Digital Holographic Interferometry for Radiation Dosimetry

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A thesis submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy

March 2014

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Abstract

A novel optical calorimetry approach is proposed for the dosimetry of therapeutic radiation, based on the optical technique of Digital Holographic Interferometry (DHI). This detector determines the radiation absorbed dose to water by measurement of the refractive index variations arising from radiation induced temperature increases. The output consists of a time series of high resolution, two dimensional images of the spatial distribution of the projected dose map across the water sample. This absorbed dose to water is measured directly, independently of radiation type, dose rate and energy, and without perturbation of the beam. These are key features which make DHI a promising technique for radiation dosimetry.

A prototype DHI detector was developed, with the aim of providing proof-of-principle of the approach. The detector consists of an optical laser interferometer based on a lensless Fourier transform digital holography (LFTDH) system, and the associated mathematical reconstruction of the absorbed dose. The conceptual basis was introduced, and a full framework was established for the measurement and analysis of the results. Methods were developed for mathematical correction of the distortions introduced by heat diffusion within the system. Pilot studies of the dosimetry of a high dose rate Ir-192 brachytherapy source and a small field proton beam were conducted in order to investigate the dosimetric potential of the technique. Results were validated against independent models of the expected radiation dose distributions.

Initial measurements of absorbed dose demonstrated the ability of the DHI detector to resolve the minuscule temperature changes produced by radiation in water to within experimental uncertainty. Spatial resolution of approximately 0.03 mm/pixel was achieved, and the dose distribution around the brachytherapy source was accurately measured for short irradiation times, to within the experimental uncertainty. The experimental noise for the prototype detector was relatively large and combined with the occurrence of heat diffusion, means that the method is predominantly suitable for high dose rate applications.

The initial proof-of-principle results confirm that DHI dosimetry is a promising technique, with a range of potential benefits. Further development of the technique is warranted, to improve on the limitations of the current prototype. A comprehensive analysis of the system was conducted to determine key requirements for future development of the DHI detector to be a useful contribution to the dosimetric toolbox of a range of current and emerging applications. The sources of measurement uncertainty are considered, and methods suggested to mitigate these. Improvement of the signal-to-noise ratio, and further development of the heat transport corrections for high dose gradient regions are key areas of focus highlighted for future development.
Acknowledgements

I really can’t thank my supervisor Dr. Juergen Meyer enough. Firstly for the initial conversation many years ago which sparked my interest in medical physics, and then for everything else I have learnt from you about how to be a scientist and how to write about science (any excessive parentheses or lack of conciseness in this thesis are my natural tendencies which he hasn’t quite managed to completely eradicate). Thank you for the continued discussions, planning, advice, reviewing, emailing and skyping, and for moving halfway around the world to a facility with convenient access to a proton beam which I could test my detector on.

To my other supervisor Dr. Jon-Paul Wells for taking on a medical physics student and teaching me about optics. Thank you for the advice readily provided whenever I needed it, and for dealing with all the acronyms that a medical physics thesis inevitably includes. Also, thank you to Dr. Richard Watts for supervision at the start of my research and helping with the initial development of the detector.

Thank you to the technical and support staff in the University of Canterbury Department of Physics and Astronomy - in particular, Graeme Kershaw for always being happy to build me test cells and other components for the detector, Dr. Bob Hurst for advice and optics ideas and Dr. Orlon Peterson for rescuing me from computer illiteracy.

Love and thanks to Juergen’s family - Louise, Finn, Zòe and Pia for looking after me while I visited Seattle and joined your family for extended periods of time.

A world of thanks to my partner Gert-Jan for looking after, pep-talking, feeding, listening to and loving me throughout. Thank you to my mum Jillian, for diligently reading through countless pages of a topic you know nothing about, to catch all my misspellings of neccessary and occurrence. To both mum and dad, Sean, for everything! Thank you also to the rest of my friends and family who have been there for me, for your encouragement and for carefully not asking me about my progress for the last 18 months.

Thank you to the Medical Physics and Bioengineering Department at the Canterbury District Health Board for taking me on as a Registrar and allowing me the extra time required to complete my PhD concurrently. The experience that I gained in all aspects of radiation oncology physics has been invaluable for my research, and I also appreciate the financial support received to attend conferences and the access to the brachytherapy source.

Thank you very much to the team at the University of Washington Medical Centre Small Field Proton Facility for allowing me access to the beam line, and providing a wealth of technical support and experience. In particular, thank you to George Sandison, Eric Ford, Rob Emery and Steven Steininger.

I am grateful for financial support I have received allowing me to present my work at international conferences, and travel to Seattle for proton beam experiments. Thank you to the Royal Society of New Zealand Canterbury Branch for a travel scholarship, Universities New Zealand for a Claude McCarthy Fellowship, and the University of Canterbury Department of Physics and Astronomy for travel assistance.
# Contents

Abstract i

Acknowledgements iii

1 Motivation 1

1.1 Introduction ........................................... 1
1.2 Research Questions ................................... 4
1.3 Outline of Thesis ..................................... 5

2 Introduction to Dosimetry 7

2.1 Principles of Radiation Dosimetry .................... 7
  2.1.1 Radiation Therapy ................................ 7
  2.1.2 Radiation Dosimetry ................................ 10
  2.1.3 Properties of Dosimeters ......................... 12

2.2 Calorimetry ........................................... 15

2.3 Dosimetry for Specialised Radiation Therapy Approaches 17
  2.3.1 High Dose Rate Brachytherapy .................. 17
  2.3.2 Proton Therapy .................................. 27
  2.3.3 Microbeam Radiation Therapy .................. 43

2.4 Concluding Remarks .................................. 49

3 Principles of Digital Holographic Interferometry 51

3.1 Fundamental Concept of Optical Calorimetry .......... 51
3.2 Optical Interferometry ................................ 52
  3.2.1 Basic Optics Principles ......................... 52

3.3 Refractive Index Determination in Liquids .......... 57
  3.3.1 Holographic Interferometry .................... 58
  3.3.2 Digital Holographic Interferometry ............ 60
  3.3.3 Experimental Configurations ................... 61

3.4 Historical Development of Interferometry for Radiation Dosimetry 69
  3.4.1 Early Holographic Interferometry Studies ....... 69

3.5 Concluding Remarks ................................... 75
### 8.5.1 Tomography at Limited Projection Angles

269

### 8.5.2 Tomography by Interferometer Rotation

272

### 8.5.3 Additional Considerations

273

### 8.6 Considerations for DHI Application to MRT Dosimetry

274

### 8.7 Other Proposed Future Applications

277

### 8.8 Concluding Remarks

281

#### 9 Conclusions

283

##### 9.1 Review of Research Questions

284

- **9.1.1 Research Question One**

284

- **9.1.2 Research Question Two**

284

- **9.1.3 Research Question Three**

285

- **9.1.4 Research Question Four**

287

**Bibliography**

289

**A List of Abbreviations**

317

**B MATLAB Code**

321

- **B.1 Graphical User Interface for Image Reconstruction**

322

- **B.2 Heat Diffusion Calculations**

349

**C Publications**

355

- **C.1 Refereed Paper**

355

- **C.2 Conference Proceedings**

355
Chapter 1

Motivation

1.1 Introduction

Cancer is one of the leading causes of death in New Zealand, with the disease responsible for some 8,593 deaths in 2010 (29% of total deaths) [1, 2]. The total number of new cancer registrations was 21,235 in 2010 [2]; with population growth and an ageing population these numbers are set to increase in coming years [3]. The average survival rate across all types of cancer five years after diagnosis was 63% in 2009 [4]. Radiation therapy, also referred to as radiotherapy, is a treatment approach which uses ionising radiation to kill cancer cells. It is one of the most effective and widely used tools for fighting cancer. In New Zealand about 50% of people diagnosed with cancer receive radiotherapy treatment, with the choice of treatment dependent on the type and stage of cancer [5, 6].

Radiation therapy exploits the biological effect of high energy ionising radiation on tissues to preferentially destroy cancerous cells within a target volume in the body. This volume consists of the tumour plus surrounding treatment margins to account for such influences as microscopic tumour invasion, set-up error and motion during or between treatment fractions. A radiotherapy treatment can be delivered with curative, known as radical, or palliative intent. This choice affects how aggressively the cancer is treated, in order to balance the chance of a cure with the quality of remaining life for terminally ill patients [7]. The paradox with radiotherapy is that the ionising radiation which damages tumour cells is also damaging to the healthy tissues surrounding them, and this causes the patient to experience various toxic side effects. The acceptable dose to healthy tissue varies according to the critical morbidity of the relevant tissues or organs, which depends on the response to radiation, called the radiosensitivity of the tissue [8]. The aim of radiotherapy is to concentrate a lethal absorbed dose of radiation to the tumour in order to optimise the probability of local tumour control, whilst minimising the dose received by the surrounding healthy tissue, to reduce the
incidence of complications. This goal is achieved by shaping the radiation dose to be as conformal as possible to the shape of the tumour. Treatment is usually conducted using the techniques of external beam radiation therapy (EBRT) or brachytherapy [9]. EBRT is performed with a linear accelerator, which produces high energy beams of electron or photon radiation which are then shaped by external collimating devices. These shaped fields are then delivered to the patient at multiple beam angles coincident on the tumour location. Brachytherapy is the use of sealed radiation sources (radionuclides) which are placed either permanently or temporarily inside the body, adjacent to or within the tumour location. Due to local radiation/tissue interactions and the inverse square law, the dose to tissue decreases with distance from the source. Treatments using either method are typically delivered as an accumulation of several smaller fractions of the prescribed dose [10]. Modern EBRT is geometrically accurate to within a few millimetres, and the prescribed dose can be delivered to within ±5% [11]. However any improvements which can be made in either geometric or dosimetric accuracy have been demonstrably shown to improve outcomes for patients; thus this is a field of widespread active research. Modern day advances in radiation therapy treatments have seen a trend towards increasing the conformity of the delivered dose to the tumour volume, and a reduction in treatment margins to decrease the amount of normal tissue irradiated. For EBRT this often involves more complex treatment plans where a fraction consists of many fields of even smaller doses, a technique called intensity modulated radiation therapy (IMRT) [12], or a technique using continuous dose deposition, known as volumetric modulated arc therapy (VMAT) [13, 14] or hypo-fractionated stereotactic radiotherapy (SRT) treatments [15]. This trend towards more complex treatments has led to a corresponding requirement for further improvements in dose quantification and localisation.

Radiation dosimetry is the calculation of the absorbed dose to some medium, typically water or tissue, resulting from exposure to indirectly and/or directly ionising radiation. When ionising radiation is incident on a medium, the interactions of the radiation with the atoms within the medium causes energy to be transferred to the medium by various mechanisms including Compton scattering, pair-production, the photoelectric effect and Coulombic interactions such as Bremsstrahlung production [9]. The extent to which each effect contributes to the dose to a specific type of tissue is dependent on the initial energy and type of the incident radiation, as well as the tissue composition. The biological impact of the radiation dose in tissue is predominantly by means of DNA strand breaks, resulting in cell damage and/or death. This biological impact is directly related to the energy transferred from the incident radiation to the medium [10]. Due to the difficulties in consistently and safely measuring
biological effects, especially in actual human tissue, water has been used as a surrogate reference medium which approximates the response of human tissue to radiation in a consistent and reproducible way [16]. Therapeutic radiation doses are therefore calculated in terms of their reference absorbed dose to water, in units of Gray (Gy), where:

\[ 1 \text{ Gy} = 1 \text{ J kg}^{-1} \] (1.1)

Accurate and consistent measurements of radiation dose are fundamental to ensure that radiotherapy clinical trial and treatment outcomes are comparable worldwide. Clinical trials and treatment outcomes are all based on a consistent scale of dose so that they can be accurately compared. Primary standards laboratories located throughout the world determine the absolute dose values and regular intercomparisons are performed between these centres. One of the roles of these laboratories is to provide a calibration service, which ensures there is a traceable link between the field detectors used for quality assurance of radiation doses delivered in individual hospital clinics back to the primary standard. Variation in dose by more than ±5% from prescribed values has been shown to have measurable detrimental effects on treatment outcomes for patients [11]. Therefore sources of uncertainty in the calibration chain must be kept as low as possible in order to ensure that the final dose can be measured to within ±5% of the prescription dose. There are many varied methods for quantifying absorbed dose to water (discussed further in Section 2.1.2) each with their own advantages, limitations and influences on the accuracies and uncertainties of the delivered dose.

Existing dosimetry techniques provide adequate solutions for the dosimetric needs of most conventional radiation therapy treatments that are widely and effectively used throughout the world today. Limitations arise from factors external to the irradiation and dosimetry process, which include individual variations between patients, imaging and tumour/organ-at-risk contouring uncertainties, patient set-up errors and misdiagnoses. However there are a number of emerging delivery techniques in radiotherapy that provide challenges which classical dosimetry techniques are not always able to fully overcome. These techniques range from new treatment modalities such as proton beams or heavier ion beams [17,18] or synchrotron generated microbeams [19,20], to increased use of small fields as part of IMRT or SBRT techniques [21–23], with each presenting its own specific set of dosimetric challenges. These methodologies are in various stages of development, from early pre-clinical studies to clinical trials to increasing implementation in clinics worldwide. There is also additional focus on the expansion of conventional treatment techniques to non-traditional tumour types and locations. In order to advance these new techniques to their full potential, dosimetry techniques
need to advance at the same or greater rate. This includes both the refinement and develop-
ment of existing dosimetry solutions, as well as the development of new approaches. An
introduction to some of these therapeutic modalities is provided in more detail in Chapter 3,
along with a discussion of their dosimetric limitations and potential approaches to overcome
these.

The aim of the present research is to adapt an optical metrology technique known as Digital
Holographic Interferometry (DHI) for application to radiation dosimetry. The fundamental
concept of the technique is to infer the absorbed dose to water from a source of radiation,
by measurement of the temperature increase induced by the transfer of energy from the
radiation to the water. This concept is the basis for calorimetry which is a fundamental
means of measuring radiation dose (see Section 2.2). DHI is a widely applied technique
in many optics applications, but in particular the technique can be used to measure small
changes in physical parameters of a transparent medium, such as the refractive index. Thus
an optical calorimetry approach can be developed, measuring absorbed dose to water by
exploiting the fact that temperature increases in water cause a predictable variation in the
refractive index. A similar method was first applied to radiation dosimetry in the 1970’s
by Hussmann [24, 25], and then Miller [26, 27] and is described in Section 3.4.1. They used
an analogue method of holographic interferometry to measure radiation dose from electron
beams. Hussmann and Miller’s detectors were ultimately limited by the technology they had
available to them and were superseded by alternative detectors of their day. The advent of
modern digital technology and the subsequent advances in optical interferometry mean that
digital holographic interferometry may again become a viable and useful tool for dosimetry,
with several properties that make it a desirable technique.

1.2 Research Questions

Advances in radiation therapy delivery have resulted in current detector technology being
a limiting factor for some emerging therapeutic approaches [17, 21, 23, 28]. There is a clear
need for advances in detector technology, including investigation into new methods, in order
to develop detectors which overcome the shortfalls of existing techniques with regard to a
range of new therapeutic options. Dosimetric limitations of radiotherapy techniques depend
on the parameters required for safe and effective treatment. These parameters cover a
broad range and include spatial resolution, beam perturbation, lack of charged particle
equilibrium, variations in stopping power ratios, dynamic range and linearity of response.
With the application of modern technology to the previously redundant dosimetry technique
of holographic interferometry there is now the potential to make advances in dosimetry in areas as diverse as proton therapy, high dose rate brachytherapy, and microbeam radiation therapy. The potential advantages are manifold, as the technique has the ability to provide high resolution absolute dose measurements of absorbed dose to water directly, overcoming several limitations of present detectors. This research applies DHI techniques to the field of radiation dosimetry in order to develop a novel radiation detector, with the aim of answering the following research questions:

1. Can the optical technique of digital holographic interferometry be successfully applied to radiation dosimetry?

2. Is it possible to develop a digital dosimeter based on the fundamental principles of calorimetry that is capable of measuring dose with high two dimensional spatial resolution?

3. Will the application of modern digital technology allow for dosimetric results which advance the early achievements of Hussmann and Miller?

4. Is there a justification for further work to explore the potential for such a detector to be used to overcome the dosimetric problems associated with emerging radiation therapy techniques?

1.3 Outline of Thesis

The aim of this work is to develop a novel DHI dosimeter to address the above research questions. This incorporates work across a variety of subject areas, from optical interferometry, radiation dosimetry and medical physics, to image processing and mathematical modelling. This thesis is written at a level which will provide a comprehensive introduction to each of these areas in terms of their relevance to DHI dosimetry, to allow for an understanding of the subject by those with limited background in one or more of these fields. Chapter 2 provides an introduction to radiation therapy and dosimetry with the aim of providing a justification for the development of a new detector. In particular, some of the developing areas of radiation treatment approaches are introduced. Each has specific dosimetry requirements, and the ways in which a DHI detector may overcome existing dosimetry problems is proposed. Chapter 3 introduces the principles of digital holographic interferometry as an optical calorimetry technique and reviews the available literature regarding previous applications of interferometry to this field. Chapter 4 progresses through the development stages of a DHI detector to describe the working prototype that was used for the remainder of this
research. This includes a discussion of the potentially advantageous characteristics of this approach to dosimetry. Chapter 5 discusses the impact and modelling of heat transport, in particular diffusion, which is a phenomenon which is critical to consider in order to obtain accurate interpretation of DHI dosimetry results. Two different approaches are proposed and implemented to account for this effect. Chapters 6 and 7 present the application of the detector to radiation measurement of a high dose rate (HDR) brachytherapy source and a proton therapy beam, respectively. Chapter 8 discusses the outcomes of the research, considering the effectiveness of DHI as a radiation detector. The various benefits and limitations are summarised and comprehensive recommendations are given in regard to the direction of further research. Consideration is given to the potential for DHI as a detector for areas such as absolute dosimetry, microbeam radiation therapy (MRT) and interface dosimetry. Chapter 9 concludes the work by revisiting the research questions posed in Section 1.2 to determine the extent to which they have been achieved. A list of all abbreviations used is included in Appendix A, whilst Appendix B contains the MATLAB code for key parts of the process. Appendix C lists the publications arising from this work.
Chapter 2

Introduction to Dosimetry

In this chapter a framework of the particular dosimetric requirements of various modern radiation therapy treatment modalities and the array of dosimetry tools that are presently used to achieve these is established. In doing so, a justification for the development of a DHI detector will be covered, by demonstrating that there is a space within this framework for investigation into new dosimetry techniques. Finally the principles of calorimetry as a dosimetry technique is introduced separately in more detail, as this will serve as the basis for a DHI approach.

2.1 Principles of Radiation Dosimetry

2.1.1 Radiation Therapy

Radiation Physics

Radiation therapy utilises ionising radiation to preferentially destroy cancerous cells within a target volume. Ionising radiation is composed of photons or particles which individually have enough kinetic energy to liberate an electron from an atom or molecule, thereby ionising it. In cells, the interaction of the subsequent free radicals with the cells nucleic acids (DNA) can result in DNA strand breaks which can ultimately lead to cell death. Ionising radiation comprises two categories of particles: directly and indirectly ionising, depending on their ionisation method. A directly ionising particle is a charged particle which can, if it has sufficient energy, ionise atoms directly via Coulombic interactions. Directly ionising particles include atomic nuclei (both alpha particles and heavier nuclei), electrons, muons, charged pions, and protons. A single particle of these types can ionise a number of atoms along its path through a medium until all of its kinetic energy is dissipated. High energy electrons in matter can produce Bremsstrahlung X-ray radiation and secondary electrons, Delta rays which can also go on to be ionising in turn. Indirectly ionising radiation includes photons
and neutrons. The photons are called gamma rays or X-rays, depending on their energy and mode of production. Photons and neutrons are electrically neutral particles, which lose their energy via interactions such as the photoelectric effect, pair production and/or the Compton effect.

**Radiation Biology**

Irradiation of any biological system with ionising radiation results in a series of processes, which can be divided into three phases [29]. The first is the physical phase, where the interactions listed above occur between the radiation and the atoms that make up the tissue. A high speed electron takes about $10^{-18}$ seconds to traverse the DNA molecule, and about $10^{-14}$ seconds to entirely cross a mammalian cell. Interactions occur mainly with orbital electrons, ionising some and exciting others. Sufficiently energetic secondary electrons can then excite or ionise surrounding atoms, leading to a cascade of ionisation events in the vicinity of the original radiation track. For 1 Gy of absorbed radiation dose from a photon beam, there are in excess of $10^5$ ionisations within the volume of every cell of diameter 10 µm. The next phase is the chemical phase, in which the damaged atoms and molecules undergo rapid chemical reactions with other cellular components. Chemical bonds are broken and ionised, extremely reactive, *free radicals* are formed. These undergo a succession of reactions, which eventually lead to the restoration of the electronic charge equilibrium within the cell. Some of these reactions are with scavenging compounds such as sulfhydryl compounds which inactivate the free radicals, whilst others are fixation reactions which can lead to stable chemical changes in molecules which are biologically important. This entire chemical phase occurs within approximately 1 ms of radiation exposure. The biological phase is the third phase, which begins with enzymatic reactions which repair the majority of the residual chemical damage, for example in DNA. Occasional lesions fail to repair, which can eventually lead to cell death after some time, even after a number of mitotic divisions. The cell deaths caused by the radiation are seen in both the tumour and in the normal tissue that is unavoidably included within the irradiated region. A tumour response of regression with regrowth not occurring, or at least not occurring within the natural lifetime of the patient, is described as *local control*.

The response of normal tissue to radiation damage from doses at therapeutic radiation exposure levels ranges from mild discomfort to life threatening conditions. The speed at which a response develops varies widely, and depends on the type of tissue, and on the dose that
each tissue receives. This varied response is key to the use of fractionation schemes, whereby the prescribed dose to the tumour is divided into a number of fractions, whereby the differentiated responses are exploited to allow for maximum detriment to the tumour and reduced normal tissue detriment. The overall goal of radiotherapy is to maximize radiation dose to the tumour while keeping the dose to the surrounding normal tissues below their respective tolerance doses. The tolerance doses define an unacceptable level or likelihood of detriment. The dose response curves showing the probability of tumour control with increasing dose, TCP, and the probability of normal tissue complications, NTCP, are depicted in Figure 2.1. The balance between the TCP and the NTCP for a given dose is called the therapeutic ratio. Figure 2.1 also demonstrates the effect of a small variation in dose. Due to the steepness of the response curves, a small decrease in dose can result in a disproportionately large decrease in the probability of tumour control. Similarly, a relatively small increase in dose can lead to a large increase in the NTCP. This is the primary reason why accurate dosimetry is crucial to safe and effective treatments.

Figure 2.1: Dose response curves showing the probability of tumour control and of normal tissue complications for various doses. The therapeutic ratio is the ratio between the two probabilities for a given dose, with a higher therapeutic ratio desirable. The disproportionate impact on the therapeutic ratio of a small change in dose from \( D_0 \) to \( D_1 \) is shown.

The shape and relative positions of the dose-response curves depends on the radiosensitivity of the cells in the tumour and normal tissue, and the fractionation scheme used, among other factors. Tumours which can be successfully treated by radiation therapy must have a response curve located to the left of the response curve for the limiting normal tissue, so that the dose required to achieve a high probability of tumour control is lower than the dose which
produces an unacceptable number of complications in normal tissue. Successful radiotherapy
treatment is most probable when the two curves are widely separated and/or when the dose
to the tumour is higher than the dose to the surrounding organs at risk. Some examples
of types of cancer that have high therapeutic ratios and therefore generally respond well
to radiotherapy are lymphoma, early breast cancers, early lung tumours, prostate tumours,
cervical cancers, and head and neck cancers [10]. Many radiotherapy treatments are given
in conjunction with surgical or chemotherapy treatments.

**Radiation Therapy Delivery Modalities**

There are three principal routes for the administration of radiotherapy: external beam radio-
therapy (EBRT), sealed source therapy (brachytherapy) and unsealed source therapy (not
discussed here). EBRT is the most common form of radiotherapy and is normally performed
with high energy electron and photon beams produced by a linear accelerator, or by gamma
ray beams from Cobalt-60 units or lower energy X-ray beams. Further treatments using
cyclotron produced proton beams (covered in Section 2.3.2), neutron beams and heavier
ion beams, as well as the more experimental techniques of laser driven proton acceleration
(Section 2.3.2) and synchrotron generated X-ray microbeams (Section 2.3.3), are also in var-
ious stages of development or clinical implementation. Brachytherapy utilises sealed sources
placed inside the tumour volume, resulting in a more localized dose to the tumour, avoiding
surrounding healthy tissues (Section 2.3.1).

### 2.1.2 Radiation Dosimetry

As demonstrated in Figure 2.1, a small variation in dose can have a high impact on treatment
outcomes. In 1976 the ICRU recommended that the dose to the target volume should be
delivered within ±5%, given as one standard deviation [11]. This is to be seen as an overall
uncertainty on the dose received by the patient at the end of all the steps contributing to
radiation dosimetry, and has many contributing factors. The accuracy can be divided into
two categories, dosimetric accuracy and geometric accuracy. However the two are inextri-
cably linked. Dosimetric accuracy requires delivering a dose that is as close as possible to
the prescribed dose. However as dose is prescribed to a target volume, geometric accuracy
is also imperative, to ensure the dose is highly conformal to the target volume.

The absolute accuracy of basic dosimetry in the energy range used in radiotherapy is consid-
ered to be approximately 1-2% [30–32]. In itself, however, this uncertainty is not a problem
for a given modality, provided all centres use the same basic physical input data, and follow compatible dosimetry protocols. The absorbed dose required to kill a tumour has been determined empirically from many years of clinical data, thus the precision in measurements is required to ensure that clinical experience from past patients and between centres can be transferred with confidence. Theoretical calculations of required doses are also limited by the accuracy of the experimental data used to validate the calculations. Thus any dosimeter must be able to measure absorbed dose in a way that is in accordance with existing protocols such as the International Atomic Energy Agency (IAEA) TRS-398, or American Association of Physicists in Medicine (AAPM) TG51 [16, 33]. These recent protocols require the determination of the absorbed dose in terms of absorbed dose to water at a reference point in a beam, and doses within the beam relative to that point.

There is a distinction to be made between different types of dosimetry, each a vital link in the chain to provide an accurate dosimetric characterisation of radiation delivered to patients in the clinic. The determination of dose is initially done in what is called absolute dosimetry. This directly yields the absorbed dose in standard units, and is based on a fundamental property of absorbed radiation such as calorimetry, which measures energy deposited as heat, or charge collected due to electrons released by ionisation. In order to facilitate accuracy and consistency, some national and international standards organisations have highly accurate absolute dosimeters which are then used as a primary calibration standard for other detectors. Thus all treatment sites should have a chain of calibration resulting in a calibration factor traceable directly back to this absolute dose measurement. Calibration measurements are performed under reference conditions, which are reproducible conditions that are consistently used for the radiation type being measured, and include such factors as ambient temperature, pressure and humidity, as well as radiation specific parameters such as field size, distance to the measurement point and detector parameters. This process is known as reference dosimetry. Using a calibrated reference dosimeter, the absolute output dose to a reference point under standard conditions can be determined for a clinical radiation situation. Relative dosimetry involves a comparison of two dosimeter readings to determine the comparative dose under different conditions. In general, few conversion coefficients or correction factors are required in relative dosimetry. Relative dosimetry can be used to make measurements which characterise a radiation source, including depth dose profiles, tissue maximum ratios, output factors, axial profiles or patient specific factors. Depth dose profiles are a key parameter for radiotherapy treatments, as they quantify the variation of dose with depth in a medium, typically water. Two factors influence the shape of the depth dose curve:
attenuation of the radiation beam through dose deposition in the medium, and the inverse square law where the radiation flux decreases with increasing distance from the radiation source. Normalising the dose at each depth to the dose at a certain point results in a relative dose scale, usually a percentage scale in terms of the maximum dose.

The generally accepted measurement quantity used for measuring the amount of ionising radiation in a biological sense is the absorbed dose $D$. $D$ is a point quantity, defined as the mean energy $dE$ imparted to a unit mass $dm$ of material by the ionising radiation, as in equation 2.1. The SI unit of absorbed dose is the Gray, $Gy$, defined as one joule of energy, $E$, per kilogram of mass, $m$.

$$D = \frac{dE}{dm} \quad (2.1)$$

The absorbed dose depends on the type and energy of the incident radiation and on the composition of the absorbing medium. The biological effect in tissue depends on this absorbed dose, but also on a range of additional factors, such as the dose rate, the fractionation scheme used and the type of tissue affected.

Dose measurements are generally calculated and calibrated as the absorbed dose to water. This convention arose because the human body is comprised of approximately 70% water with an overall density of almost 1 g cm$^{-3}$. Thus water has very similar properties to human tissue in regard to radiation scattering and absorption properties, but water provides obvious benefits for measurement purposes. There are several types of primary standards for absorbed dose to water calibration: ionometric using a graphite cavity ionisation chamber, chemical dosimetry mostly by Fricke dosimeter and calorimetry (graphite or water) [9]. These primary standards have the lowest measurement uncertainty, with values of dose deduced from first principles traced from fundamental constants. There are additional types of dosimeters which are calibrated against these primary standards and used in clinics for reference and relative dosimetry. For all of the dosimetry methods, various measured and calculated correction factors must be applied in order to determine the dose to a reference point in water, and thus relate the calibration beam to the user beam. These factors depend on dosimeter type, design and materials, and on beam type and energy. The following section describes some of the properties common to all or most dosimeters.

### 2.1.3 Properties of Dosimeters

There are many types of dosimeter which are capable of producing an absorbed dose measurement on a user beam. Each type of detector utilises a different physical principle, and
possesses some of the properties of an ideal radiation detector, however each is also limited by its physical principles and thus different detector types are better suited to different applications within radiation oncology. Detectors for the dosimetry of therapeutic radiation must be able to measure a fundamental quality of the radiation and relate this to the absolute value of the absorbed dose to water at a point. An ideal detector must also be able to measure relative dose across a volume with high spatial resolution and be able to benchmark all results against the relative dose. These properties result in the determination of a full and accurate three dimensional characterisation of the dose produced at each point within a water phantom. This detector would possess all of the properties listed below, resulting in accurate absorbed dose measurements with low uncertainties in a clinical situation.

- High accuracy and precision
- Linearity of signal with dose
- High spatial resolution
- Large dynamic range
- Independent of:
  - Dose rate
  - Beam quality
  - Direction
  - Field size
- Instantaneous readout
- Easy application in a clinical setting

In reality all current radiation detection approaches achieve a balance of the above points, with different detectors being best suited for different applications. Table 2.1 lists the main types of available methods for measuring or calculating dose and gives a few of their key advantages and limitations. This is by no means a comprehensive list.
<table>
<thead>
<tr>
<th>Detector/Model</th>
<th>Advantages</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calorimetry</td>
<td>High accuracy and precision</td>
<td>Very limited spatial resolution and sensitivity</td>
</tr>
<tr>
<td>Ion chambers</td>
<td>High spatial resolution and sensitivity</td>
<td>Not useful for beam calibration and handling</td>
</tr>
<tr>
<td>Film</td>
<td>High spatial resolution and sensitivity</td>
<td>Signal erased during readout</td>
</tr>
<tr>
<td>Diodes and MOSFETs</td>
<td>No real-time readout</td>
<td>Can be reasonably tissue equivalent</td>
</tr>
<tr>
<td>Monte Carlo simulations</td>
<td>Can verify dose within patient geometry</td>
<td>Long computational times</td>
</tr>
</tbody>
</table>

Table 2.1: Some key properties of common alternative detectors and Monte Carlo modelling, with advantages that DHI potentially shares colored red and limitations DHI can potentially overcome (or is unaffected by) are shown in blue.
2.2 Calorimetry

Calorimetry is the measurement of heat. Dosimetric calorimetry is a fundamental method of measuring absorbed dose, because the irradiation of a medium and the subsequent transfer of energy as heat causes a corresponding proportional temperature increase according to the specific heat capacity of the medium [34]. The basic components of a radiation calorimeter involve a medium which is irradiated, and one or more probes to measure the temperature increase, all contained within a large thermally insulated and shielded container to isolate the calorimeter from the effects of any external temperature changes. The container is important, because the temperature increase of water attributable to a 1 $Gy$ absorbed dose of radiation is just 0.00024 K. For this reason higher doses are used, and doses are integrated across a volume, to infer a dose to a point. The specific heat capacity of graphite is six times less than water, allowing for larger temperature rises for a given radiation dose and thus more accurate measurements, but requiring conversion of the result from absorbed dose in graphite to absorbed dose in water. Generally the measurement complexities involved in isolating the irradiated sample from ambient temperature and pressure conditions, and the high doses required to attain accurate calorimetric measurements mean that the technique is not useful as a routine tool for dosimetry in a clinical environment, but rather is used worldwide in standards laboratories as a means of absolute reference dosimetry [35]. Some key features of calorimeters are described in Table 2.1.

There are different types of calorimeters used in various standards laboratories around the world - historically graphite calorimeters have been used to establish the standards for absorbed dose, whilst now standards based on water calorimetry are available to a high degree of accuracy (having a relative standard uncertainty of $\sim 0.5 - 1\%$) [35]. Water calorimetry reduces some of the uncertainties associated with graphite calorimetry, especially for high energy X-ray and electron beams. Types of calorimeters are distinguished by different procedures, features or the medium used, such as the aqueous solution chosen, the use of motionless versus stirred water, large gas space versus no gas space, low accumulated dose versus high accumulated dose etc [36]. Whilst calorimetry is basically the gold standard for absolute absorbed dose determination, there are various complicating factors which increase the difficulty of the measurements, which are briefly covered below.

A key compounding factor for most calorimeters is the need for a probe to read the temperature. If the probe and the medium have different radiation absorbing properties then it is necessary to apply cavity theory corrections. This introduces several complications: 1) it
can be difficult to determine the variation of stopping power, especially if inhomogeneities are present, as the radiation energy spectrum is degraded throughout the medium; 2) spatial resolution is limited by probe dimensions; 3) sensor sensitivity may limit measurement of high doses or dose rates; and 4) time resolution is limited by the thermal equilibration time between the probe and the medium. This problem is overcome by either measuring integrated doses across the whole calorimeter sensitive volume; or by the use of the absorbing medium itself as a temperature sensitive body, in other words the measurement of a temperature dependent property using a non-disturbing probe, such as in a DHI approach.

A factor which must be considered is heat transfer to and from the point of measurement [35]. Because the thermal diffusivity of water is small, heat transfer by conduction is low for most irradiation conditions, although it must be calculated for more modulated beams and longer irradiation times. For some irradiation conditions convection can be a serious concern and various techniques have been used or proposed to reduce or eliminate the effects of convective flow (e.g. stirring, which would require a transfer medium to give dose at a point), sealed glass vessels acting as a convective barrier within larger phantoms, or low temperature operation at 4°C where the volume expansion coefficient of water is zero, but this increases the technical complexity of the calorimeter. This factor is also a major consideration for DHI, however it is possible that the use of optical calorimetry techniques may allow this effect to be more readily quantified and accounted for, as discussed in Chapter 5.

Another consideration for radiation calorimetry is the possible occurrence of exothermic or endothermic radiation-induced chemical reactions, which consume or release energy, thus affecting the temperature change. This is corrected for with the use of a factor called the heat defect [36]. The heat defect has various contributing mechanisms, depending on the calorimeter material and radiation linear energy transfer (LET). For this reason, the absorbing medium must be carefully selected to reduce the need for, or simplify the implementation of heat defect corrections. In water the heat defect is highly influenced by the presence of impurities in the water, which undergo radiation-induced chemical reactions. Nevertheless, several different calorimeter designs using various aqueous systems have now demonstrated results which are consistent, to 1% or better, with the absorbed dose to water obtained by more conventional techniques [35]. Water quality is important, and modern water purification is highly effective, even without distillation, but subsequent exposure to air or other materials can introduce impurities which can affect the heat defect, which is generally constant for the first 400 Gy [36]. This is also where graphite has an advantage as a calorimeter.
material, as the stability of the covalent carbon bonds in graphite mean that the heat defect is negligible.

2.3 Dosimetry for Specialised Radiation Therapy Approaches

The vast majority of radiotherapy treatments are conducted using radiotherapy approaches that have well-characterised dosimetry, with well-established protocols which enable consistent dosimetric measurement worldwide using existing detector technologies. There are a large range of radiation detectors marketed by various companies, coming in a large range of types, sizes and shapes. There are however specialized radiation therapy approaches where current detector technology has some limitations. In these areas, there is a need for improved dosimetric capabilities in order to fully exploit the therapeutic potential of the different approaches. High dose rate brachytherapy, proton therapy, in particular narrow field proton beams and high dose rate pulsed beams, and microbeam radiation therapy are three such areas, which are discussed in the following sections. For each, the main dosimetric requirements are described, along with the existing dosimetry options, from amongst the multitude of radiation detectors marketed by various manufacturers.

2.3.1 High Dose Rate Brachytherapy

Brachytherapy is a type of radiotherapy where an encapsulated radioactive source is placed on or inside the area to be treated. If the source is placed directly in the target tissue, such as for breast or prostate treatments, this is called interstitial. Alternatively, the source may be placed next to or in contact with the target tissue, either intracavitary as for the cervix, uterus or vagina, intraluminal as for the trachea or oesophagus, intravascularly within a blood vessel, or externally on a surface such as skin. The main advantage of brachytherapy is the high dose delivered to the tumour with minimised damage to the surrounding healthy tissues and a consequent reduction in side effects due to a rapid dose reduction with distance from the source. Brachytherapy treatments are limited to cases in which the tumour is well localized, relatively small and accessible by means of one of the brachytherapy approaches listed above.

Brachytherapy photon emitter sources are available in a variety of cylindrical forms, including needles, seeds and wires, but are generally sealed to prevent leakage and to provide
shielding against any undesired $\alpha$ and $\beta$ radiation emitted. The dose from a brachytherapy source depends on the isotope used, which controls the energy spectrum and type of radiation emitted, as well as the source strength, which is a measure of its specific activity. Additionally, the shielding and the different construction of the sources affects the source dose distribution, because of absorbance of radiation in the shielding material and within the source itself. The dose can be delivered over one or more short treatment periods or be permanently implanted until the source has completely decayed, depending on the dose rate of the source and the treatment requirements. Brachytherapy treatments are classified according to the dose rate of the source at a dose specification point, with high dose rate sources (HDR) producing $> 12$ Gy/h or more. HDR brachytherapy has become the most common form of brachytherapy, and this will be the focus of the rest of this section. The most common HDR isotopes are mainly photon emitters Ir-192, Co-60 and Cs-137.

The dosimetry of brachytherapy sources is complicated because of the steep fall-off of dose with distance, $d$, from the source, ranging from $\sim 1/d$ close to the source to $\sim 1/d^2$ at greater distances [37]. This means that the dose gradient in the region immediately adjacent to the source is very high, which presents considerable difficulties to most conventional radiation detectors, which are generally impractical to use within 1 cm of the source [38]. This may be due to the physical size of the source and the corresponding volume averaging effect, or due to the energy or dose rate dependence which is more pronounced in this region. As such, most dosimetric measurements have been performed at distances > 1 cm and dose values closer than this simulated using Monte Carlo models or the AAPM TG-43 algorithm [39]. However uncertainties in the dose in close proximity to the source can create problems such as hotspots in both the tumour volume and in the surrounding critical tissue. It is recommended that dose measurements be obtained at the smallest possible distance, ideally offering adequate precision and reproducibility to allow for $1\sigma$ statistical uncertainty (Type A) $\leq 5\%$ and $1\sigma$ systematic uncertainty (Type B) $< 7\%$ [30,39].

This becomes particularly important with the increasing use of HDR brachytherapy for endobronchial and intravascular treatments for both palliation and cure [38,40–42]. In endobronchial treatments hemoptysis is a common side effect, fatal in 7-32% of cases, which can be reduced by better sparing of normal tissue [40]. For these treatments, doses are often prescribed at 5 or 10 mm distances from the source, thus accurate knowledge of the dose distributions on a scale of millimetres around the source is crucial. However the steep dose gradients in this region are on the order of 40% per mm which necessitates a detector with
wide dynamic range, high positioning reproducibility and accuracy and high spatial resolution of less than 0.5 mm to avoid excessive volume averaging effects \[37,43\].

There are a number of studies that have looked at the dose distributions around brachytherapy sources in this region, using a various detectors or models, with work ongoing in many areas to achieve accurate, practical and reproducible dosimetry. The sections below introduce some of the main areas of focus.

**Source Models**

Dose distributions for a given treatment configuration are generally calculated by models which have been validated by experimental data. Conventional treatment planning system (TPS) algorithms have high uncertainties in the near source region, with uncertainties being as high as \(\pm 15 - 20\%\) of the dose \[44\]. This is largely due to the difficulty of measurements in this region meaning that models have been extrapolated often without sufficient experimental validation. A Monte Carlo algorithm is a computational tool which samples from known probability distributions to determine the average behaviour of a system, and this can be used to model radiation transport processes from HDR sources to determine dose distributions. Monte Carlo simulations are capable of higher accuracy than conventional TPS algorithms, however they still require experimental validation. There are several Monte Carlo codes which have been used to work on HDR source modelling, including BEAM, EGSnrc, PENELOPE and GEANT4 \[37,44,45\]. With appropriate experimental validation, Monte Carlo models can allow for calculation of dose distributions with unparalleled spatial resolution at all distances and angles from the source, in both water as a reference medium, and in tissue \[37,46–48\].

Monte Carlo models are also used to calculate the parameters required in the TG-43 dose formulism for calculation of dose rate distributions around photon-emitting brachytherapy sources. This code of practice stipulates that the dose calculations be divided into components of geometry, attenuation, scattering and anisotropy, with dose distribution parameters in water being the dose rate constant \(\Lambda\), the geometry factor \(G(r, \theta)\), the radial dose function \(g(r)\), and the two dimensional anisotropy function \(F(r, \theta)\) \[39,44\]. All of these are measured factors, with the exception of the geometry factor, which is a calculated value.
Radiochromic Films

Radiochromic films are widely used for brachytherapy dosimetry [49], for example for quality assurance [50], measurement of TG-43 calculation parameters [51], and for assessment of dose heterogeneity [52]. Radiochromic film as a dosimetry tool gives excellent two dimensional spatial resolution, providing information about the spatial distribution of radiation within an area of interest, integrated in a single exposure. Figure 2.2(b) shows an example of an HDR dose distribution measurement on Gafchromic film, a type of radiochromic film. Radiochromic films are made of near tissue equivalent material, that contains a dye which polymerises, changing colour, when irradiated. The polymerised dye then absorbs light affecting the optical density of the film, so the extent of the colour change can be measured using a densitometer or scanner. This is then related to the absorbed dose by means of a Hurter and Driffield (H&D) calibration curve, a measured version of the schematic shown in Figure 2.2(c). The H&D curve is non-linear with dose, with four regions: 1) fog at low exposures; 2) an increasing toe region; 3) a linear region at intermediate exposures, which is the operating region for the film; and 4) saturation at high doses. The sensitivity of the film can vary between film batches, requiring individual calibration curves to be made for each new batch of film. The most common radiochromic film is GafChromic film, which is colourless, almost tissue equivalent (9.0% hydrogen, 60.6% carbon, 11.2% nitrogen and 19.2% oxygen) and turns blue upon irradiation. The main advantages of using radiochromic film are that it is essentially energy independent, particularly for higher energy radiation, which is in contrast to radiographic film. It also has incomparable spatial resolution, being a grainless emulsion, limited only by the spatial resolution of the densitometer or optical scanner used to read it out. It does however have a limited dynamic range which limits its applicability to some high dose rate or highly modular applications, and dose response non-linearity must be corrected for in the upper dose region.

Radiochromic film can overcome many of the difficulties of near-source measurements, being flexible, with excellent spatial resolution, dynamic range and near water equivalency leading to minimal energy dependency over the relevant photon energies [43]. However film batches can have considerable non-uniformities of up to 15% [53,54], and depending on the relative differences of the energy they are calibrated at, the response in a near-source HDR measurement may be between 5-40% [55–58].
Figure 2.2: (a) A piece of Gafchromic film showing the exposure due to irradiation by an HDR source, (b) the scanned greyscale values along a horizontal (red) and vertical (blue) profile through the centre of the source, and (c) a schematic of a typical Hurter and Driffield calibration curve showing the characteristic regions of the curve.

**Thermoluminescent Detectors**

Thermoluminescent detectors (TLDs) are a type of detector which is considered by some to provide an optimum compromise between being small enough to achieve adequate spatial resolution, but still achieve a sufficient sensitivity [47]. TLDs have been used for experimental dosimetry across the entire energy range of brachytherapy sources to validate Monte Carlo simulations. TLDs operate on the principle that when certain thermoluminescent phosphorous materials absorb radiation, the transferred energy causes excitation of electrons which are then trapped in meta-stable states known as luminescence centres. At room temperature electrons can stay in these traps for extended periods of time. TLDs are then read by a controlled heating pattern which imparts energy to the material, releasing the electrons back to their ground state, resulting in the emission of light photons. This luminescence can be measured with a photomultiplier tube which detects the photon fluence with time (and thus temperature, as the heating rate is held constant), resulting in a *glow curve*. Figure 2.3 shows a typical TLD glow curve. The area under the portion of the glow curve, corresponding to electron de-excitation from trap depths they were excited to by the radiation exposure, can be related to dose. This measured value is a factor of the dose, the dose rate, the energy, the phosphoric material used and the read-out heating cycle, and is converted to an absorbed dose value by means of a calibrated dose conversion. The dose response of a TLD is linear over the range of doses used in brachytherapy. Only a small part of the energy deposited as absorbed dose is emitted as light (for example only approximately 0.4% in lithium fluoride) [48]. Correction factors required include those for dose response dependence, radiation type and energy dependence, loss of latent TL signal due to fading, and drift of the TLD reader. Precision of use in both calibration and measurement is extremely important, making TLDs rather time consuming to use, however with care, accuracy can be as high as 1.5 - 2%.
The two most commonly used phosphors for TLD dosimetry are lithium fluoride (high tissue equivalence) and calcium fluoride (high sensitivity), doped with impurities to provide the luminescence centres, used in the form of small chips, pellets or encapsulated powder. Due to their extensive calibration requirements TLD detectors are often used as relative dosimeters, most commonly in a brachytherapy sense for in-vivo dosimetry as routine quality assurance, but also sometimes used as absolute dosimeters for dose monitoring in complex treatments. The application of TLDs to near-source measurements has been relatively limited to date, but Issa et al. have achieved good results using Ge-doped optical fibres used as TLDs [59]. They achieved sub-mm spatial resolution for source-dosimeter separations from as close as 0.1 cm, with quoted agreement to models of \(2.3\% \pm 0.3\%\) along the transverse and perpendicular axes, making this a potentially suitable option for this type of dosimetry. A potential area of uncertainty is the lack of tissue equivalency of the SiO\(_2\) which makes up the fibres, although this is suggested to be small.

![Figure 2.3: A typical glow curve of LiF:Mg,Ti measured with a TLD reader at a low heating rate. Figure reproduced from Podgorsak (2005) [9].](image)

**Gel Dosimeters**

Polymer gels are fabricated out of radiosensitive chemicals which polymerize upon absorption of radiation. They are able to record a cumulative dose distribution in three dimensions to relatively high spatial resolution. The ability to measure dose in two or three dimensions is advantageous in high dose gradient situations and is useful for brachytherapy [60,61]. An example of the setup of a gel measurement for an HDR source is shown in Figure 2.4. The methodology for using polymer gels has three steps: 1) the formulation of the gel and the fabrication of a suitably shaped phantom from this formulation; 2) the irradiation of this
phantom; and 3) the scanning of the phantom to measure the three-dimensional radiation dose distribution, derived from the radiation-induced physical changes in the gel by means of comparison to a gel from the same batch that has been calibrated to a known dose. This read-out process occurs post-irradiation using magnetic resonance imaging (MRI), optical computerized tomography (optical-CT), X-ray CT or ultrasound. The fundamental spatial resolution achievable by a gel dosimeter depends on the parameters of the read-out system. In the context of near-source HDR dosimetry, Papagiannis et al. measured dose to within 3 mm of the source, albeit with considerable volume averaging effects causing deviation from Monte Carlo models of up to 25% at 1 mm [62–64].

Figure 2.4: Example of a PMMA gel phantom after exposure to an Ir-192 seed for about 29 minutes. Figure reproduced from Masillon et al. [63].

The usage and results obtained from gel dosimetry is highly dependent on the type of gel, and exact chemical composition. Suitable gels must have both a measurable dose sensitivity, stability in time and space, be radiologically tissue equivalent, and have dose rate and energy independence. Some gel types are susceptible to atmospheric oxygen and must be manufactured in an oxygen free environment, others are highly influenced by the temperature history before, during and after irradiation [60]. A slight energy-dependence has been found in many polymer gels which is of limited concern for EBRT, but may have a strong influence on brachytherapy results, as most calibration curves are conducted with high energy photons, which can lead to a systematic dose error. This has not yet been extensively studied. Further uncertainties introduced by the calibration process can be high, particularly in the lower dose regions, with dosimetrically acceptable errors of < 3% hardly obtainable. Additionally, at low energies most gels will deviate from soft-tissue equivalence [60], with
for instance in I-125 and Pd-103 brachytherapy, dose corrections on the order of 5% being required.

There are more studies showing the use of gel for near-source brachytherapy dosimetry, which present some success in the results in comparison with models and film measurements, but also raise some difficulties [65–69]. The insertion of applicators or catheters into the polymer gel can create significant dose deviations near the catheter wall due to oxygen diffusion through the wall of the cavity contaminating the gel and causing an underestimation of the absorbed dose [66–68]. Other deviations arise from MRI measurements of the high dose gradients due to magnetic susceptibility differences between the gel and the catheter [69]. To achieve the sub-millimetre accuracy required by endovascular brachytherapy applications MRI images can be utilized with stronger magnetic fields, but this can cause molecular self-diffusion of water, distorting the results [67]. It may be possible to compensate for this with a suitable calibration procedure.

**Ionisation Chambers**

Ionisation chambers are currently the standard choice for routine reference dosimetry to calibrate the sources used for HDR brachytherapy [70]. There are two means of doing this. One method is to use a calibrated Well chamber, where the source is placed inside a cavity inside the surrounding ionisation chamber in order to measure the total activity. A common commercial Well chamber is depicted in Figure 2.5(a). The alternative is the value of the dose at a certain point in-air, using a specially calibrated frame and thimble chamber combination, as shown in Figures 2.5(b) and 2.5(c). The two types of ionisation chamber are geometrically different, but have key features common to all types of ionisation chamber. The operating principle is that ionisation chambers consist of a gas filled cavity between two charged electrodes. A guard electrode and/or high quality insulator is used to define the collecting volume, improve field uniformity and reduce leakage current between the electrodes. As the chamber is irradiated, the liberated charged particles are collected on the electrodes, generating a current which can be measured with an electrometer. Because a gas filled chamber with electrodes of varying materials is not tissue equivalent, corrections must be applied in order to convert the measured charge to a dose to water or air. These corrections are determined from cavity theory, based on the chamber approximating a Bragg-Gray cavity [71]. Additional care must be taken to correct for the effect of ambient pressure, temperature and humidity conditions which affect the density of the gas in the chamber.
collection volume.

Figure 2.5: (a) A Standard Imaging HDR 1000 Plus Well chamber used for brachytherapy source calibration [72]. (b) An example of a jig used to do in-air measurements of a source using a thimble chamber. Figure reproduced from Rijnders [70]. (c) Schematic of a Farmer-type ionisation chamber used for in-air calibration [73].

As yet, there is no primary standard for directly measuring absorbed dose to water for Ir-192, the most commonly used HDR brachytherapy source, although work is ongoing in this area [74, 75]. Instead, the TG43 protocol provides a formalism to convert from the reference air-kerma strength measurements made by ionisation chambers into an absorbed dose to water value, using several calculated or measured factors [39]. For an Ir-192 source, the calibration of the ionisation chambers is done at a range of different energies because of the non-applicability of the Spencer-Attix cavity theory [76]. The calibration coefficient of a chamber at the exposure weighted average energy is indirectly interpolated from the chamber calibration coefficient determined at energies above those emitted by Cs-137 or Co-60 sources and below that of orthovoltage X-rays, a method which has been proven to have some flaws [77, 78]. Ionisation chambers are sufficient for source calibration, if used to confirm the total dose of the source is as expected, but the relatively low spatial resolution that is achievable means they are not able to give a sufficient indication of the dose distribution in the near-source region due to considerable volume averaging effects. Work on detectors that are capable of two or three dimensional measurements is of more importance in this area [49].

Other Dosimetric Approaches

A number of other previous studies have looked at the dose distribution around different brachytherapy sources [43, 59, 62, 79], using a range of detectors including diamond detectors, metal oxide semiconductor field effect transistors (MOSFET), and scintillation detectors. MOSFETs are silicon transistors in which radiation generates charge in the metal oxide
layer which becomes permanently trapped, affecting the threshold voltage in the MOSFET. The threshold voltage operates as a linear function of absorbed dose, and can be read out in real time (with the detector connected to a bias voltage) and also following irradiation. MOSFETs can be used for the full energy range of therapeutic photons and electrons although for lower energy radiation the energy response can vary and needs correction. They do not require correction for dose rate, but exhibit a small axial anisotropy (2% for 360°) [79].

Many measurements using these detectors are however only made to a closest distance of 5 - 10 mm from the source. One study showed a diamond detector and MOSFET to have dose rate dependence at distances closer than 50 mm, as did the MOSFET, lowering response by up to 10% [79].

### Absolute Dosimetry using Calorimetry

As mentioned in the section on ionisation chambers above, absolute dosimetry for brachytherapy sources is complicated by the lack of an absorbed dose to water standard for Ir-192, with the existing air-kerma calibrations shown to have several shortcomings [80]. A direct calibration in terms of absorbed dose to water of Ir-192 sources by means of calorimetry has potential to reduce some of the basic reference dosimetry uncertainties [74,75]. As the basis for the use of digital holographic interferometry, calorimetry has been described in more depth in Section 2.2. The complicating factor for absolute dosimetry is the source self-heating, which impairs reliable experimental determination of dose in the region closest to the source. Positional uncertainties also increase in this region, whilst dose decreases with distance, so the measurement conditions must find a balance between these competing effects. Sarfehnia et al. have proposed an absorbed dose to water standard for brachytherapy which considers these effects [49,74,75], and suggests that an absolute dose measurement with an accuracy of better than 5% is achievable at a distance of 2.5 - 5 cm from the source. Whilst this is not in the relevant region for the near-field dosimetry discussed in the earlier sections, it is possible that DHI dosimetry may also be useful for this application. The German Standards Laboratory, Physikalisch-Technische Bundesanstalt (PTB), has recently published proof-of-principle results for the use of water calorimetry as a primary standard to determine the dose rate constant of an Ir-192 source, quoting measurement uncertainties of 3.7% [81]. Additionally, Malyarenko et al. have successfully used a high resolution ultrasonic thermometer for calorimetry [82], which could prove suitable for application to absolute dosimetry of HDR sources, and they are considering the implementation of an optical interferometric system to further improve these results [83].

26
2.3.2 Proton Therapy

Proton therapy is a type of radiation therapy where protons are typically accelerated in a cyclotron or synchrotron to the required therapeutic energy range. A schematic showing the key components of a cyclotron is shown in Figure 2.6(a), and a photograph of a commercial cyclotron in Figure 2.6(b). Energies below 70 MeV are used for superficial tumours, with energies of up to approximately 250 MeV used for deeper clinical targets. The application of protons to radiation therapy was first proposed by Robert Wilson in 1946, due to the advantageous dose distributions produced by a proton beam [84]. The interaction of proton beams with matter results in an energy distribution which is characterized by a relatively low dose in the shallow regions of their path, rising to a sharp peak near the end of the proton range, named the Bragg peak, and then a rapid decrease to zero. This dose distribution arises due to the nature of charged particle energy loss, where once the particles reach a certain energy threshold, the interactions increase and the remaining energy is absorbed in a relatively localised depth [85]. This dose distribution allows for the delivery of a high dose to a tumour with a lower dose to the intervening normal tissues, and minimal dose to any normal tissues deeper than the tumour. This results in an increased ability to safely treat tumours located adjacent to sensitive structures such as the optical chiasm or spinal cord [17]. The use of proton therapy is increasing rapidly, however is still not ubiquitous, in large part due to the large capital expenditure required to set up new treatment centres. At the present time there are approximately 40 particle accelerator facilities worldwide which are used for proton therapy, with that number set to increase dramatically in coming years [86].

Treatment using a proton beam generally exploits the fact that the depth of the Bragg peak is energy specific, and thus modifying the beam energy allows for variation in the treatment location. Modulating the energy and intensity over a specific range can result in a spread out Bragg peak (SOBP) which allows the treatment depth to cover a larger region than a monochromatic beam, allowing better conformation to the cross-sectional depth of the tumour [87]. Figure 2.7(a) shows an example of a SOBP achieved by combining beams of several different energies so that the individual Bragg peaks combine. Figure 2.7(b) shows the relative advantage in the dose distribution that can be achieved by a SOBP compared to a photon beam. An additional benefit is that due to the relatively large mass of a proton compared to electrons or photons, there is little lateral side scatter in tissue, resulting in limited beam broadening. This further reduces the dose to normal tissue in comparison to
Figure 2.6: (a) Basic schematic of a cyclotron showing the key components used, where the dotted line indicates the path of the protons as they are accelerated. Figure reproduced from Podgorsak [9]. (b) An example of a cyclotron used for proton therapy, produced by Varian Medical Systems.

(a)
(b)

Figure 2.7: Illustration of a SOBP. (a) shows the range and intensity modulation of Bragg peaks (black lines) in order to achieve a SOBP (red line). (b) is a comparison of depth doses for 15 MV photons (black line) compared to protons with a SOBP encompassing the tumour volume. This shows that the proton SOBP can achieve coverage of the tumour volume, but also lower dose to the surrounding normal tissue and less integral dose. Both figures were reproduced from work by Smith [85].

(a)
(b)

The biological effect of proton beams is generally assumed to be slightly higher than for photon beams. The increase depends on several biological and physical factors, and for clinical application of proton radiotherapy a constant relative biological effectiveness factor, RBE, of 1.1 is used to account for this effect [17,88]. This factor is used to determine the iso-effective dose which is the dose of a photon treatment which results in the same biological effect, using the same fractionation schedule [17]. Thus for an RBE of 1.1, ten percent less dose is
needed compared to photon therapy. The reduction in normal tissue dose when compared to photon treatments leads to reduced morbidity and improved quality of life for patients, and the subsequent potential to increase dose prescription to the target volume, resulting in increased local control and disease-free survival [85].

For treatments, proton beams are generally delivered to the target volume by one of two main approaches: passive scattering, including single and dual scattering, or active beam scanning. For passive scattering techniques the proton beam is enlarged to cover the treatment volume by placing scattering material into the beam path. A single scatterer is required for small fields, whilst dual scatterers are required to broaden the beam sufficiently for a large field, whilst ensuring a uniform dose profile. Collimators and compensators are used to conform the dose to the beams eye view of the target volume. The treatment depth is controlled by the depth of the SOBP, which is obtained by use of range modulator wheels or ridge filters prior to the scatterer. Beam scanning is an alternative method in which magnets are used to deflect and steer the proton beam to effectively “paint” the treatment volume in small volume elements. This is done in successive consecutive layers, as the depth of the Bragg peak is varied. This allows greater conformity to the treatment volume in the depth direction.

As for photon and electron radiation therapies, accurate dosimetry of proton beams is vital to ensure safe and effective application as well as achieving reproducible clinical results between centres. The comparison to photon doses using the isoeffective dose is not a practical measurement for routine use. However it is generally assumed that reproduction of the physical irradiation parameters reproduces the biological response. Thus proton beam dosimetry hinges on the ability to conduct accurate measurements of the absorbed dose and its distribution in a water phantom [85]. Many measurement parameters are common with other external beam treatment modalities, including percentage depth dose along the beam central axis (PDD), beam flatness and symmetry, and the absolute output. Many parameters which are specifically required for proton beams are derived from PDD measurements, including the depth of the Bragg peak, the ratio of peak dose to surface dose, the constancy of the SOBP length, the range, and the distal dose fall off.

There are a range of different detectors which have been used for proton beam dosimetry. The choice of detector depends on the measurement aim, whether that be an absolute calibration of the dose under reference conditions, or dosimetry under non-reference conditions for characterisation and quality assurance of the beam. The 5% accuracy recommended for
photon beam treatments [89] should in principle apply to the isoeffective dose, which, given that the RBE contains inherent uncertainties, poses a serious challenge [17]. In fact this level of accuracy is currently unrealistic, as the fixed value of 1.1 for the RBE has an uncertainty in the region of 10-15% [90].

There is not yet a primary standard for absorbed dose measurement of proton beams. Different proton therapy centres rely on a range of dosimetry protocols and recommendations which are relevant or specific to proton dosimetry, including but not limited to AAPM Report 16 [91], the European Charged Heavy Particle Dosimetry (ECHED) protocols [92, 93], ICRU Report 59 [94], and the more recent ICRU Report 78 [95]. The common recommendation in most of the publications is the use of calorimetry for reference dosimetry, with ionisation chambers for routine dosimetry. ICRU Report 78 recommends the use of the IAEA TRS-398 protocol for absorbed dose to water measurements. The difference in calibration varies between the different reports by up to 2%, depending on the chamber used [96].

There are however various complicating factors when it comes to the measurement of proton beams compared to more commonly used treatment modalities. Key amongst these is the high uncertainty in the stopping power water to air ratios which are required for ionisation chamber measurements, in particular in the region of the Bragg peak [97]. Thus the use of other detector types is still very much an area of active research, as there is considerable room for development to improve on the dosimetric accuracy and measurement efficiency achievable [17]. An overview of the key types of detectors used is given in the subsequent sections, with a summary of their various advantages, disadvantages and applications.

Narrow beam proton fields

A particular subset of proton treatments is the use of narrow beam proton fields for use in proton stereotactic radiosurgery (PSRS). The beams used in proton stereotactic radiosurgery generally have a diameter of between 2-30 mm, with a diameter of 10 mm or less considered narrow beams. Narrow beams experience a host of added difficulties in dosimetric measurements [18]. The dose in a proton beam changes with depth due to three processes: multiple Coulomb scattering (MCS), nuclear interactions and a changing rate of energy loss. For beams with a large cross sectional area MCS is negligible, but for narrow beams this becomes the major factor changing the gradient of the dose decrease at the end of the Bragg peak. This is because for a narrower beam there is a lack of balance where more particles
are scattered out of each section of the beam path than into it, leading to a widening of the penumbra with depth, maximised at the depth of the Bragg peak. Within the narrower cross sectional area this causes a high degree of lateral proton disequilibrium and therefore the whole width of the beam can become part of the penumbra. This results in lower than expected dose values in the drop off after the Bragg peak. For beams with collimators of less than 5 mm diameter, and below certain energies, any SOBP region is therefore not maintained across the expected depth \[18\]. The result of these effects is that many of the detectors routinely used for clinical proton dosimetry are not appropriate in narrow beams, with the finite size of the detectors introducing perturbations which distort the dose distribution \[98, 99\]. However this must be overcome, as accurate measurements are required to input into treatment planning system models to validate treatment doses. Key parameters are the central axis depth dose and localisation of the Bragg peak, and field size dependent factors. Lateral off-axis profiles are also particularly important at varying depths near the surface and near the peak, because at the surface the beam width, measured between the positions of 50% dose level, is close to the size of the collimator with relatively consistent penumbra, but at the depth of the Bragg peak there is a more complex relationship between penumbra, beam width and collimator size, and beam energy \[18\]. A range of different detectors are recommended to optimise the measurements of narrow beams, as there is no one optimal choice for beam characterisation \[18\].

**High Dose Rate Pulsed Proton Beams**

Recent advancements in laser-driven ion acceleration (LDA) have shown the potential to create proton sources of ultra high dose rate that may be suitable for therapeutic use \[100\]. The technique is in the very early stages of investigation of its potential for therapeutic application. The major advantage of LDA is that treatment units could be extremely cost effective and compact (table-top sized), compared to conventional proton accelerators. Early investigations are ongoing into the radiobiological impact of delivering doses in extremely short but intense pulses, on the order of nanoseconds \[101, 102\]. Dose rates can exceed 100 Gy/s, with 7 Gy deliverable in a single pulse \[102\]. This results in peak dose rates of up to nine orders of magnitude greater than conventional treatments. Several studies have shown the RBE of such a pulsed beam to be between 1.2 and 1.4 \[101, 103\], with no evidence for substantially different radiobiology \[101\]. The maximum proton energy achievable to date is 40 MeV \[102\], but emerging techniques may allow for this to be significantly increased \[104\].

Accurate dosimetry of these pulsed proton beams is crucial to radiobiological measurements,
however the small dimensions and extremely high dose rates introduce considerable difficulties. Field sizes for small animal experiments are commonly on the order of 0.1 mm, scanned over areas up to 1 cm diameter [102]. The only detector presently capable of resolving the dose distributions of high doses of protons to such a resolution is film. However radiochromic film dosimetry is still subject to the limitations described in the relevant section below. An example from Bin et al. of a radiochromic film measurement of an 0.45 mm by 5 mm beam diameter pulsed proton beam is given in Figure 2.8 [102]. Bin et al. quoted total uncertainties in the proton dose of up to 33%, including a 20% error in the absolute dose. Whilst acceptable for proof-of-principle measurements, these uncertainties must be improved dramatically for clinical implementation of LDA pulsed proton beams.

Figure 2.8: Lateral dose distribution of a single pulse of an LDA generated pulsed proton beam, with a maximum dose of 7.1 Gy. The horizontal scale bar is 1 mm. Figure reproduced from Bin et al. [102].

Calorimetry

Calorimetry is the recommended method in various protocols for proton beam absolute dosimetry [92,93,95]. Direct measurement of absorbed dose to water avoids the unnecessary uncertainties introduced into the overall dose results from the beam quality factor estimation, whilst allowing for a direct measurement of dose in more complicated, non-reference fields with dose not laterally uniform in the SOBP [96]. Additionally, ion chamber measurements generally only address the double scattering proton delivery technique, which may not be applicable to scanning protocols. Water calorimeters have been successfully implemented for both passively scattered proton beams [105–109] and scanned proton beams [96, 110, 111]. At present, there are at least four primary standard dosimetry laboratories (PSDLs) that are developing a primary standard of absorbed dose to water for proton beams, three based on water calorimetry [112–114] and one based on a graphite calorimeter [115]. Calorimetry
is also used for experimental determination of the beam quality correction factors, $k_Q$, for ionisation chambers [111]. The fundamental principles associated with the use of calorimeters for radiation dosimetry have been discussed in Section 2.2. Only specific considerations relevant to the calorimetry of proton beams are discussed here.

Sarfehnia et al. have conducted some of the most recent measurements, with a calculated uncertainty on absorbed dose to water measurements of between 0.4-0.6% [96]. This uncertainty compares favourably to the 1.9% achievable from ionisation chamber measurements conducted following the IAEA TRS-398 protocol [16], with calorimetric and ionisation chamber results agreeing to within one standard deviation. A diagram of their setup is shown in Figure 2.9. These measurements demonstrate the feasibility of developing a primary standard for proton absorbed dose based on water calorimetry, for both scattered and scanned beams, similar to the standards for photon dosimetry.

![Figure 2.9: A diagram of the in-house calorimeter used by Sarfehnia et al. for proton dosimetry [96]](image)

The measurement reference point within the calorimeter for a proton beam measurement is chosen to be at a point of uniform dose, somewhere within the SOBP, where there are minimal dose variations with depth or lateral displacement [96]. This reduces the impact of positional uncertainties, and also decreases any dose volume averaging effects. The choice of reference point for narrow beam dosimetry results in higher uncertainties arising from these causes, and a dose profile correction factor for doses measured at multiple thermistor positions surrounding the reference point [96]. However the notion of a reference measurement point does broach the subject of the major limitation of calorimetric dosimetry using standard calorimeter designs - the measurement only determines dose to a point or, for some
designs, several points. The energy of the beam and the subsequent depth of the Bragg peak or SOBP must be well known so that the relevant positioning of the temperature probe to this region is well understood. Thus whilst calorimeters are the recommended choice for beam calibration, supplementary detectors are required for the full beam characterisation.

The main ways in which proton calorimetry differs from photon beam calorimetry are with respect to corrections for the chemical heat defect and thermal heat conduction. The chemical heat defect is a correction for energy consumed by chemical reactions which prevents the entire beam energy from being converted to a temperature increase. The chemical reactions which occur are specific to proton beam irradiation, and have been both numerically simulated and experimentally investigated [96, 105, 107, 108, 111, 116–118]. For water saturated with hydrogen a steady state of zero for the heat defect is reached after a certain dose accumulation, whilst for nitrogen or argon saturated water there is some exothermic heat defect of < 1%, which increases with increasing LET, to an extent slightly less than the heat defect in a photon beam. With regard to the thermal heat conduction, the difference between scattered or scanned proton beams versus photon beams is in terms of the depth dose curve, where the influence of the Bragg peak results in more of an imbalance between the measured heat distribution and the radiation dose distribution [96, 116]. This places a limit on the maximum measurement time as a function of the distance between the measurement point and the distal edge of the SOBP. For scanned beams the steep lateral dose gradients are instantaneous, which results in a much larger influence of heat diffusion, especially in between the planes of a scanned beam [117]. The presence of conductive heat transfer is limited. A smaller heat conduction effect arises from the different heat constants of the walls of the measurement vessel and temperature probes compared to that of water. The correction required is similar to that of a photon beam, but has some small differences which depend on the continuous slowing down approximation range of protons to water in the wall material [108,116].

The alternative method of calorimetry is to use a solid material such as graphite for the sensitive volume rather than water. This has the advantage of having a higher sensitivity due to the lower specific heat capacity. The disadvantages are that the thermal conductivity is higher, and notably for proton beams, that the conversion of absorbed dose in the calorimeter medium to that in water introduces relatively large uncertainties. Solid state calorimeters have been used for proton beam reference dosimetry [119,120] with absorbed dose to water calculated by consideration of the variation in the energy spectrum at different equivalent depths in graphite and water due to the production of secondary charged particles.
in each medium. Additional uncertainties are introduced from radiative power dissipation, measurement of the mass of the core and the physico-chemical heat defect [121].

An additional constraint on calorimetric measurements is the logistical effort required, in part due to the high level of thermal isolation necessary.

**Ionisation chambers**

Ionisation chambers are the standard detectors for routine proton beam reference dosimetry and beam monitoring, and commonly used in the acquisition of depth dose distributions [17,122–124]. The main advantages of ionisation chambers over other detector types is the high accuracy and reproducibility under reference conditions, with a relatively small LET and energy dependence, and the availability of a range of chamber types for different applications. The disadvantages are the corrections required for any deviation from reference conditions, which are specific to the chamber used, and which are not well characterised for proton beams, resulting in the introduction of higher uncertainties compared to photon beams.

There are an array of ionisation chamber designs available, generally classified into two main categories of cylindrical or thimble type chambers and plane parallel chambers. Cylindrical chambers are recommended for reference dosimetry as the combined standard uncertainty is lower than for plane parallel chambers [16]. For many commonly used thimble chambers relatively high accuracy and reproducibility is achievable, however the sensitive volume is often relatively large, often on the order of 0.05 cm$^3$. This limits their suitability for measurements in steep dose gradient regions such as the lateral edges of the beam, or near the Bragg peak. This imposes the limitation that the SOBP width must begin at least 2 cm deep, and span at least 2 cm in water, in order to achieve accurate measurements with reduced volume averaging effects [17]. So this is only useful for the measurement of high energy beams intended for deep seated tumours, rather than the lower 60-70 MeV proton beams with SOBP widths of less than 2 cm, such as those used for eye treatments [17]. The inaccuracies are exacerbated for narrow beams. Various pinpoint chambers with radii of less than 1.5 mm and cavities on the order of 0.015 cm$^3$ are available for narrow beams or beams with high dose gradients. These can, however, still result in a widening of the penumbra in steep dose gradient regions, whilst the reduced volume results in a lower sensitivity and accuracy [18]. A common use for these is for the verification of treatment plans in a water phantom. In general the use of ion chambers is restricted to beams with a diameter greater than 10 mm [18].
Plane parallel chambers, such as the PTW-Roos, PTW-Markus, or IBA-NACP chambers [16] can also be used for absorbed dose measurements but are used more commonly for depth dose distributions. The diameters of the measurement cavities are typically between 5 and 20 mm, with a surrounding guard ring to ensure the secondary electron fluence is in lateral equilibrium. The spacing of the electrodes is typically between 0.5 and 2 mm, which allows for higher resolution of depth dose measurements than most thimble chambers, providing the field size is sufficiently large considering the cavity diameter, with a factor of two recommended [16]. The limitation of depth dose measurements with a plane parallel chamber is the requirement to scan the detector across the relevant depths in a water phantom. To increase the measurement efficiency various multiple channel devices have been developed incorporating a stack of plane parallel ion chambers [125–127]. These contain an absorbing material between neighbouring chambers, allowing for the shape of the depth dose distribution to be determined in a single measurement. Plane parallel chambers have also been used in segmented designs allowing measurement of beam properties like flatness or lateral profiles, with spatial resolution on the order of a few mm [97, 126, 128, 129], and a stack of such detectors can achieve quasi-three dimensional dosimetric measurements [130].

A detector based on a similar approach to an ionisation chamber and which has been used for proton measurements is a Faraday cup, which is a conductive metal cup which measures the fluence of charged particles by catching them in a vacuum. The dose distribution is then derived from the fluence by the relevant stopping power ratios. These have also been used in stacked configurations for depth dose measurements [123]. They have been shown to have decreased accuracy compared to ionisation chambers for lower energy beams, due to low energy protons in the beam affecting the mass stopping power [18]. For larger field sizes they also require an accurate knowledge of the cross sectional area of the beam, which introduces uncertainties compared to ionisation chamber measurements [119, 131, 132]. However this uncertainty disappears for narrow beam measurements, where the derived quality is the laterally integrated dose [133, 134].

There are several limitations regarding the use of ionisation chambers for proton beam measurements, beyond the constraints imposed by their geometry. The main source of uncertainty is in the ratio of the stopping power of the proton beam in water to that in air, which is introduced in order to convert the dose measured in the air cavity to that in water. The stopping powers have a strong dependence on the mean ionisation energies in water.
and air. In a low energy region, such as for measurements in and around the Bragg peak, a simple ratio of stopping powers is no longer valid [135]. This results in a deviation of the stopping power ratio from those recommended in TRS-398 by up to 3% in this region. A typical uncertainty achievable using TRS-398 protocol is 1.9%, which is already considerably higher than that achievable with a calorimetric measurement. This may in actuality be even higher if this effect is taken into account [96]. Additional uncertainty arises due to limited knowledge regarding the chamber specific perturbation factors for proton beams of varying energy [17]. Current research aims to improve the accuracy of ion chamber dosimetry by reducing the uncertainty in these parameters by means of both experimental measurements, and theoretical calculations.

The second main limitation of the use of ionisation chambers, is that except for the segmented chambers mentioned above, they are only able to measure the doses from scattered proton beams rather than scanned beams [17,97]. The correction factors given in protocols such as TRS-398 are only valid for scattered beams. The limitation of a scanned beam is that the dose is deposited in a cumulative fashion, which affects the measured ionisation current. As scanned beams are becoming increasingly the modus operandi for proton therapies the need for alternative detector systems is increased.

Radiochromic Film

Radiochromic film dosimetry using various film products has been shown to be possible for both scattered and scanned proton beams, achieving high resolution measurements [136–139]. In fact film is considered by many to be the detector of choice for lateral beam profiles, especially for narrow proton beams [18]. Film is also used for measuring beam widths, and quality assurance of field geometry and homogeneity. Commercially available radiochromic films suitable for proton measurements include Gafchromic EBT or MD-V2-55 from ISP Technologies (Wayne, New Jersey, USA). The resolution of most film measurements is on the order of 85 µm, with the limiting factor being the digitisation of the film by the flatbed scanner used for the analysis [139]. Radiochromic film has been shown to be a valid tool for narrow beam geometries, except at the very distal part of the Bragg peak curve, and is often considered the preferred tool for obtaining depth dose data of beams with a diameter of less than 5 mm [18].

Radiochromic film has been shown to have an approximately linear response to dose for high
energy proton beams, which is a distinct advantage over radiographic beams. Studies have shown this linearity to be approximately 4.5% for one standard deviation, except for the low energy regions near the Bragg peak, where a 5-10% dose suppression is recorded [139]. The complicating factor is that the optical density with dose is non-linear, and the film response depends on beam quality in a more complicated fashion for proton beams as compared to photon beams [17]. As the energy of the proton beam varies, the linear energy transfer, LET, varies over a wide range, with each LET component leading to a different film response [140]. Thus for mixed fields where the SOBP is created from beams of varying energies, to reconstruct the dose from the optical density requires a knowledge of the exact composition of the beam, as well as a dose response calibration curve for each beam component. It is complex but possible to do this by modelling of the film response [140] or application of relative effectiveness factors to measure depth dose profiles by quenching the film response [137]. However most dosimetric measurements using film in proton beams are for lateral measurements in mono-energetic beams. For a monoenergetic beam, a single calibration curve can be used to evaluate films exposed at different depths in the beam [18]. These measurements achieve relative dose distributions rather than absorbed dose to a reference point within a SOBP.

Monte Carlo Beam Models

Monte Carlo modelling of many different types of radiation dosimetry problems is an area of rapidly increasing importance, with many authors reporting work on the application of Monte Carlo codes to proton therapy [141–143]. The Monte Carlo (MC) modelling technique is a computational algorithm which, in the context of radiation dosimetry, develops a model of the radiation progression through a bulk medium. An MC model simulates random trajectories of individual particles by using random numbers to sample from the probability distributions which govern the individual interactions of electrons, photons and charged particles in materials. If physical quantities of interest are tracked over a sufficient number of particles and their interactions (or histories), then a MC model is able to predict expected values of macroscopic quantities such as energy deposition and therefore dose distribution. Each MC simulation code has four main components: the cross-section data for all processes considered, the algorithms used for particle transport, algorithms to specify the geometry and the analysis to determine the physical quantities of interest. Some of the physical processes considered include energy loss, straggling, multiple Coulomb scattering of primary beam and secondary radiation and nuclear interactions [141]. The path of the radiation is calculated from a modelled source, often assumed to have a Gaussian distribution, through
a complete simulation of the treatment head geometry including beam components such as bending magnets, energy modulators and collimators, and into the irradiated material, which may be homogeneous e.g. water or air, or heterogeneous, e.g. patient body composition obtained from computed tomography (CT) scans. The interactions at each point are sampled, to calculate a resulting dose distribution within the medium. MC models can also incorporate a detector such as an ionisation chamber or film, in order to compare modelled and measured results directly. There are various MC algorithms used for radiation dosimetry of proton beams, including GEANT4 [45], FLUKA [144] and MCNPX [145]. These all use variations on the physical interaction models and transport algorithms, with their own nuclear cross section libraries and the results of each model are often compared for validation and improvement [146].

Most treatment planning systems are based on fast analytical pencil-beam dose calculation algorithms which calculate dose distributions based on a water-equivalent path length [141]. A full MC model demonstrably improves on these, by considering the physical system in far more detail [147–152].

MC models have a major limitation in that the accuracy of the model is limited by the user-defined input parameters of the proton beam, and the data on the physical processes which occur. Discrepancies in some MC models result from some of the input parameters such as the irradiation geometry, or spectrum and flux of the radiation being too crude, for example neglecting scattering within the collimators or divergence or polarisation of the beam [153,154]. The input data relies heavily on the accuracy of vendor blueprints with regard to component geometries and compositions, which may vary in actuality. Additionally, the implementation of the physical interactions is via theoretical models or interpolation of experimental data. The accuracies of these calculations can depend on the energy region in question. Thus whilst modelling can produce a general model of each particular type of radiation system, it may not incorporate the real life irregularities of the particular system into the simulations. This makes MC very labour intensive, as the algorithm must be specifically applied and validated for any given beamline. The calculations also tend to be very computationally intensive, as the accuracy increases with the number of histories run. MC codes may be underutilised for these reasons, although there has recently been some development of more user-friendly interfaces such as TOPAS [155].

An MC algorithm which has been accurately implemented and validated does have many
advantages for proton beam dosimetry. This includes the fact that there is no fundamental 
limit on spatial resolution, given sufficient accuracy of the input parameters [156]. There 
is also inherently no uncertainty in the measurement position. Thus MC is a vital tool for 
validating narrow beam measurements. Additionally, the ability to obtain multiple output 
parameters, for example both dose and LET as a function of water depth can contribute to 
the accuracy of other dosimetric tools such as film, which require additional knowledge of 
the beam spectra to achieve high accuracy.

MC is therefore an extremely useful tool for dosimetry of proton beams, however it will never 
be a standalone dosimetry method, as verification with experimental results will be required 
across the entire range of applicable measurement conditions for any given system. Thus 
there is still a strong need for accurate physical detectors for validation of the MC model.

Other Dosimetry Approaches

There are a variety of other detectors that have been applied to proton beam dosimetry. 
Most of them are solid state detectors, which have the advantage of a higher signal due to 
their higher ionisation density, allowing for a reduction in the sensitive volume and corre-
spondingly higher spatial resolution. This can result in signal saturation at the distal edge 
of a Bragg peak [17]. The detectors can be broadly categorised based on their geometry 
into point-like detectors such as silicon diodes, diamond detectors, TLDs and optically stim-
ulated luminescence detectors; two dimensional detectors such as scintillating screens; and 
three dimensional detectors such as gel and sample activation detectors. Each of these is 
briefly described.

**Silicon diodes** are detectors made of elemental semi-conductor material, which are based 
on the principles of a P-N junction diode whereby radiation introduces electron-hole pairs 
which diffuse into the depletion region, generating a current. A diode dosimeter is made 
of p type silicon, counterdoped at the surface to produce a p-n junction diode. Radiation 
produces electron-hole pairs throughout, including in the depletion layer, and then charges 
produced in the body of the dosimeter within the diffusion length diffuse into the depletion 
region. Here they come under the action of the electric field from the intrinsic potential, 
and a reverse current is generated. Operated in the short circuit mode this exhibits a linear 
relationship between measured charge and dose. The benefits of diodes are that they can be
made small in size with high spatial resolution but also high sensitivity. The disadvantages are that they demonstrate a dependence on the proton beam LET, dose rate and energy [17]. Some diodes experience a significant over-response in the Bragg peak, whilst others experience an overall decrease in response with increasing dose of approximately 0.7% [157].

Diodes are commonly used for lateral profile measurements and determination of field factors, and are the detector of choice for determination of these in narrow beam geometries. For instance the Scanditronix diode DB050 was designed for use in photon radiosurgery beams and has a width of 0.6 mm, but has also been applied to narrow proton beams to good agreement with ionisation chamber results for beams of 20-30 mm diameter, and was effective for smaller beams down to 5 mm, although volume averaging effects can still be observed [18].

Both diodes and MOSFETs are used as relative dosimeters, because they require regularly updated calibration curves to obtain the absorbed dose from the current or threshold voltage. Both detectors show a temperature dependence, and a non-linearity of response with their radiation history, so they cannot be used for beam calibration. They are more sensitive and smaller than ion chambers, with excellent spatial resolution and limited attenuation of the beam. Diodes and MOSFETs are commonly used for in vivo and in phantom dose measurements, including for routine patient dose verification, brachytherapy, total body irradiation, intensity modulated radiotherapy and intraoperative radiotherapy. Because of their small size they are useful in high dose gradient areas such as those found in stereotactic radiosurgery, electron depth dose curves or the penumbral region of beams.

**Diamond detectors** are similar in many aspects to diodes, but radiation hard. The PTW design diamond detectors function by attaching metal contacts to the edges of the diamond [158]. A metal-semiconductor barrier creates a Schottky diode on the top metal contact. Positive and negative charge carriers are generated by the incident radiation, and because they are separated by the diode field a signal current is produced which can be measured with an electrometer, without the requirement for an external bias voltage. Diamond can detect any type of radiation that generates electron-hole pairs as long as the exciting radiation is of higher energy than the band gap, 5.5 eV. Chemical vapour deposition (CVD) is used to produce diamond films with similar electrical and thermal properties to natural diamond, reducing the cost and increasing the versatility.
As for diodes, diamond detectors achieve high spatial resolution with high sensitivity. They often experience radiation type, dose rate and energy dependence [138,159]. The dose rate dependence is not dependent on the rate of linear energy transfer (LET), so values measured for photon beams can also be used for protons, but the energy dependence can be substantial [18]. A recent study by Mandapaka et al. reported a commercially available detector with 1 μm thickness and no energy dependence, for high energy beams ranging between 155 and 250 MeV [160]. Diamond detectors have been shown to be useful in proton beam calibration, and are used for lateral profile measurements for beams down to 10 mm in diameter [138,159,160]. The tissue equivalency of diamond is an advantage over that of the diode detector.

**Thermoluminescence Detectors (TLDs)** are used for proton beam dosimetry, even though they exhibit supra-linearity with dose and substantial energy dependence [161,162]. The energy response can be corrected for by measuring the energy dependence of the different glow curve peaks [163,164]. They also require correction for the density being greater than that of water. TLDs do achieve sufficient spatial resolution on the order of a millimetre, and are useful for absorbed dose calibration in narrow beams, as the proton beam quality correction factors are close to unity [18].

**Optically Stimulated Luminescence (OSL) Detectors** are based on the same principle of operation as TLDs, except that the read out is via optical excitation. OSL is widely used in personal dosimetry, but preliminary work has been reported on the use of carbon-doped aluminium oxide crystals for proton dose measurements [165]. An under-response in the Bragg peak region was reported at doses above 0.3 Gy, but they generally have a linear response with dose to high fluences, and very good spatial resolution. OSLs will be potentially useful for in-vivo dosimetry of proton beams.

**Scintillating screens** have been used for dosimetric purposes in a proton beam [166,167]. They consist of a plate coated with a scintillating material such as Gd₂O₂S:Tb, and the light emitted when a proton strikes the detector is recorded by a CCD camera. They achieve a high spatial resolution in two dimensions, a linear response over a large range of dose rates, and dose rate independence, so are suitable for measuring field size and distribution, including for narrow beams. They do experience some LET and energy dependence, so are
not suitable for depth dose measurements.

**Gel dosimetry** using ferrous sulphate gels to record the dose from a clinical proton beam allows for the subsequent optical three dimensional reconstruction of the beam [168]. However as for most of the detectors mentioned, they exhibit an LET and energy dependence, resulting in a lack of sensitivity in the Bragg peak region [169]. Polymeric gels such as BANGR are somewhat less dependent on LET [170], whilst PRESAGE has the advantage of being nearly water equivalent, relatively insensitive to oxygen and solid-state allowing the detector shape to be customised more easily [171,172], however both have been reported to still underestimate the dose in the Bragg peak by approximately 20% [173].

**Sample activation measurements** have also been used for proton dosimetry, whereby a sample with a known number of C-12 atoms is irradiated and the proton fluence determined from a subsequent measurement of the induced C-11 activity [174]. The advantage of this method is that it can be used in high dose per pulse beams such as a synchrotron.

### 2.3.3 Microbeam Radiation Therapy

Microbeam radiation therapy (MRT) and its dosimetric challenges was the initial motivation for developing a DHI detector for radiation dosimetry. No measurements of MRT radiation have yet been made with the prototype DHI detector, however Chapter 8 includes a theoretical consideration of the potential for DHI to measure microbeams, based on the experimental results achieved in the initial proof-of-principle measurements of an HDR brachytherapy source and a proton beam. For this reason, a short introduction to MRT is included here, with a focus on the dosimetric problems that it presents. Brief mention is made of some of the alternative dosimetry options being explored, however this is not intended to provide a thorough coverage of the field.

Microbeam radiation therapy is a technique which utilises the fact that normal tissue can sustain very high radiation doses without notable functional damage, if the dose is limited to a minuscule volume of tissue. This phenomenon was first discovered almost 40 years ago at the Brookhaven National Laboratory in the US [153], and applied to the field of radiation therapy about ten years ago.
Synchrotron radiation sources are used to provide an extremely intense, tuneable beam of photons with a broad energy spectrum of X-rays in the 50-150 kV energy range [19]. This high flux radiation beam is collimated into a planar, micro-lattice of narrow beams, each one typically 25 µm wide, with 200 µm separation from the next peak [175]. A schematic of a synchrotron and a cross section of the microbeams produced on a medical beam line are shown in Figure 2.10. A tumour is irradiated for a fraction of a second (possibly from several directions) by bundles of these X-ray beams, with typically several hundred Grays of radiation given in the peak doses. The high flux rate of the beams is important to avoid the “smearing out” of the dose by tissue movement [153].

Figure 2.10: a) A diagram of the layout of the Australian synchrotron, where (1) electron gun, (2) linear accelerator, (3) booster ring, (4) storage ring, (5) beamline after the electrons are converted to photons on a wiggler or other device, and (6) end stations where the measurements or treatments are conducted [176]. b) Monte Carlo model of the cross section of a microbeam array at a depth of 3 mm in a water phantom, showing typical dimensions of peaks to valleys. Image reproduced from work by Bräuer-Krisch et al. [177].

High dose synchrotron microbeam radiotherapy has been shown to be effective in animal models at causing significant growth delay or even tumour ablation, whilst causing minimal damage to normal tissues [175]. This allows for prevention of tissue necrosis within the volumes traversed by the microbeams, except in a cross-fired target (although even unidirectional exposures have been shown to have differential effects on tumour cells) [19]. MRT can significantly reduce tumour cell proliferation within 24 hours after irradiation; within 24 hours the peak and valley zones in the tumour irradiated regions become indistinguishable, due to extensive cell migration between the zones [178]. This effect is not seen in the MRT treated normal skin cells, which appear to undergo a coordinated repair response, and be exceptionally resistant to even hundreds of Grays of peak dose [175]. The exact mechanisms and cellular processes relating to this differential response are not yet fully understood. Over-
all, survival times are on a par with conventional radiotherapy, whilst there is considerably
less normal tissue damage, so therefore the therapeutic index is higher for MRT [178].

This technique may prove to be more effective than the best existing technique for several
intractable human malignancies, and therefore has the potential for therapeutic applica-
tion [179]. In particular, conventional radiotherapy has some limitations for treating brain
tumours - especially in children, as the radiation damage is intolerable to normal brain de-
velopment if applied before the age of around three years [154]. High-grade glioma is one of
the most common forms of child cancer, and MRT may be able to potentially overcome this
limitation, so for this reason alone it is well worth pursuing.

Synchrotron radiation sources are now found throughout the world, with MRT being most
actively studied at the European Synchrotron Radiation Facility (ESRF), and the National
Synchrotron Light Source (NSLS) in the USA, although other facilities also investigate this
area, including dedicated medical beamlines at SPring8 in Japan, and the Australian syn-
chrotron in Melbourne [19].

**Dosimetry requirements for MRT**

There are many questions to be answered before MRT’s potential can be fully estimated,
and before clinical application on humans. To answer most of these questions requires very
accurate dosimetry methods to determine the dose distribution throughout the irradiated
volume. There currently exist no commercial dosimetry systems capable of satisfactorily
measuring the dose distributions of MRT. Currently one of the main approaches has been
to model the dose using Monte Carlo simulations based on assumptions about the radia-
tion transport and dose deposition in water; however it is essential to have an independent,
measurement-based dosimetry system that can be used to verify these computer simulations
and measure day-to-day variations.

The primary problem is to quantify the relationship between the microbeam irradiation
parameters and the resultant tissue damage. This is important because the microbeam en-
hanced normal-tissue sparing effect is heavily dependent on the peak-to-valley dose ratio
(PVDR) and the irradiated volume [178, 180]. This correlation must be thoroughly under-
stood in order to determine the optimal geometric configurations for MRT treatments [181].
There is a certain width of the microbeams which should not be exceeded, and the valley
doses, which are proportional to the array size, subject size, tissue depth, and the increasing
ratio of beam thickness to spacing, must be minimised [180]. Therefore it is particularly important to develop a reliable means to accurately determine the PVDRs.

Lower valley doses may be achieved by temporal spacing of dose fractions, by 1-3 days, possibly at perpendicular angles, although the MRT spatial fractionation may be sufficient in most cases [178]. This needs to be investigated, along with other questions such as the extent to which the dose penetration is lower for microbeams, is there any dose build-up at depth, what is the effect of the collimator on the beam quality (relating to the beam penetration), further investigation of the bystander effect, as well as to assess the effect of greater X-ray scattering in larger target volumes of humans rather than samples.

The nature of microbeam radiation creates some difficulties in accurately characterising the dose. There are several factors to consider for MRT that are not a consideration for linac produced broad beam radiation dosimetry. The key parameters for microbeam dosimetry are:

- **PVDR**: The most crucial factor for the outcome of MRT treatments is the PVDR, as this is the limiting biological factor for MRT [28,182]. However simultaneous measurement of peak and valley doses has proven difficult for the typical MRT energy ranges of 50-150 kV [28,153,183]. This can be attributed in part to the high dose gradients (hundreds of Gray) that occur over very short distances of tens of µm.

- **Spatial resolution**: In order to have optimal use of the MRT benefits, it is important to accurately localise the peaks and valley doses, particularly if multiple treatment fractions are used. Due to the microscopic dimensions of the microbeam arrays this is not a trivial consideration.

- **Peak dose**: The absolute peak dose must also be determined. This may be less crucial than the PVDR, because when delivering hundreds of Grays of radiation (already a lethal dose) a small percentage error is negligible. However, any dosimetry system must still be able to resolve the very high dose rates, on the microscopic scale required.

- **Spectral range**: The system must be able to cope with the non-monochromatic nature of the synchrotron beam. Some traditional dosimetry methods can encounter
difficulties arising from their use of absorption correction factors which vary with photon energy. Additionally, measurements should ideally be able to be made at different depths within the irradiated material.

**Monte Carlo simulations** are used to calculate the MRT dose distributions within the tissue. Because there is a lack of experimental dosimetry systems with sufficient resolution for MRT, MC has made up the majority of approaches to this dosimetry problem in the past ten years, and has been vitally important to the development of MRT [182]. A Monte Carlo approach will never be a stand-alone dosimetry method, as any model needs verification with experimental measurements. Work by Crosbie et al. has shown large differences between film measurements and a corresponding MC model, demonstrating the need for empirical verification of MC models used for dosimetry purposes [28]. However, these simulations are still crucial for the refinement of treatment planning for clinical trials or other experiments [182]. Various MC algorithms are used, including PENELCOPE [153], PSI-Geant3, EGS4 [182], and GEANT-4 [45, 154]. These all use variations on the physical interaction models and transport algorithms, and results of each model are often compared for validation and improvement. There are a huge number of irradiation parameters and physical processes which must be carefully simulated, to try and ensure the comparability of the simulation models and experimental data. The primary mechanisms for dose deposition are the Compton scattering and photoelectric events that set electrons in motion [180]. An important factor is the models’ ability to deal with low energy electron transport, important for dose calculations in the micron-sized ranges of MRT, because the low energy electrons determine the dose scattered into the valley regions. Present discrepancies may be based on, for example, too crude a model of the real irradiation geometries (e.g. many models neglect the scattering in the collimators, or the divergence or polarisation of the beam [153, 154]. One of the main shortfalls of MC is that it is next to impossible to incorporate the real life irregularities of the MRT system into the simulations. For example the collimators used are not uniform (as in the MC calculations), actually the manufacturing process introduces significant variations and curvature, which is exacerbated by the intrinsic divergence from the wiggler on the synchrotron. One study found that for a collimator with average full width half maximum apertures of 25 $\mu$m, the actual variation was between 19-39 $\mu$m, which has a huge effect on the dose distribution [183].

**Ionisation chambers** are not well-suited for resolving the peak and valley doses for MRT due to the low spatial resolution [28]. Additionally, because the irradiated volume is so small
it becomes hard to satisfy the condition of charged particle equilibrium, and the intensity of the beam means that ion recombination becomes an unavoidable problem [20]. Despite these difficulties, low energy free air ionisation chambers have been used to measure air kerma rates and attenuation coefficients for the MRT beam at the Australian Synchrotron, with the results showing agreement to calculations to within 3% [184]. Further measurements using graphite chambers have also shown promise for integrated absolute dose determination [185].

TLDs can come in two dimensional foils which have been used to measure microbeam doses. These foils have limited spatial resolution due to the properties of the detectors, and the light scattering within the detectors, so they are not really suited to this application. Nonetheless, they have been considered a convenient tool for quality control and basic dose measurement of X-ray microbeams [186].

Solid state detectors based on an epitaxial silicon detector are under development by Lerch et al. to measure the lateral dose distribution of a microbeam array in high resolution and real time [187]. Initial results have been shown to be reproducible to within 0.5%, but with PVDRs a factor of 4.5 times less than expected due to charge recombination effects at low bias voltages. Suggested improvements to this detector may result in potential for its use for MRT in the future.

Radiographic films have been used for micro-dosimetry with reasonable accuracy, but the precision of the dose measurements is limited due to the energy dependence, speed of the film, slight changes in processing conditions, inter-film emulsion difference, conditions of the densitometer, and the uncertainty from the calibration curve (for example the difference between the energy spectra of the calibration versus the MRT radiation) [20]. Measurements can have a tendency to underestimate the PVDR, possibly due to the point spread function of the film [20].

Radiochromic film has a much weaker energy dependence than radiographic film, which is important because synchrotron radiation is produced in a wide beam spectrum rather than quasi-monochromatically [28,153]. An example of radiochromic film which has been used for MRT dosimetry is GafChromic film [28]. Aside from the calibration of the films, one of the other primary difficulties is in recording the peak and the valley doses on the same film. One study has sought to overcome this by using parallel sheets of two types of film with different sensitivities, to record peak (low sensitivity film) and valley (high sensitivity film) doses [28]. Film has the advantage of unparalleled spatial resolution - this is limited
by the microdensitometer used to read it, but film still provides sufficient spatial resolution for microbeams.

2.4 Concluding Remarks

This chapter served as a general introduction to the field of dosimetry for radiation therapy, and described the motivation behind the development of a new approach to radiation dosimetry. Radiotherapy is a widespread and effective tool against many types of cancer, and accurate measurements of dose distributions delivered to patients are critical to optimise treatment efficacy and safety. Current detectors are adequate for conventional treatment approaches, however there are various new and existing treatment types which have particular dosimetry requirements which are not fully realisable by existing technology. These include HDR brachytherapy, narrow beam proton therapy, high dose rate proton beams and MRT. The dosimetry requirements for each of these were introduced and discussed, along with the main types of dosimeters currently used to approach these requirements. While each has its own set of advantages, the fact that no dosimeter can in isolation fulfil all the requirements of an ideal dosimeter means there will always be a motivation for further development to achieve different combinations of beneficial features. The ways in which DHI may provide some advantages over existing dosimetry techniques will be discussed further in the relevant Chapters 6-8. In the next chapter, the optical technique of digital holographic interferometry is introduced.
Chapter 3

Principles of Digital Holographic Interferometry

This chapter introduces the optical principles required for digital holographic interferometry (DHI) and the history of DHI, and then includes a short discussion of the different types of DHI interferometers available with a focus on which is the most applicable for the purpose of dosimetry. The chapter concludes with a summary of the literature relating to previous applications of interferometry to dosimetry.

3.1 Fundamental Concept of Optical Calorimetry

An optical calorimetry approach to dosimetry is based on the concept that irradiation of a sample of water, or some other transparent tissue or near tissue equivalent medium, deposits a dose of energy. Most of this energy is converted into heat energy, which increases the temperature of the medium, depending on its specific heat capacity. Measurement of this temperature increase means it is possible to then infer the absorbed dose to a high degree of accuracy. This is the principle that calorimetry, which is used at several national standards laboratories as a primary standard for determining absorbed dose, is based upon. Conventional calorimetry techniques, however, whilst providing highly accurate measurements of the temperature increase, generally provide limited information about spatial distribution. Most calorimeters determine an integrated dose to the entire measurement volume of the calorimeter. They also often rely on physical probes to detect the temperature, which can perturb the radiation field and require a thermal equilibration time which limits the temporal resolution. These limitations to conventional calorimetry techniques can potentially be overcome by the use of an optical technique such as holographic interferometry to probe the temperature distribution within a test cell.
The key phenomenon that makes the use of optical interferometry possible for calorimetric measurements is that the refractive index of water is temperature dependent. This means that when the absorbed energy from irradiation of a water sample causes a temperature increase, there is a corresponding decrease in the refractive index - a parameter which is able to be quantified with an interferometer. An interferometer can measure the change in refractive index because it is able to detect the variation in the path length of light travelling through the water sample, which is a function of refractive index. These optical concepts will be covered in more detail in Section 3.2.1. The result is that by means of a type of interferometry known as holographic interferometry, it is possible to obtain information regarding the spatial distribution of the temperature variation within a cell, and thus infer the dose distribution. As this process involves no physical detector placed in the beam, there is no perturbation of the radiation beam, and no intrinsic limitation on the spatial and temporal resolution.

3.2 Optical Interferometry

The radiation induced graduated change in the refractive index of a water cell can be measured by means of optical interferometry. The refractive index variation and resultant variation in the optical path length of light passing through the water cell can be measured using a coherent light source, such as a laser. The optical phase of the laser light passing through the cell varies compared to light that does not pass through the cell. If the two wavefronts interfere after the cell, they will produce a pattern of fringes that is related to the path difference. Comparison of the fringe patterns formed before and after the cell is irradiated gives a direct measurement of the absorbed dose in the water. The most basic interferometric set-up is the Michelson interferometer [188], which was used by Hussmann for the first interferometric measurements of radiation dose [24]. An example is shown in Figure 3.1 along with an example of the type of fringe pattern that it produces. Many other configurations of interferometer have since been developed, such as the Mach-Zehnder interferometer, which has proven to have a more usable geometry for many applications [189,190]. A number of interferometer configurations will be described in Section 3.3.3.

3.2.1 Basic Optics Principles

This section introduces some of the optics principles that are fundamental to the understanding of interferometric systems.
Harmonic Light Waves

Light is a transverse, electromagnetic wave, consisting of time-varying magnetic and electric fields, which obey the Maxwell equations [191]. The wave equation which describes the propagation of light in a vacuum is:

$$\vec{\nabla}^2 \times \vec{E} - \frac{1}{c^2} \frac{\partial^2 \vec{E}}{\partial t^2} = 0$$ (3.1)

where $\vec{E}$ is the electric field strength, $t$ is the time instance, $c$ the propagation speed of the wave, and $\vec{\nabla}^2$ the Laplace operator as in equation 3.2, with $x, y$ and $z$ the Cartesian spatial coordinates, such that the spatial vector $\vec{r} = x\hat{x} + y\hat{y} + z\hat{z}$.

$$\vec{\nabla}^2 = \frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2} + \frac{\partial^2}{\partial z^2}$$ (3.2)

Transverse waves vibrate orthogonally to the direction of propagation, and are described in vector notation. The polarisation of a wave describes the direction it vibrates in. Generally for laser interferometry it is acceptable to assume that a wave is plane polarised, vibrating in only a single plane.

For a plane polarised wave, the most important solution to equation 3.1 is the harmonic wave equation:

$$\vec{E}(\vec{r}, t) = \vec{E}_0 \cos(\vec{k} \cdot \vec{r} - \omega t + \phi)$$ (3.3)

Here, $\vec{E}_0$ is the real amplitude of the wave, $\phi$ the phase, and the wave number $\vec{k}$ relates to the wavelength $\lambda$ according to:

$$\vec{k} = \frac{2\pi}{\lambda}$$ (3.4)
and $\omega$ the angular frequency of the wave, which is related to the wavelength by:

$$\omega = \frac{2\pi c}{\lambda} \quad (3.5)$$

The harmonic wave from equation 3.3 can be written in complex notation, including only the real term which represents the physical wave, where $i = \sqrt{-1}$ is the imaginary unit, according to:

$$\vec{E}(\vec{r},t) = \frac{1}{2} \vec{E}_0 e^{i(\vec{k} \cdot \vec{r} - \omega t + \phi)} + \frac{1}{2} \vec{E}_0 e^{-i(\vec{k} \cdot \vec{r} - \omega t + \phi)} \quad (3.6)$$

Figure 3.2 shows the spatial distribution of a wave moving in the $z$-direction, at time instances $t = 0$ and $t = t_1 > 0$. Each point of constant phase moves with the *phase velocity*, $c$. A *wavefront* refers to the spatial distribution of a surface of constant phase, such as the maxima, as it propagates through space.

Figure 3.2: The components of a wave as it propagates through space.

Equation 3.6 describes a plane harmonic wave, which has constant phase in all planes orthogonal to the propagation direction at each arbitrary time $t$. Ideal spherical waves do not technically exist in nature, but can be approximated in practice by the output at the focus of a convex lens, if the input is a plane wave. For a harmonic spherical wavefront, with each phase constant on each spherical surface about the origin, and $r$ the amplitude of the spatial vector, the complex description of the amplitude of the real wave becomes:

$$\vec{E}(\vec{r},t) = \frac{1}{2} \frac{\vec{E}_0}{r} e^{i(\vec{k} \cdot \vec{r} - \omega t + \phi)} + \frac{1}{2} \frac{\vec{E}_0}{r} e^{-i(\vec{k} \cdot \vec{r} - \omega t + \phi)} \quad (3.7)$$

The only parameter of light which is directly detectable by sensors, e.g. eyes, or opto-electronic sensors, is the *intensity* or “brightness” of the light wave, and more crudely, the frequency is detectable as colour. The intensity of a wave is defined as the energy flux through an area per unit time, and is proportional to the time averaged square of the electric field strength:

$$I \sim \langle \vec{E}_0 \rangle \langle \vec{E}_0^* \rangle = |\vec{E}_0|^2 \quad (3.8)$$
Refractive Index

The refractive index, \( n \), of a medium is defined as the ratio of the phase velocity of a given wavelength of light in a vacuum, \( c \), to that in the medium, \( v \) [191]. If a given medium has a greater optical density, then it has a higher refractive index, and light moves more slowly through it.

\[
n = \frac{c}{v}
\]  

(3.9)

This slowing down effect is caused by the electric and magnetic fields of the wave causing disturbances in the charges of each atom, proportionate to the electric and magnetic susceptibility of the medium [191]. These disturbances contribute additional electromagnetic waves and the light wave becomes the macroscopic superposition of all such contributions in the material, typically resulting in a reduction in phase speed according to equation 3.5. This results in a phase retardation of the wave, where the phase of the wave upon exiting the material is retarded compared to that of a wave traversing the same distance with a vacuum, or material of different refractive index.

To consider it in a slightly different way, the optical path length, \( OPL \), of light propagating through a medium is a product of the geometric distance of the path of the light and the refractive index of the medium. In a vacuum, the optical path length is always equivalent to the physical path length, or geometric distance. This can be determined according to Fermat’s principle, which is that the path light takes between two points is always the path that has the minimum optical path length. An optical path length difference \( \Delta OPL \) is the difference in the optical path length traversing between the same points along two different paths or through mediums with differing properties. The optical path length traversed determines which phase the light has at any given point.

\[
\Delta OPL = \frac{\lambda \Delta \phi}{2\pi}
\]  

(3.10)

Alteration of the refractive index by external factors can thus be investigated by measuring the change in phase of a wave passing a distance \( d \) through a medium.

\[
\Delta \phi = \frac{2\pi d \Delta n}{\lambda}
\]  

(3.11)

Interference

The term interference refers to the redistribution of energy in space when two or more waves overlap, resulting in a new wave consisting of the undisturbed superposition of the two waves. The components of the waves in each direction superimpose independently, therefore
two waves travelling orthogonally to each other will not interfere. The combined intensity, \( I \), of two waves can be calculated from their descriptions in equation 3.6. In the simplest case, it is assumed that the two interfering waves have the same frequency and polarisation, resulting in a combined intensity of:

\[
I \sim |\vec{E}_1 + \vec{E}_2|^2 
\]

(3.12)

\[
= (\vec{E}_1 + \vec{E}_2)(\vec{E}_1^* + \vec{E}_2^*) 
\]

(3.13)

\[
= (\vec{E}_0^1)^2 + (\vec{E}_0^2)^2 + 2\vec{E}_0^1\vec{E}_0^2 \cos(\phi_1 - \phi_2) 
\]

(3.14)

\[
= I_1 + I_2 + 2\sqrt{I_1I_2} \cos \Delta \phi 
\]

(3.15)

where \( I_1 \) and \( I_2 \) are the individual intensities of each wave, and \( \Delta \phi = \phi_1 - \phi_2 \) is the difference in phase between the two waves. The third term in equation 3.15 is the sinusoidal varying term which governs the interference. This term is maximum, referred to as constructive interference, when the two waves are in phase:

\[
\Delta \phi = 2n\pi \quad \text{for } n = 0, 1, 2, ... 
\]

(3.16)

Destructive interference occurs when this term is minimum because the two waves are completely out of phase:

\[
\Delta \phi = (2n + 1)\pi \quad \text{for } n = 0, 1, 2, ... 
\]

(3.17)

where \( n \) represents the order of the interference. Across any given plane through the intersection of the two light waves, this results in a pattern of alternating bright and dark bands called interference fringes. These fringes are spaced according to the variation in phase between the two light waves. This is determined by the difference in optical path length each has traversed to reach the observation point, a factor which depends on the wavelength, the angle between the waves, and the geometric distance travelled in each medium with differing refractive indices. Thus for the interference bands to be resolvable the angle between the two light beams must be small.

If the two waves have the same intensity, \( I \), then the interference pattern displays the maximum intensity modulation, from zero to \( 4I \). As the intensities of the two waves become increasingly different, the interference pattern has lower contrast \( C \), where \( C \) is described according to:

\[
C = \frac{I_{\text{max}} - I_{\text{min}}}{I_{\text{max}} + I_{\text{min}}} 
\]

(3.18)

In the above example calculating the intensity of an interfering wave, the waves are assumed to have the same frequency and polarization. This is a factor of the coherence, or correlation.
between the two light beams. Thus only two light beams which are sufficiently coherent will display this interference effect. There are two aspects of coherence, temporal and spatial. Temporal coherence describes the correlation of a wave with itself, at different time instances - in other words whether there is frequency drift over time, proportional to the distance travelled by the wave in a medium of given refractive index. A stabilized single-mode laser emits nearly perfectly temporally coherent light. Spatial coherence describes the mutual correlation of different parts of the same wavefront at a given distance from the source, both longitudinal and cross-sectional. This is a property of the light wave and is usually associated with the apparent size of the source as seen from the measurement point. The spatial coherence of laser light is associated with the transverse mode structure of the resonance cavity, so for lasers resonating in the fundamental transverse (TEM00) mode, all points on the wavefront have essentially perfect spatial coherence. Thus for many interferometry experiments, a single laser possessing sufficient spatial and temporal coherence is used, and divided into two beams which can then later be recombined after probing the medium of interest.

3.3 Refractive Index Determination in Liquids

Interferometers have been developed in a large range of different designs, and been applied to countless different applications in many fields of scientific research. The use of interferometry is indicated by the occurrence of a physical process where the optical path length is modified by various physical quantities. If this induced modification of the path length changes only the phase of the light and has minimal effect on the lateral displacement then measurement of the physical quantity is amenable to interferometry. For many years, a major application of interferometry has been for non-destructive testing of mechanical components under load or vibration; they must have diffusely reflecting opaque surfaces, such as turbine blades, pressure transducers, aircraft and automotive parts etc [192–194]. Some of the additional areas interferometry has been used for have been to investigate the propagation of bending waves after an impact [195, 196], crack propagation in glass [197], flow visualisation in fluid dynamics [198], mass distributions in mass transfer experiments [199] and measurement of electron densities in plasma diagnostics [200].

Application of interferometry to radiation dosimetry exploits the use of interferometry as a tool to non-intrusively provide temperature field visualisation and quantification in transparent gases and liquids. There are many optical techniques capable of utilising refractive index
variations in order to measure temperature fields in a liquid [201]. These include methods based around the deflection of light rays from refraction effects, including laser speckle photography [202], Talbot interferometry [203] and quantitative Schlieren [204]. Other methods infer the temperature field in a test liquid, known as a *phase object*, from measured phase differences of light due to refractive index variation. These include classical interferometry, shearing interferometry [205], and holographic interferometry [200, 206–208]. Holographic interferometric techniques have some distinct advantages in certain applications, which will be discussed in the following section.

### 3.3.1 Holographic Interferometry

Holography is a type of optical interferometry, whereby optical interferograms are created, and then a three dimensional image of the object is reconstructed. This has traditionally been done using holographic film as the recording medium, which is exposed by the interfering light waves, which consist of an unchanging *reference* beam and an *object* beam which probes the phase object and thus varies with temperature. Following exposure, the film is developed, and replaced precisely in the location where it was exposed, and re-illuminated by the reference beam. This reference beam then interferes with the interference pattern already developed on the film, causing a hologram to form - a three dimensional image of the original object to be reconstructed, in its original location.

Holographic interferometry is a further extension of this process whereby it is possible to make two holograms, which were recorded with different states of the phase object, interfere with each other. This results in a reconstruction of the phase object which shows only the changes in the object between the different states. Compared to classical interferometry, this greatly simplifies the process of obtaining information regarding the refractive index variations. For classical interferometry, variation of phase throughout the object is obtained by analysis of the recorded fringe pattern, which shows only minor variations. Comparison of two fringe patterns can allow for inference of the parameter of interest, i.e. the change in the temperature field. However for holographic interferometry, instead of having to analyse the fringe patterns directly, the reconstructed interferograms show a fringe pattern that corresponds only to the *difference* in phase, and therefore the temperature change.

The additional benefit of holographic interferometry over classical interferometry, is that less precise and therefore cheaper, optical components may be used in the interferometer [209]. For classical interferometry, very high precision optical components are required in order
to produce a fringe field with minimal distortions. Each optical component, such as beam splitters, mirrors, lenses etc. cause distortions in the wavefront which affects the uniformity of the fringes in the resultant interference pattern. This greatly enhances the difficulty of the analysis, reducing the accuracy achievable in the results. Reduction of this effect is achieved with a reference beam with an ideal shape, such as flat or spherical, and all surfaces kept optically flat to approximately one twentieth or less of the wavelength of light used, which is difficult and therefore expensive to achieve [200]. In contrast, holographic interferometry circumvents this problem by implementing a differential concept, because the output is a reconstructed interferogram showing only the differences between the two interferograms, and thus any distortions or non-uniformities effectively cancel out [209].

Holographic interferometry can be done using a real-time technique, as well as the traditional double exposure technique which captures just one time instance. An interferogram in the reference state of the object is captured, developed and re-illuminated by the interferometer as the refractive index in the phase object is altered, by heat or some other means such as varying the chemical composition. The fringe pattern of the resultant reconstructed holographic interferogram has bright fringes at the even integer multiples of \( \pi \) and so locations in the object where there is no change in the phase, or a \( 2n\pi \) change, will be in the centre of a dark fringe in the reconstructed image. Quantitative evaluation of the holographic interference patterns involves the pointwise determination of the numerical value of the optical path length change at each point, and relating that back to the physical quantity which caused it. Early techniques involved manually counting the fringes directly in the interferograms to obtain an approximation to the interference phase distribution. In more modern techniques, the resultant holograms are often captured by a camera either in video mode, or at specific time instances. A consideration is the variation caused by the observation vector, which is overcome by the observer projector theorem, which states that if the holographic interferometric fringes are localized off the object surface, they can be observed as if projected onto the object surface radially from the centre of the aperture of the viewing system [200]. The captured images can be stored for later analysis. The manual counting of the fringes is replaced by computerized techniques such as fringe skeletonising [210, 211]. These methods assume that the local extrema of the intensity distribution correspond to maxima and minima of the cosine function in equation 3.15 and that the phase at these pixels is therefore an even or odd integer multiple of \( \pi \). There are several types of fringe skeletonising methods, including some based on fringe tracking, and some related to segmentation. A processing scheme involves multiple steps, beginning with spatial and temporal filtering to improve
the signal-to-noise ratio and specification of the fringe pattern boundary, then extraction of the raw skeleton by fringe tracking, pattern segmentation, or another method, and interactive enhancement of this skeleton by removing artifacts, adding missing points, linking interrupted lines and removing line crossings. The fringes are then given interference order numbers, and the interference phase between the lines is interpolated, before the physical values of what was being measured are determined at each point.

3.3.2 Digital Holographic Interferometry

Advances in optoelectronic sensor technology such as CCD (charge coupled devices) and CMOS (complementary metal oxide semiconductor) technology, as well as in computer processing power, have made it feasible to collect the interferograms digitally, and then use numerical algorithms to reconstruct the holograms directly. This method is termed Digital Holographic Interferometry (DHI) and was first developed by Schnars and Juptner in 1994 [205, 212]. For each recorded state of the object, the intensity and the phase of the object wave can be calculated during the reconstruction of the algorithm, and the interference phase determined from the comparison of these individual phases. This eliminates the technical challenges of using film, which requires a time consuming chemical development process, as well as introducing potential uncertainties during the realignment of the film to its exact previous location in the interferometer. The results of doing this process digitally are reconstructed interferograms from which the phase information can be directly obtained, at video frequency, having high resolution and contrast, with no need to consider the observation vector. Any state of the object can be used as a reference, being the initial conditions of the object which all subsequent changes are compared to. This is a major advantage compared to non-digital methods which require the exposure of a film with a reference interferogram at a single set time instance. Because the interferogram only provides information on the evolution of the system since the reference conditions, the digital methods minimisation of the elapsed time between acquisition of the reference interferogram and later object ones increases the reliability of the results. The integration of optical recording, numerical reconstruction and evaluation into one system is also a major advantage as it simplifies and streamlines the process.

The drawback of the digital method is the lower spatial resolution of optoelectronic arrays compared to film. This means that the angle between the reference and object waves must be limited to just a few degrees, in order to satisfy the Nyquist sampling theorem [213].
However the resolution of sensors is constantly increasing, and if required it is also possible to overcome the lower resolution by magnification of the interference pattern before it impinges on the array, converting higher spatial frequencies to resolvable frequencies on the sensor. This does reduce the area that can be imaged, which is already generally smaller than film, limited by the size of the array used.

The ability to record the interferograms accurately in real time in a self contained system with none of the complications arising from film processing, and the ability to use any state as the reference, make digital holographic interferometry an appealing choice for use in dosimetry.

3.3.3 Experimental Configurations

There are a wide range of different experimental configurations and measurement techniques which have been utilised for interferometry measurements of temperature distributions in water. The choice of method depends on the specific requirements of the particular measurement application, with some approaches being more suited to different purposes. Several common configurations which were considered during the design stage are briefly introduced here, with emphasis on which is the most suitable to be used for radiation dosimetry purposes. This is not a comprehensive list, as this is a very broad field. Factors to consider for dosimetry include both the inherent sensitivity and suitability of the method for the temperature fields produced by radiation, but also practical considerations such as the availability of components, complexity of the digital reconstruction algorithms, and operating considerations such as the portability of the interferometer, the ease of alignment and the reproducibility of results.

Fourier Transform Digital Holographic Interferometry

The DHI described in Section 3.3.2 has been conducted with a range of measurement configurations of the reference and object beams. Each configuration requires specific reconstruction algorithms to account for the relative geometry of the reference and object beams. Each has its own variations on the mathematical reconstruction algorithms, however the use of the Fourier transform in the numerical reconstruction process is ubiquitous. Figure 3.3 depicts possible geometries between the reference and object beams [214].

Figure 3.3(a) has a plane reference wave propagating perpendicularly to the CCD, with the
object located unsymmetrically with respect to the centre line. This setup is simple and easy to achieve, but the positioning of the object is less effective because it is not positioned symmetrically. The major advantage however is that because it is an off-axis configuration, the real part of the image, which is the part within the reconstructed image which contains the phase information, is spatially separated from the central bright zeroth diffraction order DC term (this is defined in Chapter 4).

Figure 3.3(b) has the plane reference wave and the object wave coupled via a beam splitter, allowing for both beams to be perpendicular to the sensor. This is the geometry obtained if the common Twyman-Green type interferometer is used [215]. This is based on a Michelson-type interferometer, and an example is shown in Figure 3.4(b). One advantage of the Twyman-Green/Michelson type interferometer is that the light travels twice through the measured phase object, which doubles the sensitivity. However it also makes the setup more complicated to adjust and reduces the light efficiency, although this is not of concern for many applications [216]. Another common type of interferometer achieving this geometry is the Mach-Zehnder type, as shown in Figure 3.4(b) [217]. A key feature of these types of interferometer is that the angle that can be achieved between the reference and object beams is very small, which leads to large fringe spacings which can increase the resolution. However the major limitation for holographic interferometry is that this small angle results in the real term and the DC term being superimposed on the interferogram, which drastically reduces
the information which can be obtained. The impact of this can be experimentally reduced, but not entirely eliminated [214].

Figure 3.3(c) has the reference wave impinging on the CCD at a set angle, \(\alpha\). In order to calculate the numerical reconstruction \(\alpha\) needs to be determined to a high degree of accuracy and any uncertainty in this measurement impacts the results. The limitation of this method is that the angle between the interfering beams can vary across the sensor surface which can mean that the full spatial bandwidth of the sensor may not be able to be used, reducing the final spatial resolution [208].

Figure 3.3(d) is called lensless Fourier transform digital holography (LFTDH). The spherical reference wave is produced as a point source which is located at a distance in the same plane as the object. This approach simplifies the reconstruction algorithms, as the equation for the reference wave is able to cancel out with the spherical phase factor associated with the Fresnel transform of the interference pattern, covered in detail in Section 4.3.2. This reduces the computation time by requiring only a single Fourier transform to reconstruct the image, and removes uncertainties associated with measurement of the physical parameters of the reference beam. The other advantage is the off-axis geometry which results in spatial separation of the real image and DC term in the reconstructed image. An example of a lensless Fourier transform configuration is shown in Figure 3.4(c) [218].

**In-line Interferometry**

In-line interferometers are single beam configurations, where there is no separate reference and object beam [219]. There are a range of approaches to in-line interferometry. The methods described here do not produce holographic measurements, but were considered as they have been used for phase measurements in transparent objects. All measurements are based on interference of a single beam with itself, but this can be with either its own reflections or interference due to refraction. The general advantages of this approach are that unlike off-axis geometries, the single path of the laser means that the method is less sensitive to vibrations [220]. The components required are usually simple and cost effective, and able to be configured in a compact, simple geometry. For transmission measurements of a water cell, the lack of a reference beam can allow for more flexibility regarding where the beam passes through the test medium. Differential measurement techniques where a reference image is subtracted from all subsequent images reduce the effect of distortions from low quality optics. The disadvantages are that the analysis algorithms can be complex, with direct access
Figure 3.4: Basic schematics for common DHI configurations. M=mirror, L= lens, BS = beam splitter. (a) Twyman-Green type interferometer, (b) Mach-Zehnder type interferometer, (c) Lensless Fourier Transform type interferometer.

to the measurement phase and positioning not always directly determinable from the images.

**Common path interferometers** can be used for temperature measurements in water, with an example given by Yan and Cha [219]. This is based on the concept of a Fabry-Perot interferometer [221], where the laser interferes with its own reflections. A schematic of their detector is shown in Figure 3.5. The laser is expanded and collimated, and then passes through a beam splitter. Due to the relative size of beam splitter and test cell the beam then undergoes a further expansion and collimation, but this step may not be necessary. The
beam then passes through the test cell, and then another beam splitter and on to the sensor. The beam splitters produce a directly transmitted beam as the reference beam, and then a number of multiply-reflected and transmitted beams. These beams interfere, to produce an interferogram of the flow field, where bright fringes represent the phase differing in each round trip reflection by an integer multiple of $2\pi$. A finite fringe pattern can be produced by tilting one of the beam splitters slightly. The fringe interval with no variation in the cell phase can be calculated from the wavelength, fringe order and angle of tilt of the beam splitter. When the temperature field within the cell is varied, the variation in phase within the cell can be calculated at each point according to the distance of the point from the reference position and the extent of the variation in the fringes from the reference state. The sensitivity is doubled because each reflection represents a double pass through the cell. In order to remove the effects of any distortions in the optical components and directly visualise changes in the phase, a digital double exposure technique can be employed, whereby the reference image is subtracted from subsequent measurement images. Phase shifting techniques can be employed, as discussed in the section below.

Coherent gradient sensing (CGS) is an alternative approach to common path interferometry, which is able to detect gradients in the refractive index field [220, 222]. The approach was first used for mapping the temperature field in a fluid layer by Mishra et al., and a schematic of their detector is shown in Figure 3.6. Coherent light from a laser source is collimated and expanded, then passed through a medium with varying refractive index. The light rays undergo a phase shift as they pass through the medium, and can bend due to the presence of a refractive index gradient. The distorted wavefront containing the refractive index information is passed through two gratings, and the subsequent diffraction orders are caused to interfere using a lens, with a filtering aperture selecting the interference fringes of a particular order. The first order interference fringes represent the points having constant

Figure 3.5: A common path interferometer as used by Yan and Cha [219].
refractive index gradient. Note that, as described, this only records refractive index gradients in one direction, i.e. perpendicular to the grating direction. The fringes represent the derivative of the refractive index along the grating direction. A full three dimensional map of the temperature gradients is achieved by rotating the interferometer about the cell, and a subsequent tomographic reconstruction. Due to the finite time required to obtain all of the projections, this limits the system to measurement of systems in steady state, or with limited temperature evolution. The sensitivity is readily adjusted by modifying the grating pitch or distance between the gratings, in contrast to traditional interferometry, whereby the sensitivity is largely dependent on the wavelength.

![Figure 3.6](image)

Figure 3.6: A coherent gradient sensing interferometer, as used by Mishra et al. [220]. Additional lenses are required due to the cylindrical shape of the test cell required for tomographic imaging to achieve measurements of the three dimensional temperature field.

**Electronic Speckle Pattern Interferometry** is based on the concept that if coherent light is diffusely scattered and interfered, it can contain some information. In most types of interferometry, the speckles that occur when coherent light is diffusely scattered are a disturbance to the signal, which must be reduced as much as possible. The speckles do however carry fundamental information about the system, and can be exploited in a type of measurement technique sometimes called electronic speckle pattern interferometry (ESPI). This technique has been effectively used for visualisation of thermal distribution and diffusion in a transparent liquid [223–225]. Application of the technique for this purpose utilises a transmission mode experimental configuration where the optical path passes through the test cell and also through a diffusely transparent surface, such as ground glass, producing a speckle pattern on the sensor. An image plane hologram is recorded rather than the Fresnel diffraction field of the object [200]. The positioning of the ground glass before or after the object affects the information that can be obtained from the result, as shown in Figure 3.7. With the glass placed on the sensor side, variations in the liquid refractive index variation
affects only the optical path, so only the phase within the speckle pattern varies, resulting in a good correlation factor. Alternatively if the glass is placed on the illumination side, the fringe contrast will be geometrically altered slightly, as the refractive index variation is integrated on a truncated cone shape. This reduction in fringe quality is negligible if the distance to the ground glass is much greater than the pixel size to achieve resolvable speckles. This second approach allows for both the temperature field and any streamlines of fluid flow to be determined without requiring any experimental adjustment, which is of benefit for some applications. In general, for either approach to achieve a detectable interference, colinear reference and object waves must be used. The spatial resolution of the sensor chip places a lower limit on the speckle resolution, and if not sufficient can lead to degradation of the interference pattern.

ESPI operates under a temporal differential principle, where two speckle fields corresponding to the object states before and after the deformation are compared, producing an interference pattern in which small static misalignments of optical components are cancelled out. ESPI methods contain the same information as other DHI techniques, so in their production vibrations must be avoided, particularly with frequencies similar to or higher than the video frequency being used, especially if a phase shifting technique is used, requiring the recording of several interferograms. The evolution time of the investigated phenomena must be long enough with respect to the recording time, thus limiting the applications of this technique.

A second speckle pattern of the object is recorded and subtracted from the first in a point-wise fashion. It is assumed that the variation in the optical path of the light changes the phase but not the amplitude. Where a point in the object has had motion in a direction normal to the optical axis, the speckle pattern follows this displacement component. Thus the combined speckle patterns consists of a manifold of speckle pairs, where the distance between the points of each pair is proportional to the lateral displacement. This results in an intensity pattern consisting of a stochastic speckle noise (varying randomly across all pixels), and a low frequency modulation of the half phase difference induced by the deformation, which is the interference pattern that contains the information on the evolution of the system.

The maximum sensitivity of an ESPI interferometer is for out-of-plane variations, i.e. the direction normal to the optical axis, with the variations in optical path length required to be larger than the speckle size. Thus compared to other DHI approaches such as LFTDH, ESPI has poorer image quality and measurement range, making the approach less suited for measuring the refractive index variations produced in a dosimetric measurement. However
ESPI can be straightforward to use, as it does not require precise alignment of components, meaning it is possible to automate the measurement process [224]. The most common use of ESPI is in reflection rather than transmission mode, for deformation measurements of opaque surfaces, and in fluid mechanics where fluids are seeded with reflective tracer particles.

Figure 3.7: The effect of the positioning of the ground glass for an ESPI interferometer: (a) when the ground glass is placed between the cell and the camera, the refractive-index variation is integrated along a line, and (b) when the ground glass is located on the illumination side of the cell, the refractive-index variation is integrated on a truncated cone. Figure reproduced from Dupont et al. [223].

Phase Shifting Measurement Acquisition

Phase shifting is a measurement approach that was developed to interpret the fringe patterns on the reconstructed images obtained using film interferometric techniques [226, 227]. The reconstructed film contains a fringe pattern consisting of light intensity maps, rather than phase maps. Phase shifting allowed for the phase of the object beam to be determined from the film. The process involves rotating one of the mirrors along the path of the reference wave step-wise, causing the phase of the reference wave to shift. This results in a pattern of parallel fringes on the recorded interferogram. The principle of phase shifting interferometry is to record several (at least three) interferograms with added phase shifts between each. Any change in the phase within the object beam results in a shift of these fringes, with the extent of the shift proportional to the change in phase. Multiple phase shifts are required in order to create sufficient points at which the phase can be analysed. The object phase can then be calculated from these phase shifted interferograms via a range of available algorithms [200]. Phase shifting approaches can be applied to all of the interferometer configurations described above.

For digital holographic techniques the advantage of access to the phase information is somewhat negligible, as the phase can be determined from the complex intensity wave that is
calculated during the numerical reconstruction. There is some advantage for DHI however, in that the reconstructed image is free from the DC term and twin image, allowing the recording of higher spatial resolution images by reducing the angle between reference and object beams.

The main disadvantages of this approach are the additional experimental effort required to record phase shifted images and, crucially, the additional time that this takes, which limits measurement of processes with transient phase [228]. Unfortunately this rules out the use of phase shifted measurements for dosimetry studies except for the case of a broad beam geometry in steady state.

3.4 Historical Development of Interferometry for Radiation Dosimetry

3.4.1 Early Holographic Interferometry Studies

Hussmann was the first to apply interferometry to radiation dosimetry in 1971 [24]. He used a double exposure holographic interferometry technique to determine the radiation absorbed dose distributions from a high intensity, pulsed, approximately 2 MeV electron source collimated to be circularly symmetric about the central axis. The apparatus used was based on a modified Michelson type interferometer and is shown in Figure 3.8(a). The double exposure of the unirradiated cell and then post-irradiation was re-illuminated with the reference beam. The resulting pattern of interference fringes was recorded on the photographic plate, as shown in Figure 3.8(b). In this image, each fringe corresponds to a certain dose, measured in rad, where 1 rad = 0.01 Gy, as depicted in Figure 3.8(c). In order to calculate three dimensional dose distributions it was assumed that the dose distribution was cylindrically symmetrical around the axis of propagation of the radiation beam. This was shown to hold to within 5%. This assumption applies for any conversion of a two dimensional integrated image to a three dimensional volume. The nature of the dose analysis also required that the dose was high enough and monotonically decreasing to sufficiently small values as a function of distance from the beam axis in order to achieve a satisfactory number of interference fringes. This is a requirement for this analogue experiment, as there is no direct information regarding the light phase, so the dose is determined in segments outlined by each fringe. Hussmann sought to avoid the impact of heat diffusion by using a pulsed beam of pulse length 20 - 40 ns, and recording the image within 20 ms. A sufficiently small angle between reference and object beam was required in order to achieve the wavelength
spacing that was resolvable on photographic plates with a resolving power of 100 lines mm$^{-1}$.

Figure 3.8: The original application of holographic interferometry to dosimetry of an electron beam. (a) Schematic of the holographic interferometer, where $L_{0-3}$ are lenses, $P$ is a pinhole, $IS$ is an iris shutter, $M_{1-4}$ are plane mirrors, $CM$ is a corner mirror, $BS$ is a beam splitter, $C$ is the irradiation cell, $HP$ is holographic plate, $S$ is a screen with a small hole, and $PP$ is photographic plate. (b) shows a holographically reconstructed interferogram of the electron beam energy deposition in the water, and (c) is the corresponding absorbed dose distribution [24].

This work was continued with a slightly different focus, by Miller, Hussmann and McLaughlin in 1975 [27], who used an interferometer with a single photodiode to record fringe shifts, rather than the holographic interferometry approach. The interferometer they used is shown in Figure 3.9, which was designed so that the two light beams follow the same path and share optical components as much as possible, to reduce the impact of air turbulence and vibrations. The motivation for this work was to achieve calorimetric measurements with a fast response time. The response time of conventional calorimetry measurements depends on the rise time of the physical sensing probe in the beam path, which at its fastest is on the order of milliseconds, as it depends on the time for the probe to reach thermal equilibrium with the surrounding water, as well as the probe sensing properties such as volume or electrical...
resistance. They applied the detector to measure high flux single electron beam pulses with
30 ns half width, maximum energy of 2 MeV and broad spectral distribution, produced by
a Field Emission Corp. accelerator. The measurement cell was located 10 cm from the
accelerator exit window, with an expected dose of 1 Mrad per pulse at that location reduced
by use of a copper diaphragm with a hole in the centre. As the refractive index varied due
to the radiation induced temperature changes in the water, the fringe pattern shifted across
the photodiode, and the resulting variation in voltage was displayed on an oscilloscope. The
reported example of a typical measurement is shown in Figure 3.9(b), where the response
time achieved was 1.5 µs, and the change in phase corresponds to a dose of 10.0 krad (100
Gy). The rise time is not indicative of the transient temperature increase, but is indicative of
the response time of the photodiode and the initial masking of the refractive index increase
by a change in pressure. The refractive index is restored by emission of a shock wave, which
is visualisable on some measurements approximately 50 µs after the electron pulse. The
signal remained fairly stable for at least 1 s following the irradiation. They reported limits
of sensitivity of 350±70 rad (3.5±0.7 Gy).

Figure 3.9: (a) Schematic of the Miller et al. interferometer [27]. Components are 1=Laser;
2=Radiation shield; 3=Beam splitter; 4=Adjustment prism; 5=Electromagnetic shield;
6=Irradiation cell; 7,8=Optical flats for adjustment of fringe position and narrowing spacing
of parallel light beams; 9,10=Mirrors; 11,13,14=Lenses; 15=Microscope objective. (b) Oscil-
loscope display of a partial fringe shift on a fast time scale, where each division corresponds
to 20 mV vertically and 1 µs horizontally. The fringe shift represents a dose of 10.0 krad.

Subsequent work by Miller published in 1979 continued the initial Hussmann measurements
using holographic interferometry to gain dose distributions of electron pulses from several
different electron accelerators [26]. The interferometer layout varied from the original one,
and is depicted in Figure 3.10(a). The dose distribution achieved by a 3 MeV Van de Graaff
accelerator beam shown in Figure 3.10(b), where each fringe corresponds to a dose of 1.42
kGy. He also undertook a variation on the dose distribution measurements by carrying out
direct isodose fringe pattern imaging. This involved tilting mirror seven in Figure 3.10(a)
in between exposures of the holographic image (pre- and post-irradiation). This overlaid a
pattern of equally spaced vertical fringes on the reconstructed image. These fringes were distorted when the water was heated, with the degree of distortion at each point proportional to the temperature rise. Thus the resulting image was representative of depth dose curves. The equivalent 10 MeV Van de Graaff generated beam measurement using this method is shown in Figure 3.10(c). This method was shown to improve the sensitivity, and simplify the location of the region of maximum dose.

Figure 3.10: (a) Schematic of the Miller interferometer [26]. Components are 1=Laser; 2=Shutter; 3=Microscope objective; 4=Pinhole; 5=Lens; 6=Beamsplitter; 7=Movable mirror; 8=Irradiation cell; 9=Diffuser; 10=Holographic plate. (b) Holographic interferogram of the absorbed dose distribution, where each fringe represents an isodose curve corresponding to 1.42 kGy. (c) The same measurement, on a system with parallel fringes superimposed. The distortion of the fringes from vertical corresponds to the dose at each point.

Miller also undertook various measurements to understand the different dose absorption properties of a range of transparent mediums. He also measured the effect of back scatter from materials of different densities placed within the electron range, with results showing an increase in dose just prior to the scatterer, compared to a cell containing only water. He extended this to investigate the effect of beam perturbations around different shaped inhomogeneities in the water, simulating the presence of bone within an irradiation volume in the body. Figure 3.11 shows the aluminium rod used to perturb the dose in the cell, along with the measured dose distribution and isodose map.
Figure 3.11: Experiments by Miller showing the dose distribution around inhomogeneities in the water cell [26]. (a) The $20 \times 20 \times 20$ mm$^3$ quartz test cell with 5 mm diameter aluminium. (b) Reconstructed hologram of the cell irradiated from above, where each fringe represents an isodose curve corresponding to an absorbed dose of 142 krad. (c) The same measurement, on a system with parallel fringes superimposed. The distortion of the fringes from vertical corresponds to the dose at each point, with the peak being approximately 400 krad. Figure reproduced from Miller.

Nicolau et al. continued work on this subject in 1999, using a microprocessor to assist with image analysis [229]. They also used a double exposure holographic interferometric method based on a Michelson design interferometer. Reconstructed images were recorded with a camera, and a Z-80 microprocessor was used to record profiles across the image for analysis of the fringe pattern. The investigated different transparent liquids and the boundary phenomenon of radiation absorption across layers of different liquids, and reported an accuracy of 4%. However no further detail of the achieved results were presented.

Overall, the major limitations of the previous research is in the information obtainable by manual counting of the fringe patterns. The analogue images were interpreted by assuming the bright fringes have even integer multiples of $\pi$ phase shift, and the information gained is in terms of dose per fringe. Using the parallel fringe approach the dose depends on the shift of the fringe, but this is only measurable accurately at certain fringe locations. This could be improved by computerised fringe skeletonising techniques, however there are still fundamental assumptions inherent regarding the relationship of light intensity and phase when the data is interpolated. A digital approach allows for direct access to the phase information so the absorbed dose at each point within the measurement region can be determined independently.

The second limitation is in the double exposure technique used, where each measurement is recorded at one time instance during or following irradiation. Miller did suggest extension
to a real time holographic interferometry approach, however this was not implemented, and does introduce further uncertainties from evolution of the system whilst the reference image is developed. Digital holographic interferometry allows for video frequency recording of the phase evolution, with any time instance able to be chosen for the reference time during data analysis.

**Reference Image Topography**

Ackerley *et al.* revisited the idea of optical calorimetry, for the purposes of MRT dosimetry in 2011 [230]. They proposed the concept of digital holographic interferometry, but due to equipment availability they instead utilised a method based on a modified Schlieren approach known as Reference Image Topography (RIT) [231, 232]. RIT also maps the variation in refractive index across a test cell, based on the apparent motion of a speckle pattern projected through the test cell and imaged on a camera. As the refractive index varies the speckles appear to move, and the degree of apparent motion at each point in space can be analysed by a cross-correlation approach like that used in particle image velocimetry processing [233], and integrated to obtain the indicative temperature values. They made some preliminary proof-of-principle measurements using a heated wire in a water bath in place of a radiation dose. Despite the temperatures measured being two orders of magnitude greater than expected MRT temperature changes, the conclusions they drew were positive regarding the potential applicability of the method to MRT dosimetry, with RIT expected to be able to resolve individual heat diffused synchrotron microbeams.

**Ultrasonic Thermometry**

Malyarenko *et al.* used an approach based on the same fundamental concept as optical calorimetry: the use of a non-invasive system to measure temperature variations within a calorimeter volume, thus eliminating the complexities associated with the presence of non-water temperature sensing materials within the water phantom [82, 234]. Their approach was not actually interferometric, comprising the use of ultrasonic thermometry. This technique determines temperature variations in a medium based on their impact on the speed of sound, which is measured by detecting the variation in the time of flight of an ultrasound pulse as it passes through the medium. Their initial work achieved temperature resolutions on the order of 0.001 K, with a root mean square noise of 5 μK, averaged over a 60 cm test cell [82]. Their work included a careful consideration of the influence quantities impacting the measurement. Subsequent work extended the system to achieve spatially resolved
temperatures via tomographic measurements [234]. The detector used a 128-element transducer array covering a planar area of 230 mm x 230 mm, to acquire temperature maps by a fan beam tomographic reconstruction algorithm, to a resolution of approximately 5 mm. Measurements were achieved with a temporal resolution of four seconds. This is sufficiently low that the temperature map degradation, for the broad beam geometries considered, due to heat transport experiences blurring to less than 50% of the spatial resolution. Refinements to the instrument to potentially improve the temporal, spatial and thermal resolutions were suggested, however to some extent each suggested improvements favour one of these parameters at the expense of the others. For instance expanding the number of channels will increase spatial resolution, but also the overall acquisition time. They consider that a spatial resolution of $< 1 \text{ mm}^3$ is required in order to make ultrasonic thermometry viable as a reference standard for medical radiation dosimetry.

Preliminary work in the same research group has considered the use of a similar tomographic system but utilising an optical interferometry approach to the temperature determination [83]. The preliminary work is similar to the initial work by Hussmann, with shifts in the interference pattern recorded by means of a photodiode [24]. Early experiments on simulated heating patterns have indicated that an optical approach may result in higher sensitivity temperature resolution than that achieved by ultrasonic thermometry.

### 3.5 Concluding Remarks

This chapter introduced the fundamental concept of an optical calorimetry approach to dosimetry. The basic optical principles required to understand the process of digital holographic interferometry were introduced, including the wave equation for light, refractive indices, and the process of interference. An introduction to the use of interferometry for the determination of refractive index variations in water followed, with focus on holographic interferometry, and the subsequent development of DHI. A selection of experimental configurations which were considered during the design phase of the DHI dosimeter are described, and each has its relative advantages and disadvantages. The chapter concluded with an historical overview of previous interferometry based approaches to dosimetry. In particular is the early work by Hussmann and Miller et al. in the 1970s, of which developing this work further with the application of modern digital technology was the inspiration behind the present work. The next chapter describes the selection of a DHI approach, and its subsequent development, including a full description of the completed prototype detector
and reconstruction algorithms implemented to interpret the recorded interferograms. The chapter also describes the preliminary testing and characterisation of the detector that was undertaken during the refinement process, prior to the eventual radiation measurements.
Chapter 4

DHI Dosimeter

This chapter focuses on the design, development and refinement of a prototype interferometer for use as a radiation dosimeter. The design considerations for applying interferometry to dosimetry are discussed, with the design of the prototype developed based on these requirements. Following this, a complete description of the prototype dosimeter is presented, along with the mathematical algorithms required for the reconstruction, and an outline of the operating procedure for a series of measurements. The chapter concludes with examples of some of the preliminary tests done on the interferometer during development and testing.

4.1 Design Considerations

The choice and design of the interferometer for application to radiation dosimetry has many technical and practical considerations to take into account. The foremost of these is the consideration of which particular interferometric approach will be capable of acquiring the measurements required to a suitable standard. The key points for this choice have already been introduced in Chapter 3. The next category of design considerations encompasses the choice of equipment used to build the selected type of interferometer, including the selection of a laser, camera and optical componentry. Correct selection of equipment is required in order to optimise the results that can be obtained with a prototype detector, whilst acknowledging that there are financial constraints. Thus in some cases tradeoffs may be required to achieve an economical solution. Included within the choice of equipment is the design of the test cell which is used as a water phantom for the measurements. Another design consideration is the exact layout and construction of the interferometer to meet the physical space requirements of some potential radiation applications. The final consideration is the transportability and ease of operation of the prototype interferometer, for both initial measurements, and with an eye to potential future clinical implementation. The choice of an interferometry approach, and the exact design of the prototype dosimeter for this initial
proof-of-principle work does not rule out the use of a different design in the future if at that point it would provide advantages. Suggestions for the improvement of the final design are given in Chapter 8.

Some of the key considerations are introduced below, with a short description and discussion of how to incorporate each point into the prototype.

- **Choice of interferometry approach:** The decision of which interferometry approach to select required consideration of the advantages and limitations of each technique as described in Section 3.3.3. Some key considerations which helped to distinguish between the possible approaches included the following items.

  - The design must be able to achieve high spatial resolution and sensitivity in at least two dimensions.
  - The design must be capable of measuring transient processes, which rules out the use of phase shifting approaches.
  - To reduce the influence of external vibrations and turbulence, the design should have the light beams share optical components where possible, or fit onto a single breadboard.
  - The measurement uncertainties should be minimised where possible.
  - The design should have reconstruction algorithms with access to the interference phase.

- **Equipment considerations:** Where possible, available equipment from the optics laboratories in the Department of Physics and Astronomy, University of Canterbury was utilised in order to reduce unnecessary expenditure. A limited amount of funding was available to purchase equipment. The result of this was that some of the equipment choices whilst fit for purpose, involved tradeoffs between cost and quality. The main purpose of this work was to develop a prototype dosimeter as proof-of-principle of a DHI approach, and it is anticipated that this will provide a basis for future funding applications to further develop the work and upgrade the equipment used. With these funding constraints in mind, some of the design considerations for the equipment selection are listed here.

  - The laser chosen must have low amplitude noise, as the detection system is sensitive to variations in the light intensity and phase, and have a stable power output.
- A shorter wavelength laser will increase the sensitivity because a change in refractive index induces a larger change in optical path length, however the absorbance of the wavelength in the medium used must be negligible to avoid introduction of extraneous temperature variations.

- The laser must be of sufficient power to provide enough illumination for the short exposure times of the camera. The upper limit on the laser power is such that the camera sensor is not oversaturated. However the ability to attenuate the light beam makes this a less important requirement.

- The test medium should be water, or near water equivalent, and transparent, with consideration given to minimisation of the impact of the heat defect. A medium with a higher variation in refractive index with temperature than water could be used to increase sensitivity, but this then introduces a further step to convert absorbed dose to that in water.

- The test cell should have low thermal coefficient of expansion, although this is a minor point as the temperatures involved are extremely low.

- The test cell must also have smooth, parallel faces, with negligible reflection. The thickness must be small enough to have minimal impact on the radiation beam, and the material used should have close to water equivalence for radiation absorption.

- The width and depth of the test cell must be sufficient to allow the desired depth of measurement for a given radiation source. This is constrained by where the cell is located within the interferometer. Additionally, the distance across of the test cell in the direction of the laser line-of-sight must be optimised to allow for full measurement of the radiation, but reduce the reduction in sensitivity caused by integration across a larger distance.

- Ideally the test cell should be large enough to completely absorb the beam, however this requirement is unlikely to be fully achieved. An approximation of it may be possible for protons or low energy photons, but is unlikely for higher energy photons and electrons. At this stage the uncertainty introduced by any scattered radiation is likely to be negligible compared to the overall uncertainty.

- The camera resolution must be sufficient to resolve dosimetric features such as the Bragg peak of a proton beam.

- The frame rate of the camera must be high enough to allow any phase changes to be resolved to within an entire $2\pi$ shift in phase. This is only applicable for
potentially very high dose rates. The faster the frame rate achievable, the more accurately corrections for heat diffusion can be made, which is key for highly modulated radiation sources.

- The camera sensor size controls the size of the region that can be measured, so as large as possible is desirable. For affordable cameras, this generally becomes a trade-off between pixel number and pixel size.

- **Layout and construction of the interferometer:** There are countless variations in the design of each type of interferometer, and the exact configuration must be designed to be specific for the purpose of radiation measurement. Some of the considerations involved in this are listed here.

  - If possible there needs to be space available to incorporate shielding to protect the electronics (camera and laser) from scatter radiation if this is likely to be considerable.
  
  - It must be possible to enclose the set-up within a box to isolate it as much as possible from variations in ambient conditions/turbulent airflow etc. In practice, this entails containing the interferometer on a single breadboard.
  
  - There must be some way of damping vibrations. The use of a vibration isolated table is not feasible for any measurements of a clinical radiation source, so some other means must be considered.
  
  - The location of the test cell must have enough space available to allow for different depths of measurement and varying size test cells.
  
  - The configuration must allow for irradiation of the test cell from the side and from the top, for use in different beamlines.

- **Ease of use:** The ease of use of the interferometer and the workflow for radiation measurements is a vital consideration. This is because most radiation measurements will be in-situ in a clinical environment. Some points to consider in the design of the interferometer are listed below.

  - The interferometer must be transportable, which involves consideration of weight, ease of set-up deconstruction, and fragility of the components.
  
  - In a clinical situation most radiation sources are likely to have time constraints, with limited beam time available for dosimetry experiments. Thus the workflow for use of the interferometer must be straightforward and well planned, to reduce
measurement times required, and the chance of making unpredicted errors. The interferometer must also be easy to realign in situ if required. Additionally, with an eye to future clinical implementation, the interferometer should have the potential to be developed to the point where specialised optics experience is not required for its implementation.

- If tomographic measurements are to be considered at some point in the future this would be relatively straightforward for vertical beam sources, but far more complicated for a horizontal source (such as many proton beamlines or synchrotron medical beamlines).

- The selected camera must easily interface with a computer for data acquisition. The computer must be accessible from outside of any radiation shielding around the radiation source. Software used must be able to facilitate a straightforward, easy-to-use workflow.

- An easy to use graphical user interface should be developed to visualise and analyse the results accurately and efficiently.

### 4.2 Lensless Fourier Transform Digital Holography

LFTDH was selected as the configuration of choice for the prototype DHI dosimeter. An in-line configuration is also a potentially viable option, however LFTDH was preferentially selected because the use of a digital holographic interferometry technique allows for direct access to the phase information from the reconstructed images. The geometry of an LFTDH interferometer with a spherical reference beam allows utilisation of the full spatial bandwidth of the sensor and simplifies the reconstruction algorithms as the equation describing the reference beam cancels out. The off-axis relative positions of the reference and object beams means the reconstructed images are easily interpreted, with the real image and DC terms able to be spatially separated. This is believed to be more important for the proof-of-principle of the system than the sensitivity increase which would be achieved by the double-pass configuration of a Twyman-Green or Michelson type interferometer. The system was thought to be more influenced by vibrations than an in-line configuration would be, however LFTDH has been shown by others to be suitable for measurement of small temperature variations in water. Thus with sufficient damping of vibrations this is not believed to be of concern at this stage and the benefits achieved from the direct access to the phase in the calculated reconstructions outweigh this effect for early testing.
The geometry of the detector, whilst more complex and less flexible than an in-line configuration, is easy to adjust, and can be contained within a single breadboard. This ensures the detector is easily transportable. The components required were all readily available. Phase shifting approaches were not used for the preliminary work as the off-axis LFTDH configuration voids the benefit attained from removing the DC term from the reconstruction. Additionally, as the radiation sources used all experience high spatial and temporal variation in the dose distribution, the experimental time required to obtain phase shifted measurements would result in too high an uncertainty contribution arising from heat diffusion and continued dose deposition.

The proposed system of holographic interferometry potentially overcomes or improves on some of the problems associated with the alternative dosimetry systems, listed in Table 2.1 and discussed in Chapter 2. The following discusses the theoretical potential of the concept of using DHI in terms of the list of desirable features of a dosimeter that was introduced in Section 2.1.3. This theoretical potential of DHI justifies research into the development of DHI for dosimetric purposes. The proof-of-principle work that follows will aim to experimentally investigate the theoretical advantages and limitations given here, to determine whether DHI is a viable dosimetric approach in practice.

- High accuracy and precision: The primary benefit of DHI as a dosimetry system is that it is a calorimetric approach based on the direct measurement of absorbed dose to water. Thus the fundamental quantity of dose is measured without the need for correction factors (such as cavity theory corrections as required for ion chambers). This is especially relevant for applications where the radiation energy spectrum is not well characterised and correction factors are not yet thoroughly understood or readily available, such as proton beams or synchrotron radiation spectra. Additionally, the ‘remote sensing’ of the temperature variation means that there is no perturbation of the beam by a probe directly in the beam path, so no correction is required for non-water equivalence of the detector. This means that with the appropriate experimental set-up DHI has the potential to have very high accuracy, especially when validated by cross-calibration with other measurement systems.

The precision will depend on the repeatability and reproducibility of the measurement process and the ability to control the effects of external influence quantities such as temperature. The considerations which apply to measurements using calorimeters will be relevant to this. It should be possible to use the same approach as used for high
precision primary standards measurements to achieve similar high precision for DHI measurements.

- Linearity of signal with dose: Because DHI is based on the measurement of temperature, the occurrence of heat transport within the test cell will impact on the linearity of signal with dose. This will have minimal impact for the measurement of fields with broad beam geometry. For smaller fields with high modulation and lower dose rates or longer delivery times, the impact of heat diffusion and convection on the measured temperature distribution may be considerable. This will affect the linearity of the signal with dose. The effect can be experimentally reduced with careful experimental planning, or the use of higher frame rate cameras, or theoretically accounted for to different degrees of success by several different approaches, which are introduced in Chapter 5.

- Adequate spatial resolution: The intrinsic resolution of this method is primarily dependent on the resolution of the CCD camera used. It can be further increased by magnification of the image before recording it, as long as the photon flux is high enough to get a high signal-to-noise ratio, however this comes at the expense of a reduced field of view. The resolution of many standard scientific cameras is sufficient for most dosimetric purposes, and may even achieve suitable resolution for MRT dosimetry. Many of the advantages of calorimetry are shared, whilst also having the ability to measure the dose distribution to a high spatial resolution. There is no limitation for the measurement depth, any point in the cell can be measured, provided the appropriate experimental configuration of laser reference and object beams is achievable.

The size of the camera sensor constrains the size of the sensitive region that can be measured. For readily available sensors that are reasonably priced this is normally on the order of 1 cm$^2$, but higher pixel numbers are possible in the more advanced models. Alternatively, additional experimental efforts involving focussing a larger sensitive region onto a smaller sensor can overcome this limitation, with the corresponding decrease in spatial resolution.

- Large dynamic range: There is no inherent constraint on the dynamic range of the system, and measuring high dose and low dose regions simultaneously. There is a caveat however, that for dose distributions with high dose modulation, heat diffusion has a major impact. This can be modelled and accounted for but does provide a limitation on the method.
• Independent of dose rate, beam energy and direction: The direct measurement of absorbed dose to water calorimetrically means that DHI will be largely independent of dose rate and beam energy, however as mentioned above, the impact of heat transport can have a higher impact on measurements made of small fields at higher dose rates.

In terms of direction, the output of the interferometer is line-of-sight projections through the medium, a similar concept to planar X-ray images. This results in measurements which have no information regarding the distribution of temperature/absorbed dose in one direction perpendicular to the beam axis. In future this could be potentially dealt with by tomographic reconstructions from different angles (for some applications), or for symmetrical source symmetry by modelling the dose distribution from the known information (refer to Chapter 6).

• Ease of application in a clinical setting: With a basic understanding of interferometry, a DHI dosimeter can be easily set up, if time consuming to align accurately. However a finalised version of the detector would probably be able to be constructed in a fashion that requires limited adjustments, allowing for its fast and simple use.

Because it is a calorimetrically based method, external environmental fluctuations in temperature, pressure and air flow can have an impact on the results for some applications of the detector. The sensitivity of the detector is directly related to the ability to reduce or eliminate these influence factors. This will require an experimental enclosure to isolate the detector from temperature and possibly pressure changes. Depending on the application, this may prove prohibitive for an easily portable detector for routine clinical usage, however still allow the use of DHI for more specialised measurements.

The following sections describe the components used in the prototype detector, the mathematical reconstruction of the data, and the process of making an absorbed dose measurement.

4.3 Prototype Detector

4.3.1 System Components

Laser

The two key parameters for selection of the laser are the wavelength and the power. As the wavelength of light increases, generally the absorbance in water also increases, as shown in Figure 4.1. A 700 nm laser impinging on an area of 1 cm² of a water cell will cause a temperature increase of $1.49 \times 10^{-6}$ K mW$^{-1}$ cm$^{-1}$ s$^{-1}$ compared to $2.72 \times 10^{-8}$ K mW$^{-1}$...
cm$^{-1}$ s$^{-1}$ for 380 nm light. For comparison, a dose of 1 Gy will lead to a temperature increase of $2.38 \times 10^{-4}$ K, so this effect may have a detectable influence on measurements of very small doses, and should be corrected for if measurements of doses on this order are conducted. Shorter wavelengths also result in a greater change in phase for a given change in refractive index, meaning they are more sensitive. However interferometric studies have commonly used a Helium Neon (He-Ne) laser which produces output light in the mid-range of the visible frequencies, at 632.8 nm.

The laser used for the prototype DHI dosimeter was a He-Ne laser (Melles Griot, Carlsbad, CA, USA), with an output wavelength of 632.8 nm, and beam diameter ($1/e^2$) of 0.65 mm, with divergence of 1.24 mrad. This laser was available from the Department of Physics and Astronomy optics labs. If it proves necessary to improve sensitivity, future versions of the detector could use a shorter wavelength laser.

![Figure 4.1: Absorbance of visible light in liquid water (H$_2$O) [235].](image)

The power output of the laser was measured with a power meter and the results are shown in Figure 4.2. The laser required a warm-up period of approximately 50 minutes for the power output to stabilise, and then achieved a mean power output of 12.1 mW, with a standard deviation of 1.1%. This power proved to be more than sufficient to optimise the camera frame rate to allow for minimum exposure times, and had enough excess power to allow for the use of neutral density filtration to match the power of the reference and object arms of the interferometer.

Note that an additional laser was used for comparison during the development of the interferometer to rule out any influence of laser frequency and amplitude fluctuations on the
noise visible in the interferograms. This was an SIOS frequency stabilised model SL03 632.8 nm laser, with wavelength stability of $< 2$ nm over 1 hour, and power output $\sim 1$ mW (SIOS Meßtechnik GmbH, Ilmenau, Germany). The results of these measurements are discussed in Section 4.4.3.

**Camera**

The camera used for the prototype detector was a 1.3 Megapixel CMOS camera from PixeLINK (Gloucester, Canada). The relevant specifications are given in Table 4.1. This camera was selected as a compromise between cost and capabilities, in particular with regard to the resolution, the sensor size and the frame rate. The most important consideration between these three parameters was on having a resolution sufficiently high enough to enable potential measurement of microbeam arrays, or proton beam Bragg peaks. The frame rate was the secondary consideration, as a sufficient frame rate is required for high dose rate applications. The sensor size was chosen to be as large as possible given the spatial resolution required, and the economic constraints. The choice of a CMOS sensor versus a CCD sensor was for cost purposes, however, for the measurement specifications used for these DHI measurements the performance of the two sensor types is essentially equivalent [236].

The image acquisition was run using PixeLINK Capture OEM software (PixeLINK, Ontario, Canada). During set-up and stability measurements, the camera was connected directly to a computer with a 2 m long USB cable. For experimental measurements a 10 m long asymmetric digital subscriber line (ADSL) cable was used to network a secondary computer within the treatment bunker to the primary computer in the operator console area. The
two computers were connected with a remote desktop connection and the experiment was controlled from the primary computer, recording images using PixeLINK on the secondary computer. This was necessary because it was not possible to have a long enough USB cable which also provided sufficient power to operate the camera. The image acquisition was started and stopped manually because it was not possible to interface directly with the software used for the various radiation delivery systems to allow for automatic triggering. All images were acquired in uncompressed 16 bit Tagged Image File Format (TIFF). The exposure time was optimised for each alignment of the interferometer, to achieve the best dynamic range of the measured results and reduce overexposure, but was commonly around 0.08 ms. Most images were recorded with the full resolution of 1280 x 1024 pixels. For each measurement set the frame rate and the length of the measurement were varied as required.

Other Optical Componentry

The other optical components used in the prototype interferometer include mirrors, neutral density filters, a beam splitter, and a beam expander. These were all obtained from Thorlabs (New Jersey, USA). The absorptive neutral density filters ranged from optical density of 0.1 to 3.0. Combinations of filters were chosen for each alignment of the interferometer so that the intensity of the two beam paths was equal. The beam splitter was a BS010 400-700 nm broadband beam splitter cube with 10 mm sides. The beam expander was a BE20M with twenty times magnification. All of the optical components were mounted on a breadboard created in house, measuring 25 cm by 60 cm.
Test Cell

Multiple test cells of different sizes were constructed by the in house workshop. These were made of 1 mm thick transparent Perspex (polymethylmethacrylate, PMMA). There were two test cells used for all radiation measurements, one with internal dimensions of $3.8 \times 3.8 \times 3.8$ cm$^3$ and the other with internal dimensions of $2.0 \times 4.0 \times 4.0$ cm$^3$ with the 2 cm dimension in the direction of the laser beam on the interferometer. The two sizes were selected in order to allow for a cell which would be large enough to absorb most of the incident radiation in the axial plane, but minimising the width of the cell to reduce the distance across which the change in dose is integrated for a measurement. The surfaces of the cells which the laser passes through were highly polished and aligned parallel to each other to reduce the chance of any distortions. The cells were mounted on a Newport MB-2 optical platform (Newport Corporation, Irvine, CA, USA). One of the test cells is depicted in Figure 4.3(a). The metal pins on either side are used to hold a template in place for the purpose of measurement pixel size calibration, which is described further in Section 4.3.3.

Enclosure

For most measurements the breadboard containing all the optical components was housed within a wooden box to reduce the impact of air currents around the interferometer. A picture of the box is shown in Figure 4.3(b). The box has dimensions of height = 24 cm, width = 34 cm, and length = 74 cm. The lid of the box was removable to allow for adjustment of the interferometer, with a 10 cm by 10 cm hole covered by a moveable piece of Perspex with a 0.5 mm hole to allow access and adjustment of the HDR brachytherapy applicator. The laser was attached to the outside of the box to reduce the impact of the heating of the laser.

Figure 4.3: (a) One of the test cells used. (b) The wooden box used to isolate the system from air currents.
Interferometer Configuration

The final configuration that was used for the radiation measurements is shown in Figure 4.4. This was an LFTDH set-up, with an object to sensor distance $s = 26.5$ cm, measured between the camera sensor surface and the focal point of the reference beam. The test cell was aligned such that the centre of the cell was in line with this focal point. This arrangement of mirrors was determined with the first priority to optimise the size and position of the real image in the reconstructed image. The secondary requirements were that the entire interferometer was contained on one breadboard, excluding the laser, as well as ensuring that there was sufficient horizontal space to allow for horizontal irradiation of the test cell when required. The interferometer was disassembled for transportation, so the precise alignment of all the components was adjusted before each individual set of measurements. Section 4.4 shows some of the steps in the development of a working DHI interferometer for dosimetry, and shows some of the different configurations used for earlier measurements.

4.3.2 Image Reconstruction and Dose Determination

In this section, the analysis of the images acquired by the interferometer is discussed. This process is summarised in Figure 4.5. The process is split into two parts. The first part is the use of the interferometer set-up and digital reconstruction algorithms to derive phase information about laser light passing through the irradiated system (steps 1-4). This process is not specific to dosimetry and can be applied to a wide range of applications. The second part is specific to dosimetry, and involves the subsequent determination of the absorbed dose from the phase information (steps 5-8). Figure 4.6 expands on steps 3 and 4 to outline the process involved in obtaining interference phase information from the recorded interference patterns. There are two possible paths for this process, in the first the phase information is obtained from each image independently and then they are compared by modulo $2\pi$ subtraction, whereas in the second path the images are superimposed and a combined image reconstructed, from which the interference phase can be derived. The first path was used in the present work.

All of the analysis of the data was carried out in the MATLAB environment, using a specialised GUI written to streamline the process of obtaining the dose information. The GUI is described in Section 4.3.4, with the code given in Appendix B.
Hologram Reconstruction and Phase Determination

The concept of the image reconstruction is to digitally replicate the process of creating a physical hologram, and the interference between two holograms. This can be done via two routes, as shown in Figure 4.6. The first method involves the reconstruction of both holograms by means of the Fresnel transform to obtain the phase information, before they are digitally interfered to obtain the interference phase angle of the spatial phase variations across the laser beam $\Delta \phi(X, Y)$ between the two states of the test cell. The second method requires the two interferograms to first be combined before they are reconstructed by the same Fresnel transform. Both methods are equivalent, and will result in a differential reconstructed image where the consistencies between the two images are cancelled out, and only
Figure 4.5: Flow chart describing the steps required in the use of DHI for absorbed dose determination.

the change in the phase angle which has occurred between the two time instances remains.

The reconstruction algorithm described here uses the first approach, based on work by Hossein, Schnars and their respective collaborators [205,207,237].

The interference pattern sampled on the camera sensor plane is denoted \( I(X_H, Y_H) \), where the subscript \( H \) refers to the hologram plane in the \( X \) and \( Y \) directions. \( R(X_H, Y_H) \) is the complex reference wave amplitude distribution, and \( O(X_H, Y_H) \) the object wave. The camera sensor has \( n \times n \) pixels of size \( \Delta X \) and \( \Delta Y \). The distance, \( s \), is the distance from the sensor plane, sometimes called the hologram plane, to the plane of interest within the test cell, which is coplanar with the focal point of the converging lens that is in the path of the reference beam.

When the image is recorded on the sensor, it is a result of a combination of terms, where * denotes the complex conjugate operator:

\[
I(X_H, Y_H) = R(X_H, Y_H)R(X_H, Y_H)^* + O(X_H, Y_H)O(X_H, Y_H)^* \\
+ R(X_H, Y_H)^*O(X_H, Y_H) + R(X_H, Y_H)O(X_H, Y_H)^* 
\]  
(4.1)

The first two terms are the complex reference and object wave amplitude distribution, respectively, in the hologram plane. The last two terms represent the interference terms.

The numerical reconstruction of an LFTDH hologram is based on the Fresnel reconstruction algorithm. A wave, consisting of a reference and an object beam, illuminates the optoelec-
Step 3: Reconstruction

I₁(X,Y)
Interferogram in reference state

Superposition

Fresnel Transform

Path 1

O₁(X,Y)
Complex amplitude reconstructed hologram

Path 2

I₂(X,Y)
Interferograms during/after irradiation

Path 1

O₂(X,Y)
Complex amplitude reconstructed hologram

Path 2

Ø₁(X,Y)
Phase

抽取相位

Modulo 2π subtraction

ΔØ (X,Y)
Interference phase

ΔØ (X,Y)
Unwrapped interference phase

Step 4: Phase determination

Figure 4.6: An expansion of steps 3 and 4 from Figure 4.5 showing the two possible routes for phase determination from the recorded interferograms.

Electronic sensor with an amplitude transmittance of \( I(X_H,Y_H) \) and is then digitally illuminated by the reference wave. Mathematically, this is the product of \( I(X_H,Y_H) \) and \( R(X_H,Y_H) \). The Fresnel transform can then be used to calculate the complex amplitude of the diffracted wave in the plane of the real image [205], as in equation 4.2, where \( k \) is the wave number, \( \lambda \) the wavelength, and \( s \) the distance from the sensor to the plane of the lens focal point.

\[
O(X_I,Y_I) = \frac{exp(iks)}{i\lambda s} \left[ exp \left[ -i \frac{k}{2s} (X_I \Delta X)^2 + (Y_I \Delta Y)^2 \right] \right]
\]

\[
* \int \int_{X_H,Y_H} \left\{ I(X_H,Y_H)R(X_H,Y_H) * exp \left[ -i \frac{k}{2s} (X_H^2 + Y_H^2) \right] \right\} dX_H dY_H
\]

\[
* exp \left[ \frac{2\pi}{\lambda s} (X_I X_H + Y_I Y_H) \right]
\]

This Fresnel approximation is only valid if the sensor is in the near-field region where Fresnel diffraction phenomena can be observed [237]. This assumes that \( s \), which also describes the distance between the hologram and the real image, is much greater than the maximum

92
dimensions of the CCD chip, and thus the following condition must be obeyed:

\[ s^3 >> \frac{\pi}{4\lambda} \left[ (n\Delta X - X_I)^2 + (n\Delta Y - Y_I)^2 \right] \]  

(4.3)

The maximum possible value of \( n\Delta X - X_I \) and \( n\Delta Y - Y_I \) must therefore be considered. For a \( \lambda = 632.8 \) nm and typical hologram dimensions of \( (n\Delta X - X_I)^2_{\text{max}} = (n\Delta Y - Y_I)^2_{\text{max}} = 0.5 \) cm, \( s \) must be greater than 14 cm.

This function is digitized into a discrete form, when sampled on an \( n \times n \) matrix on a CMOS sensor, where \( (X_I, Y_I) \) and \( (X_H, Y_H) \) run in discrete steps from 0 to \( n-1 \), of width \( \Delta X \) and \( \Delta Y \), respectively. This results in:

\[
O(X_I, Y_I) = \frac{\exp(iks)}{i\lambda s} \exp \left[ -i \frac{k}{2s} (X_I\Delta X)^2 + (Y_I\Delta Y)^2 \right] \left[ \sum_{X_H=0}^{n-1} \sum_{Y_H=0}^{n-1} \left\{ I(X_H, Y_H) R(X_H, Y_H) * \exp \left[ -i \frac{k}{2s} (X_H^2 + Y_H^2) \right] \right\} \right] \]  

(4.4)

This equation is a numerical representation of the Fresnel approximation, which can be written in terms of a discrete inverse Fourier transformation. By using the Fourier transform equation, 4.5, scaled by \( 1/\lambda s \) (indicated further below in equation 4.8 by \( F^{-1}_{\lambda s} \)) this results in equation 4.6 [238]:

\[
F(u, v) = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} f(x, y) \exp(-2i\pi(ux + vy)) \, dx \, dy 
\]  

(4.5)

\[
O(X_I, Y_I) = \frac{\exp(iks)}{i\lambda s} \exp \left[ -i \frac{k}{2s} (X_I\Delta X)^2 + (Y_I\Delta Y)^2 \right] \left[ F^{-1}_{\lambda s} \left\{ I(X_H, Y_H) R(X_H, Y_H) * \exp \left[ -i \frac{k}{2s} (X_H^2 + Y_H^2) \right] \right\} \right] 
\]  

(4.6)

Additionally, the use of a LFTDH set-up produces a spherical reference wave, described by equation 4.7, where \( B \) is a constant which depends on the amplitude. Thus it is possible to eliminate the effects of the reference wave spherical phase factor from equation 4.6, resulting in a simplified equation for the reconstructed object, 4.8.

\[
R(X_H, Y_H) = B \cdot \exp \left[ i \frac{k}{2s} (X_H^2 + Y_H^2) \right] 
\]  

(4.7)

\[
O(X_I, Y_I) = B \cdot \frac{\exp(iks)}{i\lambda s} \exp \left[ -i \frac{k}{2s} (X_I\Delta X)^2 + (Y_I\Delta Y)^2 \right] \left[ F^{-1}_{\lambda s} \left\{ I(X_H, Y_H) \right\} \right] 
\]  

(4.8)
Thus the standard algorithms for a fast Fourier Transform can now be applied, which are computationally less demanding than alternative DHI approaches. The resulting matrix $O(X_I, Y_I)$ is a complex $n \times n$ function describing the amplitude and phase distribution of the wave field in the plane of the real image. This contrasts to conventional optical reconstruction from holographic film, and earlier digital techniques, which require additional experimental steps to access phase information.

The intensity in the reconstructed image can be calculated from the equation above by taking the modulus and squaring:

$$I(X_I, Y_I) = |O(X_I, Y_I)|^2 = Re^2|O(X_I, Y_I)| + Im^2|O(X_I, Y_I)|$$  \hspace{1cm} (4.9)

where $Re[O(X_I, Y_I)]$ and $Im[O(X_I, Y_I)]$ denote the real and imaginary parts of the image, respectively. The phase information is given by:

$$\Phi(X_I, Y_I) = \arctan \left\{ \frac{Im[O(X_I, Y_I)]}{Re[O(X_I, Y_I)]} \right\}$$  \hspace{1cm} (4.10)

$\Phi(X_I, Y_I)$ varies over the interval $-\pi$ and $+\pi$, as the signs of $Im[O(X_I, Y_I)]$ and $Re[O(X_I, Y_I)]$ vary independently.

**Interference Phase Angle Determination**

In the second part of the reconstruction, the interference phase is calculated from comparison of phase information from irradiated and un-irradiated states of the test cell. The corresponding amplitude transmittances $I_1(X, Y)$ and $I_2(X, Y)$, at time $t_1$ and $t_2$ respectively, are reconstructed separately, and the phase determined with 4.10. The interference phase, which is the phase difference between the two object waves from the different states of the object, is then calculated by modulo $2\pi$ subtraction, in equation 4.11:

$$\Delta \Phi(X_I, Y_I) = \begin{cases} 
\Phi_1 - \Phi_2 & \text{if } \Phi_1 \geq \Phi_2 \\
\Phi_1 - \Phi_2 + 2\pi & \text{if } \Phi_1 < \Phi_2 
\end{cases}$$  \hspace{1cm} (4.11)

The result is a digitally reconstructed two dimensional holographic interferogram, representing the phase difference, with three distinct regions as shown in Figure 4.7. From equation 4.1, describing the interfering field, the first two terms contribute to the central zeroth order of diffraction of the reference and object waves, termed the \textit{DC component}, which is considerably brighter than the real image term (shown on a log scale in Figure 4.7), affecting the dynamic range of the display of the image. Removal of the DC component by spatial filtering enhances the contrast, allowing for easier visualisation of the information of interest.
in the real image. The third term contributes to the real image, and the fourth to a twin image, which is a mirroring of the real image, reducing its size in the total reconstructed field. Off-axis geometry, where the reference and object laser impinge on the sensor with a finite angle between them, is used for the purpose of avoiding any overlap between these three components, so that the real image can be selectively analysed. The alignment of the interferometer to achieve an optimum positioning of the image components is discussed in Section 4.3.3.

![Figure 4.7: A digitally reconstructed two dimensional holographic interferogram of the test cell. (a) The central DC component, and the real and twin images, shown on a logarithmic scale and (b) cropped and scaled real image, depicted on a linear scale.](image)

**Phase Unwrapping**

The use of digital holographic techniques allows for direct attainment of the phase values per pixel, eliminating the fringe analysis that was required to interpret results of earlier analogue interferometers. However because the phase difference containing the information is obtained by modulo $2\pi$ subtraction of the phase of the object and reference images, the resultant phase maps can be discontinuous, indefinite to an additive multiple of $2\pi$. Phase unwrapping is the process of analysing these images to remove the $2\pi$ discontinuities from the phase map. In its simplest form, phase unwrapping involves detecting any $2\pi$ phase jumps and adding or subtracting an integer multiple of $2\pi$ offset to retrieve the continuous form of the phase distribution. The use of a threshold value for the unwrapping points can give some ability to deal with noise in the data. In the case of straightforward phase data with no disturbances this method is sufficient, and the output is independent of the path of the phase unwrapping. However in most unwrapping situations this method is insufficient, due to the presence of noise, under/over-sampling, object discontinuities or missing phase
information [239]. These disturbances can mean that different results are obtained depending on the order in which the pixels are unwrapped. In this case, more advanced methods are required.

Most DHI images obtained during radiation measurements will have straightforward fringe patterns because, with the exception of highly modulated dose distributions such as those produced by MRT, the phase gradients are consistently changing in the same direction. This means that fringe edges, or unwrapping points, are easily evident and the offset required during the unwrapping process is always in the same direction. However at this stage the images produced have a considerable noise component, as well as the potential to be influenced by external factors such as atmospheric variations or vibrations, which can produce wrap points in the image. For this reason the choice of phase unwrapping technique was carefully considered in order to implement the most robust phase unwrapper.

There are various approaches to solving the phase unwrapping problem for a range of applications, with varying degrees of accuracy and complexity [240]. These can be roughly categorised into local or path-following phase-unwrapping algorithms, versus global unwrapping algorithms. Local methods unwrap the phase map by following certain paths across all the pixels in the phase map to reduce the chance of incorrect unwrapping propagating around discontinuities. In these approaches, the choice of path is key to producing the most accurate results. Global algorithms unwrap the phase by formulating the solution in terms of minimisation of a global function to estimate the phase gradient, an approach which is quite computationally intensive. Many authors have made their phase unwrapping codes readily available for use by others, so it becomes a question of selecting a code which will be effective for the type of dataset.

The unwrapper selected was obtained from Herraez et al.1, along with their paper describing the algorithm [241]. This unwrapper is described as a “Fast, two-dimensional phase-unwrapping algorithm, based on sorting by reliability, following a non-continuous path (2D-SRNCP).” The algorithm is a path-following phase unwrapper which chooses the order to unwrap pixels in based on the quality of the pixels. Pixel quality is determined using the second difference quality map technique, which effectively corresponds to the amount of noise in the region of the discontinuity edge. High quality pixels are unwrapped before the lower quality ones, minimising the incidence of error propagation. This method of unwrapping

1From the website of Liverpool John Moores University: http://www.ljmu.ac.uk/GERI/90207.htm
gives better results than a straightforward flood fill technique. The key feature distinguishing this algorithm from similar path-following approaches is that the selected path is not limited to a continuous path, which improves the reliability of the results in the presence of discontinuities or noise, particularly where there are high local variations in the signal-to-noise ratio (as is the case with the DHI data). In terms of the implementation, a MEX file was written and compiled in MATLAB containing the C++ algorithm code and incorporated into the GUI, described in Section 4.3.4.

In the case of the DHI measurements, as the radiation delivery is not instantaneous, the phase map changes dynamically with time. The ideal approach is to compare not only the phase distribution across a two-dimensional region, but also the variation of this phase map over the irradiation period. This would enable the measurement of absolute doses at each point in the image, rather than being limited to a dose difference map at each point in time. Thus the phase unwrapping problem becomes three dimensional, considering two spatial directions and the temporal dimension. Two different approaches were compared for this. The first involved the unwrapping of each image individually using the Herraéz unwrapper, then a subsequent basic phase unwrapping in the temporal direction of each point within the image. This approach was adequate for some image sets, but for noisy data, the secondary unwrapping process seriously affected the previously unwrapped images at each time point. The second approach was to utilise an extension of the Herraéz unwrapper which calculates the phase unwrapping in all three dimensions directly. The code was written by Abdul-Rahman, a doctoral student from the same group, and is henceforth referred to as the “Rahman unwrapper” [242]. This was more successful on most of the datasets, but still resulted in a degradation of the quality of the individual images when compared to using the two dimensional unwrapper. A contributing factor that would worsen this impact is that the noise influences intra- versus inter-image are different, so the path-following route selection is altered for the three dimensional unwrapper as compared to the two dimensional one.

At the current stage of the development of the DHI dosimeter, there are complications in obtaining consistent measurements in the time direction, as discussed further in Section 4.4.3. This means that for some of the results analysis presented in this thesis the information from the temporal direction is not used. In these situations, the primary purpose of the unwrapper is for two dimensional analyses only, with incidental consideration of the third dimension. Thus the Herraéz unwrapper is used for the results presented in the remainder of this work, unless stated otherwise. Future development of the detector to increase consistency, enabling
absolute dosimetric measurements, will require revisiting of the most suitable approach to the three dimensional unwrapping problem.

**Converting Refractive Index to Dose**

In step 5 with regards to Figure 4.5, using the relationship in equation 4.12, the change in optical path length, \( \Delta OPL \), is determined from the unwrapped interference phase at each point, where \( \lambda = 632.8 \text{ nm} \) is the laser wavelength:

\[
\Delta OPL(X_I, Y_I) = \frac{\Delta \Phi(X_I, Y_I) \cdot \lambda}{2\pi}
\]  

(4.12)

In step 6 the change in refractive index through the test cell (of width \( d \)) is calculated according to the relation:

\[
\Delta n(X_I, Y_I) = \frac{\Delta OPL(X_I, Y_I)}{d}
\]  

(4.13)

The temperature rise caused by absorption of ionising radiation in the water in the cell is determined based on the relationship between \( \Delta n \) and \( \Delta T \) for water, reported by Bashkatov and Genina [243], and shown in Figure 4.8. A sixth order polynomial model was fitted to the inverse of this relationship. The limits of accuracy of this calculation are discussed in Chapter 8.

The dose is then calculated according to the calorimetric relation:

\[
D(X_I, Y_I) = \frac{c_m \cdot \Delta T(X_I, Y_I)}{1 - k_{HD}}
\]  

(4.14)

where \( c_m \) is the specific heat capacity of water, determined from the data in Figure 4.8. At 20°C this is equal to 4181.8 Gy K\(^{-1}\). \( k_{HD} \) accounts for the heat defect [121,245]. Corrections for the heat defect, which can amount to several percent, were not made in this work, with \( k_{HD} \) set to zero, which is discussed further in Chapter 8.

The dose determined, \( D(X_I, Y_I) \), is the dose difference within the test cell deposited between times \( t_1 \) and \( t_2 \), with each X and Y corresponding to a dose to a line integrated over the width of the test cell in the direction of the laser. Between two time points the measured dose is absolute. For the current prototype, an empirical calibration factor was determined from the HDR source measurements presented in Chapter 6, for the integration of the dose over the test cell. If the camera is operated in continuous mode, the temporal resolution of the system is determined by the frame rate. The absolute dose at each point can be determined
by phase unwrapping in the time dimension, between adjacent images, to determine the cumulative dose to each point. This process is susceptible to environmental variations such as temperature, pressure and vibrational interferences, which, if significant, mean that the absolute dose delivered between the two time instances cannot be determined with a high degree of certainty. For completeness it should also be noted that if the dose variation between frames causes a variation in phase of larger than $2\pi$ then the absolute dose may not be able to be determined. However as $2\pi$ corresponds to a dose of approximately 1500 Gy this limitation is unlikely to be encountered, except perhaps in a synchrotron MRT measurement. Even in these two situations, the relative dose across the measurement region can still be accurately measured. Thus the measured results achieve a series of two dimensional dose difference maps at each point in time.

### 4.3.3 Experimental Process

The determination of absorbed dose for clinical purposes necessarily requires a high level of accuracy. For this reason, achieving consistent and reproducible results is imperative for any dosimeter, as well as a thorough awareness of exactly what the measurement parameters are. For radiation measurement the complicating factor is that the measurement quantity is not visible to the naked eye, which means that alignment of the dosimeter requires special attention. The experimental process of taking a DHI dosimetry measurement with the
prototype detector has three main components. The first is tweaking the alignment of the interferometer to achieve the best possible image quality, the second is the geometric calibration and alignment of the dosimeter with regard to the radiation source, and the third is the actual data collection process with various parameters recorded before and during irradiation. These three processes are described below.

**Interferometer Alignment**

There are several aspects involved in the alignment of the interferometer to achieve an optimum image quality. The first aspect is the gross alignment of the interferometer components in order to both maximise the size of the real image, and its positioning relative to the DC component and the overall field of view to reduce extraneous noise. The position of the real term relative to the DC term is proportionate to the transverse separation between the reference and object beams compared to the axis normal to the camera sensor. The size of the real image is inversely proportional to the distance of the focal plane from the camera sensor. An example can be seen in Figure 4.9 of the result of poorly aligned components, with Figure 4.9(a) showing the result of a set-up where the angle between the beams is too small, causing overlap of the real image and the DC term, whilst Figure 4.9(b) demonstrates the focal point being further than optimal from the camera. Figure 4.9(c) demonstrates the desired alignment. Achieving this optimal position is constrained by aspects of the experimental components. For example, the size of the lens and holder places a lower limit on the transverse separation between the two beams, whilst the length is limited by the size of the breadboard that all the components are attached to. Additionally, the difference in path length of the reference and object beams must remain within the coherence length of the laser used, in order to achieve a meaningful interference pattern.

An additional constraint to this process is that there is an upper limit to the angle which can be used between the reference and object beams. This angle defines the fringe spacing, and is controlled by the size and resolution of the sensor. In general for all types of holography, whether digital or film, the photosensitive material must be able to resolve the complex intensity distribution resulting from interference between the waves scattered from all object points and the reference wave [205]. The maximum spatial frequency which is resolvable limits the maximum angle \( \theta_{max} \) between the two beams, according to:
Figure 4.9: Reconstructed output from the interferometer showing the impact of a non-optimal alignment compared to a well aligned set-up. (a) depicts the real term overlapping with DC component, introducing additional noise into the real image, (b) shows the real image smaller than optimal, reducing spatial resolution, whilst (c) is an example where the alignment is optimal.

\[ f_{\text{max}} = \frac{2 \lambda}{n} \sin \left( \frac{\theta_{\text{max}}}{2} \right) \]  

(4.15)

Compared to film, digital sensors have a relatively limited resolution, so \( \theta_{\text{max}} \) is limited to a few degrees, and thus only relatively small objects at larger distances from the sensor can be recorded. According to the Nyquist sampling theorem the distance between neighbouring pixels, \( n \), is the limiting factor for the maximum spatial frequency resolvable by a CCD array, as in equation 4.16 [213].

\[ f_{\text{max}} = 2 \, n^{-1} \]  

(4.16)

Thus by combining equations 4.15 and 4.16 and substituting the values of \( \lambda \) and \( n \) used in the prototype detector, an upper limit of \( \theta_{\text{max}} = 10.8^\circ \) is determined from equation 4.17.

\[ \theta_{\text{max}} = 2 \, \arcsin \left( \frac{\lambda}{n} \right) \]  

(4.17)

The next consideration is reducing the impact of any defects in the components which may cause image distortions. This step includes cleaning the mirrors, lenses and camera sensor to remove dust particles, and ensuring that the reference beam is centred on the sensor, as the intensity varies across the width of the beam due to its spherical nature.

The final factor in obtaining an optimal interferometer set-up is ensuring that the reference and object beams are of approximately equal intensity, achieved through the use of neutral density filters. This is the controlling factor for the contrast of the fringes, as discussed in
Section 3.2.1. The filters also serve the purpose of reducing the intensity of the light impinging on the sensor, to prevent saturation of the detector. The detector shutter speed can be modified to control the exposure, but the minimum shutter speed of 0.04 ms places an upper limit on the light intensity, whilst increasing the exposure time can lead to a reduced frame rate which may be a concern for some applications. The filters come in a set with certain values, so a combination of filters must be selected to meet all the above requirements as well as possible. The best choice depends on the exact configuration of the detector for a particular measurement, and must be selected after the detector is reassembled and additional positioning measurements, as described above, have been carried out.

**Geometric Calibration**

A key aspect in getting useable, quantitative results from the DHI detector is the geometric calibration. This involves both a calibration to determine the size of each pixel within the measured data, and the localisation of each measurement relative to the type of radiation used. The size calibration involves the same process for each measurement, whilst the localisation step is dependent on the experimental set-up required for measurements on each particular source.

To calibrate for pixel size a series of *templates* are used, consisting of rectangles printed onto a thin sheet of transparent plastic. These rectangles are the same relative proportions as the camera sensor, but different sizes (e.g. 100% of the sensor size, 95%, 90% and so forth). Following the alignment of the detector, a template is placed in the object beam at the focal point, positioned in the same orientation as the sensor and aligned to make sure that all corners appear perpendicular, as shown in Figure 4.10(a) The size of this template must be selected so that the full width of all the lines are visible on the image, so it will be less than 100% size. An image is then taken and reconstructed, as shown in Figure 4.10(b) and (c). A comparison of the measured number of pixels in the reconstructed image, in the $x$ and $y$ directions, to the known size of the template allows a calibration of pixel size. This process is repeated with the template two centimetres in front of and behind the focal position, to confirm that the object beam was sufficiently collimated. This means that the the pixel size of images taken with the focal point at any distance across the test cell will be consistent. There is some uncertainty in this method, due to the fuzziness of the edges of the template, but considering the width of the printed lines as well as the template dimension allows for some redundancies in the measurement, allowing for more confidence in the result.
Table 4.2: Example of data collected for a pixel size calibration

<table>
<thead>
<tr>
<th>Measurement position</th>
<th>Pixel 1</th>
<th>Pixel 2</th>
<th>ΔPixels</th>
<th>Distance (mm)</th>
<th>Resolution (mm/pixel)</th>
</tr>
</thead>
<tbody>
<tr>
<td>x</td>
<td>Outside edges</td>
<td>39 ± 1</td>
<td>383 ± 1</td>
<td>344 ± 2</td>
<td>8.00</td>
</tr>
<tr>
<td></td>
<td>Inside edges</td>
<td>50 ± 1</td>
<td>373 ± 1</td>
<td>323 ± 2</td>
<td>7.48</td>
</tr>
<tr>
<td>y</td>
<td>Outside edges</td>
<td>27 ± 1</td>
<td>248 ± 1</td>
<td>221 ± 2</td>
<td>6.47</td>
</tr>
<tr>
<td></td>
<td>Inside edges</td>
<td>30 ± 2</td>
<td>235 ± 1</td>
<td>205 ± 3</td>
<td>5.95</td>
</tr>
<tr>
<td>x</td>
<td>Outside edges</td>
<td>63 ± 1</td>
<td>406 ± 1</td>
<td>343 ± 2</td>
<td>8.00</td>
</tr>
<tr>
<td></td>
<td>Inside edges</td>
<td>74 ± 1</td>
<td>395 ± 1</td>
<td>321 ± 2</td>
<td>7.48</td>
</tr>
<tr>
<td>y</td>
<td>Outside edges</td>
<td>22 ± 1</td>
<td>249 ± 1</td>
<td>227 ± 1</td>
<td>6.47</td>
</tr>
<tr>
<td></td>
<td>Inside edges</td>
<td>34 ± 1</td>
<td>237 ± 1</td>
<td>203 ± 2</td>
<td>5.95</td>
</tr>
</tbody>
</table>

Repeated measurements on different images, with the template slightly shifted in each allows for the statistical uncertainty to be calculated from the standard deviation of the results. An example is given in Table 4.2. This process is carried out every time a major realignment of the interferometer has occurred. For actual measurements, if a visual positioning aid is required, as large a template as possible is chosen with the inner edges just visible on the edges of the interferogram. This is visible on the computer display in real time during the set-up process, allowing for alignment of the radiation source with the measurement field.

![Figure 4.10: Geometric calibration template.](image)

(a) A template attached to the test cell, (b) reconstructed image showing the template as used for pixel size calibration, and (c) interferogram showing a larger template just visible on the edges, as used for real time positioning purposes.

The localisation of the measurement field within the test cell is done using the template. Depending on the exact alignment of the interferometer for a given measurement affects which size template to choose. The choice of template requires a size where the inner edges of the template are all clearly visible on the interferogram (seen in real time using the PixelINK Capture OEM software), without impinging too much on the field of view, as shown
in Figure 4.10(c). In this work most set-ups to date have used one of the 90-100% sizes. This template can then be used as a visual point of reference of the alignment of the field of view within the test cell, in comparison to the source of the radiation. The process of aligning the template with the source is highly specific to the source of radiation being measured, and is covered further in the relevant Chapters 6 and 7.

Data Collection

For each measurement and subsequent data reconstruction particular parameters of the measurement must be collected. These may vary slightly depending on the type of radiation being measured, however fit into three general categories: set-up parameters and checks, measurement parameters and initial analysis parameters. The set-up parameters are recorded only at the beginning of any given set of measurements, and all concern the particular alignment and use of the interferometer. The measurement parameters are recorded during/before each irradiation, and include all parameters that may be varied for a given measurement, as well as a description of the radiation and the positioning of the detector relative to the radiation. The initial analysis parameters are the parameters used directly after a measurement when an image set is checked to see if it has the expected results. It is not strictly necessary to record these parameters, but has proved useful if later analyses cannot detect the same features as originally seen due to selection of different region of interest, reference image or image range. Examples of each type of parameter are listed in Table 4.3, which can serve as a record sheet for recording parameters during measurements. Future iterations of the detector may automate some more of this process, such as electronic triggering of the camera, and further image processing to automate selection of the region of interest.

4.3.4 Graphical User Interface Design

A graphical user interface (GUI) was designed in MATLAB to streamline the process of reconstructing the DHI images and the subsequent determination of the measured dose. The first step in the GUI is an input screen, as shown in Figure 4.11(a). A reference image is selected, and a series of images for analysis, which are then compared against that reference image. Specific input parameters for that dataset are entered, including the laser wavelength, image dimensions, geometric information and initial temperature. A region of interest (ROI) for analysis is selected, to correspond to one of the twin images containing the real reconstructed information. In order to determine the ROI, the button on the right
Table 4.3: Record sheet for measurement parameters

<table>
<thead>
<tr>
<th>Stage</th>
<th>Parameter</th>
<th>Explanation</th>
<th>Example value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Set-up</td>
<td>Date</td>
<td>15 March 2013</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Object to sensor distance</td>
<td>From the lens focal point, along object beam</td>
<td>20 cm</td>
</tr>
<tr>
<td></td>
<td>Position of real image ok?</td>
<td>Do a reconstruction to check the alignment of the real image compared to DC term/field of view</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Size calibration done?</td>
<td>Record values in a table similar to Table 4.2</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Test cell</td>
<td>Width of selected test cell in direction of laser</td>
<td>2 cm</td>
</tr>
<tr>
<td></td>
<td>Intensities matched</td>
<td>Check each arm of the interferometer has similar intensity and use filters to optimise to ensure sufficient contrast</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Camera exposure time</td>
<td>0.04 ms</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Baseline measurement?</td>
<td>Measured background noise and stability of system</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Template size</td>
<td>Correct sized template selected for positioning</td>
<td>90%</td>
</tr>
<tr>
<td></td>
<td>Experiment start time</td>
<td>For comparison to the external temperature tracking</td>
<td>14:56</td>
</tr>
<tr>
<td></td>
<td>Camera frame rate</td>
<td>3 f.p.s</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total measurement time</td>
<td>In case the frame rate set is unable to be achieved</td>
<td>200 s</td>
</tr>
<tr>
<td></td>
<td>Total number of frames</td>
<td>To check if the frame rate set was achieved</td>
<td>600 ✓ ok</td>
</tr>
<tr>
<td></td>
<td>Description of positioning</td>
<td>What is recorded here depends on the set-up for each radiation type; sometimes a sketch is helpful</td>
<td>HDR Applicator vertical, visible top left</td>
</tr>
<tr>
<td></td>
<td>Relevant radiation parameters</td>
<td>e.g. dose rate, dwell time and position, source activity, beam current etc.</td>
<td>170 GBq, 60 s, 1 mm from end of applicator</td>
</tr>
<tr>
<td></td>
<td>Radiation-on time/frame</td>
<td>Time is recorded between recording start to beam on, unless there is a networked control computer in which case the frame corresponding to the beam on time can be recorded.</td>
<td>Frame # 12</td>
</tr>
<tr>
<td></td>
<td>Radiation-off time/frame</td>
<td>#270</td>
<td></td>
</tr>
<tr>
<td>Measurement</td>
<td>Reference image</td>
<td>Image chosen as t = 0</td>
<td>Image #1</td>
</tr>
<tr>
<td></td>
<td>Image range</td>
<td>The range of images chosen for analysis</td>
<td>70-100</td>
</tr>
<tr>
<td></td>
<td>R.O.I. selected</td>
<td>[x y width height] where x and y are the co-ordinates of the top left corner of the region of interest</td>
<td>[200 300 200 150]</td>
</tr>
</tbody>
</table>
of Figure 4.11(a) can be selected, which opens a window showing the initial reconstruction of the full image, as shown in Figure 4.11(b). From here the box can be adjusted to exactly contain the ROI, which then automatically enters the parameters. Once all data is correctly entered, the “Reconstruct” button is pushed. This reconstructs the full image series, and then displays the results for the ROI, in Figure 4.11(c). This display has several components. The data can be depicted in various formats, using the drop down menu above each graph: phase, two or three dimensional unwrapped phase, temperature and dose. The left graph shows the reconstructed series of images, with a bar to scroll between images. A horizontal or vertical line can be selected at any point within the image, with the data in these profiles displayed in the central graph. The right graph shows the phase value at the point of intersection of these profiles, across the whole image series. These plots allow for a straightforward analysis of the data to determine any immediate trends visible, either spatially or temporally. Further analysis of the results, for example quantitative sensitivity or noise calculations, and comparison to a model dataset are conducted using the output datasets from the GUI. These have not yet been included in the GUI as there is considerable variation in the calculations required for different applications.

4.4 Detector Progression and Characterisation

The process of developing the prototype interferometer and digital reconstruction algorithm involved several stages of interferometer design, with consequent testing on a series of heating patterns. The knowledge gained from each stage in this process informed the design and use of the final prototype.

The first step in the process was the development of a system capable of doing digital holographic interferometry. This has two parts, the first is the experimental configuration, and the second is the digital image processing for reconstructing the algorithms. The first attempts focussed on a basic interferometer design based around a Michelson interferometer, to produce interferograms which were used to develop preliminary reconstruction algorithms. These were tested by producing reconstructed holograms visualising the absorption of the object beam laser light in solid objects, and then phase objects (objects which induce a phase change in the laser light without excessive absorption). Following this a set-up similar to the design used for the prototype detector was developed and the sensitivity of the system tested with the measurement of heat distributions using flames and drops of heated water. This served to confirm the measured temperatures and temperature distributions approxi-
Figure 4.11: MATLAB GUI for reconstruction of the DHI images and initial interpretation of the results. a) The initial display where measurement parameters are entered and images are loaded, b) selection of the region of interest in the reconstructions, and c) display of the reconstructed dataset for analysis.

mated those expected, which was an integral step in developing confidence in the system for the subsequent use on radiation. Heat distributions simulating radiation dose distributions proved difficult to produce with any degree of accuracy, but some of the attempts are shown. Results from each of these steps are shown, and briefly discussed in the sections below.

4.4.1 Initial Holographic Interferometer

Development, particularly initially, was limited by the experimental equipment available, so the initial experiments started with a basic Michelson-style interferometer, similar to that used by Hussmann and Miller [27]. A schematic of a basic Michelson interferometer was
shown in Figure 3.1, and the actual set-up is shown in Figure 4.12, with a test cell and heating element in the object arm. With correct alignment, the initial circular interference patterns were produced, as shown in Figure 4.13. The size of the rings is dependent on the angle between the reference and object beams, which is controlled by the tilt of the mirror in the reference arm of the interferometer.

Figure 4.12: Experimental Michelson interferometer, with key components labelled and the path of the laser indicated in red.

Figure 4.13: Initial interference patterns produced with a Michelson interferometer. (a) and (b) show centred and off-centred patterns, as well as differences in fringe patterns depending on the angle between reference and object beams, where a smaller angle produces larger rings.

Once fringe patterns were resolvable, the initial digital reconstruction algorithms were developed. These were tested with the placement of letters, printed onto a thin page of transparent
plastic, into the object beam of the interferometer. The first successful reconstruction that was achieved is shown here in Figure 4.14.

![Figure 4.14: The first successful reconstruction of a solid object.](image)

The next test attempted to refine the measurement object from a solid object, such as the letters, which prevented transmission of some of the light in the object beam, to a phase object which allowed all the light to be transmitted, but changed the phase of parts of the light. Several different approaches to this were attempted, including the use of drips of acetone on a microscope slide, and pieces of clear adhesive tape on transparent plastic. In
order to see the effects of this, the images were measured at the edges of the phase object to show the contrast between where the object was and was not. Typical results can be seen in Figure 4.15, showing the edge of the adhesive tape on an image of a letter K. It was not possible to rule out that some of the effects in the reconstructed images may have been from absorbance of light by the object, rather than solely a phase effect.

![Figure 4.15](image)

Figure 4.15: Reconstructed image showing the successful visualisation of a phase object, consisting of a piece of transparent adhesive tape bisecting a letter K printed on a piece of transparent plastic. (a) shows the recorded interferogram, (b) the reconstructed image, and (c) the phase image clearly displaying a jump in phase, which is not apparent in the reconstruction, although the edge of the tape is visible in both. The black area in image (c) is a point where the phase is wrapped over $2\pi$.

However, following these early experiments the use of a Michelson type interferometer was abandoned in favour of an LFTDH set-up, similar to that described in Section 4.3.1 [237]. The major justification for this was to simplify the reconstruction algorithm, but also to avoid the double pass of the object beam through the object. Whilst a double pass does increase the sensitivity of the measurement, it also increases the size of the real image because of the small angle between the reference and object beams, which can make it too close to the DC term. It also complicates the alignment process, affecting the resolution. It is an option to revert back to this type of set-up in future if increased sensitivity is required.

Similarly to the above results with the Michelson interferometer, initial testing of the LFTDH system measurement and implementation of the reconstruction algorithms was carried out using solid objects in the beam. A demonstration that the reconstructed interferograms are displaying what they should is an experiment where a reference image is taken, and then one of the mirrors is slightly tilted, resulting in a variation in the fringe pattern that causes consistent straight fringes in the reconstructed images, as shown in Figure 4.16.
Figure 4.16: The result of slightly tilting one of the mirrors in the interferometer vertically and horizontally after the reference image. (a) the combined interferograms, (b) the reconstructed image, and (c) the unwrapped reconstructed image.

4.4.2 Non-Radiation Induced Heating Patterns

One of the key considerations for this type of research is that access to the radiation sources such as cyclotron or synchrotron is limited and expensive, particularly for instrumentation type projects that do not have immediate clinical benefit. For this reason the DHI detector was developed as much as possible in the laboratory to maximise the chance of successful results of later radiation measurements. Up until this point, the test objects were suitable for development purposes, but not close approximations of a radiation source. Thus an additional step which was undertaken throughout the development process was to attempt to create temperature values in the cell which could be measured by DHI. The output of DHI temperature measurements is not the absolute temperature values within the test cell, but rather temperature differentials, as the temperature varies with spatial location and time. Ideally these temperature distributions could be independently quantified, however it is not a straightforward problem to simulate easily measurable and reproducible heating patterns, especially on the small temperature scales, on the order of 0.001 K, produced by irradiation of water with doses in a clinically useful range. Several different approaches were attempted with the equipment available. The results proved qualitatively that the detector was operating as expected, however exact values measured of temperature distributions could not be accurately verified. The overall process helped to inform the further development of the detector at each stage.

Flames

The next step was to visualise transient heating patterns. The first attempt was inspired by the papers by Aggarwal et al. [246] and Xiao and Puri [247], who used a DHI approach to study the heat distributions within flames, as a demonstration of the system and to investigate combustion phenomena. This was a convenient way to demonstrate the two key
aspects of the measurement of heat and transient phenomena, so some images were taken and reconstructed. A match was used as the flame source. First a reference image was taken, then the match was lit, and embedded in a piece of adhesive putty, so that the flame was in the object path of the interferometer. The reconstructed images showed the heat distribution of the flame around the head of the match clearly, as seen in Figure 4.17. Due to the limited size of the sensor the entire flame is not visible in one image. The shape of the heat distribution was as expected, with the peak temperature being some distance above the head of the match. Phase unwrapping appeared to be effective, despite the turbulent nature of many of the images. The phase shifts between the outer edge of the images and the region immediately adjacent to the match were up to $10\pi$. Temperature values were unable to be easily assigned to these phase images because there is no direct relationship between the refractive index of air and its temperature, because the temperature induced density variations do not have a straightforward correlation as the ideal gas law cannot be applied in a non-sealed volume.

![Figure 4.17: Images of a flame in air demonstrating successful visualisation of transient heating phenomena. The region shaded by the match head is visible in the bottom right of the image. (a) Measured phase difference and (b) the corresponding unwrapped phase image where red corresponds to higher temperatures and blue to lower.](image)

**Water Droplets**

The successful detection of heat distributions in a flame in air paved the way for measurements in water. The first test was done using droplets of warm water into the test cell filled with room temperature water. This was chosen because it is a straightforward way to get images of a heating pattern in water with an initially clearly defined predictable shape, as well as be able to estimate approximate temperature values. Figure 4.18 shows a water drop with a temperature of 40 °C being dropped into a cell of temperature 21 °C. The first image, Figure 4.18(a), shows the turbulence created in the moment that the water drop goes into
the water. The high turbulence in this moment meant that no meaningful phase unwrapping was possible. To confirm that it was the temperature of the water drop causing the refractive index variation, and not just the turbulence from the droplet, drops of water at the same temperature as the test cell were also tested, but showed no influence on the refractive index. The image taken three seconds after the warm water droplet entered the water, Figure 4.18(b), shows a phase change wrapped approximately four times over a $2\pi$ interval. When unwrapped and converted to temperature this corresponds to a temperature range of $1.3 \degree C$. When the integration of this measurement across the cell is taken into account, the resulting temperature increase near the surface of the water is approximately $8 \degree C$. This is of the correct order of magnitude for the expected increase, although an exact estimate for the expected temperature cannot be achieved without undertaking a more comprehensive study on the physics of heat transfer in water via droplets. This measurement was however evidence that the DHI system was working appropriately and was able to resolve two dimensional temperature difference maps.

Figure 4.18: Images of heated water drops in a test cell, with the water surface visible at the top of the image. (a) shows the wrapped phase difference image as the water enters the cell, (b) the wrapped phase difference 3 s later, (c) the unwrapped temperature distribution of image (b), with the black line defining the temperature profile displayed in (d).
Modulated Heating Pattern

A final approach to creating measurable temperature variations in the laboratory was attempted, with the creation of a more highly modulated temperature distribution. The idea was that the resultant phase changes would be both more confidently determined on the images, as well as provide some indication of the complexities that would be faced in attempting to measure more modulated radiation dose distributions, such as that produced by MRT radiation beams. An example of one such complexity is that the phase wrapping will not be only in one direction, so this may reduce the effectiveness achieved by the unwrapping algorithm. In order to simulate microbeams, the heat gradient must be high over a short distance, and created on a short timescale. A heating element was manufactured in the form of a copper heat sink with three parallel pins extruding from it, each of length 1 cm and diameter 1 mm (depicted in Figure 4.19(a)). The pins were immersed in the water of the test cell, and then resistively heated with a current of 0.5 A and 12 V voltage. A temperature probe was inserted into the centre of the copper block in order to provide a temperature value for comparison with the DHI measurements. An example of the result after a one minute measurement is shown in Figure 4.19, progressing from the recorded interferogram, to the image reconstruction, phase difference map and corresponding temperature difference map. The temperature increase around the pins is clearly visible, and the profile lines shown in Figure 4.19(e) clearly show the range of the temperatures around the heating elements. The temperature probe in the copper block measured an increase in temperature over this time period of 4.6 °C. The DHI measured temperature increase at the tip of the pins was 0.29±0.03 °C, however at 1 mm along the pins this rose to 0.81±0.04 °C. Additional measurements, not depicted here, with more of the pins visible on the interferogram, showed a temperature rise of up to 3.12±0.08 °C in the water immediately adjacent to the pins, approximately 3 mm distally from the copper block. Thus it is evident that despite the high thermal conductivity of copper, the temperature in the centre of the heat sink is not equal to the temperatures along the pins. This effect is compounded by heat diffusion which would occur over the minute-long heating up period allowing for faster transfer of heat away from the pins because of their higher surface area compared to the heat sink. In this case, the DHI measured values are on the order of magnitude that one might expect, especially considering the occurrence of heat diffusion over the one minute.
Figure 4.19: (a) The copper heat sink used to create a modulated temperature distribution, (b) a recorded interferogram with the pins visible, (c) reconstructed real image, (d) the phase distribution after one minute of heating, (e) the measured temperature differences around the pins, which are masked. The blue and red lines indicate the profile positions shown in (f), which displays the unmanipulated measured temperature values along these lines.
4.4.3 Absolute Temperature Measurements

The measurements presented in the previous sections are examples of relative measurements, where the temperature variation within the field of view is considered at one time instance. In situations where the induced temperature change does not reach all areas of the field of view, then the absolute temperature change at each point compared to the reference image can be determined. However in most situations, including most dosimetric measurements, there may be an induced temperature rise in every pixel of the field of view. Thus each image provides a measurement of only the temperature (or dose) difference at that point in time and gives no indication of the cumulative temperature increase/absorbed dose to each point. It is theoretically possible, by taking a series of measurements it is possible to determine the cumulative temperature/dose increase at each point in the cell over the entire irradiation period. This would result in a determination of the absolute dose value at each point, but remains an area of further work.

As discussed in Section 4.3.2, the series of images measured can have phase values wrapped in the time dimension, which also need to be unwrapped, using the Rahman unwrapper. The complicating factor is that the noise from atmospheric temperature and pressure variations, and vibrations will have a greater effect inter-image than they do intra-image. For instance, variation of the room temperature causes expansion or contraction of the optical componentry, which can affect the measured phase values. Additionally, there is a degree of heating induced in the water due to the laser, as calculated below. In order to do any kind of absolute dosimetry, these influences need to be quantified to determine if it is possible to correct for it. They have no impact on the individual images because, in a first order approximation, variations in these quantities will affect each point in the image to the same extent.

Laser Induced Heating

The extent to which the water in the test cell is heated by absorption of a laser in the water can be calculated for a given configuration of the interferometer. The first step is to calculate the transmittance, $T$, of the light through the sample, using the Beer-Lambert Law:

$$ T = 10^{-A} = 10^{-a \cdot d} $$

(4.18)

where $A$ is the absorbance of the medium for that wavelength of light, $a$ is the absorption coefficient, and $d$ the depth of the test cell in the laser direction. The laser power absorbed in the sample, $P_A$, can then be calculated according to:
\[ P_A = P_L \cdot BS \cdot N_D \cdot F \cdot (1 - T) \] (4.19)

where \( P_L \) is the mean power of the laser in steady state, \( BS \) is the fraction of light in the object beam after passing through the beam splitter, \( N_D \) is the fraction of the light passing through the neutral density filters and \( F \) is the fraction of the light which reaches the test cell and is not obscured by one or more of the mirrors. This last value of \( F \) involves an approximation, however it proves to have relatively negligible influence on final measured results. Additional assumptions are that the light from the laser as it comes out of the beam splitter is of homogenous intensity, that the transduction efficiency is equal to one, that there is no laser attenuation in air, and that any absorbance in the thin Perspex wall of the test cell is ignored. These assumptions should be revisited in future if improved measurement accuracy warrants this correction.

The rate of temperature rise of the test cell water in the path of the laser, is then calculated from the heat capacity of the water, \( C_m \), using the equation:

\[ \Delta \dot{T} = \frac{P_A}{C_m} \] (4.20)

where the units are K s\(^{-1}\).

For a He-Ne laser, the absorption coefficient is \( a = 0.2995 \) m\(^{-1}\) [235, 244]. For a typical measurement with the DHI dosimeter prototype, the laser had a mean power output of \( P_L = 12.1 \) mW, in an interferometer with a 50/50 beam splitter \( (BS = 0.5) \), neutral density filters with optical density 0.4 and 0.2, and with \( F = 0.8 \). The beam was incident on a cross-sectional area of the test cell of 1.57 cm\(^2\). Substituting these values into equations 4.18-4.20 gives an increase in temperature of approximately 0.4 mK s\(^{-1}\). This is compared to a radiation induced temperature increase of approximately 0.24 mK G\(^{-1}\). Thus for a dose of several hundred Gy, the impact is minimal, provided the dose rate is sufficient. However, for lower dose measurements, and for heat diffusion calculations this effect may become significant. At this stage, the projection of the dose means that the differential heating of different portions of the cell by the laser is not visible on the final image, but in future it should be included in the heat modelling, especially if low doses are to be measured.
Correlation of External Temperature Variation

Various so-called “flat field” measurements were taken, where there was no induced temperature change in the water. In the absence of room temperature variations, this should result in images that show only the small, consistent increase in temperature due to the optical heating. However, variations in room temperature may have an impact on the path length of the light passing through the interferometer. Ambient temperature increase causes decreased air density and expansion of the metal parts of the interferometer, to a different extent on the reference and object paths, thus causing a corresponding variation in the measured phase shifts and resultant temperature measurements. A separate temperature logger with 0.1 °C resolution was placed within the experimental box to record the atmospheric temperature during the measurements, to attempt to correlate this effect. If a consistent value can be achieved for the correlation of room temperature and measured temperature, then it may be possible to account for this effect, and undertake absolute dosimetry measurements.

A series of flat field images was recorded over several measurement sessions on different days. The measurement periods encompassed times when the ambient temperature in the box was consistently increasing, decreasing or unchanging. The resulting DHI measurements also showed a range of outcomes in terms of temperature variation. A sample of some of these measurements is shown in Figure 4.20. In general, when the ambient temperature increased or decreased there was a corresponding change in the measured phase difference values, averaged across each image. This corresponds to an artificial change (in the opposite direction to the phase) in the measured temperature values attributed to the water in the test cell. However some measurements where the ambient temperature showed no variation resulted in a decrease in phase measured by the detector, corresponding to apparent temperatures of up to 0.34 K min^{-1}. The source of this variation was unable to be determined and, whilst generally consistent for the period of each measurement, varied between measurements. The frequency stabilised laser described in Section 4.3.1 was used to rule out the drift being caused by some instability in the laser frequency, with results also showing similar inconsistencies. All other aspects of the interferometer were carefully considered, but at this point no suitable explanation for these results has been determined. Given this unexplained drift, a consistent correlation value between the ambient temperature values and the DHI measurements was not determined. It may prove to be due to non-homogenous temperature variation within the experimental box, or alternatively barometric variations which were not measured.
Time-variant Temperatures

An extension of the flat field measurements, was to make further measurements where an additional temperature gradient was introduced into the test cell. The test cell was filled with warm or cold water and measurements were made whilst the water temperature equilibrated to room temperature. The intention was to create effectively a one-dimensional heat gradient, where the temperature of the cell was roughly homogenous, but varies with time. A thermometer inserted in a corner of the cell was used to provide an independent measure of the temperature for comparison to the DHI results. Some slight variation in temperature between the centre of the cell and the edges was expected, as the heat exchange occurs through the boundaries of the test cell, however this is an obvious experiment to try as a first approximation to validate the temperature measurements. Preliminary measurements of water cooling over an interval from, for example, 30.6 °C to 29.8 °C showed a corresponding measured decrease in the DHI results. However due to the potential presence in the results of the unexplained drift mentioned above, it is not possible to have full confidence in the accuracy of the measured result.

The results from these initial flat field and time variant measurements do not invalidate DHI as a dosimetric approach. It means that at this stage of development of the prototype
detector measurements are limited to determining the temperature/dose differentials within an image at each point in time. Thus all further results presented in this thesis will be relative results only, which provide useful information about the absorbed dose distributions in water. Absolute temperature and dosimetric measurements will be an area for future development. It is anticipated that the use of a temperature isolating encasement for the detector, as used for calorimetry measurements in various standards laboratories, would solve the measurement difficulties described above by eliminating the effects of ambient temperature increase. This temperature control is a requirement regardless, even if a suitable correlation with ambient temperature and DHI flat field measurements was to be determined. This is because of the presence of air conditioning units in clinical treatment facilities, meaning that the ambient temperature variations can fluctuate in a fashion that does not allow for their impact within the DHI box to be accurately tracked and accounted for. Additionally, for calorimetric measurements of highly modulated sources, Sarfehnia et al. suggest that measurements be made at 4 °C to reduce the impact of convective heat transfer effects [74]. Considerations regarding the construction of an environmentally controlled experimental box are discussed in Section 8.4.1.

4.4.4 Fibre Optic Approach

During the DHI detector development process, an opportunity arose to collaborate with Dr. Frédérique Vanholsbeeck of the University of Auckland, who works in the area of fibre optic interferometry, in particular on the project of optical coherence tomography (OCT). The idea was to investigate the possibility of using a fibre optic approach to DHI. The advantage of a fibre optic system is that once set up and aligned, it can be easy to use and transported with minimal further alignment required. This is a useful feature if the clinical implementation of DHI is considered. Additionally, because dosimetry measurements expose the sensitive optical components to potentially high doses of ionising radiation, a fibre optic approach can allow for the use of optical wave guides to direct the light from detectors and a laser source that are located further away from the radiation, and thus be less susceptible to radiation damage. For the purposes of longevity of a DHI detector this may well prove to be an important consideration.

To realise the full potential of a fibre optic approach requires the use of a photodiode as a sensor, replacing the use of a camera. The photodiode is constructed from semiconductor material that converts incident visible light into a voltage. This reduces the complexities of coupling and decoupling the light from the optical fibres. An x-y scanning system is then
required to scan the field of view in the test cell and build up the measured interferogram point by point. This introduces inherent difficulties with noise, because it takes some finite time to build up the image, resulting in each pixel value being influenced differently by noise effects. This distortion may be difficult to correct for. For high dose rate radiation the measurement time variation across the image may also have an impact. The image acquisition rate can be increased in order to reduce this effect, but at the expense of the spatial resolution.

Dr Vanholsbeeck kindly allowed access to her laboratory, and with the help of her PhD student Norman Lippok, a basic Michelson interferometer was set-up and analysed for ease of use and effectiveness. A He-Ne laser was coupled into single mode optical fibre with core diameter at 632 nm of 4.3 µm using a three axis micrometre-precision injection stage. Instead of a beam splitter to create the object and reference beams, a 50/50 fibre coupler (model SM630 manufactured by OEMarket) was used. For the object beam, the light was decoupled from the fibre and passed through the test cell, where it impinged on a galvanometer consisting of a mirror driven by a motor which allowed the laser to scan across the test cell (model 6215H from Cambridge Technologies, USA). In this experiment a one dimensional galvanometer was used rather than a two dimensional scan. The light then passed back through the test cell and was recoupled into the optical fibre and, at the fibre coupler, recombined with the reference beam to impinge on the photodiode. The complicated part of this process was the configuration of lenses needed for this coupling and recoupling process to achieve a high resolution. The photodiode was attached to an oscilloscope, and a Labjack USB data acquisition (DAQ) card (model USB 1608-FS from Measurement Computing) was used to record the measured voltages to build up the scanned measurement and control the galvanometer. A schematic is depicted in Figure 4.21.

The set-up proved to be very sensitive to room and air vibrations, with a pulse of frequency 1-2 s\(^{-1}\) causing the fringes to consistently move. Makeshift cardboard shielding and the use of an air table reduced the amplitude of the pulse, but it was still considerable. For a scanned image each point in the image is influenced to a different extent, which is difficult to account for mathematically given the experimental complexities. An additional problem was that as the laser is scanned across the test cell, the gain on the photodiode varies because the amount of the light that reaches the photodiode changes with the angle of incidence to recouple the light back into the optical fibre. Under perfect alignment conditions this would not occur, but in practice it is very difficult to eliminate. It may be possible to mathematically correct the images for this during the analysis step, by comparison with flat field calibration.
images. Additionally, the influence of vibrations of the optical fibres can have a considerable effect on fibre optic interferometry. This can be mitigated to some extent by the use of a vibration isolated table, but this is likely not to be available in a clinical dosimetry situation.

Following these early experiments, further work was done on this approach by Masters student Kaidi Liang, under the co-supervision of Dr. Vanholsbeeck and Dr. Juergen Meyer [248]. He achieved successful holographic reconstructions of two dimensional interferograms, however did not achieve any conclusive temperature measurement results due to encountering various experimental setbacks. The use of fibre optic interferometry therefore remains an area to explore further for the sake of its potential advantages for transportability of a DHI detector. This approach has more complexities than the standard non fibre approach described in the rest of this chapter. There are many areas that would require consideration for this to work, including the best method of coupling the light into the fibre by the test cell, and experimental and image processing noise reduction.

4.5 Concluding Remarks

The purpose of this chapter was to fully describe the prototype DHI detector used for the radiation dosimetry measurements, based on an LFTDH configuration. The various design considerations and equipment choices were discussed in the context of how they influenced the final prototype design. A complete description of the detector and the mathematical algorithms developed to reconstruct the images and obtain measured dose values was included.
Further description of the entire measurement process was given in sufficient detail to allow for all measurements to be independently replicated. Initial measurements of various heat distributions were presented as part of the development process of the interferometer, and in order to determine that it was operating as expected. The result of these measurements was a prototype detector that successfully resolved various two dimensional temperature maps and was ready for application to clinical radiation sources.

Consideration was given to measuring temperatures/doses in terms of absolute versus dose difference distributions. Based on the absolute temperature experiments conducted to date, the present prototype detector is limited to dose differential measurements. Future development of an atmospheric controlled experimental enclosure may allow for absolute dosimetry measurements at some later stage. Future work may also include further consideration of a fibre optic interferometry approach.

The next chapter introduces the concept of heat transport within the test cell, which must be considered in order to ensure the correct interpretation of measured temperature maps when determining absorbed dose from irradiation.
Chapter 5

Heat Transfer Modelling

The impacts of heat transfer must be considered when undertaking any form of calorimetric radiation dose measurements over a finite time interval. As absorbed doses are derived directly from the temperature increases imparted by the radiation, any variations in the temperature field can be a limiting factor on measurement accuracy. This chapter introduces the basic forms of heat transfer, and their relevance to DHI dosimetry. Methods to account for the effects of heat transfer in DHI dosimetry are developed and described.

5.1 Introduction to Heat Transfer

In this context, heat is considered to be thermal energy, which can transfer from one thermodynamic system to another. There are three fundamental modes of heat transfer which are relevant to calorimetry: conduction, convection and radiation [249]. Conduction is the direct microscopic exchange of kinetic energy of adjacent particles, and is also referred to as diffusion in this work. A net flow of heat occurs when there is a temperature differential between two points, in order to reach thermal equilibrium, as described by the second law of thermodynamics. Convection is the transfer of energy due to fluid motion, as bulk flow of a gas or liquid carries heat along with the flow of matter. This process is sometimes also referred to as advection. In calorimetry the relevant type of convection is natural convection where thermal expansion of the fluid in a heated region causes buoyancy forces, establishing a circulation of heat away from the heated region. At times the term convection is used to describe the transfer of heat by both advection and diffusion, as convective heat transfer generally has an element of conduction associated with it. The third relevant type of heat transfer is thermal radiation, which occurs through a vacuum or any transparent medium, transferred by means of the absorption or emission of thermal photons in electromagnetic waves. The electromagnetic waves are generated by the movement of the charged particles (protons and electrons) within the atoms of a heated object.
The most relevant types of heat transfer for DHI dosimetry are heat diffusion and heat convection [74]. The extent to which these phenomena impact the measurement results depends on the specific application and measurement conditions. Ideally, to reduce the impact of heat transport, doses should be delivered at as high a dose rate as possible, and measurement taken concurrently or immediately subsequent to dose delivery. Sufficiently high dose rates are however, depending on the radiation modality in question, not always achievable or clinically relevant. Thus some consideration must be given to the extent of diffusion and convection occurring, and corrections made for the impacts these effects may have on the results.

Radiative heat transfer in the case of DHI pertains to the energy losses at the sides of the test cell. Considering the miniscule temperature increases expected, and the localisation of measurement regions away from the edges of the test cell, for most DHI applications this effect will have negligible impact on the total temperature distributions measured, so has not been considered further in this work.

The next section describes a framework for modelling heat diffusion, and then describes two different methods to account for heat diffusion in DHI radiation dosimetry measurements. The impact of convection on the measurements is not considered, and the effects of this omission will be discussed in Chapter 8.

### 5.2 Heat Diffusion

The occurrence of heat diffusion is unavoidable in DHI dosimetry of spatially varying dose distributions, although in some applications there will be less of an impact than in others. The rate of heat diffusion depends on the temperature gradient between two points, with higher dose gradients resulting in a higher rate of heat diffusion down the temperature gradient (towards temperature equilibrium between the two points). Thus, radiation modalities where there is a higher modulation in the dose will be more affected by heat diffusion. The most obvious example of this is MRT, where the key principle behind the approach is to have highly modulated beams, with the array of microbeams being both extremely close together and with high peak to valley dose ratios. The alleviating factor is that the dose rate is extremely high, so measurements can be made on a short time scale. For a microbeam array, the heating pattern generated by a radiation dose of hundreds of Gray in the peaks has been calculated to dissipate entirely in less than a second. This will be discussed further
in Chapter 8. A therapeutic proton beam is another example that, in this context, could be considered a highly modulated dose distribution, as the Bragg peak is a narrow region of much higher dose than at the depths adjacent to it. A situation where heat diffusion would have the least amount of impact would be an absolute dose measurement of a broadbeam radiation geometry, where the irradiated region is much larger than the measurement region of interest. In this case the temperature distribution will have limited variation over the measurement volume, reducing the impact of diffusion.

Two different approaches are suggested for quantifying and correcting for the impact of heat diffusion, displayed in Figure 5.1. The mathematical framework to describe heat diffusion in three dimensions is common to both methods, which are outlined below in Sections 5.3 and 5.4. Each method has inherent advantages and limitations, which are discussed. Method 1 requires comparison of the measured dose to an independent model of the expected dose distribution. The DHI detector test cell is then described by three dimensional heat equations, which are used to model the heat diffusion that has occurred in the system. These equations are solved numerically, in order to correct the modelled dose data to the same state as the measured data, enabling a “like with like” comparison of the two datasets. Method 2 requires deconvolution of the heat diffusion. This process has many complicating factors that mean it is not possible to achieve to the level of accuracy required for dosimetry. An alternative approach is proposed, involving determining the heat diffusion contribution to each time instance by calculating the heat diffusion of the temperature distribution at the previous time instance. This method is described and has been implemented on simulated data.

5.2.1 General Model of Heat Diffusion

Heat diffusion in a medium is steady if the overall temperature does not vary with time at any point in the medium, whilst transient heat diffusion displays a time dependence. The rate of heat diffusion in a specified direction is proportional to the temperature gradient in that direction [238,249]. The temperature gradient can be defined as the change in temperature per unit length in a given direction. In general heat distribution within a medium is three dimensional and time dependent, and can be written as the scalar quantity \( T = T(x, y, z, t) \). The transfer of heat from any given point is a vector quantity named heat flux. In certain situations the heat conduction in some dimensions is negligible, so this can result in one dimensional, two dimensional or three dimensional heat diffusion problems. Solving heat transport problems in one dimension has a much lower level of complexity so is generally
Figure 5.1: Two approaches to account for heat diffusion. The yellow region indicates data that is available: the measured dose distribution, and a model of the radiation dose (such as a Monte Carlo model). The dotted lines indicate these datasets corrected for heat diffusion. Method 1 involves a forward correction of the modelled data in order to compare the measured data to, whilst Method 2 involves an inverse correction of the measured data to account for heat diffusion.

used to develop an understanding of the principles involved. Solutions to one dimensional problems can often be extended to a three dimensional situation [249–251].

The rate of heat conduction $\dot{Q}_{\text{cond}}$ across an area $A$ between two points in a medium is measured in Watts. $\dot{Q}_{\text{cond}}$ is proportional to both the temperature difference across the medium and the area normal to the direction between the two points, but is inversely proportional to the distance between the points. This is expressed by Fourier’s law of heat conduction (equation 5.1) [238].

$$\dot{Q}_{\text{cond}} = -kA \frac{\partial T}{\partial x} \quad (5.1)$$

In this equation, $k$ is the thermal conductivity of the material, which describes its ability to conduct heat, and $dT/dx$ is the temperature gradient in the $x$-direction, i.e. the slope of the curve on a temperature versus distance diagram, as shown in Figure 5.2(a). The water in the test cell can be considered to be isotropic in nature with regard to $k$ at each location. This is not strictly true, as the value of $k$ depends on the temperature of the water at each location. However given the miniscule temperature changes induced by the radiation the assumption can be considered valid. For a detector operated at room temperature, a dose of 100 Gy, resulting in a nominal temperature increase of 0.024 K would result in a negligible
variation in \( k \) of \(< 0.007\%\) (calculated using thermal conductivity versus temperature values taken from the Handbook of Chemistry and Physics [244]). This value scales proportionately for smaller doses. The water cell is in a state termed \textit{transient} diffusion, because the temperature distribution of the water in the test cell changes as a function of time.

![Figure 5.2: (a) The temperature gradient \( \frac{dT}{dx} \) is the slope of the temperature curve on a temperature versus distance diagram. (b) The heat transfer vector, \( \dot{Q}_n \), is always normal to an isothermal surface and can be resolved into its components.](image)

Because heat is conducted in the direction of decreasing temperature, the temperature gradient is negative when heat is conducted in the positive \( x \)-direction. The negative sign in equation 5.1 ensures that heat transfer in the positive \( x \)-direction is a positive quantity.

For a general relation for Fourier's law of heat conduction in a medium with a three-dimensional heat distribution, consider an isothermal surface within that medium, as shown in Figure 5.2. The heat flux vector at any point \( P \) must be perpendicular to the surface, pointing in the direction of decreasing temperature, \( n \). The rate of heat conduction at that point, in the direction \( x \), can then be expressed by Fourier's law as:

\[
\dot{Q}_n = -k A \nabla T
\]  

(5.2)

In Cartesian coordinates the heat conduction vector can be expressed in terms of its components as shown in Figure 5.2(b) and described by the following equation:

\[
\dot{Q}_n = \dot{Q}_x \mathbf{i} + \dot{Q}_y \mathbf{j} + \dot{Q}_z \mathbf{k}
\]  

(5.3)
where $\vec{i}$, $\vec{j}$ and $\vec{k}$ are the unit vectors, and $\dot{Q}_x$, $\dot{Q}_y$ and $\dot{Q}_z$ are the magnitudes of heat transfer in the $x$-, $y$-, and $z$- directions, respectively. These can be described individually as:

$$
\dot{Q}_x = -kA_x \frac{\partial T}{\partial x}, \quad \dot{Q}_y = -kA_y \frac{\partial T}{\partial y}, \quad \text{and} \quad \dot{Q}_z = -kA_z \frac{\partial T}{\partial z} \quad (5.4)
$$

Here, $A_x$, $A_y$ and $A_z$ are the heat conduction areas normal to the $x$-, $y$-, and $z$- directions, respectively.

The generation of heat per unit volume $g$ within the DHI test cell is a volumetric phenomenon, equal to the absorption of the ionising radiation within a specific volume (less any effects of the heat defect) multiplied by the density of the medium $\rho$ [34]. The total heat generated $G$ is equal to $g$ integrated over the volume, $V$. As the density of the water can be considered effectively constant throughout the test cell, the rate of heat generation $\dot{G}$ (in $W$) is directly proportional to the rate of absorbed dose to water $\dot{D}_W$ (measured in $Jkg^{-1}s^{-1}$).

$$
\dot{G} = V\dot{g} = V\rho \dot{D}_W = A\Delta x\rho \dot{D}_W \quad (5.5)
$$

To develop equations to model the heat transfer, the system is simplified by limiting the direction of heat transfer to one dimension. A thin element of the medium at position $x$, of thickness $\Delta x$ in the direction of heat transfer and cross-sectional area $A$ is considered, as shown in Figure 5.3. This element has mass $m$ and is assumed to have density $\rho$ and heat capacity $C$. An energy balance of this element over a small time interval $\Delta t$ shows that the rate of heat conduction at $x$, less the rate of heat conduction at $x + \Delta x$, plus the rate of heat generation inside the element is equal to the rate of energy change of the contents of the element. This can be expressed as:

$$
\dot{Q}_x - \dot{Q}_{x+\Delta x} + \dot{g}A\Delta x = \frac{\Delta E_{\text{element}}}{\Delta t} \quad (5.6)
$$

The change in energy content of the element can be written by substituting the calorimetric equation (4.14, with $k_{HD} = 1$) to give:

$$
\Delta E_{\text{element}} = E_{t+\Delta t} - E_t = mC(T_{t+\Delta t} - T_t) = \rho A\Delta xC(T_{t+\Delta t} - T_t) \quad (5.7)
$$

Substituting this into equation 5.6 and dividing by $A\Delta x$ yields:

$$
-\frac{1}{A} \frac{\dot{Q}_{x+\Delta x} - \dot{Q}_x}{\Delta x} + \dot{g} = \rho C \frac{T_{t+\Delta t} - T_t}{\Delta t} \quad (5.8)
$$
Figure 5.3: One dimensional heat conduction through a volume element.

Taking the limit as $\Delta x \to 0$ and $\Delta t \to 0$ gives:

$$\frac{1}{A} \frac{\partial}{\partial x} \left[ kA \frac{\partial T}{\partial x} \right] + \dot{g} = \rho C \frac{\partial T}{\partial t} \quad (5.9)$$

since, according to the definition of the derivative [252] and Fourier’s law of heat conduction (equation 5.2),

$$\lim_{x \to 0} \frac{\dot{Q}_{x+\Delta x} - \dot{Q}_x}{\Delta x} = \frac{\partial \dot{Q}}{\partial x} = \frac{\partial}{\partial x} \left( -kA \frac{\partial T}{\partial x} \right) \quad (5.10)$$

With constant values for $k$ and $A$, equation 5.9 becomes:

$$\frac{\partial^2 T}{\partial x^2} + \frac{\dot{g}}{k} = \frac{1}{\alpha} \frac{\partial T}{\partial t} \quad (5.11)$$

where $\alpha = k/\rho C$ is the thermal diffusivity of the medium, representing how fast heat propagates through the material. This equation can be extended to three dimensions, with coordinates as shown in Figure 5.4, and is then known as the Fourier-Biot equation [250]:

$$\frac{\partial^2 T}{\partial x^2} + \frac{\partial^2 T}{\partial y^2} + \frac{\partial^2 T}{\partial z^2} + \frac{\dot{g}}{k} = \frac{1}{\alpha} \frac{\partial T}{\partial t} \quad (5.12)$$

All the equations above were developed using an energy balance on all the interior elements of the medium. No consideration was paid to the thermal conditions on the surface, however these will have an impact on the internal heat flux and temperature distribution. When solving the Fourier-Biot equation for any given system, these surface conditions are included in the calculation as boundary conditions. In general, to give a unique solution for a system with heat transfer, two boundary conditions are required for each dimension of heat transfer. This is equal to the number of arbitrary constants that would be present in a general solution to the differential equation. There are various types of boundary conditions, including specified temperature (for example $T(x, y, z, 0) = f(x, y, z)$), heat flux (with
special cases being an insulated boundary, or thermal symmetry), convection, and radiation, or some combination of these.

Solution of a heat diffusion problem can be done by analytical or numerical methods. An analytical solution results in a solution function of the temperature at each point in the medium. Generally an analytical solution will go through the following process of: 1. Define the heat transfer problem, 2. Mathematical formulation of the differential equation and boundary conditions, 3. Determine a general solution of the differential equation, 4. Apply boundary conditions to obtain a unique solution. However, for three dimensional cases in particular, the partial differential equation can be complex, and often difficult (if not impossible) to determine a solution to [250]. In order to find a solution the approach is limited to highly simplified problems with basic geometries, and thus the approximations required may introduce unacceptable inaccuracies into any solution obtained. Numerical solution methods can achieve sufficiently accurate approximate solutions generated by a computer, without the time consuming and complex process of solving the differential equation [249,250,253,254]. Using a superposition approach called the product approach, a basic one dimensional system can be extended to three dimensions and then solved numerically to achieve a three dimensional approximation. Numerical methods replace the differential equation with a set of $n$ algebraic equations. Simultaneous solution of these equations gives the temperature values at each of the $n$ discrete points. This approach often allows for a more realistic model of the system to be solved compared to an analytical solution, so despite the ‘approximate’ solution output, the result can often be more accurate. The numerical approach to finding a solution for the DHI dosimetry heat diffusion system is described in the following section.
5.2.2 Numerical Modelling

The numerical approach used to solve the heat diffusion problem for DHI is a finite difference formulation using the energy balance method [250, 255–257]. This method does not require having the differential equations before the analysis. In this method, the volume is discretised into a sufficient number of volume elements and then an energy balance is applied to each element. The centre of each volume element is a node where the temperature is to be determined. The edges of each element pass through the midlines between each node. The node represents the average properties of the element in terms of temperature and the rate of heat generation. Figures 5.5(b) and 5.5(a) show the co-ordinate system for nodes and elements, simplified to one and two dimensions respectively.

Initially the numerical approach to a one dimensional situation is presented here, before this is expanded to the three dimensional case required for DHI. The length $L$ of the region is divided into $M$ equal elements of thickness $\Delta x = L/M$ in the $x$-direction, as shown in Figure 5.5(a), with the centre of each element taken as the nodes. Therefore there are $M + 1$ nodes, labelled as $0, 1, 2, \ldots, m - 1, m, m + 1, \ldots, M$, with the $x$-coordinate of any node $m$ being $x_m = m\Delta x$ and the temperature denoted as $T_m$.

![Diagram of finite difference mesh for one-dimensional case](image)

![Diagram of finite difference mesh for two-dimensional case](image)

Because the DHI problem involves a transient temperature situation, the problem must also be discretised in time as well as position. A suitable time step $\Delta t$ is selected and the unknown nodal temperatures are solved at each time instance until a solution at the desired
time is achieved. As $\Delta t$ is reduced the solution becomes more accurate, however there is a corresponding increase in computation time. The superscript $i$ is used as an index of time steps, with $i = 0$ corresponding to the initial state of the system and each time step $i$ corresponding to a time of $t = i\Delta t$. $T_m^i$ represents the temperature at node $m$ at time step $i$.

Then a general difference equation for the interior nodes is obtained by considering the element represented by the node $m$, and the neighbouring modes $m + 1$ and $m - 1$. Taking heat conduction into an element to be positive, the energy balance on the element during $\Delta t$ can be expressed as the rate of heat conduction at the left surface ($\dot{Q}_{\text{cond,left}}$), plus that at the right surface ($\dot{Q}_{\text{cond,right}}$), plus the rate of heat generation inside the element ($\dot{G}_{\text{element}}$), which is set equal to the rate of change of the energy content of the element [249, 250]. This is expressed in the following equation:

$$
\dot{Q}_{\text{cond,left}} + \dot{Q}_{\text{cond,right}} + \dot{G}_{\text{element}} = \frac{\Delta E_{\text{element}}}{\Delta t}
$$

Using the equation for heat generation (5.5) and Fourier’s equation (5.2), the rate of heat conduction towards the node $m$ at the left and right surfaces can be expressed as:

$$
\dot{Q}_{\text{cond,left}} = kA \frac{T_{m-1} - T_m}{\Delta x} \quad \text{and} \quad \dot{Q}_{\text{cond,right}} = kA \frac{T_{m+1} - T_m}{\Delta x}
$$

The change of the energy content of the element is, similarly to the one dimensional case (5.7),

$$
\Delta E_{\text{element}} = mC \Delta T = \rho V_{\text{element}} C \Delta T
$$

where $\rho$ is density and $C$ is the heat capacity of the element.

Substituting equations 5.5, 5.14 and 5.15 into equation 5.13 gives the change in temperature of the node between the time steps $i$ and $i + 1$:

$$
kA \frac{T_{m-1} - T_m}{\Delta x} + kA \frac{T_{m+1} - T_m}{\Delta x} + \dot{g}_m A \Delta x = \rho V_{\text{element}} C \frac{T_{m+1}^i - T_m^i}{\Delta t}
$$

Simplifying by cancelling the surface area $A$ and multiplying through by $\Delta x/k$ results in:

$$
T_{m-1} - 2T_m + T_{m+1} + \frac{\dot{g}_m \Delta x^2}{k} = \frac{\Delta x^2}{\alpha \Delta t} (T_{m+1}^i - T_m^i)
$$

This equation is based on the assumption that the temperature varies linearly across the element, an approximation which becomes increasingly accurate as the distance between
nodes (Δx) and thus the size of the elements is reduced. Note that in the limiting case of Δx approaching zero, the formulation becomes exact and becomes a differential equation.

For simplicity in the computations, the equation can be simplified further by describing a dimensionless mesh Fourier number as:

$$\tau = \frac{\alpha \Delta t}{\Delta x^2}$$

(5.18)

As the nodal temperatures change during each time step, the temperatures from either the previous time step $i$ or the new time step $i+1$ can be used for the left hand side of equation 5.17, called the explicit and implicit methods respectively. Both methods result in approximately the same values for the calculation of $T^{i+1}$ values, however the explicit method is easier to implement but has a time limit on the maximum size time step $\Delta T$ which can be solved. The implicit method has no such time limit but requires all $M+1$ equations to be solved simultaneously. The explicit method is used in the following work, because for an implicit approach, the large number of equations required (equal to the number of pixels sampled) means that a direct method of solving the system of simultaneous equations is computationally prohibitive.

Substituting Equation 5.18 into Equation 5.17, assuming no heat generation and rearranging using the explicit approach to solve for $T_{m}^{i+1}$ results in:

$$T_{m}^{i+1} = \tau(T_{m-1}^{i} + T_{m+1}^{i}) + (1 - 2\tau)T_{m}^{i}$$

(5.19)

Using an implicit solution, the result is:

$$(6k\tau + 1)T_{m}^{i+1} - k\tau(T_{m-1}^{i+1} + T_{m+1}^{i+1}) = T_{m}^{i}$$

(5.20)

This equation is applicable to each of the $M-1$ interior nodes. The two additional equations for the elements at the boundaries (which are half sized) are obtained by using the boundary conditions of the system, which can involve any of specified temperature, specified heat flux, convection and radiation boundary conditions.

The choice of implicit versus explicit solution hinges on the stability criterion for the explicit solution, which limits the largest permissible value of $\Delta t$, in order to prevent the solutions
from oscillating wildly and diverging from the actual solution. The choice of a suitable time interval requires that the coefficients of all $T^i_m$ in the $T^i_{m+1}$ expressions are greater than or equal to zero for all nodes. For the one dimensional situation described by Equation 5.19, the coefficient of $T^i_m$ for all the interior nodes is $1 - 2\tau$, which is independent of mode number $m$, thus the stability criterion requires that $1 - 2\tau \geq 0$, and thus:

$$\tau = \frac{\alpha \Delta t}{\Delta x^2} \leq \frac{1}{2} \tag{5.21}$$

In the three dimensional DHI case, the stability criterion becomes $1 - 6\tau \geq 0$. At 25 °C the thermal conductivity of water is 0.6071 W K$^{-1}$ m$^{-1}$, the density of water at 1 atm is 997.05 kg m$^{-3}$ [244] and for a voxel size of $1 \times 10^{-4}$ m the largest allowable time step becomes:

$$\Delta t \leq \frac{1 \Delta x^2}{6 \alpha} = \frac{(1 \times 10^{-4} \text{ m})^2}{6\left[\frac{(0.6071 \text{ W K}^{-1} \text{ m}^{-1})}{(997.05 \text{ kg m}^{-3})(4181.8 \text{ J kg}^{-1} \text{K}^{-1})}\right]} = 0.0114 \text{ s} \tag{5.22}$$

The limiting factor for an implicit solution is the size of the numerical array required in order to simultaneously solve for the temperature at each point in the system. The solution has a number of elements equal to the square of the product of the dimensions in each direction. Thus for instance for a cube with 10 mm sides, and resolution of 0.1 mm, the size of the three dimensional solution array required is $10^6 = 1 \times 10^{12}$ or approximately $9 \times 10^5$ MB which is computationally infeasible on many systems. MATLAB code to determine the implicit solution was developed in order to compare with the explicit solution, however the largest size three dimensional array that was solvable on the available Department of Physics and Astronomy hpc1 server was 40 by 40 by 40 elements. The code for this is included in Appendix B. There are mathematical methods for decreasing the computational load [258], however implementation of these are beyond the scope of the present work and unnecessary as the explicit approach has proved sufficient. A brief comparison of the output of the implicit and explicit methods is given in Section 5.3.1, but for the ongoing application to DHI an explicit approach was used.

### 5.2.3 Expansion to Multiple Dimensions

The previously described one dimensional numerical approach can be extended to three dimensions by working through the same process described above [249–251]. A three dimensional cubic mesh is applied to the system. The nodes have a coordinate in the $x$, $y$ and $z$ directions denoted as $m$, $n$ and $p$ respectively, with sizes of the cubical volume element in
each direction of \( \Delta \eta \). Equation 5.13 is expanded to describe a volume element, becoming:

\[
\dot{Q}_{\text{cond, left}} + \dot{Q}_{\text{cond, right}} + \dot{Q}_{\text{cond, top}} + \dot{Q}_{\text{cond, bottom}} + \dot{Q}_{\text{cond, front}} + \dot{Q}_{\text{cond, back}} + \dot{G}_{\text{element}} = \frac{\Delta E_{\text{element}}}{\Delta t}
\]  

(5.23)

Expanding equations 5.5 and 5.14 to all dimensions of the volume element, and then substituting these, along with 5.15 into equation 5.23 results in:

\[
k \Delta \eta^2 T_{m-1,n,p} - T_{m,n,p} + k \Delta \eta^2 T_{m+1,n,p} - T_{m,n,p} \\
+ k \Delta \eta^2 T_{m,n-1,p} - T_{m,n,p} + k \Delta \eta^2 T_{m,n+1,p} - T_{m,n,p} \\
+ k \Delta \eta^2 T_{m,n,p-1} - T_{m,n,p} + k \Delta \eta^2 T_{m,n,p+1} - T_{m,n,p} \\
+ \dot{g}_{m,n,p} \Delta \eta^3 = \frac{\rho \Delta \eta^3 C}{k \Delta t} (T_{m,n,p}^{i+1} - T_{m,n,p}^i)
\]  

(5.24)

Solving for \( T_{m,n,p}^{i+1}_x,y,z \), followed by substitution with equation 5.18, as well as choosing an explicit method solution results in:

\[
T_{m,n,p}^{i+1} = \tau (T_{m-1,n,p}^i + T_{m+1,n,p}^i + T_{m,n-1,p}^i + T_{m,n+1,p}^i + \dot{g}_{m,n,p} \Delta \eta^2 k) \\
+ T_{\text{node}} (1 - 6\tau)
\]  

(5.25)

The solution of this equation for each element is straightforward for each location \( m, n, p \).

Following a similar process for an implicit method solution gives:

\[
(6k\tau + 1)T_{m,n,p}^{i+1} - k\tau (T_{m-1,n,p}^{i+1} + T_{m+1,n,p}^{i+1}) \\
+ T_{m,n-1,p}^{i+1} + T_{m,n+1,p}^{i+1} + T_{m,n,p-1}^{i+1} + T_{m,n,p+1}^{i+1} = T_{m,n,p}^i
\]  

(5.26)

The solution to this requires the simultaneous solution of each element within the temperature array.

### 5.3 Method 1: Forward Modelling

The first method used to account for heat diffusion uses a non-direct, comparative approach to correct for heat diffusion via forward modelling of a comparison dataset. The independent model of the radiation modality being measured is corrected for what the temperature distribution at the measurement time would have been, considering both the temperature due
to the dose deposition and the effects of heat diffusion. This method is not novel, and there are commercially available software programs such as the COMSOL Multiphysics software Heat Transfer Module which are capable of such calculations. This is the software used by Seuntjens et al. and Malyarenko et al. for their work on calorimetry [116,234,245]. However, lack of access to such software meant that the computations had to be implemented by hand in MATLAB, and applied to the specific radiation measurements studied. The process used for the calculations is described here, and the code is included in Appendix B.

The independent modelled dose data, referred to from here on as the “dose model”, generally consists of a treatment region divided into voxels at a certain spatial resolution, with the dose represented by the average value of the absorbed dose within each voxel. The voxels correspond to elements in the framework for numerical analysis of the heat diffusion described in the previous section, and each dose value corresponds to the dose at a node. The calorimetric equation, equation 4.14, is used to convert the dose at each node to the equivalent temperature rise expected from that absorbed dose. As the dose is directly proportional to the increased temperature (neglecting any loss due to the heat defect), the temperature field can be calculated before or after applying the heat diffusion analysis. Equation 5.25 is used iteratively to calculate the heat diffused temperature field in time increments of \( \Delta t \).

The heat diffused temperatures of the external/boundary voxels are determined by specifying the temperature to be equal to the interior node immediately adjacent to it. This is justifiable for the DHI test cell, because the change in temperature is minute and relatively far removed from the edges of the test cell where the temperature change is generated. Thus \( T_0 \) is set to be equal to \( T_1 \) and \( T_M \) is set equal to \( T_{M-1} \) for each dimension and at each time instance, rather than solving an equation for these nodes. The result is a set of simultaneous equations that can be solved to determine all the independent variables (internal voxel temperatures) at each time instance.

The heat generation in the system due to radiation (the \( \dot{g}_{m,n,p} \) term in equation 5.25) does not require modelling as a function for inclusion in the equation, but is added as a constant, known temperature change at each time instance. This is possible because the dose is deposited at a constant rate, resulting in a corresponding constant temperature increase. The distribution of this temperature increase is known from the dose model. If the dose model was calculated over a total time of \( t \), then the incremental temperature increase at each point is equal to \( T_{M,N,P} \Delta t \). This allows the simpler approach of determining the change in temperature of each node after each time period \( \Delta t \) by summing the corresponding temperature
distribution due to the radiation deposition to the calculated $T^{i+1}$ values from the previous time instance. This process is conducted iteratively until the total time $t$ is reached. The entire array of nodes is termed $T_i$, with superscripts $UC$ (uncorrected) and $C$ (corrected) used to indicate if the temperature array is directly as measured, or whether the heat diffusion equations have been applied. The subscript $i$ refers to the time instance. The term $T_i^{UC}$ is therefore the incremental temperature increase due to radiation. The heat diffusion calculation is represented by the function $F(T)$, shown in equation 5.27.

$$T_i^C = F(T_i^{UC}) = \begin{cases} f(T_i^{UC}) + T_i^{UC} & \text{if } i = 2 \\ f(T_{i-1}^C) + T_i^{UC} & \text{if } i = 3, 4, \ldots, \frac{t}{\Delta t} \end{cases}$$ (5.27)

The overall process was implemented in MATLAB using the following steps:

**Step 1:**
Initialise a three dimensional array with the volume and resolution required to give sufficient comparison data to the measured data. Smaller voxels will increase accuracy, with the lower limit on voxel size being the resolution of the dose model data. The size of the volume is limited by the size of the modelled dose data, but should ideally be at least equivalent to the size of the test cell. If this results in a number of equations that is computationally unfeasible to solve, the resolution can be reduced or the size can be reduced in the plane orthogonal to the laser beam. The model size must always at least encompass the entire measurement data region. Size reduction should be done with the awareness that there is a reduction in accuracy closer to the perimeter of the calculated volume.

**Step 2:**
Select a suitably small time step for $\Delta t$. This may have an upper limit, if the explicit method for solving the equations is used. A smaller time step will increase the accuracy but also the computation time.

**Step 3:**
Calculate $T_1^{UC}$ from the dose model.

**Step 4:**
Starting with this temperature distribution as $T_i$, apply the heat diffusion equations to each point within the three dimensional array, and add another $T_i^{UC}$ to determine
$T_{i+1}^C$, according to equation 5.27. Any external voxel should have $T_{i+1}$ set equal to the $T_i$ of the closest internal voxel.

**Step 5:**

Using a `for` loop, repeat step 4 until the total measurement time $t$ is reached.

**Step 6:**

Determine the magnitude of the dose which would have caused the temperature values achieved, by conversion using the calorimetric equation. Compare the heat corrected dose model to the measurement results. A direct comparison requires an integration of the modelled data across the width of the test cell in the direction of the laser.

### 5.3.1 Application to Radiation Dose Distributions

The method described above was applied to the dose models of an HDR source and a proton beam. Details of the dose models are described in the following chapters specific to each of the radiation modalities (Chapters 6 and 7). For the purposes of developing the heat diffusion modelling it is sufficient to have modelled dose distributions which approximate the magnitude and configuration of a possible measurement, with the specific parameters set to generic values. The effects of various parameters in the model were analysed to evaluate the model and determine its limitations.

**Heat Diffusion of Proton Beam Model**

The proton beam model used is a Monte Carlo model of the relative dose distribution of a small field proton beam of 2.0 mm full width half maximum, which is being developed for radiobiology research at the University of Washington [259]. The voxel resolution is 0.1 mm in each direction. The model was calculated as a relative dose distribution because the absolute doses delivered from the cyclotron with the particular settings used for the DHI tests were not well characterised at the time of measurement. An example of heat diffusion of the proton beam model is shown in Figure 5.6. The actual temperature differences are displayed in Figures 5.6(a) and 5.6(b), showing axial and transverse profiles through the peak position. Figures 5.6(c) and 5.6(d) show the same data normalised to the peak temperature, and Figures 5.6(e) and 5.6(f) display two dimensional plots of the average temperature in the direction of the laser for the whole field of view. The normalised plots demonstrate that the heat diffusion causes the peak position in the temperature distribution to be closer to the entrance point by 0.4 mm (for this particular dataset).
Figure 5.6: Example of the temperature distribution of a heat diffused proton beam with peak dose of \( \sim 200 \text{ Gy} \) averaged over the width of the test cell, where the black line is the original beam model and the red is the comparative heat diffused model after a 17 s irradiation. (a) Profile orthogonal to beam direction, through the peak position, (b) profile along the beam central axis, (c) and (d) the same data normalised to the peak position, (e) and (f) two dimensional plots of the distribution respectively without and with heat diffusion modelling applied.
The determination of the absolute temperature difference from a model that only represents the relative doses requires some knowledge of the absolute dose expected. For the proton data an absolute peak dose was approximated for the measurement conditions used. In step 3 of the process above, the peak dose is used to determine the dose rate for a given measurement time, allowing for the calculation of a temperature increment over each time interval chosen. The choice of absolute peak dose is based on the parameters used in actual measurements, however if this is estimated incorrectly then the heat diffusion calculation will not match the measured result. The error in the dose translates to the same percentage error in temperature at each point in the volume. This means that, if the data is normalised to give relative temperature differences, the heat diffused models arising from different peak doses are in agreement, as long as all other parameters are the same. This is demonstrated in Figure 5.7 for a 5% variation in peak dose.

![Figure 5.7](image)

Figure 5.7: Example of the resulting heat diffused model after the input dose was increased by 5%. The black line shows the heat diffused temperature distribution along the central axis at 200 Gy peak dose, and the red dots are at 210 Gy. (a) The absolute temperature differences, showing a 5% variation at each point. (b) The normalised temperature distributions showing the relative temperature distribution is unaffected by the estimated input dose.

Only achieving relative temperature differences is obviously a limiting factor for this approach, as the absolute dose is not always known for an experimental measurement. However, if the relative temperature distribution of measurement and heat diffused model is in agreement then an absolute dose can be determined iteratively by finding an initial dose that would result in a temperature distribution as measured. This process is covered in Chapter 7.
Heat Diffusion of HDR Source Model

The HDR brachytherapy source model used was the treatment planning system BrachyVision™ (Varian Medical Systems, Palo Alto, California, USA), with voxel resolution of 0.5 mm in each direction. More details of the model are given in Chapter 6. The dose distributions predicted by the model were converted to temperatures using the calorimetric equation (4.14), then the heat diffusion model was applied. For the initial proof of principle the influence of the non-water materials in the applicator were not considered. For short irradiation times this is not anticipated to have a large effect on the result, but should be considered in future work. An example of heat diffusion of the model is shown in Figure 5.8(d) for a 20 second irradiation by a source with activity 4.6 Ci. Unlike the proton beam, the absolute dose for a given irradiation time is known to sufficient accuracy for the HDR source, so the dose/temperature differences can be reported directly, rather than as values relative to some reference point. As expected, the heat diffusion results in a greatly reduced peak dose, with increased doses further from the peak. The radial distance away from the source at which the heat diffused dose shifts from lower than the non-heat diffused dose to higher, depends on the source activity and the irradiation time. In the example given in Figure 5.8(d) this occurs at 2.3 mm from the centre of the source, or 0.7 mm outside of the applicator. It should be noted that with a voxel resolution of 0.5 mm there is some considerable smoothing of the dose from the real shape especially around the peak, which introduces some uncertainties to this crossover point.

Sensitivity Analysis of Heat Diffusion Parameters

There are various parameters involved in the calculation of heat diffusion by the above method, and potential areas where an incorrect selection of parameter value may cause unnecessary uncertainty to be introduced to the result. These areas were investigated and are presented here. The proton beam model is used to demonstrate these effects as the model is known to higher resolution, thus small effects are more apparent and can be more accurately quantified.

Time Step

The key parameter when calculating heat diffusion in this fashion is the size of the time step, \( \delta t \) which is selected. The upper limit on the size of the time step when using an explicit calculation method is given in equation 5.21. For the proton beam model data, with voxel dimensions of 0.1 mm in each direction the maximum time step is 0.0114 s, as calculated in equation 5.22. If a value larger than this is chosen, the result oscillates wildly, diverging from
Figure 5.8: Example of the temperature distribution of a heat diffused HDR source model (activity 4.6 Ci, irradiation time 20 s) averaged over the width of the test cell, where the black line is the original source model and the red is the comparative heat diffused model. (a) Profile across the applicator at the source position, (b) normalised to the peak dose at the source, (c) and (d) two dimensional plots of the distribution respectively without and with heat diffusion modelling applied.
the actual solution, as shown in Figure 5.9 for a $\delta t$ of 0.02 s. A longer time step within this constraint is the most efficient as the heat diffusion is calculated after each time interval up to the total irradiation time, however the ideal solution is obtained as the time step reduces to zero. Thus 0.01 s was chosen as the base value for the time step. This was compared to shorter time steps to quantify any introduced variation in the results. Errors are attributable to two factors. The first factor is the discretisation of the dose into time-step increments, which means any heat diffusion of the dose increment in this time is not included. This effect is generally negligible for the time scales considered. The use of a longer time step has the highest impact in the peak region where heat diffusion is the most rapid, resulting in an overestimation of dose, and there is a slight underestimation in the regions surrounding the peak. The second factor is in the calculation of the heat diffusion, and in particular the assumptions made for the boundary conditions. A longer time step results in a slight overestimation of dose close to the boundaries. An example is given in Figure 5.10 of the variation in the heat diffused model (averaged across the test cell) for a time step of 0.001 s compared to 0.01 s. The maximum percentage temperature difference at any point in the medium is -0.18%, whilst the mean discrepancy is 0.0022% with a standard deviation of 0.0010%. The spatial variation across the two dimensional temperature difference map agrees with the theory above for what impact the time step will have. In the context of this preliminary proof-of-principle study, and in the interests of computational efficiency, this introduced uncertainty is considered acceptable as it is negligible when compared to the total uncertainty burden, thus $\delta t = 0.01$ s time steps was used henceforth.

Figure 5.9: The impact on the heat diffusion model of using a time step larger than that calculated by the stability criterion, $\delta = 0.02$ s. (a) The profile through the peak position of the proton beam model, (b) the central axis of the proton beam model.

**Thermal Conductivity**
Figure 5.10: Comparison of a heat diffused proton beam model calculated with $\delta t$ of 0.01 s compared to 0.001 s. (a) The central axis dose averaged across the laser path through the cell, with the black line showing 0.01 s and the red line 0.001 s. (b) The percentage difference of the two dimensional temperature maps generated with each time step value.

Another parameter in the heat diffusion calculation that is important is the value chosen for the thermal conductivity of water, $k$. Whilst it was stated in Section 5.2.1 that the water can be considered isotropic with regard to $k$, because the radiation induced temperature variations are small enough to have a negligible impact on the value of $k$, it is still imperative to input an accurate value of $k$ to the calculations. $k$ values are temperature dependent, and varying the temperature of the water (in equilibrium with the ambient room temperature) by 1 K varies $k$ to the extent that it impacts on the heat diffusion results. An example is shown in Figure 5.11 for varying the temperature between 21 °C ($k = 0.6001 \text{ W m}^{-1} \text{ K}^{-1}$) and 22 °C ($k = 0.6018 \text{ W m}^{-1} \text{ K}^{-1}$). This results in a maximum difference of 1.2% with a mean difference of 0.28% and standard deviation 0.04%.

Thus it is important to measure the water temperature for a given measurement as accurately as possible, or measure the room temperature and ensure that the water in the test cell has sufficient time to equilibrate before irradiation begins. The $k$ value for any given temperature has been obtained by fitting a quadratic curve to $k$ versus $T$ values, as shown in Figure 5.12 [244]. With a temperature uncertainty of ±0.2 K the corresponding mean error introduced to the heat diffusion model is on the order of 0.055% with a standard deviation of 0.007% and a maximum of 0.20%. These values can vary slightly depending on the model data and calculation parameters.

**Model Dimensions**

The size of the model used for the heat diffusion calculation is important because of the
Figure 5.11: Demonstrating the impact of a change in ambient water temperature on the heat diffusion model, via the impact on the thermal conductivity of water. (a) The central axis of the heat diffused proton beam model, where nearly no change is noticeable with the 21 °C case shown in black and the 22 °C case in red. (b) The corresponding two dimensional temperature difference map showing that the largest impact is near the edges of the field.

Figure 5.12: Thermal conductivity of water as a function of temperature. Black points are the data [244] and the red line is the quadratic fit used, with a corresponding equation of $k = -9.37e^{-6} T^2 + 0.00212 T + 0.56$
approximations made around the edges of the model. The model must therefore be considerably larger than the size of the sensitive region of the test cell to ensure that the edge region in the heat diffused model does not overlap with the measured data when the two are compared. The HDR brachytherapy model was used for this comparison as a larger dataset was available, allowing for the heat diffused model to be closer to the “ideal” solution for variation of this parameter. A comparison of a 20 second irradiation heat diffused HDR model which extends 50 mm in each direction from the source location to one which extends 6 mm in each direction is shown in Figure 5.13. As expected, the error in the smaller volume is around the edges of the model. The mean dose difference in the smaller volume is 10.6% with a maximum of 48.6% error. This large error however is negligible in a region that is at least 3 mm in from each edge, reducing to a mean error of just 0.19% which is acceptable in the context of the overall uncertainty budget. So the model data must extend at least 3 mm in each direction past the DHI measurement volume.

Figure 5.13: The effects of determining the heat diffusion over a smaller region, shown for the HDR source. The black line is the model calculated over 50 mm in each direction from the source, and the red points for a model extending 6 mm in each direction. (a) Profile through the source. (b) The corresponding two dimensional temperature difference map showing that the largest impact is near the edges of the field.

**Absolute Dose**

The dose models are input with a certain absolute dose value and the heat diffusion is calculated over the measurement time period. If there is an error in this measurement period it affects the calculated dose rate which impacts on both the total input dose entered and the heat diffusion. For the proton beam, for a 5% increase in the input measurement time from 17.0 s to 17.85 s the mean error introduced to the heat diffused proton beam model is 4.9%, with a maximum of 21%. The uncertainties however are predominantly towards the
edges of the calculated temperature map, as shown in Figure 5.14. A reduced region of the calculated temperature map is also displayed in this figure, extending 2 mm to either side of the central axis of the beam and from 30 mm to 90 mm deep. This corresponds to the same size as the DHI detector sensitive area. In this region the mean error from the 5% time error is reduced to 0.51% with a maximum of 2.8%. These are much reduced, but still notable, so it is paramount to achieving accurate measurements that the correct measurement time is input into the system with as little uncertainty introduced as possible.

Figure 5.14: Effect on the heat diffusion model of having an error in the measurement time period. This figure shows the two dimensional difference map for a 5% error in the input time. (a) The full model region, with reduced region indicated in red, (b) the reduced region shown in (a) corresponding to the size of the DHI measurement sensitive region.

**Positioning**

An experimental parameter which can introduce uncertainties is in the localisation of the position of the irradiation region within the cell in the direction parallel to the path of the laser. This position is not visible in the final recorded images, thus cannot be validated during the analysis process. This is unlike the position in the other two dimensions which can be confirmed on the measurement images. For the proton beam measurements this localisation is more difficult as there is no physical object in the beam, but the error introduced by positional uncertainty is minor because the beam is relatively narrow compared to the width of the test cell with steep fall-off away from the central axis. An example is shown in Figure 5.15 where the proton beam model is shifted by 1 mm within the test cell. The mean error introduced is 0.036% with a standard deviation of 0.027%. As anticipated, the difference is higher towards the edges near the surface entrance side of the beam, where the overall integrated dose is lower so the percentage difference is higher.
Figure 5.15: The difference in the heat diffusion model if the proton beam location is displaced by 1 mm in the direction of the laser path. (a) The proton beam central axis, where black is when the model is centred in the test cell, and red is when it is displaced by 1 mm. (b) The corresponding difference map.

The localisation of the physical position of the applicator means the HDR brachytherapy measurements have less positional uncertainty, but the introduced error is relatively higher than for the proton beam because the dose drop off is less steep further from the source. An example of a 1 mm shift in position of the HDR model is given in Figure 5.16. The mean dose difference is 0.90% with a standard deviation of 0.075%. As for the proton beam, the difference is higher further from the region of peak dose.

Figure 5.16: The difference in the heat diffusion model if the HDR applicator is displaced by 1 mm in the direction of the laser path. (a) A profile through the HDR source, where black shows the applicator centred in the test cell, and red a displacement of 1 mm. (b) The corresponding difference map.
5.3.2 Efficacy of the Method

The above sensitivity analysis has shown that heat diffusion can be accurately calculated to a level of uncertainty sufficient for use in DHI dosimetry, provided attention is paid to the measurement and calculation parameters used. The heat diffusion model was further validated using experimental data. Preliminary HDR source measurements showing agreement with modelled data, upon implementation of the heat diffusion model, with results presented in Chapter 6.

5.4 Method 2: Quasi-Inverse Modelling

The second method implemented for accounting for heat diffusion in the DHI measurements is based around an inverse correction of the measured data to enable it to be compared directly to the model. This idea is intuitively appealing, as it allows for the DHI results to be used without the need for an independent dose model. However there are many difficulties to achieve this approach which mean it is unlikely to be a stand-alone method. The most feasible way of implementing this concept is proposed here, based on a quasi-inverse approach.

The temperature distributions measured in DHI are characterised by a gradual smoothing of the initial temperature distribution by the flow of heat from warmer to colder areas. On the surface, this would appear to involve a deconvolution of the measurement with a heat diffusion kernel. However the difficulties in this approach are that the extent of the heat diffusion at each time instance is dependent on the state of the system, so therefore the kernel is spatially and temporally variant. This makes the calculation both complex and computationally prohibitive. Additionally, there is degeneracy in the solution, as different starting points can tend to the same equilibrium position. This means that taking a single state of the system and attempting to deconvolve the heat diffusion to determine an earlier state results in a range of possible solutions. Determination of the correct solution would require input of features of the expected result. This process risks selection bias in the final solution to agree with the expected result, and is therefore not necessarily reliable.

An alternative approach was instead taken, which approximates the solution by iterative forward correction of a series of measurement images. The result achieves a measured dataset which is corrected to allow for a direct comparison to the model, hence the description of this as a “quasi-inverse” approach. The theory behind this approach is described in Section
5.4.1. The key mathematical algorithms required to implement it are introduced in Section 5.4.2. In order to analyse the efficacy of this approach the method was implemented on simulated data, and various limitations were determined, which are discussed in Section 5.4.3.

5.4.1 Description of Approach

The basic theory underlying Method 2 is to determine the rate of incremental dose deposition throughout the irradiation time. Accumulation of the incremental doses results in the total dose and its distribution. This method is based on the theory that for any given time instance $t_n$ the temperature map is a result of the heat diffusion of the temperature map at some previous time instance $t_{n-1}$ plus the dose deposited in the intervening time interval.

The aim is to separate these two components so that the absorbed dose can be isolated to be quantified independently of the heat diffusion. By taking the image at $t_{n-1}$ and forward calculating the expected effects of heat diffusion, it is then possible to subtract this value from the image at time $t_n$, and obtain the incremental increase in temperature $T_1$ for each time period $t_n - t_{n-1}$.

The data consists of a series of reconstructed images which represent the temperature distribution at each point in time. The shortest possible time interval $t_n - t_{n-1}$ should be used, in order to reduce variation in the diffused temperature map due to dose deposited during the intervening time. The minimum time interval achievable is dependent on the frequency of image acquisition, $f$. This is a balance between the maximum frame rate achievable by the sensor, and the need to achieve an acceptable signal to noise ratio, and should be carefully selected. Adjacent images should then be analysed. Analysis using larger time intervals can be achieved by examining two or more pictures that are multiple frames apart, in order to estimate the extent of the errors induced by this discretisation approximation which incompletely considers the conductive effects. Therefore the values of $t_n$ represent the time instances of image $n$, where $n = 1, 2, \ldots t \cdot f$, where $t$ is the total measurement time and the actual time for each image is calculated by $\frac{n}{f}$. The final temperature array is therefore referred to as $T_t$.

The Method 2 function used for calculating heat diffusion is shown in equations 5.28 and 5.29. This method incorporates the heat diffusion function $F$ from Method 1 equation 5.27. Note that the subscripts $C$ and $UC$ for corrected and uncorrected temperature matrices refer
to correction of the measurement data rather than the model. So in contrast to Method 1, $T^C$ refers to a temperature array which has been corrected for the effects of heat diffusion, while $T^{UC}$ is the original measured temperature distribution.

\[ T_1 = T_n^{UC} - T_{n-1}^C = T_n^{UC} - F_{n-1}(T_1^{UC}) \]  (5.28)

\[ T_i = \sum_{n=1}^{t_f} T_i \]  (5.29)

To accurately calculate the effects of heat diffusion the three dimensional temperature distribution must be known. However each image in the series of measured DHI images is the two dimensional projection of the temperature distribution in the test cell. Thus in order to use this approach, it is necessary to approximate a three dimensional temperature distribution from each of the measured images in the series. This limits the approach to use in situations where symmetry in the geometry of the radiation dose distribution allows for approximation of three dimensions from a two dimensional map. Both of the approaches presented in this work can be assumed to possess cylindrical symmetry about a central axis. Generally the way that HDR sources are fabricated in terms of their core and encapsulation results in effective cylindrical symmetry of the dose distribution to their longitudinal axis [37]. The proton beam, after passing through a circular collimator, can be assumed to have cylindrical symmetry about the central axis. Cylindrical symmetry allows for a mathematical formulation called the Abel transform to be used to convert the projection map from two to three dimensions [260].

### 5.4.2 Implementation of the Abel Transform

The Abel transform is an integral transform, which is often used for the analysis of spherically or cylindrically symmetric functions [260]. The forward Abel transform is used to project a symmetric three dimensional function onto a plane. The reverse Abel transform is used to calculate the radial cross section from a projection across that area. This is the process which is relevant to the current problem. In the case of cylindrical symmetry, the function can be used in its two dimensional form, and applied to one line of the projection image at a time, in order to build up an approximation of the full three dimensional function.
An example of the geometry for a two dimensional Abel transform is shown in Figure 5.17. Given a function, $f(r)$, with radial dimension $r$ and longitudinal dimension $y$, the two dimensional forward Abel transform is described by equation 5.30 [260].

$$F(y) = 2 \int_{y}^{\infty} \frac{f(r)r \, dr}{\sqrt{r^2 - y^2}}$$  \hspace{1cm} (5.30)

The reverse Abel transform is correspondingly shown in equation 5.31, converting the line of sight projection back into the radial function.

$$f(r) = -\frac{1}{\pi} \int_{r}^{\infty} \frac{dF}{dy} \frac{f(r)r \, dr}{\sqrt{r^2 - y^2}}$$  \hspace{1cm} (5.31)

The radial function can then be converted into the two dimensional plane by assuming symmetry about the origin, and using the relationship between polar and Cartesian coordinates, shown in equation 5.32.

$$r = \sqrt{x^2 + y^2}$$  \hspace{1cm} (5.32)

Figure 5.17: Example of the geometry of the two dimensional Abel transform. The observer looks along a line $I$, parallel to the x-axis, at a distance of $y$. They see the line of sight projection of the circularly symmetric function $f(r)$.

The use of this expansion to mathematically obtain a radial distribution from a two dimensional projection is fundamental for Method 2 of the heat diffusion calculations. It is also useful for interpretation of measured DHI results, with the assumption of symmetry allowing the results to be presented in a format that is more familiar when compared to alternative dosimetry systems. The Abel transform is referenced in the results section of the HDR measurements due to its usefulness in determining radial dose functions for comparison of results according to established dosimetry protocols.
The numerical implementation of the inverse Abel transform is not straightforward, due to
the presence of the derivative of the projection function. Numerical differentiation tends to
amplify noise, which is of concern for the relatively noisy data achieved with the current
DHI detector. There are various methods of implementing this function to improve this.
A conventional approach is to convolve the derivative of a Gaussian with the function we
wish to differentiate and then perform an inverse transform to recover a smoothed numerical
derivative. A similar approach uses an iterative Fourier-Bessel expansion. MATLAB code
for both of these approaches was written and implemented on simulated test data. A third
approach, which was the selected approach for further work for DHI, was a Fourier-based
algorithm, as proposed by Pretzler [261,262]. This approach is based on fitting the measured
profile to a set of cosine-based expansion integrals. The Pretzler approach is less prone to
error in the determination of the object centre, and relatively insensitive to noise [262]. The
algorithm has already been implemented in MATLAB, with the code for the abel.m made
available through the MATLAB file sharing website www.mathworks.com [263]. These m-
files were checked against simulated data, and found to be operating correctly. The approach
was found to be more accurate than the other two at reproducing the original distribution
of simulated data.

The Pretzler approach incorporates a series expansion, with a lower frequency limit of 1,
and the upper frequency limit selected to control the level of noise filtering required. This
parameter defines the number of cosine expansions used. Lower values act as low pass filters,
reducing the noise, but also potential features of the image. Higher numbers also increase
the computation time. By analysis of the modelled proton beam data an upper frequency
of 20 was selected, however for noisy data this may need to be reduced.

5.4.3 Implementation of Method 2

The Method 2 approach for calculating the heat corrected temperature/dose distribution was
developed using simulated proton beam data. The Monte Carlo beam model was modelled
for heat diffusion as described in Method 1. The result was then converted into projections,
in the form that would be recorded by DHI measurements. This process has no noise intro-
duced, so it is an idealised dataset. It would be possible to add noise if further exploration
of the limits of accuracy in a controlled condition was to be explored. The calculation of
Method 2 equations 5.28 and 5.29 were applied in MATLAB, in an attempt to reproduce
the original MC model. The process is split into the following steps:
Step 1:

Determine the axis of symmetry of the data. For instance, assuming a horizontal axis of symmetry, e.g. for the proton beam and for horizontal location of the HDR applicator, find the horizontal line within the image with the maximum values. This is assumed to be the central axis. Due to the symmetry of the Abel transform reconstruction only data on one side of this line is included. If the central axis is offset from the center of the image, then the side with the most data is chosen. For an HDR source, if the line of maximum dose is not horizontal, this could be due to the source not being straight within the applicator. If the data has been smoothed sufficiently, then the maximum point in each vertical line can be used for the Abel transform, but care should then be taken to align the images correctly for the heat diffusion calculations.

Step 2:

Decide the calculation parameters. A frequency of 5 Hz was used for the current DHI measurements, so the time interval between images is 0.2 s. The next parameter is the measurement time of interest, $t$: this may be the entire irradiation period, or some shorter interval within that. The other key parameters are those used for the heat diffusion calculations, as described for Method 1 in Section 5.3. A value of $\Delta t = 0.01$ s was used for the heat diffusion calculation time interval.

The following steps 3-6 are conducted for every time instance for $n = 1, 2, \ldots, t \cdot f$.

Step 3:

Apply the Abel integral to the data, one projection at a time. The result must be divided by two, as the algorithm assumes data is only integrated from central axis, not across the whole width of the beam.

Step 4:

Create rotationally symmetric outputs of each projection of the Abel transform. Stack these to achieve a three dimensional dataset of the temperature distribution, $T_{n}^{UC}$. This is effectively a reconstruction of the temperature in the whole sensitive volume of the test cell system, including the influence of heat diffusion. Crop the image to match the original dataset size (required if the central axis of the beam was non-central in the image).

Step 5:

Calculate the heat diffusion for each image, $F_{n-1}(T_{n}^{UC})$, over the time increment until the next image.
Step 6:
Determine the iterative temperature change between each image, $T_I$ by subtracting each heat diffused image from the subsequent measured image prior to calculating the heat diffusion $T_{UC}^n$.

Step 7:
Calculate the cumulative dose, by summing the series of $T_I$ over the measurement time. The result is a final temperature/dose map, corrected for heat diffusion. If the dose rate is constant, then each of the increments should be equal. This redundancy allows for statistical analysis to estimate the uncertainty in the final result by analysing the standard deviation for the total dose at each pixel, with variation arising from noise in the original measurement images.

Step 8:
Compare the result with the original model data, or to alternative dosimetric measurements.

The process is extremely computationally intensive, due to the size and quantity of datasets being processed. Steps 3 - 5 are completed for each image within the irradiation time period of interest. For each, the Abel transform is applied, rotational symmetry determined, and then the heat diffusion calculated. This process can be on the order of 20 minutes or more per time instance, so the overall calculation can take several hours. This limits the practical application of this approach.

5.4.4 Efficacy of Method

Using simulated data with no noise as both the measurement data and the original model, it should be theoretically possible to obtain close to complete agreement between the inverse corrected result and the input data. However this is prevented by several factors. The first factor, is the presence of losses due to the finite size of the time increment used for the Method 2 calculations. As the irradiation time increases, there is a relative increase in the extent of influence of heat diffusion compared to the radiation dose deposition. This means that the loss of accuracy due to this effect increases with time. The other main factor is the introduction of errors by the use of the Abel transform, particularly for the shape of the dose distributions studied. The inability to correctly reproduce the three dimensional function from the two dimensional projection severely limits the applicability of this method. As the
method relies on an accumulation of small dose contributions at each time instance, the error was relatively low for any one increment of dose but became excessive for the total calculation. In fact, with the current algorithm used for the Abel transform, the variation is such that errors in the three dimensional distribution are actually greater than the incremental temperature difference. Thus the results have discrepancies which means that the feasibility of this approach for actual DHI measurements is low, unless the following problems can be solved.

The Pretzler algorithm for numerically implementing the Abel transform was the best of the three approaches attempted, however in regions of steep variation in the dose gradient the result does not manage to completely conform. Unfortunately, the proton beam profile is sufficiently varied across the measurement region so as to encounter this problem, with an example is shown in Figure 5.18. The agreement in the rest of the volume is reasonable, however due to the iterative nature of Method 2, when small discrepancies are cumulatively summed to determine the total dose, there is considerable disagreement with the true value. This is particularly the case in the peak region, but also affects the shape of the entire dose distribution. The noise level achievable with the current measured DHI datasets would exacerbate this problem.

Further discussion of the use of the Abel transform is included in Section 8.3.3, with analysis into the specific limitations. References to newer algorithms which claim to improve on some of the shortcomings of the Pretzler algorithm are provided. In future work, these new algorithms could be trialled for the DHI measurements, to determine whether there is scope to improve this approach sufficiently to make it a useful technique for DHI dosimetry of proton beams and HDR sources.

The method was also tested without the use of the Abel transform, to determine whether that is the only limiting factor. This was done by repeating the process, but omitting the initial step where the model test data was projected across the test cell region and then reconstructed to three dimensions. Method 1 was applied to the original three dimensional model data to determine the expected heat diffusion. Then Method 2 was applied to see whether the original data could be recreated, and to estimate the extent of the accuracy of this approach, for the measurement conditions. Figure 5.19 shows an example of a 5 s proton beam irradiation, with a frame rate of 5 Hz. The figure shows the Method 2 reconstructed dose compared to the expected dose if heat diffusion had not occurred, and in the absence of
Figure 5.18: Abel transform of simulated proton beam data demonstrating the difficulty in reproducing regions of steep dose gradient variation. (a) Central axis dose map of the original data for comparison, (b) the corresponding integrated and then Abel transformed dose map, (c) central axis profiles of the original (black) and Abel transformed data (red), (d) a similar cross plane profile through the peak position, and (e) a cross plane profile at 1 mm depth.
any noise. The results show that the agreement between the two dose distributions is higher in regions away from the peak dose. However the disagreement in the peak region is high enough that the current experimental conditions need improvement in order to make this approach suitable for accounting for heat diffusion.

The addition of noise to the model, by adding random noise of ±0.5 Gy to each pixel in the original model, increased the discrepancies further. However increasing the frame rate of the camera in the model, and decreasing the total image acquisition time improved the results considerably. This is expected, because the method is limited by the influence on the changing temperature field due to heat diffusion compared to radiation deposition, particularly as the irradiation period increased (the degree to which this effect occurs is explored further in Section 8.2.1). These are experimental improvements which can be made, with care taken to achieve a suitable balance between improvement of these aspects, and decreasing the signal-to-noise ratio.

![Figure 5.19: An example of the Method 2 heat diffusion calculation, when a three dimensional dose distribution is used as the starting point so the Abel integral is not required. (a) The central axis plane of the dose model without any heat diffusion applied, for a 5 s irradiation with a DHI frame rate of 5 Hz; (b) the expected distribution after application of Method 2 to correct for the effects of heat diffusion; (c) the dose difference between the two models.](image)

Overall, the results of shown in Figures 5.18 and 5.19 suggest that Method 2 has some considerable obstacles to overcome before it has any possibility as a viable option for DHI dosimetry heat diffusion corrections. It is shown to be possible to approximately quantify
the extent of heat diffusion in the measured results, however care must be taken with the experimental situations to which this method is applied. Currently this approach is limited to the measurement of dose distributions which do not have steep dose gradients. In these situations however, heat diffusion has a lower influence on the measured temperature map. The use of Method 2 could potentially improve accuracy for these conditions, if it proves necessary. For situations with a more modulated dose, Method 2 will not currently allow the true dose distribution to be accurately determined from the measurement. Varying the experimental parameters as described above may help with this. Additionally, for highly modulated doses, a mathematical algorithm which is more robust towards steep gradient variations and noise than the Abel integral is required. Alternatively, to avoid this step, a first order approximation could be used based on approximating the effects of heat diffusion directly on the two dimensional projection images. This could be done by a two dimensional heat transfer calculation and the use of a proportionality constant to account for contributions from out-of-plane regions. For data such as the HDR source, where the dose gradient is predominantly in one direction, this approximation could have some degree of accuracy. This would also avoid another uncertainty in the DHI HDR correction, where the sharp edge in the image created by shading from the applicator results in an incorrect Abel reconstruction in that region.

5.5 Concluding Remarks

Calorimetric based measurement processes must consider the impact of heat transfer on the measured results. The basic mechanisms of heat transfer have been described, and the mathematical formulations for considering the extent of heat diffusion were introduced.

Two different approaches were developed to account for heat diffusion in the DHI measurement process. Method 1 is a forward correction of the model comparison data, to allow a “like with like” comparison with the form of the measured data. This approach was successfully implemented, and was found to introduce a total uncertainty on the order of 0.75% to the interpretation of DHI measurement results. The fundamental limitation of this approach is that it relies on a set of model data to compare to, so measurements can only be used in conjunction with a model or alternative measurement approach. Method 2 is based on an inverse correction of the measured data to remove the effects of heat diffusion. The approach was to iteratively determine the dose deposition rate by comparison of the calculated heat diffusion in subsequent measurement images. This approach is appealing because it removes
the dependence on an alternative dosimetry system, which would increase the versatility of the DHI results. However Method 2, whilst theoretically possible, was limited by the constraints of the Abel integral and the cumulative nature of the calculation, with these effects resulting in discrepancies that render this approach infeasible at this time for radiation distributions with high variation in dose gradients. Improvements to the mathematical algorithms used for reconstructing the three dimensional dose, experimental reduction of the noise and increase in the image acquisition frequency may allow for reconsideration of this method in the future. The implementation of a three dimensional measurement acquisition method such as tomographic imaging would eliminate the need to approximate the temperature distribution by means of the Abel transform, and the advantages and disadvantages of this approach are also discussed.

The effects of heat convection have not been considered in the current work. The validity of this assumption is also considered in Chapter 8.
Chapter 6

HDR Brachytherapy Source Measurements

HDR brachytherapy was selected as a suitable radiation source to test the DHI detector prototype. These measurements were intended to demonstrate the feasibility of a DHI approach to radiation dosimetry by measuring the miniscule radiation induced temperature variations. An HDR source was a practical choice for the initial measurements because of the availability of a source at Christchurch Women’s Hospital. The source by definition has a high dose rate, which is also highly spatially variant in the region close to the source. This results in a high relative dose range and subsequent temperature variation, which should be resolvable on each of the DHI images.

The primary aim was to provide an initial proof-of-principle of DHI as a radiation dosimetry approach, characterise the dosimeter and identify issues for future improvements. The secondary aim was to investigate the potential for DHI to contribute to the field of near-source dosimetry described in Section 2.3.1.

6.1 Methods

6.1.1 Measurement

All measurements were acquired according to the general process described in Section 4.3.3 and measurement parameters recorded as in Table 4.3. Details specific to the HDR measurements are given below.
HDR Brachytherapy Source

The HDR source used in this study was an Ir-192 source supplied by Varian Medical Systems (Paolo Alto, USA), owned by Canterbury District Health Board (CDHB) and located at Christchurch Women’s Hospital (Christchurch, New Zealand). Ir-192 has a complex gamma ray spectrum with energies ranging from 136 keV to 1.06 MeV and an average energy of 380 keV. The source consisted of a cylindrical Ir-192 pellet of length 3.5 mm and diameter 0.6 mm, housed within a stainless steel capsule of length 4.52 mm and diameter 0.9 mm. The source was attached to a flexible stainless steel wire, housed within a Varian Medical Systems GammaMed Plus afterloader. The manufacturer’s quoted specification for the positioning accuracy of the wire is ±1 mm relative to the indexer. At the time of measurement the air kerma rate of the source at 1 m distance was 18.7 mGy h$^{-1}$. The corresponding activity was 170.1 GBq (4.597 Ci). A calibrated well chamber was used at the time of source installation to validate the manufacturer’s quoted source strength source, achieving agreement to within 0.3%, well within the 2% tolerance required for clinical usage.

For all measurements the source was housed within a Perma-Doc Phantom Applicator (Varian Medical Systems), which is a straight aluminium applicator of diameter 3 mm. The distance between the external tip of the tandem and the source centre is 3.75 mm when the source in the end dwell position. This relatively thick applicator was selected rather than the much smaller plastic catheter used for source calibration in the well chamber, because it had a much higher rigidity. The movement of the source from where it was housed in the afterloader to the end of the applicator causes movement of the applicator. All measurements are made comparatively by subtracting a reference image taken before the source was in place from images taken during irradiation, thus if a non rigid applicator is used, any change in position of the applicator due to source movement leads to inaccuracies in the results. With the applicator that was used, the closest measurable point was 1.5 mm from the central axis of the source. For closer measurements alternative applicators could be used if required.

DHI Detector

The DHI detector used was the configuration shown in Figure 4.4. The object-to-sensor distance was 26.5 cm. The detector in situ is pictured in Figure 6.1, from one of the preliminary measurements. The box which was used to isolate the detector from air flows is not pictured, but was used during the subsequent measurements, results of which are presented in this chapter. A burette stand was used to suspend the applicator in the test cell. Care
was taken to keep the applicator tube from the afterloader as straight as possible, to reduce the positional uncertainty arising from bending of the source wire.

The test cell used was a $4 \times 4 \times 4 \text{ cm}^3$ open-topped Perspex cube, with wall thickness of 0.15 cm. The test cell was filled with tap water, which had been allowed to equilibrate to room temperature before measurements began.

![Image of DHI dosimeter set-up for an HDR brachytherapy measurement.](image)

Figure 6.1: The DHI dosimeter set-up for an HDR brachytherapy measurement. The photograph is from a preliminary measurement, without the box used to prevent air flow, and using a polystyrene base to reduce the influence of vibrations. The applicator was held in place by a burette stand.

**Measurement Process**

Prior to any radiation measurements the DHI detector was aligned to achieve an optimal position for the real image in Fourier space. Baseline measurements were made to quantify detector stability and background noise levels for the particular alignment of the interferometer and its location within the brachytherapy room.

For each radiation measurement the applicator was suspended vertically in the test cell using the burette stand. By inspecting the real-time image preview from the camera, the applicator was aligned. For the first sets of measurements the applicator just impinged on the top
of the cross-section detected by the camera sensor, whilst for the latter measurement sets it was just visible on one side. Geometrical alignment and size calibration of the test cell was achieved by use of a rectangular template, according to the process described in Section 4.3.3.

For each measurement set the camera began recording the evolving interference pattern prior to the source leaving the afterloader. The first image was taken to be the initial reference image. The image series was acquired at a frequency of 1 Hz, with an exposure time of 15 ms, over irradiation times of up to 600 s. After the recording was started, the source was driven to the end dwell position (130 cm), which took several seconds. Thus the initial frames are when the source is still in the afterloader or during transit. The frame number for when the source reached its position was recorded, as was the frame when irradiation ended. All measurements were carried out at room temperature. The initial absolute temperature was obtained by the use of a digital thermometer with 0.1 K precision.

6.1.2 Analysis

Treatment Planning System Model

Measured results were compared to the dose distribution as modelled by the BrachyVision\textsuperscript{TM} Treatment Planning system (Varian Medical Systems). Absorbed dose to water was modelled in a water phantom extending at least 100 mm in each direction from the source. BrachyVision makes no allowances for non-water equivalent media, so this size was chosen to be larger than any test cell which may potentially be used. There are therefore discrepancies between model and actual dose distributions near the edges of the test cell. The voxel size was 0.5 mm in each direction, which was the smallest allowable with the BrachyVision software. This is not negligible compared to the dose gradient, so will inevitably result in some degree of volume averaging in the voxel closest to the source. This is approximated in Figure 6.2 by using an inverse square fall off with distance, where a calculation voxel of size 0.5 mm is compared to size 0.01 mm. It can be seen that for the first 1 mm distance from the source there is an overestimation of the dose due to the volume averaging effect of the larger voxel sizes. Beyond 1 mm, where the dose gradient is more shallow, the doses agree with negligible differences. BrachyVision is known to not be an accurate model in this region regardless, due to it’s use of the TG-43 algorithm [264]. The error in the > 1 mm region is acceptable for validation of the DHI detector results for the present proof-of-principle study. Care must be taken if results closer than 1 mm to the source were to be interpreted, however with the present applicator having a radius of 1.5 mm this effect will not impact on the comparison to DHI results. For future application to higher accuracy near-source dosimetry measurements
a higher resolution Monte Carlo model should be used for comparison purposes.

Figure 6.2: Comparison of the impact on the radial dose distribution from an HDR source of the use of 0.5 mm voxels compared to 0.01 mm voxels. Dose distribution is approximated by the inverse square law and does not take any other geometric or dosimetric factors into account.

In order to compare the model to the measured results, Method 1 for heat diffusion correction was used (refer to Chapter 5). The heat equation was applied in three dimensions to the modelled data to account for effects of heat diffusion over the measurement period. Convective motion was not considered in the model for these preliminary measurements, as with the experimental parameters used, the impact on the overall uncertainty is likely to be relatively small, as discussed in Section 8.2.2. The modelled dose data was then integrated across the depth of the test cell ($d = 4$ cm) in the direction of the laser path, in order to compare equal quantities.

**Image Processing**

The pixel size calibration was done for the measurement dataset according to the method described in Section 4.3.3. The source position was determined from the visible edge of the applicator on the image. The relative size of the applicator compared to the sensor area means that the entire semicircle end of the applicator may not be visible, which introduces some uncertainty to the source position, quantified in Section 6.2.1.

As part of the image reconstruction process each image was compared back to the first image from the series as a reference image, which was taken pre-irradiation. The movement of the source into the designate position within the applicator caused the applicator to vibrate, which caused slight but visible distortions on the images. The first such image was taken
to be the first time instance of irradiation, however only later images where the picture had stabilised were used for analysis.

There are two types of noise inherent in the measurements made by the optical system. These both cause the phase values measured on each sensor pixel to fluctuate with time and/or position, in the absence of any irradiation. The first is ambient noise due to ambient influence quantities, including air flow, temperature fluctuations, vibrations, and variation of the temperature within the test cell. The impact of these was minimized by housing the detector in a box to isolate it from air motion, with a rubber base to absorb vibrations. However these influences could not be entirely eliminated for the prototype detector, and impacted on the measurements. The second type of noise is intrinsic noise, which is a consequence of the optical components used and their exact alignment. An example can be seen in the ring pattern visible in the bottom left corner of Figure 6.4(a). Both types of noise combine to influence the dose measurements. A low pass Gaussian filter was used to reduce the impact of the noise in order to examine the dose distribution. Before applying the filter the applicator was masked in the image, to avoid excessive influence by the arbitrary but wildly fluctuating phase values which are seen in the region shaded by the applicator.

Direct Comparison to Model Results

The results presented later in Section 6.2.4 show the direct comparison of the measured datasets to the BrachyVision model data, which has been corrected for heat diffusion and integrated over the width of the test cell. The DHI measurement values showed the relative dose difference between the different points in the sensitive region, plus some amount that depended on the absolute phase of the measurements, which has an arbitrary value between 0 and $2\pi$. The process used to normalise this dose difference is referred to as “difference normalisation” throughout the remainder of this work. A normalisation point was chosen at a point as far away as possible from the applicator. The exact distance achievable depended on the location of the applicator within the field of view, whilst consideration was also given to avoiding any visible distortions in the measured image. The measured dose value at this difference normalisation point was then subtracted from every pixel in the image. However the limited sensitive region of the present version of the prototype detector meant that, for longer irradiations, even the most distant point of the image experienced a non-negligible increase in temperature. Thus in order to benchmark the dose difference to a value that allowed the results to be meaningfully compared to the model, the dose determined by the
model at the location of the distance normalisation point was added to the measured dataset, so that the dose differences of the model and the measured data could be compared directly. This approach is equivalent to also doing a difference normalisation of the model to the same normalisation point, however allows for the values of the dose to be compared at the actual dose values. This allows for more meaningful uncertainty metrics, with the percentage uncertainty for instance being a valid tool to consider the agreement of measurement and model.

In Section 6.2.4 dose profiles along axial and longitudinal axes from the applicator are presented, at a range of distances from the source centre. Two dimensional dose distribution maps at different time instances are shown. In order to quantify the results by calculating dose difference maps of measured versus modelled data, the datasets must have the same resolution. The conventional approach to this would be to resample the measured results to match the lower resolution of the model, however this has a major downside in that it loses the benefit of the higher resolution of the measured results in the region of the source where the model may be less accurate. Additionally, the presence of the applicator distorts the resampled results in this region. The alternative approach is to interpolate the model data, using a MATLAB spline interpolant function, to have the same dose grid spacing as the measured dataset. This approach allows for a better comparison of the data near the source, as long as due consideration is accorded to the impact of interpolation on the model dose profile in this region. Both approaches are compared in the results section.

Section 6.2.5 presents the results in a more conventional fashion by comparing radial dose functions of the measured and modelled data. This is in contrast to the results in the rest of the comparison, which are in terms of the integrated dose across the distance of the test cell, which is not a metric which is commonly encountered in radiation dosimetry. The radial dose function is a measure of the dose along any given profile in a radial direction from the source longitudinal axis, and is required in the TG-43 algorithm [39]. The Abel transform, which was introduced in Section 5.4.2 in the process of calculating the heat diffusion, can be used to determine the three dimensional distribution of a cylindrically symmetric measurement. This does not add any information to the measurements presented above, indeed it actually risks losing some information about any asymmetries in the source positioning which may be detected by the standard DHI measurements. It may however make the results of the DHI detector more accessible by presenting them in a means that medical physicists may be more familiar with.
Uncertainties

In order to determine the sensitivity of the detector, and quantify the accuracy of the dose distribution measurements the uncertainty in the measurement parameters are determined. There are various points in the experimental process where errors can be introduced, but they can be divided into dosimetric uncertainties and positional uncertainties. Their impact must be quantified in order to put a limit of accuracy on the results in order to determine the sensitivity of the DHI dosimeter. The final values used for both dosimetric and positional uncertainty are reported in Section 6.2.3. The methods of quantifying them are described below.

A main contributing factor to the dosimetric uncertainties is noise in the measurement system. The two types of noise already mentioned, ambient and intrinsic noise, are inherent in the dosimetric uncertainty. At this point, both of these effects are grouped together in order to estimate the total dosimetric uncertainty. As all dose measurements are determined via a differential comparison with an initial reference image, an estimate of the noise in the system can be obtained by quantifying the phase variation from the reference image, for a series of images prior to each irradiation beginning, effectively giving flat-field null measurements. As these measurements were only concerned with the dose difference maps at each time instance, rather than absolute dose, the mean value of the arbitrary phase difference of each image was subtracted from that image. This resulted in a series of null images where the phase fluctuated across the image. The standard deviation of the calculated dose values in each image was determined, and then the total standard deviation of the image series determined by taking the square root of the sum of the variances of each image. The data from the null images was analysed by several means to determine if it obeyed a normal distribution. The first method was a straightforward visual comparison of a normal distribution function with a relative frequency histogram of the data, using the Freedman-Draconis rule [265], given in equation 6.1, to select a bin width of 0.413 Gy. This selects the bin width based on a comparison of the interquartile range, \(IQR\), of sample \(x\) to the number of data points, \(n\).

\[
\text{Bin size} = 2 IQR(x) n^{-1/3}
\]

In order to give the visual method some degree of statistical significance, the chi-square goodness of fit test against the null hypothesis that the data is normally distributed was calculated, via the built-in MATLAB function \(\text{chi2gof.m}\). This returns one if the test rejects the null hypothesis at the 5% significance level, and zero otherwise. The test groups data into \(N\) bins, and then calculates the chi-square test statistic to compare the observed,
\( O \), and expected, \( E \), counts for those bins according to:

\[
\chi^2 = \sum_{i=1}^{N} \frac{(O_i - E_i)^2}{E_i}
\]  

(6.2)

If there was any uncertainty in these results then an additional test of normality was also calculated by constructing a normal probability plot for the data, using the MATLAB function `normplot.m`, where if the points are linear then the data has a high positive correlation to a normal distribution. In this test, the x-axis is transformed so that a cumulative normal density function will be plotted as a straight line. Then the mean and standard deviation are calculated from the data and transformed to the standard normal values, i.e. where the mean is zero and the standard deviation is one. The data points are then plotted along the fitted normal line.

If the results of this null testing for each individual irradiation measurement showed a sufficient correlation with a normal distribution, then the dosimetric uncertainty arising from the measurement influence quantities was taken to be the standard deviation, \( \sigma \), of the calculated dose values of the preliminary images, which corresponds to the 68.2\% confidence interval. Standard deviations from the individual images \( \sigma_i \), were summed according to equation 6.3.

\[
\sigma = \sqrt{\sigma_1^2 + \sigma_2^2 + \ldots + \sigma_i^2}
\]  

(6.3)

The other contributing factor to the dosimetric uncertainty in the measured DHI results is termed relative shift. This is the uncertainty that arises from the difference normalisation process, where an absolute value is used to benchmark the dose difference distribution for comparison to the model distribution. The uncertainty is dependent on the possible error due to the relative positioning of the normalisation point on the measured versus the modelled data. The normalisation point is chosen to be at the lowest possible dose value, in a region where there are no evident distortions in the measured dose distribution. An estimate of the uncertainty introduced is obtained by comparing the normalisation value from the model at that point with the dose at a distance of 0.5 mm in either direction, to account for possible positional errors between the measured and modelled data. The total dosimetric uncertainty is the sum of the relative shift and the combined ambient and intrinsic noise.

The dosimetric uncertainty in the BrachyVision data was determined using the comparison by Zourari et al. of the BrachyVision data with a state of the art Monte Carlo model [266] in order to attest to the capability of BrachyVision to accurately account for the scattering conditions in any homogeneous geometry. They benchmarked the dose distributions
created by BrachyVision with Monte Carlo models, for single Ir-192 sources in homogeneous bounded water geometries, so their results are applicable to the DHI situation. They found that at points close to the longitudinal source axis BrachyVision results present a dose rate over-estimation of 1-3% which is statistically significant, although some of it can be attributed to the Monte Carlo model statistical uncertainty. The remaining difference is attributed to spatial discretisation. The rest of the points are within agreement to less than 1%, with BrachyVision slightly underestimating the dose. Based on these results, for the proof-of-principle comparisons a conservative estimate of ±3% uncertainty was assumed on the BrachyVision data. Future studies may investigate this further and possibly reduce this estimate.

An additional dosimetric uncertainty arises from the temporal uncertainty. The time of the HDR measurement was selected according to the current image numbers when the applicator reached its end dwell position. For a measurement rate of 1 Hz, this has an inherent uncertainty of ±0.5 s. This was incorporated in the dosimetric uncertainty for the model, with the value proportionate to the length of the irradiation time. Thus for a twenty second irradiation there is an additional 2.5% uncertainty, but this value decreases with longer irradiation time. This is an influence which can be greatly reduced in future iterations of the detector by automating the timing of the image acquisition by automatic triggering.

The heat diffusion calculations induce some uncertainties, which were discussed in Chapter 5. The relevant uncertainties for the HDR model heat diffusion calculations were summed, with the total of 0.75% added to the above uncertainties. This number incorporates the impact of applicator positional error when calculating the integrated dose, variation in ambient temperature from that used in the calculations, and the effects of timing error on the heat diffusion calculation. The overall dosimetric uncertainty in the integrated, heat diffused HDR model was thus 3% + 2.5% + 0.75% = 6.3%.

The other type of uncertainty to be considered is the positional uncertainty of the reported distances for the model and the DHI results. For the model data, the resolution is 0.5 mm in each direction, and so the presumed uncertainty is half of that, i.e. 0.25 mm. The uncertainty in the positioning of the DHI measurements is determined during the pixel calibration, and reported in Section 6.2.1.
Accuracy Determination via Gamma Analysis

The gamma test is a metric for considering the agreement between a pair of two or three dimensional dose distributions. The gamma test was developed by Low et al. [267] from two simpler approaches, the dose difference comparison (as used in the previous section) and the distance-to-agreement (DTA) comparison. A dose distance comparison is a straightforward comparison of the dose at the corresponding points in the two dose distributions under comparison. Generally a passing criteria is used, for example 5%, whereby if the absolute dose difference at each point is less than the passing criterion then the measured dose distribution is considered to “pass” at that point. This approach has a major drawback in that it is not robust in high gradient regions, where a small misalignment can cause a disproportionately large dose difference. An alternative method which is often used in conjunction is the distance-to-agreement (DTA) method, where for each point, if the dose within a certain radius matches the dose at the corresponding point in the model then that point passes. This techniques is more robust against misalignments in high gradient regions, because the matching dose will still be nearby, but is more prone to failure in low dose regions, where small misalignments can require a large radius to find the matching dose level. In order to overcome these limitations in the high and low gradient regions, these two tests are often used in conjunction with each other, by evaluating them separately, and determining each point to be sufficiently accurate if it passes either test [268,269]. The gamma test is a more sophisticated combination of the two approaches, whereby they are combined into a more abstract metric which resembles a distance.

The gamma test is implemented mathematically according to equations 6.4 and 6.5. Comparison of two dose distributions is done pointwise, with a dose $D_a(r_a)$ in the first distribution, $a$, at point $r_a$, and a dose $D_b(r_b)$ at the corresponding point $r_b$ in the second dose distribution, $b$. The first term in the square root of equation 6.4 describes the DTA condition. A threshold passing value, $\delta_{DTA}$ is defined, for example 2 mm. The DTA condition is fulfilled when $D_a(r_a) = D_b(r_b + r)$ where $r$ is an arbitrary point some distance $|r|$ away from $r_b$. This describes an isodose contour in the second dose distribution around point $r_b$. For a simple DTA test, any value smaller than the threshold is considered a passing value. The gamma test uses $\delta_{DTA}$ to normalise the DTA value, so that a normal passing value would become unity. The second term in equation 6.4 describes the dose difference at the corresponding points, $|D_a(r_a) - D_b(r_b)|$, with the use of a pass/fail threshold $\delta_{DD}$ to also normalise the result of a normal passing value to unity. The DTA and dose difference terms are combined by squaring them, summing them and then taking the square root, to achieve a distance-like
metric, $\Gamma$. $\Gamma$ is only defined for values of $r$ such that $D_a(r_a) = D_b(r_b + r)$, which are those values geometrically located along the DTA isodose contours.

The actual gamma index, $\gamma$ is then determined as in equation 6.5 from the minimum value of $\Gamma$ by varying $r$, which corresponds to the point along the isodose contour where DTA is the smallest. The convention is for a gamma test to pass when $\gamma \leq 1$ and failing if $\gamma > 1$.

$$\Gamma = \sqrt{\frac{d^2_{DTA}\left((r_a, r_b) + r\right)}{\delta^2_{DTA}} + \frac{|D_a(r_a) - D_b(r_b)|^2}{\delta^2_{DD}}} \quad (6.4)$$

$$\gamma(r_a, r_b) = \min\{\Gamma(r_a, r_b), \forall r\} \quad (6.5)$$

The gamma test was applied to compare some of the measured data to the model, using threshold passing values of $\pm 10\%$ and $2$ mm. These criteria were chosen based on the performance of the measured data, in order to gain an understanding of where improvements are most necessary. The results are shown in Section 6.2.6 and the usefulness of the gamma index as a metric for dose distribution evaluation for the purposes of DHI is discussed in Section 8.3.4.

### 6.2 Results

The results presented in this Chapter are intended to be a representative sample of the measurements. As such, results with the applicator in two different positions within the cell are shown. Dataset 1 shows the applicator just impinging on the right hand side of the image, and is an example of a measurement with generally high agreement between the measured and modelled dose distributions, over a relatively short irradiation period. Dataset 2 shows the applicator just impinging on the top of the image, and was chosen as it has some more distortions in the measured dose distributions that were typical of many of the measurements. Both datasets show increasing disagreement with the model as irradiation periods increase. An example of the interferograms and subsequent reconstructed images from measurements taken with the applicator in a central versus a lateral position are shown in Figure 6.3. The calibration template is visible in these images, but for the analysis of the measured results a smaller region of interest was selected just inside this outline.
Figure 6.3: (a) and (b) show examples of the recorded interferograms for datasets with the applicator in a lateral and central position, respectively. The applicator is visible as a shaded region on the image. (c) and (d) show the corresponding reconstructed real images with the applicator and template visible.
6.2.1 Pixel Size Calibration

The pixel size calibration resulted in measured resolutions of $0.0232 \pm 2 \times 10^{-4}$ mm/pixel in the x-direction (corresponding to 43 pixels/mm), and $0.0292 \pm 3 \times 10^{-4}$ mm/pixel in the y-direction (corresponding to 34 pixels/mm). With this calibration, the width of the applicator in the x-direction as seen on the reconstructed image was 3.03 mm, which is in agreement with the actual width of 3 mm, to within 1% uncertainty. Thus any positional uncertainty in the x-direction arising from determining the visible edge of the applicator will be less than 0.03 mm. However there can be some slight variation in the positioning of the source within the applicator due to bend in the wire. Thus for the purposes of comparison to the model data which assumes exact placement of the source, the positional uncertainty to the centre of the source is taken to be $\leq 0.2$ mm. In the y-direction, if the full width of the source is visible on the reconstructed image then the uncertainty in position is also 0.03 mm. Accurate source positioning within the applicator was confirmed prior to measurement, with a margin of error of 0.3 mm, so the total uncertainty in the y-direction is taken as $\leq 0.33$ mm. In the case of a measurement where the full width of the source is not visible, such as in Figure 6.3(c), the peak position can be determined with less confidence so the uncertainty in the edge detection is increased. Only measurements where this could be confidently determined to within 0.1 mm were used, resulting in uncertainties of up to 0.4 mm in the x-direction for comparison to the model data.

6.2.2 Raw Data and Noise Filtering

Figure 6.4 shows an example of the data measured in raw form for an irradiation of 20 seconds, with the dose difference determined from the measured phase values. It can be seen that the data is at an arbitrary absolute value, but that the dose differences are showing a decrease in dose with distance from the source. Also note the random values reported in the region shaded by the applicator.

For filtering the data, different parameters for a low pass Gaussian filter were tested in order to find the most appropriate values, as described in the method section above. Parameters of $\sigma = 6$ Gy and width = 30 pixels provided the best compromise between retaining the features and slope of the data and reducing random noise, in most of the measurement field. However, in the region close to the applicator this large width value resulted in the dose being undervalued. For this reason, a two mask system was found to be the most effective way to retain the accurate dose distribution close to the applicator, whilst smoothing the
Figure 6.4: An example of the data obtained in raw format, showing an image from Dataset 1 following a 20 second irradiation. (a) is the reconstructed image converted to a temperature and dose map. The black and blue lines indicate the dose profiles depicted in (b) and (c). In (b) the area to the right of the red line is the area shaded by the applicator, so the values are arbitrary.
noise sufficiently in the remainder of the image. This approach involved increasing the region that was masked over the applicator, by ten pixels in each direction to create a perimeter region around the applicator. Within this region the parameters for the Gaussian filter were chosen as $\sigma = 6$ Gy and width $= 10$ pixels. The resultant filtered image was then combined with the original filtered image of the whole region to produce the final result. An example of the results after this process is depicted for two different positions of the applicator in Figures 6.5 and 6.6. For the two datasets shown the mean residual between the smoothed data and the raw data is -0.114 Gy and 0.559 Gy for Dataset 1 and Dataset 2, respectively.

6.2.3 Detector Sensitivity and Dosimetric Uncertainty

As described in Section 6.1.2, the uncertainty on each measurement point is made up of dosimetric and positional uncertainty. The initial sensitivity measurements which were taken as the first few images pre-irradiation, in the image series of each irradiation, were analysed to determine the noise contribution to the dosimetric uncertainty. This also allows an estimation of the limits of the sensitivity of the prototype DHI detector.

Various tests were done in order to determine whether the noise fits a normal distribution. An example is presented of the data from one of the HDR measurements, Dataset 1, with the applicator at the right hand side of the sensitive region. An example of one of the flat field reconstructed images, converted to dose, is shown in Figure 6.7(a), with the region shaded by the applicator masked. Figure 6.7(b) shows a histogram of the data points, in 0.413 Gy bin widths, with the corresponding normal distribution displayed for comparison. Figure 6.7(c) shows the normal probability plot of the data which compares the measured data spread with the spread expected from a normal distribution. For the dataset shown, the standard deviation was 2.90 Gy. The chi-square test confirmed agreement with the normal distribution. The normal probability plot shows that there is some deviation from a normal distribution, with the S-shape indicating that there was less variance than expected. This means that the standard deviation was somewhat higher than the 68% confidence interval, thus this was considered an acceptable estimate for the noise induced uncertainty in the data. For each of the datasets the first five images were analysed and the total standard deviation of the noise was calculated, according to equation 6.3. For Dataset 1 this resulted in an uncertainty estimate of $\sigma = \pm 3.01$ Gy.

Determination of the relative shift uncertainty is shown in Figure 6.8. For a normalisa-
Figure 6.5: Data filtering, Dataset 1. (a) The raw temperature/dose data after 20 seconds of irradiation, showing the mask applied over the applicator region. Profiles of interest marked in black and blue. (b) The same image after application of a Gaussian filter ($\sigma = 6$ Gy, width = 30 pixels), (c) the mask used for the region adjacent to the applicator where the Gaussian filter had width = 10 pixels. (d) Blue points are the data points from a profile orthogonal to the applicator in the raw dataset (black line in (a)). The green line marks the edge of the applicator, and signal to the right of this is arbitrary. The black line marks the smoothed data without the additional region shown in (c), displaying how the values are lower than they should be near the applicator. The red line shows the smoothed data with the two mask regions. (e) is the profile along the solid blue line from (a) and (f) is the dotted blue line.
Figure 6.6: Data filtering, Dataset 2. (a) The raw temperature/dose data after 20 seconds of irradiation, showing the mask applied over the applicator region. Profiles of interest marked in red and black. (b) The same image after application of a low pass Gaussian filter ($\sigma = 6$ Gy, width = 30 pixels), (c) the mask used for the region adjacent to the applicator where the Gaussian filter had width $= 10$ pixels. (d) Blue points are the data points from a profile along the central axis of the raw dataset (red line in (a)). The green line marks the edge of the applicator, and signal to the left of this is arbitrary. The black line marks the smoothed data without the additional region shown in (c), displaying how the values are lower than they should be near the applicator. The red line shows the smoothed data with the two mask regions. (e) is the profile along the solid black line from (a) and (f) is the dotted black line.
Figure 6.7: (a) A flat field image from Dataset 1, with noise with a standard deviation of 2.90 Gy. (b) A histogram of the data from the entire image except the masked applicator region, with a normal distribution plotted in black for comparison. (c) Normal probability plot of the data, with the ideal linear fit shown in red.
A normalisation point at 6 mm distance from the applicator central axis, and assuming a positional uncertainty between the measured and modelled data of 0.5 mm, a maximum relative shift uncertainty of 0.969 Gy is determined for a twenty second irradiation. As the dose rate is constant, this is equal to 0.0485 Gy s\(^{-1}\), and can be scaled up or down for longer or shorter irradiation periods. This ignores the impact of heat diffusion, thus overestimating the uncertainty for longer irradiation periods.

![Image](a)

![Image](b)

![Image](c)

Figure 6.8: Determining the relative shift uncertainty arising from the difference normalisation of the measured result in order to compare it to the model. (a) Measured data, 20 second irradiation, filtered, Dataset 1. The X marks the selected normalisation point, chosen to be in a low dose region, but avoiding the slight fluctuations in dose near the lower edge of the image. The artefact marking the edge of the inner filtration mask is visible around the applicator. (b) The corresponding heat diffused BrachyVision model data, with the normalisation point marked, and the red line showing the profile depicted in (c). (c) shows the possible variation due to positional uncertainty of the dose used to do the difference normalisation. The larger value is used as the relative shift uncertainty.

The total dosimetric uncertainty for Dataset 1 is taken to be equal to the standard deviation of the null images, which is constant with irradiation time, plus the relative shift uncertainty, which varies with irradiation time. For a twenty second irradiation period, the total dosimetric uncertainty is ±3.98 Gy. This implies that there is a lower limit of sensitivity on the present version of the detector of 4 Gy, where integrated dose values less than this amount will not be resolvable with high confidence. The same process was undertaken for all datasets analysed.
The total uncertainties for Dataset 1 and its comparison to the BrachyVision model consist of a dosimetric uncertainty on the DHI results of $\pm 3.98$ Gy for a 20 s measurement, and $\pm 5.92$ Gy for a 60 s measurement, with a positional uncertainty of $\pm 0.33$ mm for measurements where the full width of the source was visible, and $\pm 0.40$ mm if it was obscured to some extent. The corresponding percentage uncertainty depends on which region of the curve is considered, as the dose difference at each point varies. The model data had a dosimetric uncertainty of $\pm 6.25\%$ for a 20 second measurement, with a positional uncertainty of $\pm 0.25$ mm. The uncertainty for other datasets were calculated in a similar fashion to that described for Dataset 1. Dataset 2 had a dosimetric uncertainty on the DHI results of $\pm 3.94$ Gy and $\pm 5.88$ Gy for the 20 s and 60 s irradiations, respectively.

6.2.4 Direct Comparison to BrachyVision Data

The DHI measured results were compared to the BrachyVision model data, corrected for heat diffusion, and integrated over a width equivalent to the test cell. Figures 6.9-6.11 present the results from Dataset 1 after 20 seconds of irradiation. The measured dose distribution image is shown, along with the corresponding modelled dose distribution for comparison. The one dimensional dose profiles along different lines from the two dimensional maps are shown in more detail. The profiles shown were selected to show the dose in both the radial and axial directions, adjacent and relatively distant to the source position. The top horizontal profile was chosen to be the closest position to the centre of the source, constrained by the resolution of the model data to 0.5 mm intervals. The source centre is located 3.75 mm from the distal end of the applicator, whilst the profile shown is at 3.5 mm. The lower horizontal profile was selected to be in line with the end of the applicator. The vertical profiles were chosen as 2 mm and 6 mm away from the centre of the applicator, thus 0.5 mm and 4.5 mm respectively from the visible edge of the applicator.

From the profiles shown in Figures 6.9(c)-(f), it can be seen that there is excellent agreement between the dose differences in the measured and modelled data. All points in the image agree to within the experimental uncertainty values, except for a region to the lower left of the image, $>5$ mm from the applicator, where the doses are slightly higher than expected. As described in Section 6.2.2 the filtering of the measured data means that the dose is under-reported next to the applicator, which is visible in Figure 6.9(c).

Figures 6.10 and 6.11 inspect the relative dose distributions across the image in more detail.
Figure 6.9: Dose distributions from Dataset 1 at 20 s irradiation. (a) The dose distribution measured by the DHI detector. The coloured lines mark the position of the profiles depicted in (c)-(f). (b) The corresponding BrachyVision model data, corrected for heat diffusion and integrated across the width of the cell. (c) - (f) The measured dose (black with red horizontal and vertical error bars) and the model dose (blue) along the profiles from (a), where (c) = black line, (d) = green line, (e) = blue line and (f) = red line.
As mentioned in Section 7.1.2 the results are compared by two different methods - Method 1: interpolating the model data to match the resolution of the measured data; and Method 2: combining pixels in the measured data to compare to the model directly. These images are shown in Figure 6.10. Following the determination of dose maps with matching resolution, they are compared by subtracting the modelled data from the measured data. Both the difference map, and the percentage difference maps are shown for each method, in Figure 6.11. The major difference in the results from the two approaches was in the region adjacent to the applicator. The underreported dose adjacent to the applicator due to filtering means that when the pixels are combined to equal the size of the model pixels, this lower region is spread out to cover a larger region further from the applicator. Additionally, there was some distortion visible arising from the averaging of pixels in the region of the applicator, meaning that the mean calculated percentage error for the whole image may have inaccuracies introduced.

For the 20 s irradiation for Dataset 1, the mean of the percentage difference for Method 1 was -2.7% with 68.0% of the measured points agreeing to within 5%, and 72.7% of points agreeing to within 10% of the model data. For Method 2, the mean of the percentage difference map was -1.5%, with agreement of 70.1% of the points to within 5% and 74.1% of points to within 10%. These results are promising, and show that the detector is able to resolve the temperature changes on the scale required, with good agreement in the shape of the dose distribution.

For longer irradiation periods, the agreement between the measured and the modelled data reduced progressively. An example of 60 seconds of irradiation for Dataset 1 is shown in Figures 6.12-6.14. Compared to the 20 s irradiation the slightly longer irradiations showed less agreement with the model. For Method 1 of comparison, the mean of the percentage difference map was as high as 23.4%, with only 18.2% of the points agreeing to within 10% of the model results. However in the region within 3 mm of the source the results agreed well, with the gradients of the dose differences being very similar for the measured and modelled data. The discrepancies arose with distance from the source, where the measured data was unexpectedly high, due to a lower gradient. Thus time of measurement is proving to have an impact on the results, potentially because this leads to an increased time interval between the reference image pre-irradiation and the later measurement images. Thus there is a higher chance of ambient conditions affecting the measured results. This result will be discussed further in Section 6.3.
Figure 6.10: Two dimensional maps to compare the measured and modelled dose distributions from Dataset 1 at 20 s irradiation, showing (a) the model dose distribution at original resolution of 0.5 mm pixel dimensions, (b) model dose distribution interpolated to the resolution of the measured data, (c) DHI measured dose distribution at original resolution, and (d) DHI measured dose distribution with pixels combined to equal the model resolution.
Figure 6.11: Two dimensional maps to compare the measured and modelled dose distributions from Dataset 1 at 20 s irradiation, showing the comparisons, with (a) the dose difference map of Figure 6.10(c) minus 6.10(b) (Method 1 comparison), (b) the corresponding percentage difference map for Method 1, and (c) the dose difference map of 6.10(d) 6.10(a) (Method 2), with (d) the corresponding percentage difference map.

The next results presented are from a set of measurements, referred to as Dataset 2, in which the applicator was located at the top of the images. The dataset provides an example of a result with more discrepancies from the model, representative of typical results achieved with the DHI measurements. This is shown because consistency in dosimetric measurements is vital, thus in order to present a full picture of the performance of the prototype detector, it was considered important to show measurements that cover the range of results achieved, rather than just the optimal measurements. There is somewhat less agreement with the model compared to Dataset 1, but the results still show dose distributions in general agreement with the model results.

Figures 6.15-6.17 show the results from Dataset 2 after 20 seconds of irradiation, whilst Figures 6.18-6.19 show the results at 60 seconds of irradiation. For both time instances
Figure 6.12: Dose distributions from Dataset 1 at 60 s irradiation. (a) The dose distribution measured by the DHI detector. The coloured lines mark the position of the profiles depicted in (c)-(f). (b) The corresponding BrachyVision model data, corrected for heat diffusion and integrated across the width of the cell. (c) - (f) The measured dose (black with red horizontal and vertical error bars) and the model dose (blue) along the profiles from (a), where (c) = black line, (d) = green line, (e) = blue line and (f) = red line.
Figure 6.13: Two dimensional maps to compare the measured and modelled dose distributions from Dataset 2 at 60 s irradiation, showing (a) the model dose distribution at original resolution of 0.5 mm pixel dimensions, (b) model dose distribution interpolated to the resolution of the measured data, (c) DHI measured dose distribution at original resolution, and (d) DHI measured dose distribution with pixels combined to equal the model resolution.
Figure 6.14: Two dimensional maps to compare the measured and modelled dose distributions from Dataset 2 at 60 s irradiation, showing the comparisons, with (a) the dose difference map of Figure 6.13(c) minus 6.13(b) (Method 1 comparison), (b) the corresponding percentage difference map for Method 1, and (c) the dose difference map of 6.13(d) minus 6.13(a) (Method 2), with (d) the corresponding percentage difference map.
the dose difference in the region close to the applicator agrees reasonably well to the model values. However it is clear that there is some distortion in the lower part of the images at increasing distance from the applicator, which is clearly visible on the dose map. In particular, Figure 6.15(e) clearly shows a distortion in the dose attenuation curve. The distortion results in the dose values measured by DHI being lower than expected from the model. For the 20 second measurement only 57% of the points agree to within 10% of the model, with discrepancies mostly beyond a 2-3 mm radius of the applicator. It should be noted that the dose values are small in this region, thus a high percentage uncertainty is actually a low absolute uncertainty. This effect worsens with time, as seen in the results from the 60 s irradiation, shown in Figures 6.18 and 6.19. This disagreement is surmised to be due to variations in the ambient conditions, and possibly the effects of heat convection which have not yet been incorporated into the model. This is discussed further in Section 6.3.

In Figure 6.15(a) it appears that there is some asymmetry of the dose distribution around the visible end of the applicator, with a slightly higher dose occurring on the left hand side of the image adjacent to the applicator. It is possible that the source was not perfectly centred inside the applicator tube during this particular measurement. This detection of such a misalignment serves to underscore the need to experimentally validate modelled dose distributions. The ability to detect this to high spatial resolution is a useful outcome of the DHI measurements, although this is limited to situations where the error has some component in a direction perpendicular to the laser path.

It is obvious from Figures 6.16(d), 6.17(c), and 6.17(d), that Method 2 for comparing the two dose distributions, which involved the reduction of the measured resolution to match the model, is not appropriate in all situations. The way the applicator protrudes into the image and is masked when the data is filtered, means that there are a large number of pixels where the average dose cannot be determined to any degree of accuracy. This means that the comparison doses will result in an artificially lower agreement than using Method 1, and much information about the agreement of the measured and modelled data is lost, particularly in the important region in the vicinity of the source. Thus despite the obvious shortcomings of interpolating the model data, this method is preferred for the comparisons.
Figure 6.15: Dose distributions from Dataset 2 at 20 s irradiation. (a) The dose distribution measured by the DHI detector. The coloured lines mark the position of the profiles depicted in (c)-(f). (b) The corresponding BrachyVision model data, corrected for heat diffusion and integrated across the width of the cell. (c) - (f) The measured dose (black with red horizontal and vertical error bars) and the model dose (blue) along the profiles from (a), where (c) = black line, (d) = green line, (e) = blue line and (f) = red line.
Figure 6.16: Two dimensional maps to compare the measured and modelled dose distributions from Dataset 2 at 20 s irradiation, showing (a) the model dose distribution at original resolution of 0.5 mm pixel dimensions, (b) model dose distribution interpolated to the resolution of the measured data, (c) DHI measured dose distribution at original resolution, and (d) DHI measured dose distribution with pixels combined to equal the model resolution.
Figure 6.17: Two dimensional maps to compare the measured and modelled dose distributions from Dataset 2 at 20 s irradiation, showing the comparisons, with (a) the dose difference map of Figure 6.16c minus 6.16b (Method 1 comparison), (b) the corresponding percentage difference map for Method 1, and (c) the dose difference map of 6.16d minus 6.16a (Method 2), with (d) the corresponding percentage difference map.
Figure 6.18: Dose distributions from Dataset 2 at 60 s irradiation. (a) The dose distribution measured by the DHI detector. The coloured lines mark the position of the profiles depicted in (c)-(f). (b) The corresponding BrachyVision model data, corrected for heat diffusion and integrated across the width of the cell. (c) - (f) The measured dose (black with red horizontal and vertical error bars) and the model dose (blue) along the profiles from (a), where (c) = black line, (d) = green line, (e) = blue line and (f) = red line.
Figure 6.19: Two dimensional maps to compare the measured and modelled dose distributions from Dataset 2 at 60 s irradiation, showing (a) the model dose distribution at original resolution of 0.5 mm pixel dimensions, (b) model dose distribution interpolated to the resolution of the measured data, and (c) DHI measured dose distribution at original resolution. The direct comparisons are shown with (d) the dose difference map of (c) - (b) (Method 1 comparison) and (e) the corresponding percentage difference map.
Temporal Measurements

One of the key features of the DHI approach which distinguishes it from film, which is currently a primary, high resolution, dosimetric tool for HDR, is the ability of DHI to make continuous measurements to show the evolution of the dose distribution. Post measurement analysis can then later select any of the time instances of interest. An example is shown in Figure 6.20, showing the evolution of the dose difference along a profile in a radial direction from the applicator, at the depth of dose maximum. This clearly shows the increase in dose difference with time, with the region close to the source developing into the expected inverse squared fall off.

![Figure 6.20: An example showing the capability of the DHI detector to measure the temporal evolution of the dose distribution, from Dataset 1. The dose difference is shown along the profile perpendicular to the source longitudinal axis, at the position of dose maximum. Each time instance is normalised to have the most distant dose be zero.](image)

Extended Irradiation Periods

When the measurements were made, despite being aware that heat transport and external influences would probably be an issue, each irradiation was measured for a period of ten minutes. As predicted by extrapolation of the trends, when the full datasets were later analysed, the effects that are visible in the one minute measurements that are already presented have served to make the measurement unable to detect any irradiation. This occurred despite the fact that the overall dose increased significantly, however because the parameter of interest in the present measurements is dose difference at each time point, this increase did not lead to a more visible dose distribution. For completeness sake, an example is shown in Figure 6.21. In future versions of the prototype detector, if it becomes possible to cumulatively...
measure absolute dose, as discussed in Section 4.4.3, then it is expected that the overall increase in dose would be clearly visible if this experiment was repeated.

![Diagram](a)

![Diagram](b)

Figure 6.21: An example of (a) the modelled and (b) the measured dose distributions after a ten minute irradiation.

### 6.2.5 Comparison via Radial Dose Function

Implementation of the Abel transform to the filtered, reconstructed images meant it was possible to derive a full three dimensional dose distribution, assuming cylindrical symmetry of the system. This then makes it possible to compare the measured data with model by comparison of the radial dose function, a metric which is often required for characterisation of an HDR source. The Abel transform was applied to Dataset 1. A radial profile through the centre of the source at 20 s irradiation time is shown in Figure 6.22(a). In general, there is good agreement between the curves, with the measured absorbed dose having the correct magnitude. The slope of the dose decrease with distance from the applicator is somewhat steeper for the measured dose than the modelled dose. This is the opposite to what was seen on the integrated dose measurements, indicating that the regions further from the applicator are disproportionately high. In the images presented earlier, this result was seen in the plane of the measurement, however must also occur in the direction parallel to the laser beam. The Abel transform encounters difficulties when areas of sharp change occur, such as the region within 0.25 mm of the applicator, and the resulting wild oscillations are visible in this region in Figure 6.22(a). The transformed data in this region is therefore unreliable.

To confirm the validity of the Abel transform for these measurements it was also applied to the model data. The three dimensional model was integrated across the direction of the laser path, and then the integrated result was transformed back to three dimensions by use
of the Abel transform. The result of this can be seen in Figure 6.22(b), where a radial profile through the central axis of the source is seen. It is clear that the Abel transform has some effect on the slope of the curve. This probably contributes somewhat to the steeper curve noted in the measured data in Figure 6.22(a). Additionally, there is under sampling of the dose in the peak region, an effect which again arises from a sharp change in the gradient of the curve. These results should be considered when utilising the Abel transform to calculate radial dose, and are discussed further, along with other limitations of the approach in Section 8.3.3.

Figure 6.22: (a) An example of the radial dose function calculated from the measured results by means of the Abel transform. The red points mark the measured radial dose profile through the source central axis from Dataset 1 at 20 s irradiation, whilst the blue line shows the model radial dose function at the same position. The position of the applicator edge is marked in black. (b) Analysis of the error introduced by the Abel transform calculation for this dataset. Comparison of the original model data radial dose function (red) to a model radial dose function calculated from the integrated model data by means of the Abel transform (black).

6.2.6 Gamma Index Evaluation

A gamma index evaluation was undertaken on the image from the 20 second irradiation from Dataset 1. The threshold passing values selected were $\delta DTA = 2$ mm, and $\delta DD = 10\%$. Given the uncertainties in the measurement due to noise, an agreement to within $10\%$ provides a sufficient indication of the validity of the approach. The 2 mm is a fairly tight parameter, but was selected as one of the key benefits of DHI is the high spatial resolution achievable, thus 2 mm provides a good indication of the method’s capabilities. The resultant gamma index map is shown in Figure 6.23. As expected, the gamma test failed in the region of high distortion that had been previously noted in the bottom left of the image. There was also some discrepancies around the distal end of the applicator. The overall pass rate was
83%. It should be noted for context, that for routine external beam IMRT measurements, the gamma test parameters are usually 3 mm/3%, with a pass rate of >85-90%, however low dose regions are routinely ignored by applying a 10% threshold [270].

Figure 6.23: An example gamma index evaluation for the 20 second irradiation from Dataset 1 with the applicator on the right side of the image. Gamma index threshold passing values set to $\delta_{DTA} = 2$ mm, and $\delta_{DD} = 10\%$, and a pass is shown as red, with a fail as blue.

An additional gamma index evaluation was done on the same data, using the sum of the uncertainty estimates of the measured and modelled data as the threshold criteria. The result is a gamma test map which shows all the points where the dose distributions agree to within the measurement uncertainties. The positional uncertainty was $\pm 0.25$ mm from the model added to the $\pm 0.33$ m from the measured dataset. For this time instance the dosimetric uncertainty in the model was $\pm 6.25\%$, and $\pm 3.98$ Gy for the measured data. The percentage uncertainty was converted to an absolute value by comparing to the maximum dose value of the model, thus overestimates the uncertainty for the rest of the model, which leads to a more conservative test. Figure 6.24 shows the result of this gamma test. There are more regions of disagreement than the previous test, which is as expected, as the test parameters are stricter. The overall pass rate decreased to 76% of pixels.

### 6.3 Discussion

The preliminary tests of the application of the DHI detector to measurements of an HDR brachytherapy source show that the system has promise as a dosimeter for high dose rate radiation applications. The detector was able to resolve temperatures to the correct order of magnitude as the expected radiation induced temperature increases. The measured dose distribution maps were qualitatively correct, with high doses measured near the source, approximating an inverse square law decrease with distance from the source. For some
measurements the DHI measurements agreed well with doses modelled by the BrachyVision treatment planning system. Discrepancies visible in some of the measurements show that further work is required to develop the detector to a state where it can achieve reproducible and reliable measurements. The agreement was higher for shorter irradiation times and higher dose regions, suggesting that measurements of sources with higher dose rates will lead to more accurate and consistent results. Shorter irradiation times will also result in less influence by heat diffusion, and less chance for small errors in the heat diffusion modelling to be amplified. The extent of this influence with increasing irradiation time is demonstrated in Section 8.2.1.

The measurements also showed the ability of the prototype detector to be transported, reassembled on site, and undertake successful measurements in a clinical situation, with the inherent constraints on accessibility and time. The system for making measurements was streamlined to be both efficient and thorough, with as many influence factors as possible considered. The successful results validated both the optical set-up of the detector and reconstruction and analysis algorithms.

There are however obvious areas to where further work is required on the detector. The major one is the isolation of the detector from the ambient environmental conditions of temperature and pressure fluctuations. It is speculated that the main discrepancies between the measured data and model that result in the accuracy of the measurement results diminishing at longer irradiation periods are attributable to these effects. As these influence factors are not predictable they are not able to be accounted for by increasing the margins of uncer-
tainty. Indeed, the variation in the results that would be induced by incorporating it into the uncertainties would result in a loss of profile shape information. Chapter 8 includes a more thorough analysis of the uncertainty budgets, discusses the use of the radial dose function and gamma index as evaluation metrics, and discusses in further details the impact of heat transport.

6.3.1 Potential for Contribution to HDR Brachytherapy Dosimetry

The primary aim of these measurements was validation of the detector rather than demonstrating its use for accurate HDR dosimetry. However, some consideration was given to the potential of DHI to contribute to the limitations in the present array of HDR dosimetry options that were introduced in section 2.3.1. A full understanding of the potential of DHI in this field will require improvements to the detector, which are recommended in Section 8.4, however based on the preliminary results some indication of a more developed DHI detectors usefulness can be conjectured.

The key area of focus where DHI may be able to contribute is in the field of near source dosimetry, where measurements down to 1 mm spatial resolution are required. The preliminary measurements with the prototype detector have achieved a resolution of approximately 0.03 mm or better, with potential for improvement. This is a very high spatial resolution compared to most alternative dosimetry options, which is only surpassed by the spatial resolution achievable using film. The measurement shown in Figure 6.13 where some slight asymmetry in the source positioning is visible indicates the potential for DHI to be used to validate various parameters of Monte Carlo models in the near source region.

The estimated uncertainties in the present measurements are higher than those achievable by alternative approaches such as measurements using film or gel dosimetry. The uncertainties assumed in this work are discussed further in Section 8.3 and it is expected that with careful experimental design and implementation these values will be able to be much reduced.

The fact that DHI dosimetry is directly measuring the absorbed dose to water, and has no inherent energy or dose dependence is a favourable aspect in comparison to measurements using most other detector types. It is feasible therefore that a future iteration of the detector could contribute to the field of absolute and standards dosimetry for HDR, in a sim-
ilar fashion to the development of the ultrasound thermometry by the NIST laboratories [82].

The major limitation at this stage is the lack of a sufficient method to account for heat diffusion directly in the experimental results. At this stage all measurements are relevant only in terms of comparison to a heat diffused model of the source, integrated across the width of the test cell. With continued work on the inverse modelling of heat diffusion that was suggested in Chapter 5, this may be able to be overcome, allowing a more versatile use of DHI for HDR brachytherapy measurements.

6.4 Concluding Remarks

This chapter covered the application of the prototype DHI detector to the dosimetry of an HDR brachytherapy source, in measurements intended to provide a proof-of-principle of the DHI approach. A series of measurements were taken, with results from two of them fully analysed and presented in this chapter. The measurements presented were chosen in order to provide a fair indication of the capabilities and limitations of the detector. A full analysis of the measurement uncertainties was included, with all areas of potential error considered and if appropriate incorporated into the results. The process of filtering the data to reduce the excess noise in the images was described, including means of reducing the dose underestimation near the source due to volume averaging effects. The data was compared to a model produced by the commercial treatment planning system BrachyVision. Some of the measurements were in relatively good agreement with the model, within the range of experimental uncertainties. Other measurements displayed clear distortions in the recorded images, and further experimental work will be required to reduce the impact of these effects. Overall, the results were promising, with the measured dose differences for irradiations of limited duration clearly displaying a dose distribution similar to that predicted by the model, however with some areas of discrepancy. Improvements to the experimental process are suggested in Chapter 8 which aim to increase the accuracy and reproducibility of the measurements in order to improve the quantitative agreement of the DHI results to the model. The next chapter presents the results from application of the DHI detector to the dosimetry of a small field proton beam.
Chapter 7

Proton Beam Measurements

Dosimetry of a proton beam was selected as a second approach to provide proof-of-principle of the DHI detector because the opportunity arose to access the small field proton beam at the University of Washington Medical Center (UWMC) cyclotron facility. As was the case for the HDR source measurements, this was intended primarily as a pilot study for detector development and refinement purposes, with the secondary effect of investigating the possibilities for the detector to contribute to the area of small field proton beam measurements. The localisation of the Bragg peak and determination of the peak dose are key parameters of interest.

7.1 Methods

7.1.1 Measurement

All measurements were acquired according to the general process described in Section 4.3.3 and measurement parameters recorded as in Table 4.3. Details specific to the proton measurements are given below.

Proton Beam

The proton beam used in this study was produced on a Scanditronix MC50 Cyclotron at the UWMC. The cyclotron is primarily used for the Clinical Neutron Therapy System, however there is an additional experimental proton beam research station [271]. This produces a beam of $H^+$ ions of up to 50.5 MeV with a 2 mm diameter and a 7-8 mm Bragg peak, primarily for purposes of comparative radiobiology. Dosimetric methods which have already been applied to the beam include Monte Carlo modelling, radiochromic film and ionisation chamber measurements. An example of the Monte Carlo models and film measurement is
shown in Figure 7.1.

Figure 7.1: Central axis relative depth dose results from a previous dosimetric study of the proton beam, showing two MC models (with different source modelling) compared to an experimental radiochromic film measurement. Unpublished image, courtesy of Manisha Naranayan

For the DHI measurements, the proton beam incident energy was 28.9 MeV, with an energy spread of 1.5%, corresponding to an approximately 8 mm deep Bragg peak. For these initial measurements the proton beam was set to deliver the highest practical dose rate, under conservative constraints on the operating parameters of the beam. The purpose of this was to minimise the heat diffusion and maximise the achievable signal-to-noise ratio. The beamline was under development, and the output was controlled by limiting the charge accumulated in a Faraday Cup. For each measurement the proton beam was set to deliver a total charge of approximately 4.57 nC, delivered at the highest beam current allowed, which was the maximum amount that the proton beam was known to safely deliver. These parameters correspond to an expected dose in the Bragg peak of approximately 400 Gy, according to the previous ionisation chamber measurements, at a peak dose rate of approximately 20 Gy s⁻¹.
DHI Detector

The DHI detector used was in the same configuration as that for the HDR measurements, and is pictured in situ for proton beam measurements in Figure 7.2. The object-to-sensor distance was 26.5 cm. The test cell used was a $2 \times 4 \times 4$ cm$^3$ open-topped Perspex cube, with wall thickness of 0.15 cm. The 2 cm distance was aligned parallel to the direction of the object laser path. The test cell was filled with tap water, which had been allowed to equilibrate to room temperature before measurements began. Air bubbles which had settled on the test cell walls were removed manually before irradiation.

![Figure 7.2: The DHI dosimeter in situ for a proton beam measurement. The red lines indicate the paths of the laser light, and the green line indicates the path of the proton beam. A smaller test cell than that shown in the photo was used, with a width of 2 cm in the direction of the laser path across it.](image)

In Figure 7.2 it is possible to see that there is a frame attached to the proton beam gantry and a rail extending parallel to the beam direction. These were used for alignment of other dosimetric systems, and could not be removed for the DHI measurements. These constructs meant that the interferometer had to be reassembled around the protruding pieces, meaning there was not very much flexibility in the position of the detector relative to the proton beam. It also meant that the wooden box which had been used for the HDR DHI measurements was unable to be utilised to isolate the system from extraneous air flows. To achieve the best isolation under these circumstances, a wooden frame was constructed and thick plastic sheeting was used to enclose the region surrounding the detector. This is shown in Figure 7.3. The plastic sheeting was taped closed in an attempt to seal any gaps, however the complicated geometry due to the position of the gantry, frame, rail and supporting table meant that this could not be completely achieved, as will be shown in the results presented in Section 7.2.
Figure 7.3: The makeshift cover used to isolate the DHI detector from air flow during proton measurements. (a) With an opening for adjustment of the interferometer, and (b) fully enclosed for measurement.

Measurement Process

Prior to any radiation measurements the DHI detector was aligned to achieve an optimal position for the real image in Fourier space. Baseline measurements were made to quantify detector stability and background noise levels for the particular alignment of the interferometer and its location within the proton room.

The relative positioning of the proton beam within the test cell of the detector was somewhat more complex than for the HDR measurements, as the lack of an applicator within the sensitive region meant that there was no inherent reference point common to both sets of data. Geometrical alignment and size calibration of the test cell was achieved by use of a rectangular template, according to the process described in Section 4.3.3. By inspecting the real-time image preview from the camera, the transparent rectangular template was then used to localise the measurement region within the cell. The distance from the edge of the test cell to the edge of the template was recorded, in order to determine the horizontal depth of the measurement region within the test cell. The distance from the proton beam nozzle to the test cell was approximately 16 cm. This value varied slightly in accordance with the position of the test cell and subsequent depth of the measurement region in the test cell, as the rail and frame around the proton beam meant the interferometer could not be repositioned. This is not considered to be an issue, as the source to surface distance has minimal impact on the depth dose distribution of a proton beam.
The vertical position of the proton beam within the measurement region, as delineated by the template, was controlled by adjusting the height of the optical components. Fine adjustments were made by raising and lowering the stand that the test cell was on, but this motion was constrained by the rail which ran directly underneath and parallel to the path of the proton beam. The position of the proton beam was determined by using a set square to approximate the path of the proton beam perpendicular to the exterior surface of the proton beam nozzle, in line with the 2 mm circular aperture. Following this approximate positioning, the measurements were recorded, and images reconstructed. The final determination of the position of the beam was done experimentally, by determination of the position of the beam central axis from the reconstructed images. The errors introduced in this process are estimated in Section 7.2.1. If the beam was not sufficiently centred, the test cell height was adjusted, and the measurement repeated.

The position of the test cell in relation to the beam in the direction of the laser was aligned in a similar fashion, in order to achieve an approximately central positioning of the beam. This is so that the model dose could be accurately integrated across a width equivalent to the test cell. Small offsets from the central position would have a slight effect on this result, however given the very low doses deposited outside the 2 mm beam cross section, this would have limited impact. However in the interests of accuracy the beam was centred as carefully as possible, however this was unable to be experimentally confirmed in the fashion of the vertical positioning described above.

The camera on the DHI detector is powered by the USB2 cable which collects the data. In order to achieve sufficient power to the camera, the maximum length of USB cable which can be used is limited. Thus due to the distances involved, the computer running the OEM camera recording software was in the proton bunker. Due to the lack of a suitable conduit to conduct a network cable, and no wireless access to the bunker due to the four metre thick concrete door which is required to prevent excess neutron scatter in the beam control area, it was difficult to connect to this computer. Initial measurements ran a network cable along the bottom edge of the door, however damage to the cable or to the network port on the secondary control computer meant that for most of the measurements there was no external control of the camera acquisition whilst the beam was on. For this reason, most of the measurements were acquired by first starting the camera recording and concurrently starting a handheld stopwatch. The time taken to exit the bunker, close the doors to clear
the door interlock and then start the beam, was measured and recorded. This was usually on
the order of 30-35 seconds. When the image series for each measurement was analysed the
time was benchmarked against this stop watch measurement to determine the measurement
time relative to the beam duration. The inherent uncertainties introduced by this approach
are described in Section 7.2.1.

For each measurement delivering the total charge of approximately 4.57 nC had an expected
dose in the Bragg peak of approximately 400 Gy, determined from extrapolation of previ-
ous measurements. Delivering this charge at the maximum current took between 18 and
20 seconds, depending on the precise parameters, corresponding to an expected peak dose
rate of approximately 20 Gy s\(^{-1}\). The precise measurement times of beam on and beam off
were recorded from the stopwatch. Due to the uncertainties in the total dose value it was
only utilised for the calculation of the extent of heat diffusion, and all comparisons between
measured and modelled data were made in relative terms. The normalisation point chosen
for each measurement is detailed when the results are presented.

### 7.1.2 Analysis

#### Treatment Planning System Model

The Monte Carlo model used for comparison to the experimental results was kindly supplied
by Manisha Naranayan, a graduate student at the UWMC, from a model developed specif-
ically for the UWMC proton beam. The model uses GEANT-4 based TOPAS software to
model the existing beam [259]. Previous comparison with experimental measurements show
less than 2% disagreement in the depth of the Bragg peak and better than 3.5% agreement
in lateral profiles.

The model was provided as a two dimensional dataset of relative dose distribution, nor-
malised to 100% at the surface depth on the central axis. The model had resolution of 0.1
mm in each direction, to a total of 3 cm in the direction perpendicular to the beam (this
component is henceforth referred to as “vertical”), and 1 cm in the beam direction (referred
to as “horizontal”). Beyond this region the dose deposited is negligible. For the purposes of
heat diffusion calculations, and to integrate the expected dose across the width of the test
cell, the two dimensional dose map was expanded to three dimensions by assuming cylindri-
cal symmetry about the central axis. The consequent three dimensional dose map was then
used to calculate the expected heat diffusion over the measurement period, as described in
Chapter 5. For this process the relative dose distribution was converted to absolute doses using an estimation of the dose to the peak delivered with the beam parameters used for the experimental DHI measurement. Uncertainties introduced by this estimation were considered in Section 5.3.1.

For the heat diffusion calculations, a volume equivalent to the size of the test cell was used, with the incremental dose deposited into this volume according to the MC model. The model assumes an infinite medium of water, thus the effects of lack of scatter from the smaller size of the test cell were not included in the calculations. Additionally, variation in the beam attenuation due to the Perspex walls of the test cell, as opposed to that of water, was not considered. These effects are expected to be negligible with regards to the overall uncertainties in these initial measurements, but should be incorporated for future measurements. Convective motion was not considered in the model for these preliminary measurements, as with the experimental parameters used, the impact on the overall uncertainty is likely to be relatively small.

The heat diffused MC model of the dose was then integrated across the depth of the test cell \( (d = 2 \text{ cm}) \) in the direction of the laser path, and renormalised to the surface, in order to compare like quantities with the measured data. The model was subsampled to be at the same resolution as the measured data.

**Image Processing**

The pixel size calibration was done for the measurement dataset according to the method described in Section 4.3.3.

As part of the image reconstruction process each image was compared back to a selected reference image. This was selected from the series of pre-irradiation images recorded in each measurement dataset, with the chosen image having low random noise, no repeated visible distortions compared to the adjacent images, and being shortly prior to the beginning of the irradiation.

A feature based noise reduction process was applied to the reconstructed images, whereby the average of several of the pre-irradiation images was subtracted from the final reconstruction. This was considered to be a useful technique because the noise in the fringe patterns
was not completely random, having instead an underlying pattern to it, likely arising from slight misalignments of the interferometer. The differential approach of the DHI technique should remove this effect, however by using a single reference image, which can itself be noisy, the concept is not fully realised. This noise reduction approach is effectively similar to using a time-averaged image as the reference image. The results from this noise reduction are presented in Section 7.2.1.

Following this process, a low pass Gaussian filter was then applied to reduce the impact of the random ambient noise from vibrations and air movement etc. Unlike the HDR measurements the proton measurements did not have an applicator disrupting the measured temperature maps and, especially when considering the effects of heat diffusion, no steep changes in dose gradients, thus a single filter was applied to the entire image dataset. The selected optimal filter parameters for the proton beam measurements are listed in the results section.

**Direct Comparison to Model Results**

At this stage of development of the DHI detector, the process of comparison of preliminary measured datasets to the proton Monte Carlo model data is complicated by several factors, which will be described below.

As described in the HDR DHI results, the DHI measurement values give a relative dose difference across the points within the sensitive region of the test cell, plus some amount which depends on the absolute phase of the measurements and is arbitrary between 0 and $2\pi$. The Monte Carlo model on the other hand is relative data, normalised to the surface depth on the central axis. Thus in order to compare the measured DHI results to the model requires first an estimate of the dose at a certain depth in the cell so that a difference normalisation can be conducted, where the measured dose value at a selected difference normalisation point was subtracted from every pixel in the image. The choice of normalisation point was fairly arbitrary, and the anticipated absolute dose is selected from the model based on an estimated dose to the peak region. After the measured results were difference normalised, they were then normalised by division to give a dose of 100% at the surface. Due to the limited sized sensitive region of the current detector, not all measurements include the surface, complicating the normalisation. In these cases the measurement and the model doses are normalised relative to the most superficial depth in the measured result. Estimates of the uncertainties that this process introduces are included in Section 7.2.1.
Due to these considerations, the comparison of the DHI detector results to the model is predominantly qualitative, with improvements to the prototype detector to enable accurate quantitative measurements suggested in Section 8.4. Two dimensional dose distribution maps and contour plots are presented, with difference maps giving qualitative indication of the agreement of model and measurements. Examples of relative dose profiles along axial and longitudinal axes from the proton beam path, at several beam depths are shown. Uncertainties in the localisation of these profiles are discussed in Sections 7.1.2 and 7.2.1.

Uncertainties

Whilst the focus of these measurements was on determining the required experimental parameters for future experimental applications of DHI to proton dosimetry, it is still germane to consider the sources of uncertainty in the measurement process, and the process required to quantify the uncertainties. The uncertainties to consider are both the dosimetric and positional uncertainty in the DHI measurements, and the final values used are reported in Section 7.2.1. As any uncertainties in the MC model doses, such as the effects of the Perspex test cell walls, are likely to be negligible in comparison the DHI data these are not considered. Future measurements with a refined detector may be able to help verify the accuracy of this assumption by validating the model.

As for the HDR results, in order to determine the sensitivity of the detector and quantify the dosimetric uncertainty of the results, the influence of intrinsic noise on the measurements must be considered. The process is the same as that described in Section 6.2.3. The average noise in a series of flat-field null images prior to each irradiation was determined by subtracting the mean value of all the pixels, and determining the standard deviation by taking the square root of the sum of the variances of the pixels across each. Only images where there were no obvious gradients in the temperature dose map were included in these calculations. This value is included in the dosimetric error bars on the measured DHI results.

For these proton measurements, the geometry of the beam source nozzle and resulting inability to use a solid enclosure to shield from air flow meant that despite best efforts with a flexible barrier, there was more scope for ambient noise to influence the results. The effects of this were considered by inspecting the maximum size and direction of variation in the temperature fields in the series of images immediately preceding the beginning of irradia-
tion. This effect was not included in the uncertainty error bars as any airflow if present could be a larger effect than the total dose measured. Rather, this phenomenon was inspected in order to draw conclusions as to the reliability of each of the sets of results.

Some systematic uncertainty in the dose values arises from the relative shift occurring as part of the difference normalisation process, as described in Section 6.2.3. An estimate of the relative shift uncertainty is determined by comparison of the dose expected at 0.5 mm in either direction from the normalisation point. This accounts for any positional uncertainties in the value used to calculate the difference normalisation.

An additional source of systematic uncertainty in the results is due to the temporal uncertainty. Due to the difficulties with networking to the camera control computer inside the treatment room, from the control room, the potential temporal inaccuracy in the measurements is relatively high. The temporal uncertainty arises from both possible variations in the camera acquisition rate, and timing uncertainties with the use of the stopwatch to record the camera start time compared to beam on/off times. A conservative estimate is that the temporal uncertainty could be up to 4 seconds. Over a 30 second measurement this corresponds to up to 13% of the expected total dose at each point. This was converted to an absolute uncertainty for each pixel by comparison to the MC model data normalised to the dose expected in the peak. This is an influence which can be largely eliminated in future iterations of the detector by automating the timing of the image acquisition by automatic triggering when the beam is turned on and off.

With regards to the dosimetric uncertainties, the percentage uncertainty at each point in the dose map was determined from combining the noise, relative shift and temporal uncertainties with the uncertainty introduced in the heat diffusion calculations (quantified in Chapter 5) and comparing them to the value of each pixel. To gain an understanding of the overall uncertainty, the maximum and minimum percentage uncertainties at different positions across each dose map are quoted. However at the low doses that are deliverable, when considering the integration across the test cell, the percentage uncertainties are considerable and outweigh any potential agreement of measurement and model. In particular, the percentage influence of the temporal uncertainties is excessive for all measurements not taken at the end of the irradiation period. For these reasons, in order to consider the qualitative shape of the dose distribution results, the uncertainty values are stated in the results section, but not incorporated in depictions of the results.
Positioning uncertainty is more complex than for the HDR as there is no applicator to act as a physical benchmark of the position of the image against the position of the radiation beam. The horizontal positioning by means of measuring the position of the template, as described in Section 4.3.3, had considerable inherent uncertainty. It is estimated that there is uncertainty of up to 2 mm using this method. This arises from several factors, including alignment of the set square against the proton beam nozzle, measurement error from reading the ruler, and the width of the template lines. This uncertainty value is too large to enable an accurate measurement of the Bragg peak positioning with the current detector, and a discussion of how to reduce this value is contained in Section 8.4. The vertical positioning uncertainty was less of a concern, with the vertical location of the proton beam determined directly from the measured images, by locating the beam central axis for each series of measurements. There is some slight uncertainty due to the accuracy of the size calibration of the pixels, which is taken to be 1%, as determined in Section 6.2.1.

7.2 Results

Considering the sensitivity of the present detector, the proton beam irradiation parameters that were possible for these measurements (notably the limitation on dose rate), and the limitations in the experimental conditions, the expected signal was within the range of the measurement noise. The result of this was that limited information regarding the proton beam could be achieved by the measurements at this stage. Due to this, the focus of this results analysis is to determine the refinements to the detector required to achieve useful measurements in the future.

The expected values for the beam with the irradiation parameters used are shown in Figure 7.4. In order to demonstrate the effects of heat diffusion and integration across the width of the cell, the process of modification of the original Monte Carlo model is depicted. To facilitate a realistic visualisation of the proton beam this is shown with an assumed dose to the peak of 400 Gy, although for the purposes of comparison to the measured results at this stage only the relative dose distribution is required.

7.2.1 Uncertainty Quantification and Image Post-Processing

As illustrated in Figure 7.4(e), the “dose” peak value measureable by the DHI detector is approximately 10 Gy. Note that this is not the actual dose value because of the heat diffusion
Figure 7.4: The process of obtaining the modified Monte Carlo model for comparison to measurement results, for an 18 second irradiation achieving 400 Gy peak dose. Note the different scales in each pair of images. (a) Unmodified MC model through the plane of the central axis, (b) unmodified MC model central axis depth dose, (c) heat diffused MC model in central axis plane, (d) heat diffused MC model central axis depth dose, (e) heat diffused MC model integrated across the width of the test cell, (f) integrated heat diffused model depth dose, (g) normalised integrated heat diffused MC model, (h) normalised integrated heat diffused MC model depth dose.
and integration across the test cell, however for the sake of simplicity it will be referred to as the “measured dose” for the remainder of this chapter. Given the small sensitive region of the detector, the maximum dose difference that can be detected along a depth dose profile is approximately 7.5 Gy. This value is not significantly greater than the dosimetric uncertainty on each point in the images, which is calculated next.

In the same fashion as for the HDR results, the inherent noise contribution to the dosimetric uncertainty in the image series for this set-up of the detector was determined by analysing the null images from the beginning of each measurement set. For one of the measurement sets presented in this section, the standard deviation of the noise over the first six images was 3.7 Gy. This number is typical of the results achieved for all the datasets, and is an estimate of the sensitivity of the detector for relative dose measurements. The uncertainty in the heat diffusion calculations of approximately 0.75% also impacts on the relative dose distribution. This 0.75% results in a maximum uncertainty in the peak of 0.1 Gy. The relative shift uncertainty was determined from the variation in dose across the positional uncertainty of 2 mm, at the difference normalisation point. As the difference normalisation point was usually in the low gradient pre-Bragg peak region of the curve this value was relatively low, and was taken to be 0.5 Gy for all measurements. The temporal uncertainty is up to 13% of the dose at each point. Combining all of these uncertainties results in an absolute uncertainty for the measured value of each pixel of between 4.2 - 5.6 Gy.

Thus from the above values it is evident that with the present sensitivity of the detector, and the limitation on deliverable dose rate, limited interpretation of the measured results is possible.

In an attempt to maximise the information that can be achieved from these DHI proton measurements, post-processing of the images to reduce the noise contribution to the dosimetric uncertainty by means of feature based analysis was conducted. This process was based on the observation that the noise in each image does not appear completely random, but rather some component is attributable to some significant artifacts which are visible across the series of images. By combining null images and subtracting the mean of the combined images from each image, a slight reduction of artifacts was achieved. A repeat calculation of the standard deviation within each image was then calculated. Some image series showed no improvement, and some showed noise uncertainty in the dosimetric values reduced by up to 1 Gy. This value is relatively small, in agreement with the assumption
that the noise in the images is largely random noise, but has some basis from artifacts in
the optical system. However there was a lack of consistency in producing this reduction.
It is estimated that this may be due to disproportionate influence of external temperature
variations on some measurement sets. For this reason, at this point this processing was not
used in the subsequent image analyses, but could be considered for future iterations of the
detector.

A low pass Gaussian filter was applied to the results to reduce the impact of the random
noise. The parameters used in optimal settings used for this were taken to be the same as
for the HDR measurements, with parameters of $\sigma = 6\text{Gy}$ and width = 30 pixels, in order to
retain any features and slope of the data but reduce excessive random noise. An example of
a profile line taken across a null image before and after application of the low pass filter is
given in Figure 7.5. This magnitude of filtration is necessary with the current level of noise
in the images, however care must be taken for future measurements that the filter settings
are such that the images can be accurately interpreted without unnecessary smoothing of
the data.

![Figure 7.5: An example of a profile line taken across a pre-irradiation null image before (blue) and after (red) application of the low pass filter.](image)
Consistency of Image Series

The results from the proton beam measurements were more affected by inconsistencies across and between the images than the previous HDR source measurements. This can partly be attributed to the difficulties encountered in creating a sealed enclosure around the detector to reduce air flow. The other factor is that the limit on the proton beam dose rate meant that high dose gradients were not achievable, so therefore fluctuations in the measurement of several Gy were of much higher significance when interpreting the results. Ideally these inconsistencies would be eliminated for measurements, high dose gradient or not, however if they are unable to be eliminated then a metric needs to be introduced to quantify the influence that they have. This is complicated by the fact that the very nature of the inconsistencies means that they are not necessarily predictable, and measuring the variations at one point in time does not necessarily correlate with what is occurring during the actual irradiation period. The proton beam measurements do however have a relatively large set of images from pre-irradiation compared to during irradiation, necessitated by the difficulty in networking the control computer and the long time taken for the proton room door to close before measurement could begin. Thus by examining the fluctuations in the series of pre-irradiation images, any trends can be extrapolated to estimate the impact of non-radiation induced variations on the measurement data.

The smoothed null images were inspected for any kind of gradient in the measurement field. The maximum gradient in each image was determined from the maximum and minimum points, and quantified as a percentage of the expected measurement value for a given time instance. This allows for an estimation of the impact of this effect on the validity of any measured results. Additionally, the direction of the gradient between those points was quantified in order to give an indication of the variability with time, whether the effect was just a drift in one direction, and how constant the variation was.

An example of an image series recorded at one second intervals is shown in Figure 7.6 to give an indication of the variation in the results. The long term drifts from serval datasets are presented in Figure 7.7. This figure presents the size of the maximum dose gradient, and it’s direction for each image in a 40 second series prior to the irradiation of each of the actual measurement datasets. It was found that the influence was predominantly a vertical temperature gradient, with very little variation across the horizontal plane. The fluctuations were relatively unpredictable, oscillating between approximately 0 and 10 Gy deviation from the initial reference image at most time points, but with occasional sections of larger devi-
ations up to the order of approximately 20 Gy. In Figure 7.6(c) there is more variation in the direction of the temperature gradient, but corresponding to very low values.

Figure 7.6: A set of null images at one second intervals, with a typical amount of drift visible.
Figure 7.7: Direction and size of the drift gradient with time. Data from four different measurement sets, acquired at a frequency of 5 Hz.

These results are consistent with the fluctuations being largely due to variation in ambient air temperature, where convective forces cause gradients in the air temperature. The presence of some variation in non-vertical forces suggests an additional influence of air currents, but this effect is secondary. The fluctuations can not be directly related to the temperature in air, because the unconstrained volume means the relationship with pressure and temperature and the refractive index is variable. Equally, the variations visible in the results shown here indicate that even if a consistent relationship existed, it would not be possible to correct for it as the fluctuations themselves are too inconsistent. Perhaps the most straightforward approach to overcoming this issue would be to conduct measurements in a room with no air-conditioning system. This results in much higher consistency in the gradients seen in measured null images. This is not always possible in a clinical setting however, as many facility climate functions are centrally controlled. Thus in order to control the predominant variation it will be necessary to isolate the system from ambient temperature variation.

Controlling the ambient temperature to the extent that is required to limit these fluctuations to make the dosimetric measurements useable is not a trivial task. The temperature would need to be controlled to at least a mK level, and preferably µK. This would need to be done in such a way as to minimise or completely avoid the presence of convective air currents.
Without the use of experimental temperature isolation it may be possible to conduct statistical analysis of the results and potentially compensate for temperature variations. This would only be possible if, as in the examples shown in Figure 7.6, the drift is predominantly in one direction only. In this case local trends could potentially be established in the null images and extrapolated forward to the measurement time. This approach would not be possible for all datasets, and the accuracy achievable by this method would be limited in any case. Additionally, the approach would become more complicated by the consideration that the fluctuations are not necessarily consistent across the entire image, but are sometimes only visible in sections.

7.2.3 Analysis of DHI results

As described in the previous sections, at this stage of development of the DHI system, the results are not at a sufficient level of sensitivity to allow for meaningful interpretation. However, despite the fluctuations in the images visible due to random noise and ambient temperature drifts, it is still possible to envision dose maps which are approximating the expected shape of the proton beam. To avoid the possibility of observer bias in the results, the entire series of images over the irradiation period was analysed for each dataset. Due to the temporal uncertainty of the image timestamps, this also included images in the immediate pre-and post-irradiation periods. Those datasets where a consistent pattern emerged over most of the later images were assumed to have some degree of reliability. If the anticipated shape of the dose distribution was only present in a small number of images this was considered to be potentially just a random effect. An example of central axis dose profiles which appeared to be a potentially valid representation of the absorbed dose are shown in Figure 7.8, showing both the raw data signal, and the filtered signal from a 5 second irradiation. Figure 7.8(a) shows the side of the sensitive region closer to the surface, with the difference normalisation performed so that the values read zero at the edge of the test cell. Note that in reality these would be somewhat greater than zero. Figure 7.8(b) was measured with the test cell further across, in the region of the Bragg peak. The difference normalisation was performed to agree with the corresponding point in the first image. The Monte Carlo model for the corresponding time instance is included in Figure 7.8(c). Due to the size of the uncertainties compared to the signal value, the uncertainty bars have not been plotted in the figures. The size of the uncertainty bars when included, is greater than the differences between the measured and modelled data.
Figure 7.8: Example of a DHI central axis depth dose distribution from a 5 s proton beam irradiation. (a) The surface region leading towards the Bragg peak. Blue is raw data and red is with the filter applied. (b) The Bragg peak region. (c) The corresponding Monte Carlo model, integrated across the test cell and normalised to the irradiation conditions.
Radial dose functions of the proton beam data are not presented at this stage, as the limitations of the present detector did not allow for sufficiently accurate results to warrant this level of comparison. This analytic would be possible to use in the same fashion as for the HDR measurements, assuming cylindrical symmetry about the central axis.

It was evident from some of the more reliable datasets obtained that the measured reading was too high in the penumbral regions of the beam. This may be attributable to discrepancies due to the extremely low signal to noise ratio, or possibly incorrect heat diffusion equations underestimating the extent of heat flow.

7.3 Discussion

The initial aim of these measurements was to test the DHI detector following successful HDR brachytherapy source measurements. It was hoped that the DHI detector may be able to contribute to the task of commissioning and validating the UWMC proton beamline for animal research. However the experimental difficulties faced, coupled with the limited time available at the facility meant that the main achievement from these measurements was to investigate the detector capabilities and experimental process required to potentially enable successful measurements in future proton beam dosimetry experiments. The opportunity to apply the improvements to the detector was not available at the time of measurement, due to time constraints in the clinical setting. Some of the lessons learned that are specific to the proton beam are discussed here, whilst general improvements to the DHI detector are covered more fully in Chapter 8.

7.3.1 Beam Settings

The beam settings for the pilot study were limited to the highest value known to be able to be safely delivered. The total charge delivered of 4.57 nC at a current of approximately 0.23 nA resulted in a dose to the Bragg peak of approximately 400 Gy over approximately 20 s. The steepest dose gradient achievable on the central axis, when corrected for the DHI measurement conditions of heat diffusion and integration across the test cell, was approximately 5 Gy/mm. Since the pilot study was completed it has been determined that it will be possible to safely operate the proton beam at a vastly increased dose rate three to five orders of magnitude greater than that used in these initial measurements. This will result in much
higher doses being able to be achieved, with the subsequent increase in the dose gradients meaning that the dose distribution will be much more measurable using a DHI detector. For example, if the beam current is increased by a factor of 10,000, for an irradiation time of 10 seconds, the total absorbed dose in the Bragg peak would be 100 kGy. After accounting for heat diffusion and integration across the DHI test cell, this would result in dose gradients on the central axis of up to 2000 Gy/mm. This increase in dose means that even with the current detector set-up and measurement process, the increase in signal-to-noise ratio means that even the lowest dose gradient region at the surface on the central axis should be resolvable with the current sensitivity of the DHI detector.

A key advantage of a DHI detector compared to many other dosimetric approaches is the inherently high dynamic range, so that even at high dose rates the dose in the Bragg peak will be simultaneously measurable with that in the surface or fall off region. The limiting factor on this is the impact of heat diffusion, which has a higher impact in the presence of high temperature gradients. However the high dose rate also allows for a much faster dose deposition time for a given dose, which counteracts this effect. Additionally, the extent of the heat diffusion can be mathematically corrected for.

One caveat to note on the process of increasing the accuracy of the DHI measurements by dramatically increasing the dose rate is that this moves the system far beyond any settings which might be used clinically with current treatment protocols. Caution would have to be taken extrapolating the results of these measurements to a characterisation of the beam at clinical dose rates. It is possible that with the ability to produce ultra high dose rate beams that there may be some clinical benefit to this, similar to the MRT beams described in Section 2.3.3, with dose rates on the order of 100 - 1000 Gy s\(^{-1}\) [175]. Notably, a high dose rate and the subsequent short delivery time reduces the impact of intrafractional organ motion on the target volume and organ at risk irradiation. Additionally, with the recent developments in the field of laser driven ion acceleration proton beams, as described in Section 2.3.2, investigation of DHI as a dosimetric tool for cyclotron generated high dose rate beams may lead to possibilities for its application in the dosimetry of LDA protons.

### 7.3.2 Monte Carlo Model

When comparing the DHI measurements with the Monte Carlo model, the main limitation was the fact that only a relative dose distribution comparison could be made. This is because
the Monte Carlo model provided was not specific to the exact beam current settings and irradiation time used, resulting in uncertainty in the absolute dose delivered. Whilst this still produces an accurate relative dose distribution, it limits the utility of the comparison for absolute dose. The comparison effectively becomes qualitative, comparing the shape of the dose distribution rather than specific values. Variation of the absolute dose will still result in some relative dose effects visible, with the extent depending on the normalisation point chosen. However these variations will be less obvious than if an absolute dose distribution could be compared.

The best approach would be to run the Monte Carlo model with input of the exact settings used for the irradiation. This would allow for a proper validation of any future DHI measurements against expected values, which is vital for the further development of the system. In particular this process is fundamental to the development of the detector capabilities for determination of absolute dose. This also has the added benefit of removing dosimetric uncertainty in the processed DHI measurements which results from normalisation to a point with considerable uncertainty. The uncertainties in the results, and the extent of discrepancies between measurement and model would then be able to be quantitatively determined, in terms which are readily understood and transferable to other methods.

7.3.3 Detector Dosimetric Sensitivity

The first conclusion from the initial pilot measurements of the proton beam are that in order to achieve useable results, the sensitivity of the measurements must be increased. This could be achieved either by improving the detector responsiveness, or by increasing the signal from the proton beam. A traditional definition of signal to noise ratio (SNR) is the average signal value, $\mu$ divided by the standard deviation of the background, $\sigma_{bg}$. The signal value considered in the case of a DHI measurement is the mean difference between two set points, which are separated either spatially or temporally. This difference is used rather than the absolute value of a point, as the absolute value is arbitrary, depending on the starting conditions and phase. In order to achieve meaningful results, the SNR of a dataset must be greater than one. If the noise is determined as the standard deviation of a null image, then for a signal to noise ratio of one, the confidence in this result will be $\sim 68\%$. To increase this confidence interval, data must be acquired with a higher SNR. Consider here that a SNR calculated from one standard deviation gives the 68% confidence interval, whilst to achieve a 95% or higher confidence interval requires two or more standard deviations. Thus to have useable
reliability in the determination of the relative dose distribution requires the signal to be at least greater than twice the standard deviation of the measured signal. The additional dosimetric uncertainty in the measurement adds to this requirement. In actual terms, this requires a dose difference of at least 7 Gy, but up to 12 Gy, in order to achieve a reliable signal for the proton beam measurements. Improvements to the detector will reduce this requirement.

To improve the sensitivity of the detector by improvement of the SNR, a key approach could be to use a test cell with narrower width. This would mean that the projected dose measured is averaged over a shorter distance and thus appears larger. The noise would not be affected to the same proportion, resulting in an improved SNR. The main caveat to this approach is that by reducing the size of the test cell the system moves further away from being in full scatter conditions. A correction factor to account for this effect may need to be applied. As the test cell is already relatively small, it may already be appropriate to determine and apply such a factor to the current measurements. The factor could be determined with the use of Monte Carlo modelling. A related consideration is that the test cell must remain wide enough to encompass the entire width of the beam. An alternative method to increase the sensitivity could be to apply a double pass configuration to the present cell or a smaller cell. A potential configuration is proposed in Section 8.4.1.

A test such as the Minimum Resolvable Temperature Difference Test (MRTD) developed by Lettington and Hong could be modified for use with future versions of the detector to verify the limits of its sensitivity [272]. This would experimentally validate the theoretical calculations of achievable sensitivity.

### 7.3.4 Detector Sensitive Region

A key improvement to the DHI detector which would increase usability and reduce uncertainty for future proton beam measurements would be an increase in the size of the detector sensitive region. This region is currently constrained by the size of the collimated laser object beam which passes through the test cell and impinges directly on the camera sensor. The size of the region with the current detector configuration and hardware is approximately 7.5 mm x 6 mm. With the inclusion of the template used for positioning, this size reduces slightly further. Thus with the energy of the proton beam used, and the corresponding Bragg peak depth of between 7 and 8 mm, the full penetration of the beam is not able to be imaged in
one instance. This results in increased positional and dosimetric uncertainty. An increase in the detector sensitive region to encompass the full depth of beam penetration would remove a major source of potential error from the results. This is particularly important if normalisation techniques are used to analyse the data, as a consistent point could then be used across all datasets.

There are three different approaches that could be taken to expand the sensitive region. The first is the incorporation of a camera with a larger sensor area. Such cameras are available, but to achieve a sufficiently larger sensor without compromising the spatial resolution would represent a significant cost increase. A small reduction in spatial resolution may however be acceptable, as the Bragg peak would be readily resolveable even with somewhat reduced pixel sizes. The alternative approach would be the use of a second lens system to focus a larger region of interest in the test cell onto the camera sensor. This approach would also reduce the spatial resolution, proportionate to the amount of the magnification. This is approach requires minimal additional hardware, however may introduce some more complexities into the reconstruction equations. These would need to be carefully examined to determine that no discrepancies or distortions are introduced.

The third approach to increasing the size of the sensitive region could be the use of a micrometer controlled translation stage for the test cell. By accurately being able to measure the shifts of the cell relative to the camera, it could be possible to “stitch” multiple datasets together to achieve a compound image of a larger region. With sufficiently accurate movements this would not necessarily increase the uncertainty by any meaningful amount. However the main caveat to this approach is that it would only be possible if the stability of the detector has improved enough to make absolute dosimetric measurements possible. Without this ability, the normalisation of the images would be difficult. It is possible that the images could be normalised so that the values at adjacent edges are in agreement, but this risks introduction of errors. In particular, this approach relies on constancy of output of the machine. If an absolute Monte Carlo model is produced, this could potentially be used to validate this approach and the multiple difference normalisations required.

7.3.5 Experimental Process

There are three key improvements to the experimental process which could be implemented for future proton beam measurements. The first is the most obvious: to improve the isola-
tion from ambient conditions, in order to reduce the noise. Suggestions for this process are covered in Section 8.4.1.

The second key improvement would be in terms of access to the image acquisition computer. Direct access to the computer controlling the camera would mean that the excessively high numbers of images acquired in the present measurements would not have been necessary. Being able to synchronise the beginning of data acquisition with the proton beam irradiation would significantly decrease the temporal, and therefore dosimetric, uncertainty. The simplest approach to this is the method that was intended to be used in the pilot study: networking of an in-room camera control computer to an external control computer. This is possible, but not ideal, through the doors of the maze. The presence of an existing cable conduit from the room was undetermined, but if existing, this would be the preferred route for the cable. The use of an alternative camera with its own power source, rather than USB powered, would also allow for the direct connection of the camera to an external computer. This was not possible with the current camera as the length of the USB cable that would be required meant that the power transfer was not sufficient. The external control computer can be manually triggered when the proton beam irradiation begins and ends. The ideal solution would incorporate automatic triggering via a signal from the cyclotron control console. This would minimise the temporal uncertainty, however requires considerable technical support and cooperation from the operators of the proton beam.

The third key improvement to the experimental process which would result in a reduction of the uncertainties would be the incorporation of a three dimensional translation stage for accurate positioning of the test cell. The use of such a stage would result in a reduction of uncertainty in the position of the image relative to the beam, and in the positioning of datasets relative to each other. This is particularly significant in the case of a sensitive region which is smaller than the total dose field.

7.4 Concluding Remarks

The pilot study of the application of DHI dosimetry to a small field proton beam helped to develop the process for the use of the detector in a clinical setting, and the analysis of uncertainty influences. At this stage there is no mandate to say that DHI can contribute usefully to small field proton dosimetry. Despite the limited outcome in terms of accurate dosimetry
measurements the process was still of value in the understanding of detector response. If the system and experimental process is developed further, then the potential improvements mean that the use of DHI for proton dosimetry should be revisited. Practical improvements over a range of areas were suggested, including the proton beam irradiation settings, the Monte Carlo model, the detector dosimetric sensitivity and the size of the sensitive region in the test cell, and the overall experimental process.
Chapter 8

Discussion

The main intention of this work was to develop a novel working DHI dosimeter, to investigate the feasibility of the approach for radiotherapy dosimetry. The development of the system included initial construction of the detector, designing a process for making dosimetric measurements, and initial proof-of-principal radiation measurements. An understanding of the various sources of uncertainty in the process is a key aspect of characterising the current and potential performance of the detector. This chapter discusses various aspects of the detector design and performance, including advantages and limitations of the approach. An analysis of the uncertainty budget used determines areas where improvements can be made, and overall improvements to the detector design are suggested. Consideration is given to the potential application of DHI to different radiation modalities, and the issues to consider in a possible extension to full tomographic measurement are raised.

8.1 Proof-of-principle Results

The proof of principle of DHI dosimetry was demonstrated by application of the detector to two different radiation modalities: an HDR source in Chapter 6 and a small field proton beam in Chapter 7. The general outcomes of the measurements will be discussed in this section. Specific results relevant to the individual modalities were discussed in their respective chapters.

The following sub-sections include the achievements and limitations specific to the current prototype detector. The enhancement of these key achievements of the DHI detector which may be possible following further development are discussed in Section 8.4, along with an estimation of the magnitude of the improvement which may be achieved by implementing these changes. Suggestions for the development of future versions of the detector, to over-
come the limitations described here are also covered in Section 8.4. This section will also include a discussion of the fundamental limitations posed by this approach which will require considerable effort to overcome.

8.1.1 Achievements

The preliminary development of the detector using transmittance objects and alternative heat sources clearly validated the optical configuration of the detector and the reconstruction algorithms used, prior to any radiation measurements. The measure of confidence in the detector that was thus developed was essential to justify the application to hospital-based radiation sources, which have limited availability due to clinical constraints. These initial measurements showed that calorimetric temperature differences in the test cell could be probed non-invasively with good spatial and temporal resolution. Measurements achieved two dimensional maps of the relative temperature/dose distributions, to equal accuracy across the entire test cell sensitive region. The spatial resolution achieved by the system was excellent, with reconstructed pixels being on the order of $2-3 \times 10^{-2} \pm 2 \times 10^{-4} \text{ mm/pixel}$, corresponding to approximately 40 pixels/mm. This is superior to most alternative dosimetry options, except for film. Compared to alternative calorimetry based methods the ability to measure in two dimensions is a key feature.

The subsequent proof-of-principle measurements of the HDR source clearly showed that the DHI approach to radiation dosimetry is capable of resolving the miniscule temperature changes induced by radiation absorption within a test cell [273]. The dose distributions were resolved to the correct order of magnitude expected by comparison with modelled results, and qualitatively correct. Except for the presence of drifts introduced in the values from atmospheric influences on the system, the measurement results were within experimental uncertainties of the results expected from the model. The doses were measured in the difficult dosimetric region immediately adjacent to the source applicator, and a possible slight asymmetry in the positioning of the HDR source was determined, as was shown in Figure 6.13.

The proton beam results were also valuable, despite being somewhat more limited than the HDR results, due to the limitation of the achievable signal-to-noise ratio because of restrictions on the proton beam maximum dose rate. The measurements clearly demonstrated the practical aspects of the detector feasibility, such as its transportability. The prototype DHI
detector was able to be disassembled, transported halfway around the world, reassembled on site, and used to undertake measurements in a clinical situation, with the inherent constraints on accessibility and time. The measurement process was thorough and included consideration of the possible influence factors.

A key feature of the detector was that precisely the same detector could be used for measurements of both a proton beam and a gamma ray-emitting HDR brachytherapy source. There was no need to make any adaptations to the detector for measurements of a different energy or radiation type, and no need to account for this with any correction factors. In fact with the exception of the heat defect, and possible consideration of the lack of a full field scatter environment, the DHI detector has effectively no need for correction factors, as the detector can directly infer the absorbed dose to water from the measured temperature changes.

The modelling of heat diffusion for any three dimensional temperature field was successfully implemented, allowing for adaptation of the relevant dose models to account for the DHI measurement conditions, and allowing for a comparison of measured and modelled results.

### 8.1.2 Limitations

Whilst the preliminary results of the novel detector were promising, there are several areas which limited the results achievable. Most of the areas can potentially be improved by a refinement of the experimental design and measurement process, to the extent that they will not be limiting factors to the measurement of accurate radiation dose distributions. Suggestions to improve or overcome each of these limitations are more specifically addressed in Section 8.4.

Flat field measurements prior to irradiation found standard deviations of the noise in the range of 2.5 Gy - 6 Gy, which is considerable given that the maximum dose differences measured across the test cell were only approximately 40 Gy, when the averaging effect of the projection through the test cell was considered. This results in best case uncertainties of ±15%. These results effectively limit the current detector to measurement of radiation at high dose rates, where there is a high modulation of dose across the sensitive region. This was shown when the measurement of the proton beam dose distribution was limited because of the restricted dose rates achievable. To overcome this limitation requires a reduction of the noise in the system. Additional dosimetric uncertainties arising from dose difference
normalisation and temporal localisation can potentially be reduced by improvements in the measurement process.

The current detector has a fairly limited sensitive region due to the small size of the camera sensor. The result of this is that a limited region of the HDR dose distribution could be visualised, so the full applicator was not included in the measurements, resulting in increased uncertainty in the positioning. Additionally, the full extent of the proton beam dose distribution could not be measured in one image, with the surface dose and the Bragg peak being separated by a distance greater than the horizontal length of the sensitive region.

The outcome of the measurements being a temperature/dose map of the projection of the variation of this parameter through the test cell is a limitation, which affects the usability of the results. This is a measurement type which is not directly relatable to other dosimetry approaches, limiting the comparisons which can be made with alternative systems. Comparison with a three dimensional dose distribution is the only possible option, unless the dose has symmetry about a central axis. In this case the Abel transform can be used to convert the measured DHI dose to a full three dimensional array which can be compared to other dosimetric measurements, however there are also inherent limitations in the accuracy of the Abel transform which must be considered.

Discrepancies visible in some of the measurements show that further work is required to develop the detector to a state where it can achieve more reproducible and reliable measurements. The most major shortcoming was the influence on the detector from the ambient environmental conditions of vibrations, and temperature and pressure fluctuations. It is speculated that the main discrepancies between the measured data and model at longer irradiation periods are attributable to these effects.

Section 8.4 recommends various improvements to the detector, each designed to overcome or reduce the impact of some or all of these limitations.

8.2 Impact of Heat Transport

In other calorimetric dosimetry measurements the heat transport correction factor, often termed $k_{ht}$, is one of the most significant correction factors [35, 74, 106, 116]. For calorimetry
systems where the integrated dose is determined by measurement at a single point, \( k_t \) consists of the ratio of the ideal temperature rise at the measurement point due solely to locally deposited absorbed dose, to the actual temperature rise, with the effects of heat transport accounted for. For the DHI dosimetry, accurate consideration of the heat transport becomes more complex, and arguably more important, as due to the two or three dimensional nature of the measurements a single factor cannot be used. Ideally, irradiation in conditions that limit the impact of heat transport is ideal. For instance, in relatively flat broad beam geometries with limited temperature gradients, heat transport may be negligible. Measurements adjacent to or containing a penumbral region will be more affected. However, in order to exploit the key benefits of DHI dosimetry, most measurements are likely to be of applications where this radiation profile is not ideal for limiting heat transport. For this reason modelling heat transport is an integral component of an accurate DHI measurement. Additionally, to develop the potential for any sort of reference dosimetry for dynamic or non-uniform beams, the three dimensional effects of heat transport must be thoroughly understood [274].

For a full consideration of heat transport as it applies to calorimetric measurements, models of both heat conduction and heat convection should be included. For the prototype DHI system, conduction was modelled using the process described in Chapter 5. The validity of the model used and various assumptions made are covered in the next three sections. Heat conduction was ignored at this stage, with the justification for this covered in Section 8.2.2.

### 8.2.1 Evaluation of Heat Diffusion Model

The extent of the influence of heat diffusion on the DHI measurement results varies depending on the measurement conditions. The steeper the dose gradients present, the more heat diffusion occurs, and the higher the uncertainty in the heat transport calculations. For an external photon beam, the dose gradients are relatively small, so the heat diffusion would be a smaller problem. For the narrow proton beam with a sharp Bragg peak, and steep lateral dose drop-off, it becomes much more significant [275].

The finite element model based on heat balance equations which was used to determine the heat diffusion with the test cell during the irradiation was shown to have a mean uncertainty of less than 1% for the types of experimental conditions that the prototype detector was tested on. The accuracy of the model is dependent on the assumptions which were in the calculations, which are described in the following section. The accuracy achieved at this stage is sufficient, as the limiting factor in the measurements is the noise in the experimental
system rather than consideration of heat diffusion. To improve the heat diffusion model, the parameters used for these calculations can be optimised further to be more specific to the measurement situation, although there will fundamentally be some inherent limits on the achievable accuracy of the system. Potentially an alternative calculation approach such as the thermal-electric or thermal-dynamic analogy methods could further improve the model [276].

A further consideration is that, for longer irradiation periods, there is a greatly increasing relative impact on the temperature distribution due to heat diffusion compared to that due to more radiation dose deposition. This means that any inaccuracies in the heat diffusion model will be exacerbated and accurate modelling takes on a higher importance. An example of this for the irradiation conditions presented in Chapter 6 is shown in Figure 8.1. In this example, the HDR source was modelled for a 20 second irradiation, and the subsequent 0.2 s period was analysed, as this corresponds to the next frame of the image acquisition. The results are converted to a dose value to facilitate a more intuitive understanding of the impact of this issue on the measured results, but it should be remembered that the actual change is in the temperature field. The change in the anticipated temperature distribution over this time period was modelled separately for the effect of heat diffusion only (Figure 8.1(a)), and then for the effect of a further 0.2 s of incremental dose (Figure 8.1(b)). Figure 8.1(c) compares the change in temperature distribution for each effect directly, and Figure 8.1(d) shows the residual of the two. These results show that after a 20 s irradiation by the HDR source, the change in the temperature map due to the radiation dose still slightly outweighs that due to the heat diffusion, but it is close. This emphasises the importance of accurate heat diffusion modelling. At some point an equilibrium would be reached when the two effects are equal. Measurement once this steady state is achieved may reduce the uncertainties in the measurement, by reducing the need for accurate measurement timing, and by validating the heat diffusion model.

Validity of Assumptions

In order for the heat diffusion model used to be completely valid, there are various conditions: (1) the thermal conductivity coefficient $\lambda$, specific heat capacity $C_m$ and density $\rho$ are constants, independent of both pressure and temperature; (2) the velocity vector is equal to zero; (3) there is no exchange of heat energy between the surface of the test cell and its surroundings; (4) the temperature on the surface of the test cell is homogeneous and only a function of time. Some of these conditions are very difficult, or even impossible to satisfy.
Figure 8.1: The extent of influence of heat diffusion compared to radiation dose deposition on the temperature distribution for a 20 s HDR source measurement. Results converted to their equivalent dose values to facilitate interpretation. Radial dose profiles show the modelled dose distributions for: (a) 20 s distribution (blue), 20.2 s after only heat diffusion has occurred (red); (b) 20 s distribution (blue), 20.2 s after only additional radiation dose has been deposited (green); (c) comparing the change due to heat diffusion (black) and radiation dose (green) over the 0.2 s period directly; and (d) the residual difference between the two effects.
entirely. The validity of many of the calculation parameters chosen was verified in Section 5.3.1 when the variation in the heat diffusion results under different calculation conditions was determined. For instance for points 3 and 4, if the ratio of the irradiated volume to the test cell volume is small, the boundary effects were shown to be negligible. As the ratio increases, which may be required to increase the measurement sensitivity for some future DHI applications, the boundary effects become superimposed on the radiation heating pattern, resulting in distortions around the edges of the model, and errors of up to 50% exhibited in preliminary calculations.

An unrelated area to consider is the radiation model that the heat diffusion was calculated on. In order to achieve accurate estimates of the expected heat distribution, it was assumed that the radiation parameters were constant during the entire beam irradiation period. Variation in for example, dose rate, beam symmetry or flatness, or instabilities in the lateral dose distribution altered the reality compared to the generic model. For the HDR source this assumption is reasonably valid, but for the proton beam this may be worth investigating further. Sarfehnia et al. found that a significant contribution to the uncertainty in the heat transport models was due to the variation in irradiation times due to variations in the accelerator output dose rate and, in the case of scanned beams, the required time to change energy layers [96]. As the irradiation period increases the cumulative distribution will approach the expected distribution of the model, however there will be subtle variations in how the heat is deposited, resulting in small errors in the heat diffusion model. With decreasing size of the radiation beam, instabilities in the beam have an increasing impact on the uncertainties in the heat diffusion calculations [275].

**Cell Wall Influence**

The presence of the non-water cell wall was not accounted for in the heat diffusion calculations. According to Sarfehnia et al. this has the largest influence on calculation of the $k_{ht}$ factor [74, 96]. The deviation of $k_{ht}$ from unity was found to increase with increasing wall thickness, up to values of up to 4.7% for their irradiation conditions. However these measurements were made using a glass vessel, with glass likely to have a more significant impact than the Perspex used for the DHI dosimeter. Additionally, the substantially longer measurement times would also increase the extent of the wall influence. Simulations by Palmans et al. have shown that the impact of conduction from a glass vessel only appears approximately three minutes following the end of a two minute irradiation, with negligible
effect within the two minute irradiation period [277]. For these reasons, the choice to not include the wall effects in the present calculations is reasonable, and is unlikely to have adversely impacted on the accuracy of the results. For future development of the system, reduction of uncertainties wherever possible may be desirable, increasing the justification for modelling of the influence of the wall effect on heat diffusion. This can be done by defining the system with boundary conditions reflecting the impact of the cell wall material.

The additional effect which was not yet considered was the perturbation effects of the cell wall on the radiation field, due to attenuation of the primary beam and variation in scatter conditions. This effect is generally small, with various studies showing it to be less than 0.2% for glass test cells [277]. The irradiation properties of Perspex/PMMA are more equivalent to water than glass is, due to the average atomic number and density being more similar. Two groups have shown that for proton beams irradiating a PMMA vessel with similar size and wall thickness to the DHI test cell, the attenuation correction factor is equal to 1.000 ±0.00012 [277]. The values for photon beams are very similar, with only small variations due to differences in the relevant interaction cross sections, i.e. mass stopping powers for protons and mass energy absorption coefficients for photons [17]. If required it would be possible to include this influence into any Monte Carlo model of the radiation source, however those results suggest this may not be necessary.

### 8.2.2 Consideration of Heat Convection

The pilot studies completed with the prototype DHI detector ignored the influence of heat convection on the results when comparing the measured values to modelled values. This assumption is likely to be valid for the time frames of the irradiations measured. Natural convective motion occurs due to buoyancy forces created in a gravitational field by density variations within a medium [218]. In water convection is generally said to occur when the Rayleigh number exceeds 1000 [75]. The Rayleigh number is proportional to the thermal expansion coefficient, and a function of the temperature gradient relative to the distance to the medium barriers. In the context of DHI, the temperature gradients arising from irradiation of water and source self-heating are small enough that there is some lag time before the onset of convective effects. Additionally, if any convection does occur, the small size of the test cell used means that the cell walls act as a convective barrier, which decreases the effect of convective flow within the cell.
Malyarenko et al. who modelled the heat conduction and heat convection when their calorimeter was illuminated by a heat lamp to simulate the temperature effects of a radiation beam [234]. Their experiment resulted in a total temperature increase of 0.016 K after 30 seconds, increasing to 0.024 K after 90 seconds. These values correspond to the temperature change that would be induced by a radiation dose of 67 Gy and 100 Gy respectively. This is equivalent to or lower than the doses measured with the prototype DHI detector, with decreasing temperature gradients and therefore decreasing influence of heat transport, both convection and conduction. Figure 8.2 shows that significant convective effects do not take effect until 30 seconds after the start of the irradiation. As all the DHI measurements were made in a period of 20 seconds or less, the choice to ignore convection would appear to be validated. If longer irradiation periods are to be used, convection will need to be considered and accounted for.

Water has its highest density at a temperature of 3.98 °C, where the coefficient of volume expansion is zero [96]. If a calorimeter is operated in a narrow band around this temperature, then convection is minimised. However if a high degree of accuracy in the measurements is required, a small correction may need to be made for the effective depth of the measurement. This is due to the slight change of density of water at 4 °C compared to that of the standard reference conditions, usually 20 or 22 °C. The magnitude of the correction is less than 0.05% [96].

Figure 8.2: Figure reproduced from Malyarenko et al. [234].
Another consideration for limiting the formation of convection currents is the direction of the radiation induced temperature distribution. If the regions of higher temperature are located above the regions of lower temperature, then there may be negligible buoyancy forces produced. If the irradiation equipment permits, the irradiation conditions should be arranged to produce this effect as much as possible. For instance, external beam irradiation of a test cell in a vertical rather than horizontal direction creates a situation where decrease in dose with depth, outside of the initial build-up region, creates a vertically diminishing temperature profile. Measurement of a radiation source, as conducted in the early DHI HDR source measurements produces the same effect, if the source is partially submerged from the top. There are obviously situations where it is not possible to engineer this sort of dose distribution, for instance if the radiation gantry is only able to be horizontal, as is often the case for proton beam or synchrotron radiation measurements. An additional limitation for a proton beam even if a rotating gantry is used, is that the relatively long region of build-up dose before the Bragg peak means that the buoyancy forces can still be created, and therefore this approach cannot be used to reduce convective effects.

There may be situations for a given set of measurements where experimental limitation of convection via a short irradiation period, small volume test cell, operation at 4 °C and vertically decreasing and low temperature gradients, is not suitable. In these cases, then the convection could be modelled using the incompressible Navies-Stokes equations [278]. This approach has been used in other radiation calorimetry experiments [96, 234]. The result from Malyarenko et al. shown in Figure 8.2 appears to show some agreement with measured data in terms of the temperature at the sample point levelling off with time, but does not completely characterise the trend after the source is turned off. Alternative calorimetry approaches however are concerned with the dose at the point or points of measurement, rather than the full two or three dimensional dose field of DHI. Thus the correction for heat convection often consists of a single factor, which accounts for the cumulative effects of heat motion around the measurement region. Any discrepancies in the exact shape of the temperature map are likely to be averaged out. However the two or three dimensional DHI results must be corrected at a much greater number and density of measurement points. Therefore any discrepancies in the modelled convective currents, due to assumptions in the model or incomplete knowledge of the initial conditions will be more visible in DHI. For this reason it is anticipated to be difficult to conduct convection modelling to the extent necessary to be able to remove its influence entirely from the DHI results. It may be possible to optimise any model of the convective motion used for particular DHI irradiation conditions,
as described in the next section. However to achieve the highest degree of accuracy in the results the methods introduced for limiting or circumventing convection should be applied where possible.

8.2.3 Experimental Validation of Heat Transport Models

The multi-dimensional output of DHI is a key advantage over alternative point-based calorimetry techniques, and allows for the potential use of DHI for a fundamental evaluation of the accuracy of the heat transport models for radiation dosimetry. By recording DHI images after the irradiation has ended, any evolution of the temperature distribution map is due to heat transport effects. Taking the final irradiation frame as the initial conditions for the various heat transport models, the efficacy of the models can be tested without the complication of additional heat being added from an external source. Alternative calorimetric studies have reported similar measurements to validate their heat transport models, but the results are fundamentally constrained by the limited number of measurement points [74, 82, 96]. This could be of particular use for validating models of heat convection, where the exact temperature flow is much harder to predict than heat diffusion. By removing the modelled effect of the heat diffusion, the resultant images will represent the heat convection alone. This method can be used to quantify the extent of convection occurring, determine any predictability in the flow and optimise models if they are shown to be required. This would only be able to be achieved for systems where the heat transport results in temperature gradients which are of greater magnitude than the noise in the system. Validation of this sort could also potentially help to reduce the uncertainties introduced by the heat transport correction factors required in alternative calorimetric dosimetry systems.

8.3 Analysis of Uncertainty Budget and Evaluation Metrics

The method used for DHI dosimetry has many areas where uncertainty is introduced into the system. Some of the uncertainties are inherent to the DHI method, such as the noise in the system and the uncertainty in converting measured phases to absorbed dose. Other uncertainties are specific for the radiation type under measurement, and the measurement process required. These types include dose temporal and positional uncertainty, the influence of the heat defect, and the potential need for scatter and attenuation corrections. Uncertainty
analysis can be divided into two different types, known as Type A and Type B [279]. A combination of these approaches was used to determine the uncertainty estimates presented in Chapters 4-7.

Type A uncertainty estimates are represented by a statistically estimated standard deviation. The metric is based on deviation from the true value being due to random errors, with the measurement reproducibility acting as an indication of the uncertainty. The determination of phase by DHI was considered to be associated with Type A uncertainties. This analysis incorporates the uncertainties due to noise in the measurement system, beam output variations and some variation in ambient conditions. The extent of these uncertainties were well characterised in Chapter 6.

Type B uncertainties are based on scientific judgement of the possibility of error in specific measurement parameters, and represent possible systematic uncertainties in a measurement dataset. The anticipated range of possible values is considered, and bounds placed on the extent of certainty which can be achieved in a result. For the DHI analysis, these sorts of uncertainties included positioning errors, possible errors in the radiation model or subsequent heat diffusion model, and uncertainties in the conversion factors used to quantify absorbed dose from the measurement of the light phase variation.

The overall uncertainty budgets that were calculated for the HDR source and proton beam measurements. The gamma index analysis conducted on the HDR results in Chapter 6 was a first order check of these, by setting the dose tolerance to the level of the relative uncertainty on each point of measured and modelled data. Excluding the random distortions attributed to variations in air flows and external temperature effects, the results showed that the uncertainties were not underestimated. It is probable that there are redundancies in the way uncertainties were calculated, for example incorporating the dosimetric impact of a positioning error may mean that the uncertainty on dose was overestimated and can be reduced. Future investigation of this for the next iteration of the DHI detector will allow for accurate comparison of detector advantages and disadvantages.

An alternative way to check some of the assumptions inherent in estimating uncertainties, would be to devise a controlled test that can accurately produce temperature variations on the same order as those induced by absorbed doses. Due to the very small temperature variations involved, this is not a trivial matter. A possibility would be the use of incandes-
cent lamps, collimated and attenuated to produce small temperature changes in water, as used by Malyarenko et al. However the crude estimates of the spectral composition is still a limiting factor on the accuracy, and they only showed measurements to a sensitivity of approximately $100 \, \mu \text{K s}^{-1}$, which may not be enough to provide useful analysis of some of the system uncertainties.

Most of the sources of uncertainty in the DHI system are covered in other sections throughout this discussion chapter, when some key considerations and suggested improvements for the different aspects of the measurements are discussed. The following sections include mention only of those sources of uncertainty which have been accounted for in the uncertainty calculations but may require further consideration, and have not been discussed elsewhere. Many of the uncertainties in the measurements can be divided into two categories: positional uncertainties and dosimetric uncertainties.

### 8.3.1 Positional Uncertainty

Positional uncertainties arise where the positioning of the measured sensitive region with respect to the water surface and the radiation is not accurately known. This geometric error effectively results in the dose to specific locations being misrepresented in the results. These uncertainties were less significant for the HDR source measurements as the applicator was clearly visible on the measurement image; although due to the small size of the measurement region, only a small section of the applicator was visualisable, resulting in some uncertainty. Additionally, the excess internal space within the applicator and the potential asymmetry in source position could be a contributing factor. Both of these could be overcome by larger field of view measurements, so the entire applicator could be located, and the symmetry of the measured dose distribution around it calculated. For the external beam measurements, there were more potential errors introduced in the positioning. The template around the region of interest helped to reduce these, and the addition of a micrometre controlled translation stage to hold the test cell, and more accurate measuring equipment to locate it relative to the gantry would reduce these further. For this reason the positional uncertainty is considered to be a relatively trivial problem that in the future could be experimentally reduced to negligible levels.

An additional consideration in terms of positional uncertainty is the relative resolution of the DHI measurements, as opposed to any model or alternative measurements that it may
be compared to. For lower resolution comparison data, error in the positioning can be more readily introduced. Additionally, signal averaging in higher dose gradient regions may occur, which will also impact on the comparative doses. If this is of concern, then a higher resolution model should be used, which is easily achievable with Monte Carlo approaches. It is however also potentially useful to compare the DHI results with the output from a treatment planning system in clinical use, which is likely to achieve lower resolutions. In this case, the introduced positioning uncertainty due to resolution is unavoidable, and will need to be incorporated in the uncertainties.

8.3.2 Dosimetric Uncertainty

Uncertainties in dosimetry can be divided into two types: those which affect the relative dose, and those which affect the absolute benchmarking of that relative dose. Some of the dosimetric uncertainties contribute to both categories, while some are specific to one category. The contribution to dosimetric uncertainty from the relative shift will not be relevant if the stability and consistency of the measured results is improved in future versions of the detector, so that cumulative absolute dose values can be used. Additionally, a notable source of uncertainty in the current results is the fact that all data is compared back to a single reference image. With the current distortions visible in some of the measurements, careful selection of a reference image is important, to avoid propagating a single discrepancy through the entire image set. The selection of the reference image should be made by analysis of the image series acquired prior to irradiation starting, and selecting high quality images, with limited distortion, and phase values representative of the image series. It is also possible to average some of the image series, to reduce the influence of random fluctuations. Care should be taken not to introduce a systematic shift in the dosimetry values by averaging images that display some kind of artificial trend.

A different aspect of the dosimetric uncertainty which has not yet been considered is the small size of the test cell that was used. This means that the absorbed dose is measured in a volume which is not necessarily representative of full scatter conditions, especially for higher radiation energies. This may result in a somewhat lower dose than expected, however the effect is likely to be small for the limited field sizes in the present measurements, but would be worth considering if broad beam type geometries are studied in the future, or higher energy radiation. The exact extent of these irradiation conditions can be easily investigated with the use of a Monte Carlo model with active volumes of varying sizes.
With the present levels of noise in the measurement system, the choice of mathematical filter makes some difference to the measured doses. The filter smooths out noise, but potentially contributes to discrepancies in the shape of the measured dose distribution from what it should be. The use of Type A uncertainties based on the standard deviation of null images should account for these effects, but correct selection of a filter should prevent loss of information, the overestimation of the level of uncertainty required, or the recording of apparent signals which are actually artificially features of the noise. The choice of filter will therefore be dependent on the structure of the radiation, and the sensitivity of the system. As for the HDR source measurements presented in Chapter 6, multiple different filters can be used within an image in order to optimise the situation. Whilst the largest uncertainty in dose arising from the standard deviation of pixel values from the mean was used, further refinement of the uncertainty analysis may allow for a tightened uncertainty budget in some regions, depending on the filtration level required.

Temporal uncertainties are also another key component of the overall dosimetric uncertainty. Accurate timing systems should be developed, in order to allow effective time stamping relative to both the time of the reference image and the irradiation period. The current results approximated these time periods, and checked the validity of the results by confirming the number of images collected with the expected number. However this system could be improved upon, as suggested in Section 8.4.

**Calculation Parameters**

There are several calculation parameters used when converting from the measured phase change of the laser to the absorbed dose. These include the variation in refractive index with temperature and the specific heat capacity. Also for the heat diffusion modelling to be valid, there is a condition that the specific heat capacity and the thermal conductivity coefficient be independent of both pressure and temperature.

The first step when calculating dose is to convert between the refractive index variation in the water, as measured from the phase change, and the temperature change. This process was conducted using a sixth order polynomial fit to data reported by Bashkatov and Genina [243], as was shown in Figure 4.8. In order to estimate the accuracy of the fit, for the temperature region of interest for DHI dosimetry, a sixth order polynomial was also fitted to the inverse of the data. By converting from refractive index to temperature and
back again, it is possible to estimate the induced uncertainty as half of the variation in the value of the refractive index. Thus with the current data and fit used, an uncertainty of 0.5% should be added to this parameter. This value is only required for any future absolute dosimetry measurements, where an absolute temperature or dose measurement is required. For the relative dosimetry measurements, i.e. the spatially varying dose differences at each point in time, the error is negligible. This is because for the relative measurements, the dose difference between points is small enough that the uncertainty in the refractive index to temperature variation is very similar at each point, so therefore cancels out in the dose difference.

The next step is the conversion of temperature change to absorbed dose. It is assumed for the calculation of absorbed dose and for the heat diffusion model, that the specific heat capacity of water is constant with temperature. Over the temperature ranges of interest this holds true. As shown in Figure 4.8, a trend line was fitted to the plot of the temperature versus specific heat data from reported values [244]. From this it was determined that for a 0.001 K temperature variation, which encompasses the range of measurements used, the value of the specific heat capacity of water varies by less than $1.2 \times 10^{-5}\%$ [244]. If the ambient temperature in the water cell is incorrectly measured, the impact is also negligible. Variation by 1 K introduces only an 0.01% error into the value of the specific heat capacity. Controlling the temperature of the water and measurement of the water temperature is easily achievable to better than 1 K, so this error is effectively negligible, provided accurate source data is used for the specific heat values. This agrees with the analysis by Karger et al. and Medin et al. that the relative standard uncertainty for the water specific heat capacity used in the uncertainty budget for their calorimetric measurements be set at 0.05%, after they experimentally validated the heat capacity measurements [17,111].

In calculating the heat diffusion the value of thermal conductivity is assumed to be constant with respect to temperature. In reality, according to the data of thermal conductivity versus temperature obtained from The Handbook of Chemistry and Physics [244], in the range of normal room temperatures (20-25 °C), there is a 1.1% difference per degree in the calculated thermal conductivity value. The impact of this on the calculated heat diffused temperature distribution was quantified in Section 5.3.1, where the mean deviation for a typical proton measurement was found to be 0.28%.
Heat Defect

The heat defect is a key consideration in all calorimetric dosimetry measurements, as described in Section 2.2. No experimental efforts were made to reduce the heat defect for the initial proof-of-principle DHI measurements, as the influence is negligible compared to the other uncertainties in the system. However as the DHI detector is refined, reducing noise to gain increasing sensitivity, it will become increasingly important to limit or account for the heat defect.

The contributing mechanisms for heat defect depend on the impurities in the water and the LET of the radiation source. There is no inherent difference between DHI and alternative calorimetry systems in this respect, so the choice of a suitable medium can be considered by reviewing work in this field. The presence of oxygen gas in water has been shown to cause a strong transient exothermic effect when irradiated, of up to 10% [96]. Sarfehnia et al. used high purity water saturated with hydrogen gas for their proton measurements, and noted that any notable delay between measurements resulted in trace oxygen leakage into the system, and observable heat defect [96]. Sassowsky et al. have also reported a heat defect of effectively zero, to an uncertainty of ±0.3%, once hydrogen gas was used to remove all traces of oxygen from the system and following pre-irradiation until a steady state was reached [117]. These experimental results are in agreement with various numerical simulations of heat defect for proton beams [105, 106, 111, 116, 117, 277]. There are also a considerable number of studies investigating and accounting for the heat defect for low-LET beams, such as photon or electron beams, and similar results have been found regarding saturation of the system with hydrogen, nitrogen or argon gas [36, 245].

For DHI dosimetry therefore, experimental reduction of the heat defect should be achieved using hydrogen saturated water in a sealed test cell. This will require some modification of the current test cell as an open-topped design is currently used, and glass may be a more effective material to use to ensure the system is air tight. For measurements such as the HDR source, a complicating factor is the need to introduce a physical applicator into the test cell to house the source. It may be possible to incorporate an applicator through a small port, with air tight seals around it. If the DHI detector achieves sufficiently sensitive measurements then it should be possible to prove that this approach limits the influence of the heat defect to be negligible.
8.3.3 Use of the Abel Transform

Implementation of the Abel transform to estimate the three dimensional dose distribution overcomes a major limitation of the current DHI approach, which produces information on the dose distribution as integrated across the test cell. This means that it is in a format that physicists are inherently less familiar with, which can limit the understanding of the results, and potential utilisation of the method. Additionally, the unmodified DHI results have limited comparability with non-three dimensional point dose or planar detectors, except via a three dimensional model. In irradiation conditions with cylindrical symmetry, the use of the Abel transform overcomes these limitations, allowing a visualisation of any plane and therefore any point within the test cell. Provided the Abel transform results are interpreted with understanding of the regions where there are increased errors in the determined dose values, and used in conjunction with the original integrated dose results, this approach can add utility to the results of the DHI detector.

The mathematical solution to the Abel transform that was presented in this work was based on that proposed by Pretzler [261, 262]. This is a numerical solution based on the principle of Fourier-analysis, where the unknown radial distribution is expanded in a series of cosine functions, and the amplitudes then calculated by a least-squares fitting of the Abel transformed series to the measured data. In contrast, the conventional approach to the Abel transform determines the radial distribution iteratively in increments from the edges into the centre. The advantage of the Pretzler approach, and the reason it was selected for the initial implementation in this work is that it is known to be relatively insensitive to noise and errors in the determination of the location of the centre of the object. MATLAB code implementing this function was available from www.mathworks.com, the MATLAB file exchange [263]. An implementation of the basic algorithm was programmed in MATLAB for comparison purposes, and it was confirmed that the Pretzler code was superior at reconstructing radial dose functions with a higher level of agreement to the expected values, especially for noisy data and areas of sharply changing gradients.

The key limitations with the use of the Abel transform for this purpose is that there is a fundamental loss of information when the algorithm is applied to the measured data. Despite the improvements of the Pretzler algorithm on earlier methods, there is still loss of signal when the dose gradient varies, with the exact radial dose function unable to be precisely reproduced. Additionally, the presence of noise in the data can result in extreme oscillations within the result of the transform. Both of these situations occur in the HDR measurements,
the noise being inherent, and a very sharp change in phase occurring between the high doses adjacent to the applicator compared to the region where the sensor is physically shadowed by the applicator. Thus comparison of measured results to a model by means of radial dose function is inherently unreliable in the region immediately adjacent to the applicator. This may be of less concern for alternative radiation therapy modalities which do not experience such a sharp phase variation. Additionally, the assumption of cylindrical symmetry of the dose distribution risks losing any information garnered from measurement about any asymmetries in source positioning or beam flatness which may be detected from the measured results.

The Pretzler code was also utilised for the initial development of the second approach to heat diffusion that is described in Section 5.4. For this method the limitations of the code were more evident. This is because of the cumulative effect of the errors in the Abel transform, resulting in the final errors being proportionately higher than the signal being measured. As described in that section, in order for that approach to be implemented alternative improved versions of the Abel transform would be required. There are multiple groups in the field of mathematics working on this problem, with a variety of approaches reporting promising results for noisy data which look like they may be of use for these DHI results [280–282]. For example, Dribinski et al. report an Abel transform approach based on a variation of the basis-set expansion approach used by Pretzler which improves the accuracy in particular in the region close to the symmetry axis [280]. Gonzalez-Ramirez et al. and Dixit et al. have developed approaches which achieve stable numerical inversion of experimental intensities distorted by noise, using a Kalman filter approach and a direct operational matrix of integration approach respectively [281, 282]. Further study is required into these algorithms to understand the benefits and limitations of the different approaches, implement them in MATLAB and conduct a comparison study as to which will provide the most advantages for the specific requirements of DHI, in particular for the Method 2 heat diffusion calculations.

The Abel transform could also be potentially useful if a tomographic approach to DHI is developed (this is described in Section 8.5). A tomographic DHI with sufficient beam angles to allow for a full tomographic reconstruction would inherently determine a three dimensional dose distribution. This may not be possible to achieve however, in which case the most successful approach may prove to be a limited projection approach such as for tomosynthesis. This would involve a refined estimate of the three dimensional image reconstructed from projections at a finite number of angles, likely to be limited to two or three. In this
situation, the use of the Abel transform of each of the images could provide a comparison to estimate the accuracy of the reconstruction algorithm. Additionally, multiple measurement angles could be used to prove the cylindrical symmetry of the radiation, in which case a limited projection tomographic reconstruction may actually provide less information than just using the Abel transform directly on one or all of the images.

Radial Dose Function as an Evaluation Metric

The radial dose function is used for cylindrically symmetric geometries, and is a measure of the dose along any given profile in a radial direction from the longitudinal axis of the dose distribution. For HDR source dosimetry, it is a key parameter in the TG-43 algorithm, and for proton dosimetry it is a useful parameter for comparison of measurements from different dosimetric approaches. The radial dose function can be calculated from the current DHI results by means of the Abel transform [260].

The radial dose function was calculated for a subset of the HDR prototype measurements. Reductions in noise of the measurements would allow for improvements in the accuracy of this function. The extent of the noise in the images for the HDR results determined the distance from the applicator that was affected by the wild oscillations in the Abel transform result, as was shown in Figure 6.22(a). For datasets with increased standard deviation of the noise, the radial position to which the Abel radius was approximately accurate was further from the central axis. An exact correlation for the extent of this effect was not able to be determined from the limited datasets, because the extent of the noise had a limited range across all the measurements. Future measurements could consider investigating this effect further in order to provide an estimate on the limits of accuracy of the Abel transform.

Improvements in the Abel transform implementation, as described above, as well as experimental improvement of the signal to noise ratio should improve the applicability of the radial dose function as an evaluation metric. It may become possible to use DHI to validate some aspects of the TG-43 protocol.

8.3.4 Gamma Index as an Evaluation Metric

The gamma index is commonly used in radiotherapy dosimetry as an evaluation metric for considering the agreement between two or three dimensional dose distributions [267].
metric was developed as a means of overcoming the limitations inherent in using dose difference or distance-to-agreement comparisons, which were prone to failure in low dose and high dose gradient regions respectively. Understanding of the areas of limitation of the metric are important when interpreting the results of a gamma test. As the gamma index is likely to be a very useful tool in evaluating results of future DHI measurements, an introduction to these uncertainties is given here.

The gamma index is a more useful metric for the comparison of three dimensional dose distributions than two dimensional distributions, because for a two dimensional dose distribution the degree of agreement with the two datasets can be more easily visualised without additional calculational methods. However a gamma test is still of value, as it provides a quantitative result, which is comparable between multiple dose distribution comparisons. The output of a gamma index test is a numeric indicating the percentage of points within the test region or volume which passed the gamma criteria (e.g. had a gamma value of less than one). Results should be interpreted with caution however, because in the presence of excessive dose differences in the high dose gradient region and/or large DTA discrepancies in low dose gradient regions, the result could still be a high value, as the test does not distinguish between those datasets that failed grossly on a large number of points, from those which are close to passing. The test is generally more prone to failure in low dose regions compared to any other region, but the failure is more likely to be of less significance in terms of absolute dose, so these regions should often be ignored using a low dose threshold. Grouped failures in high dose or high dose gradient regions are more likely to be of significance. Thus examination of a sole gamma index value is not sufficient for fully determining the degree of agreement between datasets. Studies on the use of the gamma index for use in QA of IMRT treatment plans have suggested that simple pass/fail use of the gamma test may not be the best way to determine the quality of the agreement of the measured dose distribution with the model [283]. Alternative suggestions include the use of further parameters based on the gamma test, including maximum gamma index value, average gamma index value and connected area of evaluated points with gamma index $>1$ [284–286]. These methods may also be of use if a gamma test is used to quantify the agreement of DHI measured dose distributions with the expected values.

An additional consideration is that the gamma test is also highly dependent on the normalisation method used [285]. The choice of normalisation position (e.g. maximum dose, dose to a local point, surface dose etc.) is important, because the percentage value used for the
uncertainty will result in quite different absolute dose differences which are being compared, depending on the dose value of the normalisation point.

The degree of noise in the two comparison datasets is also of importance [287]. The impact is asymmetric, with the levels of noise in the reference data versus the evaluated data having differing effects on the gamma test pass rate. When the gamma test is conducted, each point within the evaluated data is considered in turn, and the surrounding points in the reference image are searched to determine the closest match. As would be expected intuitively, the presence of noise in the reference data makes this search more likely to find a good match for each point, so the gamma index becomes lower and the test pass rates increase. Alternatively, noise in the evaluated image moves the values at each point away from the reference, decreasing the likelihood of locating a good match, so the gamma test pass rate decreases. With increasing standard deviation of the noise the trends in both cases are exacerbated, with higher impact from random noise than from spatially correlated noise. For this reason, it is important to consider the relative noise in the datasets when selecting the reference data compared to the evaluated data. In the case of the DHI results, generally the calculated model results will have lower noise than the experimental results, so this should be used as the reference dataset in the gamma comparison. If two empirical datasets are compared, which are both affected by noise, then the gamma index could be calculated twice with switched roles for the reference and evaluated images, to determine a composite result. An additional important consideration is the impact of the image resolution on the noise. A decreased image resolution results in lower noise, which will affect the gamma pass rate. For this reason the standard deviation of image noise should be stated when reporting a gamma index, as it can give an idea of the uncertainty inherent in the gamma test evaluation.

The approach taken when analysing the HDR results (Section 6.2.6), in determining the points where the two dose distributions agree to within experimental uncertainty is a useful concept for analysing the results of the DHI measurements in terms of the validity of the uncertainty estimates for both dosimetric and positioning error. If sufficient magnitude uncertainty is included then the gamma test should show a 100% pass rate when the total uncertainty values are used as the threshold criteria. This is complicated by the fact that the dose deviation parameter is global, i.e. proportionate to the signal, as the gamma test uses a single threshold value across the whole region based on a percentage of the maximum dose. It would be possible to implement the test with variable threshold values across the dataset, which would allow this to be accounted for. This may be an area of interest to
achieve a simple three dimensional evaluation of measurement accuracy and estimation of experimental uncertainties, which could be used for future development of the DHI detector, or any other multidimensional dosimetry approach.

8.4 Recommendations for Experimental Improvements

Based on the preliminary testing of the detector on the proton beam and HDR source, a range of possibilities for improving the detector have been determined. The improvements which apply specifically to the proton measurements have been described in Chapter 7. This section will describe more general improvements to the system, and summarise the specific improvements. The extent of the gains achievable by implementing these modifications are estimated where possible, based on the understanding of the abilities of the current system, and by comparison to literature results of DHI measurements of temperature distributions in alternative industries.

There are various types of modifications which could induce notable improvements in the current results: from the precise configuration of the interferometer, hardware choices, and measurement conditions, to improvements and extension to the experimental process. These aspects are combined to achieve some of the aims described in the sections below.

8.4.1 Independence from Ambient Conditions

From analysis of the initial pilot study results on the HDR source and the proton beam, it is evident that considerable improvements to the reliability and usability of the results could be achieved by better isolation of the detector from variations in the ambient conditions. Ambient temperature and pressure fluctuations, and the resulting air flows vary the conditions experienced by the laser beam. The major cause of noise and extraneous signal is the temperature and pressure variations in the air portion of the laser path. A less significant cause is temperature induced expansion or contraction of the optical components. These effects alter the phase of the laser light, creating a signal which is conflicting with the phase variations due to the radiation induced temperature increase in the test cell. The phase of the laser light varies throughout the interferometer, with the signal measured being the difference in phase, and therefore optical path length, between the reference and object.
beams of the laser. The only part of the system which is producing the signal of interest is the variation in phase of the water contained within the test cell. The inherent assumption when interpreting the results is that the phase change of the entire reference beam, and the object beam everywhere except the test cell, is temporally constant. This was shown in the pilot study measurements to not be the case however. This is consistent with results from other calorimetric based studies, where thermal drift in the laboratory is detected in baseline measurements, even for systems with good experimental isolation [111, 116, 234]. For measurements at a single point of reference, this can often be approximated as a linear background drift, and subtracted out to obtain accurate radiation induced temperature increases. Unfortunately for the two dimensional nature of the DHI images, the variations have been demonstrated to be not easily predictable, and can vary quasi-randomly both spatially and temporally. This problem is exacerbated because the magnitude of the changes required to noticeably interfere with the results is relatively low.

There are two different approaches for dealing with this problem. The first is to correct for aspects of this issue with the use of careful control measurements. The second approach is to attempt to reduce or eliminate the external influences. The second approach is fundamentally a better approach, however may be technically difficult to realise in practice. Methods to undertake each approach are proposed in the next sections, along with a discussion of the advantages and limitations of each.

**Simultaneous Control Measurements**

The first approach to reducing the influence of variations in the environmental conditions is by the use of simultaneous control measurements. This concept is similar to the use of a reference ion chamber to correct for beam output variations during linear accelerator water tank measurements. For DHI, the principle is based on the theory that two laser beams, if they are sufficiently close together and pass through as many of the same optical components as possible, will experience the same change in phase. So the proposal is to build an interferometer configuration, with an inbuilt second interferometer which closely mimics the path of the first, except the object beam will not pass through the test cell. A proposed design is suggested in Figure 8.3.

The inclusion of multiple extra optical components for the control interferometer, and the need for larger mirrors and space for the beam path would probably require a larger breadboard. More efficient clamps and holders for some of the optical components could allow
The control interferometer would be reconstructed using the same algorithm as has been used for the test interferometer in the prototype DHI detector. This would allow the control images to be subtracted directly from the test image, in order to remove the influence of possible atmospheric effects. This system would not account for all possible effects, as the spatially separated paths of the reference and object beams means they may still encounter slightly different patterns of airflow. As shown in Section 7.2.2 however, the predominant airflows visualised in the proton room were vertical convective air currents. With sufficient casing around the system this is likely to be the rule rather than the exception. The vertical gradients are less spatially localised, so it is hypothesized that there will be reasonable equivalence between the test and control measurements. This system would also account for any pressure variations in the room, and, if the same types of optical componentry are used for each path, similar expansion effects on the components.
The space constraints of this design may complicate the application of the further suggestions made in the remainder of Section 8.4, however with careful implementation this is believed to be a valid approach to accounting for the impact of ambient condition variation on the results. If successful, this benchmarking of the phase change allows for the phase variation in the test cell to be successfully isolated. This would allow the system to achieve absolute dosimetric measurements, where the cumulative dose over the measurement period could be accurately determined. This concept is discussed further in Section 8.4.3.

Isolation from Air Flow and Temperature Variation

The second approach to reducing the influence of variations in the ambient conditions is more direct, and involves isolation of the system as much as possible from the surrounding environment. This requires the use of an improved housing system for the optical system. There must be an external window to the system for the radiation beam to enter. This has the negative impact of introducing an additional attenuating object in the beam, however if a suitable material and thickness is chosen this could be acceptable. Additionally, the laser and the camera sensor should probably also be located outside of the temperature controlled housing, so that the heat generated while they are running does not impact on the controlled temperature. The windows for these may distort the results slightly, although this is unlikely to have a significant effect.

It may be useful for the housing system to be temperature controlled. A key advantage of this would be the ability to control the temperature down to a level of 4 °C, which is the recommended temperature for calorimetric radiation measurements \[35,36,276\]. This temperature is when the density of water is maximal, and measuring here optimises the reliability of the value of the specific heat of water \[116\]. Operating the system at this temperature would increase the sensitivity, and lower the uncertainties achievable by the system, compared to operating it at room temperature. The use of controlled temperatures may also allow for the finite size of the test cell to be incorporated more accurately into the heat diffusion calculations, as the extent of the heat diffusion through the walls of the test cell would be more consistent and predictable.

There are several considerations with regards to the design of temperature controlled housing. The temperature must not be maintained by pumping air through the housing, as this would introduce air flows of varying temperatures. The design of the temperature controlled system which was utilised by Seuntjens \textit{et al.} for their calorimetry measurements of an HDR
source is a good model to base the design for DHI housing on [116]. Their portable water calorimeter was built in-house, and utilizes active cooling by controlling the temperature of a copper shroud using a Neslab RTE-7 refrigerated bath/circulator, rather than through air circulation. The casing consists of two 5 cm Styrofoam slabs, separated by a 5 mm copper plate, with the entire system encased in a 1 cm thick plywood box. The temperature of the copper plate can be easily and accurately adjusted to counter for variations in internal temperature as measured by temperature probes in the internal cavity and in the copper. The Styrofoam has insulating properties to reduce the rate of any heat transmission from varying external conditions. The entire system can be controlled to a temperature of 4 °C. The lack of airflow within the system means that slight variations in temperature which are not detectable by the independent temperature probe will not be of impact on the qualitative images of the dose distribution.

Improving the detector housing would be key in limiting the influence of air movement and temperature variations on the DHI measurements. The housing would however increase the weight and complexity of the system which would limit the portability, which is a key requirement of the DHI detector. It would also not isolate from any ambient pressure variations, however as the pressure is generally relatively stable in the absence of changing weather conditions, this is believed to be a much less significant effect.

An alternative approach which may be easier to implement, but has certain downsides, would be to utilise a fibre-optic-type system, like that described in Section 4.4.4. This would reduce the impact of temperature flows and slow changing temperature gradients, however the system would still be subject to these in some sections of the system, and the impact of vibrations would significantly increase, due to vibrations of the optical fibres. Section 4.4.4 described some of the key advantages and limitations of this approach, which will not be repeated here. The limitations in terms of environmental influences are that there would still be potential for expansion of the components and optical fibres, and pressure fluctuations would not be accounted for. However, the conversion would be relatively straightforward and not encounter the space constraints of the control interferometer approach, or the bulk of the temperature controlled housing.
8.4.2 Sensitivity Improvements

Improving the sensitivity of the DHI detector is key to increasing its accuracy and potential for application to lower dose rate measurements. There are two approaches to improving the effective sensitivity of a measurement: decrease the experimental noise, or increase the signal. Noise in the system includes the impact of vibrations and any inherent defects in the image quality, as well as the influence of ambient conditions described in the previous section. Brief suggestions of methods to reduce the vibrational noise and improve image quality are introduced below, as well as considerations for means to increase the signal.

Consideration of Vibration-Induced Noise

The influence of vibrations on the results is a key source of noise, reducing the sensitivity of the measurements. In order to reduce the impact of vibrational noise, it is necessary to identify the sources of the vibrations, and take steps to mitigate them where possible. There are several different types of vibration which are relevant to the DHI detector, including seismic vibrations, acoustic vibrations, and forces on the working surface. Seismic vibrations occur when the floor under the experimental set-up is caused to vibrate, which is transmitted to the working surface. The sources of these include wind on the building, people moving around, nearby traffic, and building ventilation. Many common seismic sources also generate sound, or acoustic vibrations, which are detected as local air pressure variations within the experiment, although these are generally of less significance than mechanical motions. Forces on the working surface are generated by any vibration sources which are directly coupled to the experimental set-up, such as fans within equipment or moving translation stages. For instance the slight movement caused by the HDR brachytherapy source as it extends from the afterloader may be a source of this type of vibration. Vibration types can be further classified as periodic or random. Periodic vibrations occur at a given frequency, for instance a vacuum pump. Random vibrations are from unpredictable sources, such as wind, traffic and people.

In any given clinical situation the types of vibrations present will be specific to the surroundings. There is often an ambient noise spectrum due to structural and acoustic vibrations. It may be possible to isolate the source of a vibration based on the measured characteristics of amplitude and frequency of the spectral components. Typical frequencies in a laboratory situation are between 4 - 100 Hz [288].

Whilst it is a good general principle for interferometric experiments to limit the contributing
sources of vibration as much as possible, due to the need for transportability and ease of use of the DHI detector in a clinical setting it is not necessarily feasible to incorporate a high quality vibration isolated table into the transportable DHI set-up. If it is possible to incorporate a vibration isolated table, it should be selected to have suitable damping characteristics for the magnitude and frequency of the vibrations present. The present prototype DHI detector did incorporate half tennis balls under the breadboard to reduce the transmittance of mechanical vibrations, with a measurable reduction, however the influence of vibrational noise cannot wholly be eliminated by this method. Therefore as far as possible the contributing sources of vibrations should be limited at their source.

Air conditioning systems are a key factor in the ambient noise spectrum, producing periodic vibrations as the fans rotate. The reduction of influence from ambient conditions was discussed in the previous section, however if possible the air conditioning should be turned off entirely during the measurement times. This is often not possible due to the location of the clinical room within the facility’s wider air-conditioning network, in which case if possible the outlets should hermetically sealed for the duration of the measurements. Other vibration sources such as random noise due to nearby people, traffic, and machinery may be reduced by conducting measurements out of normal hours. However it should be noted that experiments have found that the local phase can fluctuate by several tenths of a radian over measurements even for measurements performed at night, in an empty building with ventilation turned off, and a vibration insulated table [289]. This is due to local eddies and air disturbances. For instance any power source such as for the laser or computer may produce small temperature differences which moderate the refractive index of air on a small scale. The impact of this can be minimised with effective housing of the interferometer as described in Section 8.4.1.

Improvement of Image Quality

All of the reconstructed images from the prototype DHI detector showed some degree of inherent defects in the images due to scattered light. The interference patterns formed overlaid on the main image, resulting in the so-called null images not being completely uniform. Various methods are suggested to overcome this issue in future iterations of the detector, including the use of higher quality optical components, the use of tubing surrounding the paths of the laser light to prevent dust and extraneous reflections from impinging on any of the mirrors, and a reconfiguration of the detector to avoid creating the unwanted reflections
and scattered light in the first place. All of these approaches should help to reduce the measurement noise, thereby improving the sensitivity of the detector. Alternatively, pulsed low coherence light sources have been shown to be efficient at taking away disturbances from other scattering surfaces during speckle interferometry, so this is an avenue which could be explored for DHI [289]. The use of a low-coherence source effectively defines the volume in space in which the information detected is isolated, and effectively filters out information outside this volume.

**Interferometer Configuration**

A fundamental method to increase the measured signal strength from the radiation induced temperature change is to sample it multiple times. This can be achieved with the use of a double pass interferometer configuration, where the object beam of the laser passes through the test cell, and then doubles back directly on itself before impinging on the sensor. This approach would inherently increase the signal strength by a factor of two. The noise in the system is unlikely to increase to the same extent, resulting in an improvement in the signal to noise ratio, and thus a more sensitive detector.

There are various ways in which a double pass interferometer can be configured, including the basic Michelson Interferometer described in Chapter 3, and pictured in Figure 3.1. Care must be taken that the selected configuration results in the path of the laser in each direction through the test cell being exactly coincident upon itself, otherwise the spatial resolution of the system is reduced. Additionally, the laser cannot pass more than twice through the test cell, or there will be multi-order interference patterns produced, which will make the determination of phase extremely complex. These requirements limit the interferometer types which can be developed to include a double pass probe. For instance, an extension arm on the LFTDH would be possible, however the test cell must then be located a significant distance from the rest of the detector, in order to constrain the angle between the two test cell paths. This would have some advantage in terms of locating the optoelectronic components away from the region where they are likely to undergo radiation induced damage. It would also reduce any impact of scatter from the high density components in the interferometer. However physical separation of some optical components from the remainder of the interferometer may result in the varied influence of vibrations upon different parts of the system, and more influence from ambient environmental conditions. This would result in comparatively more noise in the images, however this may be of less extent than the increase
in the signal due to the double pass geometry, meaning this may still be a viable option.

**Choice of Sensing Medium and Laser Wavelength**

Water is the medium of choice for dosimetric measurements, as the absorbed dose to water is the operative quantity used in all modern radiation dose prescriptions, as a representative of tissue dose. For this reason, most dosimetric techniques go to some lengths to convert dose in a non-water medium to dose to water, introducing a level of uncertainty via the correction factors used. Therefore for DHI dosimetry water is the obvious choice for use as the sensitive medium. Conveniently, water has a sufficiently well characterised relationship between refractive index and temperature, as well as between absorbed dose and temperature. The exact conditions in which the water should be used in order to reduce the impact of any heat defect are described in Section 8.3.2. However in the context of increasing the sensitivity of the detector it is possible that other mediums may have a more favourable relationship between these physical parameters.

In the original holographic interferometry dosimetry experiments by Hussmann and Miller [24, 26], the use of an alternative medium with a lower specific heat value or higher ratio of refractive index to temperature was proposed to improve the sensitivity. Miller also made measurements in isopropyl alcohol, glycerine and an unspecified high atomic number solution, to compare the relative depth dose curves achieved. No account was given of how they calibrated the system to correct for the variation in refractive index with temperature, or any heat defect, if indeed they did so at all.

Ideally any medium would have a higher refractive index to temperature ratio as well as a lower thermal conductivity, \( k \). This would both increase the sensitivity and decrease the uncertainty arising due to the influence of heat diffusion. This combination of parameters tends to occur more in non-polar substances. Table 8.1 shows values for some commonly available liquids [290].

An alternative approach which has been considered is the use of DNA based solutions. This is based on the principle that alterations to the DNA can cause a variation in the refractive index. This phenomenon has been used by many groups for studying processes associated with DNA, such as by Sun *et al.* who looked at DNA hybridization [291]. The theory is that the primary mode of lethal radiation damage to cells is due to irreversible damage to

262
Table 8.1: Ratio of refractive index to temperature and thermal conductivity for common liquids.

<table>
<thead>
<tr>
<th>Liquid</th>
<th>(\frac{dn/dT}{k}) (cm W(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>-0.013</td>
</tr>
<tr>
<td>Methanol</td>
<td>-0.19</td>
</tr>
<tr>
<td>Acetone</td>
<td>-0.31</td>
</tr>
<tr>
<td>Benzene</td>
<td>-0.44</td>
</tr>
<tr>
<td>Isooctane</td>
<td>-0.5</td>
</tr>
<tr>
<td>CCl(_4)</td>
<td>-0.57</td>
</tr>
</tbody>
</table>

the DNA, and therefore that a valuable metric for dose is to determine DNA damage. Variation in the refractive index of damaged DNA plus that of the water solution could increase the sensitivity of the medium. However as far as could be ascertained no studies have yet been conducted on the extent of the variation of the refractive index of DNA with radiation damage, and it is believed the effect is likely to be relatively low.

For any alternative mediums, including a DNA solution however, it is thought unlikely that the increase in dose resolution with any alternative medium would have a significantly large benefit as to warrant the complications and uncertainties of accurately calibrating the relationship of absorbed dose to water and the refractive index of the medium. Particularly for the DNA solution, the relevant parameters have not yet been independently quantified. The calibration would require determination of both the extent of radiation damage to the DNA, the subsequent effect of this on the refractive index, plus the existing considerations of determining the temperature increase of water, and whether the presence of the DNA has any influence on this. If DHI does become an established dosimetry technique however, this opens an avenue for its potential usefulness for examining the extent of radiation damage as it occurs.

The other approach to improving the sensitivity of the system without changing any of the key process would be to use a laser with a shorter wavelength than the 633 nm He-Ne laser currently utilised. The shorter wavelength leads to a greater change in phase for a given change in refractive index, meaning they are more sensitive. This will also have the benefit of a decreased absorbance of the laser light in the water, with 380 nm laser causing a temperature increase four times lower than that of a 700 nm laser. Most modern digital sensors are generally sensitive to light in the UV range, depending on the filters used, if any [292]. A non-filtered CMOS sensor can usually measure UV photons down to a wavelength of 200 nm, thereby achieving three times the sensitivity of a He-Ne laser. That being
said, it is the signal to noise ratio which is the current limit on resolvability of the measured doses, and the more sensitive laser would also be proportionately more prone to noise, so no experimental gain is to be achieved by this until the noise is reduced. The lower limit on sensitivity with the current wavelength light should be reasonable for most dosimetric purposes.

Image quality and sensitivity can also be artificially improved by post-processing the images, in a mathematical equivalent to measurement procedures such as phase shifting, as described in Section 3.3.3. An example is the work by Demoli et al. who propose a pointwise operation which can achieve a manifold increase in apparent sensitivity, limited only by the noise in the system [293].

**Irradiation Configuration**

One means to increase the sensitivity of the DHI detector is to configure the irradiation of the test cell such that the only variation in dose is effectively limited to one or two dimensions, rather than three. If broad beam geometry is able to be used for the irradiation, whereby the test cell is fully contained within the range of the flat part of the radiation beam with no penumbra, then the only significant variation in absorbed dose is with depth. This means that the signal is effectively not averaged across the width of the test cell in the direction of the laser beam. Whilst this does not actually impact on the signal to noise ratio, it does mean that the measured values will be able to be recorded as the actual dose values, and not the projected dose values. Additionally, in one direction on the recorded DHI images the dose profiles should be constant, allowing for signal averaging. This results in a depth dose curve that has an improved signal to noise ratio due to any random noise across the image being decreased, and increasing the statistical significance of the measured dose.

The limitations of this approach are the reduction of the acquired dose information to one dimension, which reduces one of the advantages of DHI over the point or volume integrated doses acquired in conventional calorimetry. Additionally, it is not always feasible to apply this approach, depending on the radiation modality. For instance measurement of an HDR source would not be able to exploit this technique. The measurement of other radiation systems is also generally limited by the collimation systems that are available.
8.4.3 Absolute Dosimetry

The output of the prototype DHI detector is currently the measurement of relative dose distributions, rather than absolute or total absorbed dose in the medium. The result is a series of dose difference maps showing the variation in dose across the field of view at each time instance. Due to the lack of temporal stability in the phase values of the images, an absolute dose value is not able to be determined to benchmark the dose differences against to determine total dose. This limits the measurements to those where the dose modulation in at least one dimension is high enough to be detected. Any dose that is applied evenly across the whole field of view is not measurable. The ability to measure relative dose distributions means that DHI could be a useful tool for many highly modulated radiation types, however with some improvements the system has the inherent potential to do absolute dose measurements, which would greatly expand its usefulness. Accurate absolute dosimetry would allow for the investigation of the use of DHI for reference dosimetry for a range of radiation types, as well as measurement of radiation that has only low dose gradients across the field of view. It would also allow for validation of the methods to account for heat diffusion, as described in Section 8.2.3. This would be required for any potential use for reference dosimetry.

In principle the dose measured at each point in a DHI image should be able to be compared directly back to the reference image to determine the total dose represented by each pixel, according to the measured phase difference. If there is sufficient dose to cause a phase change of greater than $2\pi$ this phase jump could be determined by visualising the series of images. It would also be possible to compare each image to the previous image rather than an original reference image, and obtain the total dose by the accumulation of the series, which should give the same result. This approach relies on their being no extraneous influences causing the phase to vary independently of any radiation dose. If the suggested modifications to the DHI detector which were described in Section 8.4.1 are implemented, this may allow for the stabilisation of the phase sufficiently to allow for absolute dosimetry to become possible. The degree of accuracy achievable would be the same as for the relative dose distribution measurements, limited only by the extent to which the phase stability is achieved. The accuracy may in fact improve, as there would no longer be uncertainty introduced by the difference normalisation process, which was described in Section 7.1.2.

In order to achieve accurate temporal resolution for the DHI results, a high quality three dimensional phase unwrapper may be required. Three dimensional phase unwrapping is more complex than the two dimensional problem with the complications being due to excess noise.
in the measurement system. If there is no noise in the system, three dimensional unwrapping is straightforward. However with increasing levels of noise, pixels which appeared to be correctly dealt with in one plane may cause discrepancies in other planes. So in order for successful absolute dosimetry to occur, a suitably robust phase unwrapper should be chosen, and the noise of the images, both within each image and between images, should be reduced as much as possible.

An additional step to improve the accuracy of the results in order to enable absolute dosimetry, could be to encase the test cell within a larger block of water equivalent material in order to create full scatter conditions. Appropriate paths for the reference and object beams would need to be drilled through, and alignment could be more complicated, however this approach would provide a more clinically relevant result.

8.4.4 Spatial Resolution and Sensitive Region Size

Modifications to the system to potentially increase the size of the sensitive region were covered in Section 7.3.4, and will not be re-described here. Improvements in the size of the sensitive region would be of benefit to measurement of all types of radiation, especially if the spatial resolution is not significantly decreased. In fact in some cases it would be desirable to increase the spatial resolution, even if this comes at the expense of a decreased sensitive region. The discussion in Section 7.3.4 did not mention this concept, but all of the techniques which were described can also be used to increase the spatial resolution. A camera sensor with higher inherent resolution would be the primary means to achieve this. An alternative approach is to expand the reference and object beams after they are recombined, and project the expanded version on to the original resolution sensor. This increases the measurable resolution within the image features, although reduces the measurement size. Theoretically the only inherent limits in the extent that the resolution can be increased to are the random noise in the system, the need to retain a usable measurement region, and the power of the laser beam that is used. So overall, the spatial resolution and sensitive region size can be tweaked depending on the particular experimental requirements of any given dosimetric aims.

8.4.5 Experimental Process

A further improvement to the experimental process of acquiring a DHI measurement would be the use of a micrometre controlled three dimensional translation stage for accurate po-
sitioning of the test cell. This would reduce the uncertainty in dose measurement and heat diffusion calculation introduced by uncertainties in the exact localisation of the sensitive region relative to the radiation beam, as quantified in Chapter 5. This would also allow for improved consistency in positioning of subsequent datasets, which effectively increases the sensitive region of the detector by being able to “stitch” together data acquired in different irradiations. This process would then allow for a more accurate normalisation of the data, which would be particularly useful for comparing to model datasets or measurements by other detector types. Accurate positioning would also allow for the more precise understanding of the true dose values by allowing for the integration of dose across the test cell to be calculated to a much smaller region by ensuring the beam is centrally located.

Another consideration for the experimental process is the timing accuracy of the measurements compared to the irradiation time. The current method introduces a significant amount of uncertainty into the system. Incorporation of a trigger system whereby the time-stamps of the camera recording are accurately benchmarked against the radiation would be extremely beneficial. The exact means for achieving this depends entirely on the control system of each radiation source and whether it is possible to link external devices to this. For this reason no specific method has been proposed here, and the possibilities should be discussed with the control room scientists when specific measurements are planned.

8.5 Considerations for Extension to Tomographic Acquisition

A key limitation of the basic DHI dosimeter is that the dose information is obtained from the phase change occurring along the projection of the laser path across the test cell. This integrated dose measurement means that at this stage the DHI detector cannot be used to find dose at a point, or true relative doses between points in a three dimensional volume, unless the dose distribution is cylindrically symmetric or effectively two dimensional. This limits the applicability of the method, and validation of the DHI detector requires the use of a three dimensional model of the dose distribution which can be compared to the DHI results by integrated over the same volume. The ability to obtain three dimensional or quasi-three dimensional dose distributions by expansion of the DHI technique to a tomographic approach would increase the usability of the measurements. The optical mechanics behind implementing this technique are achievable, but the process would not be without difficulties, particularly for the measurement of time-variant irradiation processes.
There are many studies reporting the use of tomographic reconstructions to achieve three-dimensional temperature distribution measurements by means of interferometry \[201,220,294\]. Tomography is the process of collating image data taken from projections taken at varying angles through a sample, mathematically reconstructing the three dimensional properties. The mathematical reconstruction is an inverse problem, obtained by considering the integrated effect of the variable along lines in different directions through the medium. The most fundamental method of tomography is filtered back projection using the Radon Transform \[295\], but more modern approaches are based on iterative reconstruction \[296\].

The quality of the calculated three dimensional dose distribution is increased as the number of projections included in the reconstruction increases. For a DHI set-up, there are two approaches for achieving multiple measurement angles for use in the reconstruction: 1) separate interferometric measurements at a range of set angles, and 2) continuous image acquisition with rotation of the interferometer about the sample. Both approaches have specific advantages and limitations concerning the spatial resolution, temporal resolution and dosimetric accuracy.

Discussion of each of these approaches for DHI dosimetry is compared to the tomographic ultrasound thermometry system developed by Malyarenko \textit{et al.} \[234\] which has a distinctly different approach to tomography than possible with the current type of DHI detector, but was chosen for comparison as the approach is also a calorimetric dosimetry method using a remote temperature probing technique, and as such has encountered many of the same considerations. Their approach was based on the use of a circular array of 128 ultrasound transmitters and receivers, which probe a single plane of the irradiated volume, based on a fan-beam geometry data acquisition technique. The approach could be extended to three dimensions with the use of multiple rows of ultrasound transducers, in the same fashion as a cone beam CT. The average temperature along each ultrasound path is determined by each receiver in turn, and then the results tomographically reconstructed. The sensitivity in temperature measurements achieved for a single ultrasound line results achieved for a single ultrasound probe were temperature measurements as small as 3.2 µK along each ultrasound line, sufficiently sensitive for therapy level radiation doses \[234\]. This value was somewhat reduced under the tomographic acquisition conditions, however temperatures on the order of mK were still resolvable. The nominal spatial resolution achieved at the centre of the reconstruction volume was on the order of half the transducer spacing, or 4.4
mm, decreasing towards the circumference of the region, with significant artefacts occurring towards the edges. The total diameter of the measurement plane was about 36 cm, but the useable central region was 12 cm diameter. The temporal resolution of the system was stated as 4 s, although they also suggested refinements for the detector to achieve temporal, spatial and thermal resolutions approaching 1 s, 1 mm and 1 µK, respectively. An example of their temperature field measurement of an infrared lamp simulating a radiation beam is shown in Figure 8.4.

![Figure 8.4](image)

Figure 8.4: Temperature profile reconstructions in a water tank from a fan-beam tomographic acoustic experiment with 64 projections, 45 rays per projection. (a) The radiation source (heat lamp) off; (b) radiation source on for 30 s. Area dimensions: 300 pixels × 300 pixels (230mm × 230mm); the relative height of the temperature dome is approximately 9 mK. Figure reproduced from Malyarenko et al. [234].

### 8.5.1 Tomography at Limited Projection Angles

The first approach, taking measurements at multiple finite beam angles, could be achieved by either of two means. The first is to have a permanent set-up with two or more interferometers in one system, with orthogonal coverage of the test cell as a minimum. An example of possible geometry for an orthogonal LFTDH interferometer is shown in Figure 8.5. For an LFTDH approach, the increasing numbers of optical components required mean the detector would be complex to configure and align, and expensive, due to the replication of components. However other configurations should be explored that would reduce the complexities, for example it may be feasible to use an inline approach, such as that described in Section 3.3.3. The second method would be to make measurements at varying angles by recording each angle in turn, allowing the water to return to equilibrium between, and re-measure at the
same time instance comparative to the start of the irradiation. The DHI interferometer could be used without modification, as long as the angle of the laser path relative to the position of the radiation was accurately known. This approach would allow for any arbitrary number of projection angles, but hugely increase the time required to make a measurement, along with a corresponding increase in the dosimetric uncertainty. Additionally, for measurements such as for HDR brachytherapy, it relies on consistent reproducibility of source positioning, or for other radiation modalities it relies on a constant beam output and symmetry.

Figure 8.5: A schematic of an LFTDH configuration interferometer with a suggested configuration for incorporating a second orthogonal detector.

The major limitation with these methods however, is that in practice both will result in a limited number of projection angles. The iterative reconstruction process is an inverse problem, and as such is ill-posed and can be highly prone to error. With limited projection data, the reconstruction matrix is ill-conditioned, with a number of unknowns greater than the number of equations. In this case, the convergence of the iterations to any particular solution depends on the initial guess, noise in the projection data and selection of reconstruction parameters [294]. The result is to decrease both the spatial resolution and the confidence in the dosimetric accuracy. However, results achieved with tomosynthesis detectors such as

270
used for breast cancer screening, using expectation maximisation reconstruction algorithms, have been shown to have a high degree of accuracy, and the same principles are applicable to the DHI results [297].

The advantage of this limited angle method over an approach like the Malyarenko system however is that the measurements at each of the projections could be made at the same relative time instance compared to the start of irradiation. Whether that be a simultaneous measurement, or a series of repeated measurements, the consequence is that the time resolution would be accurate to a high degree. This means that measurements of radiation distributions with high dose gradients could be measured and the impact of heat diffusion could be accounted for in the same fashion as the current two dimensional DHI results. Because the measurements at each time instance would be resolved in three dimensions, with careful selection of the measurement intervals, it would be possible to directly account for the heat diffusion in the results without the limitations encountered by the inaccuracies introduced by the Abel transform.

The main difficulty would be achieving sufficient spatial resolution in each direction. As the entire test cell volume would be probed by each projection, there would not be the limitation experienced by the Malyarenko fan beam approach whereby the periphery regions of the test area experienced lower spatial resolution. Additionally, with the size of the pixels in the DHI detector vastly exceeding the spatial resolution of the ultrasound transceivers, the potential spatial resolution achievable would be orders of magnitude less than the approximately 5 mm they achieved. Optical CT scanners used for gel dosimetry have reported resolution on the scale of 1 mm³ [61,173], with sensors with pixel sizes similar to that used for the DHI detector. Resolutions this fine would not be achievable with limited projection angles however, as this results in a reconstruction process where the measured distributions are smeared out over a volume which is inversely proportional to the number of projections. Additionally, the reconstruction process and dosimetric uncertainty would be negatively impacted by the magnitude of the noise in the recorded images, the impact of which is reduced by the increasing redundancy in the reconstruction achieved by having a greater number of projection angles [294]. Implementation of a basic reconstruction algorithm for the DHI results at various numbers and angles of projections would allow for an estimate of the potential three dimensional resolution that could be achieved with each given experimental set-up, but this remains an area of further work.
If this limited angle approach were to be implemented, the number of angles used would be determined from the balance of multiple factors, including the cost of the system components, the space and configuration constraints on the optical system, the finite apertures of the test cell, the transportability of the set-up, the increase in experimental time required, and the resolution achievable.

8.5.2 Tomography by Interferometer Rotation

The second approach to DHI tomography, rotating the interferometer, means that depending on the speed of rotation and the acquisition rate of the camera, an unlimited number of projection angles can be achieved. This will allow for a three dimensional reconstruction with high spatial resolution and accuracy. However, this approach means that the measurements used are acquired over some time period, rather than instantaneously. For measurements of transient phenomena, such as the temperature distribution introduced by radiation absorbed dose this complicates the reconstruction immensely, and introduces a much higher level of uncertainty, dependent on the rate of image acquisition. Note that the test cell must be independent of the rotating detector, to avoid the introduction of undesired body forces in the fluid medium which would affect the temperature distribution.

The Malyarenko approach effectively used this approach, as the ultrasound transducers were measured consecutively around the circular array, with a total acquisition time of 4 s for the entire dataset. They overcame the limitations associated with variation of the heat diffusion by measuring a temperature source with a relatively low rate of temperature increase, and no steep gradients. They also had a relatively low spatial resolution of approximately 5 mm. Thus the resultant degradation of the signal due to heat transport over the 4 s measurement acquisition time resulted in an effect smaller than the spatial resolution. Thus the measurement acquisition time was not a limiting factor in the approach.

For the DHI detector, similar measurements could be made, which, if the sensitivity of the detector could be increased and noise reduced sufficiently, would allow for the measurement of clinically relevant dose distributions such as those used for IMRT [234]. However if tomographic measurements of radiation modalities such as HDR or proton beams are to be made, the relatively high dose rates and dose gradients relative to the achievable resolution will complicate this somewhat. The resolution achievable by this approach is limited only by the noise in the images, rather than an inherent limit on projection angles. Thus to achieve measurements where the signal degradation due to heat transport is less than the
ability to spatially resolve the beam, a very fast measurement acquisition time should be used. This will be limited by the maximum camera frame rate and speed of rotation of the system. With the camera used in the present DHI prototype, frame rates of up to 30 Hz are achievable, however scientific cameras with frame rates of several hundred Hz are commercially available, although the corresponding reduction in the signal to noise ratio is a consideration. Assuming the system can be accurately rotated at rates of up to 2 Hz, it would be possible to achieve a similar number of reconstructions as the Malyarenko approach, with a measurement acquisition time on the order of 0.5-4 seconds. This is still a considerable time, and depending on the radiation source will impose an inherent limitation on the temperature/dose resolution achievable at a given spatial resolution.

It is possible that a modelling approach could be used to account for the variation in dose deposition and heat transfer which occur with the varying time instances of each projection image. This process would be complex and require an iterative reconstruction method to be used which optimises the volumetric dose distribution based on a cost function which incorporates the models for heat conduction and convection. If this could be successfully implemented and validated against alternative three dimensional dosimetry approaches, then it would vastly increase the usability of the DHI system.

It should be noted that when the interferometer is rotated this must occur about an axis of rotation coincident with the centre of the test cell, but that the test cell must not rotate. This is so that the alignment of the temperature distribution map remains correlated to the direction of the radiation dose distribution, and so there is no additional blurring from the water getting dragged around by the walls of the cell. Additional error can also be introduced if there is some deviation between the centre of rotation of the interferometer and the test cell, causing the projection data to be collected at angles different to those assumed for the calculations.

8.5.3 Additional Considerations

A consideration with the use of tomography during holographic interferometry measurements is the shape of the test cell. Unless a limited projection approach is used with projections only at two cardinal angles, then a cubic test cell will result in the occurrence of artefacts due to the edges of the test cell being thicker and less transparent than the bulk of the walls of the cell. Additionally, the temperature/dose determined at each point in the projection
across the cell will be affected by different averaging effects depending on the radial location of the point of interest. This will complicate both the interpretation of the DHI temperature maps, and any tomographic reconstruction. This could be reduced by the use of a cylindrical test cell which impacts the phase of the light to the same extent regardless of the direction of the projection. This will cause added complexities in reconstructing the holograms to determine the DHI temperature maps, due to uneven refraction of the light as it traverses the cell walls. The extent of this effect should be investigated, and it should be ascertained whether successful reconstructions can be performed, prior to the use of a cylindrical test cell in any tomographic measurements.

Another practical consideration with tomographic DHI for radiation dosimetry is that it would be extremely difficult to make a tomographic detector for a beam delivered horizontally, such as the proton beam or a synchrotron beam, because the rotational axis for the projection angles is coincident with the central axis of the radiation beam. This would require rotation of a breadboard or similar with all the optical components attached, however in order to achieve rotation about the test cell there would not be a single axis of rotation for the breadboard, instead it must traverse a circle about the measured point, similar to the operation of a computed tomography (CT) machine. This would be difficult to achieve mechanically to a high level of accuracy, as well as present many difficulties in the process of shielding the system from ambient conditions. In particular if a temperature controlled environment for the detector is required, as recommended for absolute dose measurements, the size of the container would be prohibitive and render the detector difficult to transport. This could still be feasible in the context of a standards laboratory, however reduces the use of the approach for many applications.

8.6 Considerations for DHI Application to MRT Dosimetry

The initial motivator behind the development of a DHI detector was the need for improved detectors for synchrotron generated microbeam radiation therapy (MRT), as described in Section 2.3.3. The initial development of the detector and proof-of-principle measurements were first required to prove the potential viability of the method to build a solid justification to apply for scarce beam time on a medical beamline. Based on the results achieved to date for the HDR source and proton beam measurements, and the anticipated future improvements to the system, this section is intended to give an estimate of the possible utility of
this method for MRT.

The key parameters to consider when discussing the theoretical potential of DHI for MRT are the spatial resolution and the dynamic range - i.e. the ability to accurately resolve the dose in both the peaks and the valleys of the highly modulated microbeams. The fundamental independence of DHI to beam energy means that the beam spectrum does not need to be considered.

The present detector achieved spatial resolutions on the order of 25 $\mu$m. This would be not quite sufficient to accurately spatially resolve the peak sizes used in MRT, as there would only be approximately one pixel per peak, resulting in a high uncertainty in the peak localisation. However the resolution could be readily improved, by the means discussed in Section 7.3.4, to the extent that spatial resolution is not the limiting factor in the possible application of DHI to MRT.

In order for DHI to be used with the current detector design (and all anticipated future designs), the MRT collimator must be horizontal. This is due to the horizontal orientation of the object beam of the DHI detector which probes the water sample. If the collimator is vertical then all the details of the peaks will be obscured. Details of the orientation of the collimator at all synchrotron medical beamline facilities are not known, although it is noted that the collimator in use at the Australian Synchrotron is horizontal. The angle of the DHI detector must be carefully aligned with the collimator, otherwise dose averaging will occur due to partial occlusion of the dose distribution.

The key limiting factor to consider will be the presence of heat diffusion. Although the dose deposition rates are extremely high by conventional radiotherapy standards, the high dose modulation means that the heating pattern quickly dissipates. This means that the rate of image acquisition must be high compared to the time scale of the irradiation.

A basic heat diffusion calculation on a simulated MRT beam was modelled in MATLAB in order to investigate the measurement parameters required. A typical MRT beam consists of 25 $\mu$m wide peaks, with a 200 $\mu$m peak separation [175]. This was approximated by sharp peaks at this spacing, convolved with a Gaussian function, as a first approximation for the expected blurring due to collimator scatter and scatter within the test cell at the measurement depths. The dose was normalised to correspond to a dose delivery rate of 2000 Gy/s
in the peak region. A beam consisting of ten peaks was modelled, to optimise calculation
time, although larger arrays are more common. For the calculations, a time increment of 0.1
ms was used. The use of a test cell with a lateral dimension smaller than the width of the
microbeams was assumed, so that the dose is not further reduced due to integration with
regions of no irradiation across the test cell.

The calculation was performed for several measurement times. The results are shown in
Figure 8.6. The choice of measurement time in reality depends on the achievable frame rate
of the camera used for the DHI, and also the limitations on minimum MRT irradiation time
due to the finite time required to physically shutter the beam. For increasing irradiation
times the effects of heat diffusion result in a decrease in the measurable peak to valley dose
ratio (PVDR) but an increase in the overall dose difference between peak and valley. The
values for both of these at depths greater than that reduce accordingly with the decreasing
depth dose. The results are summarised in Table 8.2.

![Figure 8.6: MRT beam profiles showing the extent of heat diffusion for varying measurement
times, where the black line is the ideal dose distribution in the absence of heat diffusion,
and the red line shows the measurable heat diffused signal. a) 0.5 s measurement, b) 0.1 s
measurement and c) 0.01 s measurement.](image)

It is apparent from these results that at peak dose rates of 2000 Gy/s, DHI is unlikely to
be a viable tool for use in measurement of PVDRs. If the dose rate is increased so that
Table 8.2: Results of MRT heat diffusion calculations showing the modelled decrease in PVDR due to heat diffusion for increasing measurement times for a beam with dose rates of 2000 Gy/s in the peaks and peak separation of 200 µm.

<table>
<thead>
<tr>
<th>Measurement time (s)</th>
<th>Ideal peak dose (Gy)</th>
<th>Ideal valley dose (Gy)</th>
<th>Measurable PVDR</th>
<th>Measurable dose difference (Gy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.01</td>
<td>20</td>
<td>0</td>
<td>53.22</td>
<td>4.9</td>
</tr>
<tr>
<td>0.1</td>
<td>200</td>
<td>0</td>
<td>1.65</td>
<td>8.3</td>
</tr>
<tr>
<td>0.5</td>
<td>1000</td>
<td>0</td>
<td>1.13</td>
<td>9.9</td>
</tr>
</tbody>
</table>

measurements become more instantaneous, the time for heat to diffuse decreases. If a measurement could be made on a short enough timescale relative to the irradiation then the PVDRs would be more resolvable.

The use of DHI to just localise the peak positions is possible. In order to do this, the dose difference needs to be high enough relative to the achievable noise levels in order to allow for confidence in the true position of the peak. For the present detector this level is approximately 6 Gy, which corresponds to one standard deviation of the background noise level. For future versions of the detector it is likely this value will be decreased.

DHI could potentially be used as a non-invasive temperature probe to calorimetrically determine the total MRT dose integrated across the test cell volume. The lack of beam perturbation may have some advantages over other calorimeters, as this removes the spectral dependence of correction factors. In order for this type of measurement to be possible, the absolute dosimetric abilities of the DHI detector must be improved, as was described in Section 8.4.3.

### 8.7 Other Proposed Future Applications

DHI has potential to be used for a range of dosimetric applications. For most of these proposed applications, for DHI to be a viable dosimetry option the sensitivity of the detector, and in particular the signal to noise ratio, will need to be substantially improved. In some cases this will need to be by up to an order of magnitude. Significant system refinement by implementing the suggestions from Section 8.4 is likely to lead to considerable improvements in these results, sufficient to allow for DHI application to the measurements briefly introduced in the following sections.
Small Field Measurements

For external beam radiation therapy, there is an increasing trend towards treatments consisting of a larger number of smaller, more highly modulated treatment fields than those used for conventional conformal radiotherapy. Treatment techniques such as intensity modulated radiation therapy (IMRT), volumetric modulated arc therapy (VMAT), and various stereotactic radiotherapy treatments (such as SABR and SBRT), allow the dose distribution to conform better to the target volume, which allows for dose escalation to the tumour. The fields can be sub-centimetre in size, considerably smaller than the traditional radiotherapy fields of greater than approximately $4 \times 4$ cm in size. Clinical dosimetric uncertainty is amplified by both cumulative errors from the increased number of fields, and the challenges inherent in accurate measurement of smaller field sizes. Whilst there are recommendations from organisations regarding appropriate dosimetry tools for this situation, improving the accuracy of small field measurements further is an area of very active research.

The dosimetry of small fields is challenging due to the non-equilibrium conditions created as a consequence of the secondary electron track lengths compared to the field width resulting in a lack of charged particle equilibrium. This limits the use of ionisation chambers, which are affected by the lack of lateral scatter. There are also prolonged electron tracks in the presence of low density inhomogeneities. Radiation detectors introduced into the field perturb this disequilibrium, in a fashion that is harder to quantify in a reliable way [21, 22]. Additionally for a small field, partial blocking of the beam source by the collimating system results in pronounced and overlapping penumbra. Many detectors have less accurate measurements in penumbral regions due to the dose gradient, and traditional definition of the field size by the full width at half maximum will not be accurate. Detectors must have a resolution which is considerably smaller than the magnitude of the small field they are measuring, as well as not be affected by the variations in the electron spectrum inducing changes in the stopping power ratios. The choice of a suitable detector from amongst the commercially available options is challenging, with various guidelines and recommendations suggested in the literature [21, 22]. Each detector type has different perturbations and corrections which may become relevant at different sizes. Thorough consideration of these is required in order to have full confidence in their dosimetric accuracy.

Das et al. and others have stated the requirement for new detector types, with the state-
ment “Small volume detectors ion chambers, diodes, and others will be developed that have minimum perturbations due to its presence and composition. Also, such detectors will have minimum energy, dose, and dose rate dependence” [21]. DHI appears to have the potential to achieve many of these, provided a sufficient level of sensitivity could be achieved.

DHI has the potential to be a useful contributor to the problems of small-field dosimetry. Malyarenko et al. from NIST proposed the use of their ultrasound tomographic detector to assess the absorbed dose in IMRT-type beam conditions [234]. The logic applied is also relevant to a DHI detector. In order to achieve sufficiently accurate measurements, the temperature resolution needs to be sufficient to resolve the small dose gradients that occur in this sort of treatment. Their premise for this approach is that calorimetric standards for primary reference dose are the most suitable for time-resolved spatial distribution measurements because they are “constructed of a uniform, extended medium that could contain and faithfully register the spatial features of the beam over time.” The influence of heat diffusion is an obvious caveat to this assumption, although for the small dose gradients present for IMRT this will have a much lower impact than the high dose gradients measured in other applications. In order to achieve measurements of these kinds with a DHI detector, the sensitivity of the detector will need to be improved by at least an order of magnitude.

Investigation of the Impacts of Tissue Inhomogeneities and Boundary Interface Dosimetry

Some of the original interferometric dosimetry measurements by Miller in 1979 began to use the technique to investigate the effect of various beam perturbations on the absorbed dose distribution [26]. The work included a range of initial studies designed to help investigate different aspects of beam perturbation, in order to help increase the accuracy of treatment plans. For instance he measured the change in depth dose curves with varying backscatter materials and thicknesses, at various penetration depths of the electron beam. This is valuable for increasing understanding of the dose in the region prior to different density materials, for instance the higher density of bones. Another measurement actually visualised the distortion in the isodose lines caused by a solid object intruding into the field, again a useful simulacrum of a bone.

Measurement immediately adjacent to solid objects is possible for DHI (or the earlier film-based systems) to an extent not possible for most alternative dosimetry systems. Achieving two or three dimensional distributions concurrently would be a key advantage of DHI for
this purpose. The inherent energy independence of DHI is another key advantage, as the variations in scatter from solid objects alters the energy spectrum of the radiation at each point. For detectors that require various beam quality-based correction factors or calibrations, this introduces potential errors in the result, which would be circumvented by the use of DHI.

Future improved versions of the DHI detector could be used to extend the measurements begun by Miller. Results achieved with sufficient accuracy could be used to validate the output of treatment planning system dose distributions around regions of varying density in transparent phantoms, for various algorithms. A very exciting possibility is the potential for the use of DHI to quantify the extent of the beam perturbation around other detector types. For instance the dose distribution around an ionisation chamber could be measured, which may be useful to help experimentally verify correction factors and reduce uncertainties associated with the parameters for TRS-398 reference dose measurements. Such factors could include stopping power ratios and the beam perturbation factors for specific chamber types which are incorporated in the beam quality correction factor $k_{Q,Q_o}$. This would be particularly of use for more complex systems, such as scanning proton beam dosimetry [96], where these parameters are more difficult to accurately calculate. Measurement of other detectors such as in-vivo diodes also has an obvious benefit of quantifying the extent of the influence on the dose distribution from in-vivo measurements. The potential beam perturbations are an area of concern when conducting in-vivo dosimetry measurements, especially for patients with short treatment courses of five or less fractions. Accurate measurement of the resultant beam perturbations could allow for a greater measure of confidence in the patient treatments in these cases, and potentially allow for safer extension of in-vivo measurements to every fraction.

**Surface Dosimetry**

Conventionally, dosimetric measurements in the regions close to the surface are difficult to measure. This is due to various complications including, amongst others, the partial volume averaging effect, detector build-up requirements, rapid variation in beam spectra for electron beams, and different scatter properties. Current methods for accurate measurement of surface doses in linear accelerator beams include extrapolation chambers for low energy photon beams, and parallel plate or extrapolation chambers for higher energy beams. Improving the flexibility of surface dosimetric measurements would be particularly beneficial for treatment techniques where fields are matched adjacent to each other, either to extend the treatment
region, or match different radiation types or energies. There are currently considerable un-
certainties in the surface dose for such techniques, which can have considerable effects on
the efficacy or risks of the treatment. The DHI detector, after further development, has the
potential to contribute to this type of problem.

8.8 Concluding Remarks

This chapter covered points of possible uncertainty and potential improvement across the
whole range of the DHI system, from the optical set-up, to the irradiation and image acquisi-
tion, to the image reconstruction and analysis. The intention was to provide a comprehensive
discussion of all aspects of the measurements, in order to fully investigate the potential of
the DHI detector for radiation dosimetry. Whilst the initial proof-of-principle results using
the prototype detector were positive, there are a range of areas where future iterations of the
system could be improved upon in order to fully realise the potential of the approach. The
limitations of the system were discussed, with suggestions for how improvements could be
implemented. Sources of uncertainty were analysed, and aspects of the uncertainty budget
which were not fully covered in earlier Chapters were described. Key sources of uncertainty
are the noise in the system, and the calculation of the impact of heat transport on the re-
sults, including the use of the Abel Transform. A comprehensive range of recommendations
were made, to improve all aspects of the detector performance. Considerations regarding
the possible extension to tomographic image acquisition were fully discussed. Other possi-
ble applications which would benefit from the possibilities presented by the features of DHI
dosimetry were introduced, with a brief description of the possibilities.
Chapter 9

Conclusions

This work aimed to develop a novel DHI detector capable of measuring small temperature changes in water and apply the system to radiation applications as proof-of-principle of DHI as a dosimetry tool. A full framework was established for the process of acquiring a DHI measurement, including:

- Interferometer configuration and alignment of optical components
- Detector transport and re-building for in situ radiation measurements
- Optimising the region of interest localisation and the irradiation conditions
- Control and recording of influence factors
- Mathematical image reconstruction and subsequent absorbed dose determination
- Dose distribution analysis by comparison to model results
- Methods for accounting for heat diffusion of the measured temperature field
- Analysis of uncertainties of the system and methods to mitigate or quantify these
- Itemization and discussion of areas that should be considered for accurate and useful dosimetric measurements

The pilot study measurements on an HDR source and a small field proton beam successfully demonstrated all of the above processes. The results of the HDR source measurements proved that the DHI system was capable of resolving the small temperature gradients resulting from radiation absorbed dose to water. The proton beam measurements were useful for consideration of the ability of the prototype detector, with the results used to inform a comprehensive set of recommendations for future experimental improvements of the detector. The potential of the system for application to alternative radiation types was conjectured...
based on the results of these measurements and the anticipated improvements.

9.1 Review of Research Questions

The initial work set out to answer four research questions which were posed in order to focus the direction of the investigation into DHI as a potential dosimetry tool. The results achieved by the DHI detector, that were fully described in the remainder of this work, will therefore be summarised in the following sections by answering the research questions.

9.1.1 Research Question One

Can the optical technique of digital holographic interferometry be successfully applied to radiation dosimetry?

The DHI measurements of the HDR source have experimentally demonstrated that the prototype detector is capable of measuring radiation dose distributions. The results which were achieved in the initial field testing predominantly agreed to within experimental uncertainties when compared with an independent source model. The measured results achieved dosimetric accuracy on the order of 4-6 Gy. This value consists of a combination of the standard deviation of the noise, and the additional systematic dosimetric uncertainties in the measurement.

The prototype detector was constructed using available materials as a proof-of-principle system for the pilot studies. The successful results are therefore very promising for the future development of the detector now that the initial achievements justify the investment of time and financial resources into improving the system. The limited areas of deviation from complete agreement between the expected and measured dose distributions will be able to be mitigated by developments such as improving the detector housing, and the quality of the optical components.

9.1.2 Research Question Two

Is it possible to develop a digital dosimeter based on the fundamental principles of calorimetry that is capable of measuring dose with high two dimensional spa-
The development of the DHI dosimeter has successfully resulted in a non-invasive optical method of probing the radiation-induced temperature variation of a water sample. This overcomes the two key limitations of most calorimetric dosimetry systems; those being the perturbation of the beam by the temperature probe, and the lack of spatial resolution due to the very limited number of measurement points. DHI also achieves the same main advantage of other calorimetric systems, which is the direct measurement of the fundamental quantity of thermal energy transfer as a measure of absorbed radiation dose. Whilst in all systems there are inevitably correction factors and parameters contributing uncertainties to the result, calorimetric measurements are intrinsically suited for radiation dosimetry, and preferable to all other dosimetry options in certain circumstances. To expand the benefits of calorimetric measurement to include determination of the dose distribution in two dimensions, as DHI has achieved, has the potential to be very useful. The further extension of the two dimensional projections of the dose in the test cell to a three dimensional system would require considerable development of the experimental set-up.

The resolution achieved by the prototype DHI detector was on the order of 0.025 mm/pixel, over a sensitive region of approximately 7.5 mm by 6 mm. Compared to other dosimetry options, this resolution is only surpassed by film. Additionally, there is the possibility to further improve the resolution of the system for future versions of the detector. The fact that the prototype DHI detector was able to calorimetrically measure dose to a very high spatial resolution is a major advantage of this approach, and justifies the further development of the system.

9.1.3 Research Question Three

Will the application of modern digital technology allow for dosimetric results which advance the early achievements of Hussmann and Miller?

The novel DHI dosimetry work has advanced the results of the early interferometric dosimetry measurements by Hussmann, Miller and McLaughlin by availing the key fundamental concept of all the advantages of modern digital sensors and the associated computational power [24–27]. It is difficult to directly compare the results, as the available radiation sources were quite different. Their initial measurements using analogue detection systems were in the range of 6000-22000 Gy, delivered almost instantaneously in 20 - 40 ns [24,27], although
later measurements were of relatively lower doses of between 100 - 1500 Gy [26]. The stated dose resolution for the later work was 3.5 Gy, with an uncertainty of 20%. These kind of dose rates were unfortunately not available for the DHI measurements, as they are optimal conditions for accurate DHI measurements as well as the film based systems. The dosimetric accuracy achieved by the DHI system appears comparable with this result, given favourable measurement conditions.

Some of the original measurements presented by the early pioneers of this work were based on single point measurements using a photodiode as the sensor of the interferometric fringes [26, 27]. There were also some film measurements presented with a two dimensional dose distribution measuring isodose lines and depth dose curves. The spatial resolution of the film measurement was demonstrated by other cited authors of the period to be about 1 \( \mu \text{m} \). In contrast to this, the DHI results spatial resolution was lower than the film measurements, but patently better than single point photodiode measurements. The size of the film sensitive region was also larger than that of the current DHI prototype, however theoretically the DHI size can be expanded indefinitely, with the use of sufficient magnification, so this comparison is negligible.

The key advantage demonstrated by the digital approach over the earlier film method is the ease of data collection, reconstruction and analysis. Multiple images can be recorded at high frequency to allow for analysis of the data at any point in time before, during or after an irradiation. This allows for the progression of the dose deposition to be directly viewed, and avoids the introduction of excessive uncertainties due to timing errors triggering the single shutter of a film image acquisition with the irradiation time. Additionally, the DHI measurements at multiple close time increments means that the data can be used to help account for heat diffusion. Interferometric film measurements are by nature limited to single shot images. This is particularly important for most of the radiation techniques which are relevant to modern radiation therapy. The increasing dose modulation, temporal variation and dose rates used in many techniques mean that the capabilities of DHI are better suited to the needs of modern radiation dosimetry technology. Additionally, with DHI there is also no need for an expensive and time consuming film processing service which was an additional requirement of the film interferometry methods used by Hussmann et al. All of the other possible sources of uncertainty remain fairly consistent between film and digital systems.

The additional advantages of DHI of being readily able to digitally process the images, have
direct access to the phase values at any point, and use high power computing to evaluate compare measured and modelled data. All of these features mean that the development of the early interferometric measurements to a modern digital system is a demonstrable improvement on the earlier measurements. With developments applied to increase the DHI spatial resolution and measurement sensitive region, as suggested in Chapters 7 and 8, DHI will undisputably be an improvement to build on the early results using film interferometry.

9.1.4 Research Question Four

Is there a justification for further work to explore the potential for such a detector to be used to overcome the dosimetric problems associated with emerging radiation therapy techniques?

According to Karger et al., regarding ion beam dosimetry: ”Although methods for ion beam dosimetry have been established, there is still room for developments. This includes improvement of the dosimetric accuracy as well as development of more efficient measurement techniques.” This principle also applies to most other emerging radiation therapy techniques and some aspects of many other established techniques. For instance development of an absolute dose standard for brachytherapy Ir-192 sources, accurate quantification of proton beam Bragg peak, accurate penumbral measurements in small field dosimetry applications, and surface dosimetry and beam perturbation measurements for a range of radiation types. In some cases the lack of suitable dosimetry options is the limiting factor in the therapeutic advancement of the technique. Additionally, the development of novel systems based on fundamental principles of radiation dose measurement allows for potential contribution to validation of “gold standard” Monte Carlo dose distribution models and measurement correction factors. The application of the detector to MRT beams could allow for macro measurements of the microbeam array, but considerable improvements in measurement temporal resolution and accuracy would be required to overcome heat diffusion limitations on resolving the individual microbeams and measuring PVDRs.

Based on the results from the initial field testing on an HDR brachytherapy source, combined with the theoretical understanding of the system potential gained from implementing the DHI detector measurement and analysis system suggest that DHI is also a promising technique to approach some of these dosimetric challenges. There is a clear justification that it would be worthwhile to implement the modifications recommended to improve the system
which were described in Chapter 8.

Many of the key advantages of a DHI system which make it potentially suitable for many different applications were realised with the prototype detector. The measurements were achieved to a high degree of temporal and spatial resolution, without perturbing the radiation beam by insertion of a physical probe. Additionally the calorimetric nature of the measurements means that the measurements are fundamentally independent of radiation type, energy and dose rate (excluding the influence that the dose rate has on the extent of the heat diffusion occurring). The direct determination of absorbed dose to water, the key measurement quantity for radiation therapy purposes, and the possibility of absolute dose measurements, are also key attributes.

The initial HDR brachytherapy results indicate a mandate to investigate the use of DHI as an absolute dosimetry system for Ir-192 sources. The sensitivity of the current prototype detector limited the system to high dose rate radiation measurements, meaning that the initial field testing on the proton beam did not successfully resolve the radiation dose distributions. However the theoretical potential of the method warrants focus on improving the sensitivity by increasing the signal to noise ratio, and further development of the heat diffusion corrections.

Further work based on the framework described in this thesis for measurement, analysis and future development of the DHI dosimeter, has the potential to contribute to the dosimetric toolbox for a range of radiation applications. At this stage it appears unlikely that the approach would be of use to routine clinical measurement of small field photon beams such as those used for IMRT. In principle it would be possible to measure these, avoiding some of the pitfalls of current detectors which perturb the beams significantly, and do not always respond well in regions of no lateral electronic equilibrium. However the lower limit on measurable doses by the current system was on the order of 4-6 Gy, for projection doses of 20 Gy. For a typical small field of treatment, the doses would be as much as 100 times less. Therefore the sensitivity of the detector would need to be improved by at least an order of magnitude. Doses considerably higher than those used clinically could be delivered, however this would avoid the reduction in the heat diffusion issue which small fields generally produce. At this stage the idea that DHI could contribute in this area of relatively low dose measurements would be speculation.
Bibliography


298


310


# Appendix A

## List of Abbreviations

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Full Form</th>
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<tbody>
<tr>
<td>AAPM</td>
<td>American Association of Physicists in Medicine</td>
</tr>
<tr>
<td>ADSL</td>
<td>Asymmetric digital subscriber line</td>
</tr>
<tr>
<td>BE</td>
<td>Beam expander</td>
</tr>
<tr>
<td>BS</td>
<td>Beam splitter</td>
</tr>
<tr>
<td>C</td>
<td>Corrected</td>
</tr>
<tr>
<td>CCD</td>
<td>Charge coupled device</td>
</tr>
<tr>
<td>CDHB</td>
<td>Canterbury District Health Board</td>
</tr>
<tr>
<td>CGS</td>
<td>Coherent gradient sensing</td>
</tr>
<tr>
<td>CM</td>
<td>Corner mirror</td>
</tr>
<tr>
<td>CMOS</td>
<td>Complementary metal oxide semiconductor</td>
</tr>
<tr>
<td>CT</td>
<td>Computed tomography</td>
</tr>
<tr>
<td>CVD</td>
<td>Chemical vapour deposition</td>
</tr>
<tr>
<td>DAQ</td>
<td>Data acquisition</td>
</tr>
<tr>
<td>DC</td>
<td>Direct current</td>
</tr>
<tr>
<td>DD</td>
<td>Dose difference</td>
</tr>
<tr>
<td>DHI</td>
<td>Digital holographic interferometry</td>
</tr>
<tr>
<td>DNA</td>
<td>Deoxyribose nucleic acid</td>
</tr>
<tr>
<td>DTA</td>
<td>Distance-to-agreement</td>
</tr>
<tr>
<td>EBRT</td>
<td>External beam radiation therapy</td>
</tr>
<tr>
<td>ECHED</td>
<td>European Charged Heavy Particle Dosimetry</td>
</tr>
<tr>
<td>ESPI</td>
<td>Electronic speckle pattern interferometry</td>
</tr>
<tr>
<td>ESRF</td>
<td>European Synchrotron Radiation Facility</td>
</tr>
<tr>
<td>FPS</td>
<td>Frames per second</td>
</tr>
<tr>
<td>GUI</td>
<td>Graphical user interface</td>
</tr>
<tr>
<td>H&amp;D</td>
<td>Hurter and Driffield curve</td>
</tr>
<tr>
<td>HDR</td>
<td>High dose rate</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Full Form</td>
</tr>
<tr>
<td>--------------</td>
<td>-----------</td>
</tr>
<tr>
<td>He-Ne</td>
<td>Helium neon</td>
</tr>
<tr>
<td>IAEA</td>
<td>International Atomic Energy Agency</td>
</tr>
<tr>
<td>ICRU</td>
<td>International Commission on Radiation Units and Measurements</td>
</tr>
<tr>
<td>IMRT</td>
<td>Intensity modulated radiation therapy</td>
</tr>
<tr>
<td>IQR</td>
<td>Interquartile range</td>
</tr>
<tr>
<td>IS</td>
<td>Iris shutter</td>
</tr>
<tr>
<td>L</td>
<td>Lens</td>
</tr>
<tr>
<td>LDA</td>
<td>Laser driven ion acceleration</td>
</tr>
<tr>
<td>LET</td>
<td>Linear energy transfer</td>
</tr>
<tr>
<td>LFTDH</td>
<td>Lensless Fourier transform digital holography</td>
</tr>
<tr>
<td>M</td>
<td>Mirror</td>
</tr>
<tr>
<td>MC</td>
<td>Monte Carlo</td>
</tr>
<tr>
<td>MCS</td>
<td>Multiple Coulomb scattering</td>
</tr>
<tr>
<td>MOSFET</td>
<td>Metal oxide semiconductor field effect transistor</td>
</tr>
<tr>
<td>MP</td>
<td>Megapixel</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
</tr>
<tr>
<td>MRT</td>
<td>Microbeam radiation therapy</td>
</tr>
<tr>
<td>ND</td>
<td>Neutral density filter</td>
</tr>
<tr>
<td>NSLS</td>
<td>National Synchrotron Light Source</td>
</tr>
<tr>
<td>OCT</td>
<td>Optical coherence tomography</td>
</tr>
<tr>
<td>OEM</td>
<td>Original equipment manufacturer</td>
</tr>
<tr>
<td>OPL</td>
<td>Optical path length</td>
</tr>
<tr>
<td>OSL</td>
<td>Optically stimulated luminescence</td>
</tr>
<tr>
<td>P</td>
<td>Pinhole</td>
</tr>
<tr>
<td>PDD</td>
<td>Percentage depth dose</td>
</tr>
<tr>
<td>PMMA</td>
<td>Polymethylmethacrylate/Perspex</td>
</tr>
<tr>
<td>PSDL</td>
<td>Primary standard dosimetry laboratory</td>
</tr>
<tr>
<td>PSRS</td>
<td>Proton stereotactic radiosurgery</td>
</tr>
<tr>
<td>PTB</td>
<td>Physikalisch-Technische Bundesanstalt (German standards laboratory)</td>
</tr>
<tr>
<td>PVDR</td>
<td>Peak-valley dose ratio</td>
</tr>
<tr>
<td>RBE</td>
<td>Relative biological effectiveness</td>
</tr>
<tr>
<td>RIT</td>
<td>Reference image topography</td>
</tr>
<tr>
<td>ROI</td>
<td>Region of interest</td>
</tr>
<tr>
<td>SABR</td>
<td>Stereotactic ablative radiotherapy</td>
</tr>
<tr>
<td>SBRT</td>
<td>Stereotactic body radiation therapy</td>
</tr>
<tr>
<td>SNR</td>
<td>Signal-to-noise ratio</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td>SOBP</td>
<td>Spread out Bragg peak</td>
</tr>
<tr>
<td>SRT</td>
<td>Stereotactic radiotherapy</td>
</tr>
<tr>
<td>SSDL</td>
<td>Secondary standard dosimetry laboratory</td>
</tr>
<tr>
<td>T</td>
<td>Temperature</td>
</tr>
<tr>
<td>TG</td>
<td>Task group</td>
</tr>
<tr>
<td>TIFF</td>
<td>Tagged image file format</td>
</tr>
<tr>
<td>TLD</td>
<td>Thermoluminescent detector</td>
</tr>
<tr>
<td>TPS</td>
<td>Treatment planning system</td>
</tr>
<tr>
<td>TRS</td>
<td>Technical report series</td>
</tr>
<tr>
<td>UC</td>
<td>Uncorrected</td>
</tr>
<tr>
<td>USB</td>
<td>Universal serial bus</td>
</tr>
<tr>
<td>UWMC</td>
<td>University of Washington Medical Center</td>
</tr>
<tr>
<td>VMAT</td>
<td>Volumetric modulated arc therapy</td>
</tr>
</tbody>
</table>
Appendix B

MATLAB Code

There were many aspects of the DHI measurement and analysis process which used code written in MATLAB. The key processes included the GUI created for the initial digital image reconstruction and conversion to dose values, as well as the heat diffusion calculations, and comparison of measured doses to modelled values. The fundamental code for the first two of these processes is included here, with annotations where required for clarity, denoted with a “%” sign.

For the analysis of the results, the scope of this appendix does not extend to the inclusion of the ancillary coding required to adapt the basic process for the specific measurement, model and analysis requirements of a given radiation application. This is because these can vary considerably depending on the measurement conditions and available model parameters. For instance there are considerations to do with: adjusting relative spatial resolutions to allow direct comparisons, measurement geometry, lines and regions of interest, masking of the measurement region for analysis and image filtration, type of filtration, and calculation of noise and trends within and between images. For this reason, a specific example of the code is not often directly applicable to other applications. These included tasks such as masking of the measurement region, adjusting resolution of measured and modelled images to facilitate comparison. Additional code developed when testing and characterising the DHI system is also not included, but involved implementation of both the implicit and the explicit method for solving heat diffusion equations, implementation of the heat diffusion process (included in this Appendix) for Method 2 of accounting for heat diffusion, testing different phase unwrappers and image filters, calculating radial dose functions and gamma indices and calculating the extent of the uncertainty in interpolating data such as the refractive index to temperature conversion values. Additionally, code which was initially obtained from external sources is not included, but links to sources of the code were referenced in the
relevant chapters.

B.1 Graphical User Interface for Image Reconstruction

The following nine codes make up the GUI that was created to both streamline and standardise the initial reconstruction of the dose distribution images from the measured light intensity maps collected on the sensor. This image reconstruction is specific to the geometric requirements of an LFTDH interferometer. The output was described in Section 4.3.4.

DigitalHolographicInterferometry.m

```matlab
% Based on an LFTDH setup as presented by M. Hossain et al. in Optical Engineering, 45(10), 2006.
% Input: Holograms (2 different states)
% Output: Reconstructed interferograms(- intensity & phase)

% Initialization tasks
if iscell(par.FilenameObj) % more than 1 files selected
    NoObjHolograms = length(par.FilenameObj); % no of object holograms in sequence
else
    NoObjHolograms = 1;
end

% initialize reconstructed interferograms and others
O1 = double(zeros([par.ROIFourier(4) par.ROIFourier(3)])); % note index 4 is before 3 -> to get dimensions right
O2 = double(zeros([par.ROIFourier(4) par.ROIFourier(3) NoObjHolograms]));
O3 = double(zeros([par.ROIFourier(4) par.ROIFourier(3) NoObjHolograms])); % O1+O2
theta1 = double(zeros([par.ROIFourier(4) par.ROIFourier(3) NoObjHolograms]));
theta2 = double(zeros([par.ROIFourier(4) par.ROIFourier(3) NoObjHolograms]));
dtheta = double(zeros([par.ROIFourier(4) par.ROIFourier(3) NoObjHolograms]));

UnwrappedPhase2D_Herraez = double(zeros([par.ROIFourier(4) par.ROIFourier(3) NoObjHolograms]));

UnwrappedPhase3D_Rahman = double(zeros([par.ROIFourier(4) par.ROIFourier(3) NoObjHolograms]));
AbsTemp_Rahman = double(zeros([par.ROIFourier(4) par.ROIFourier(3) NoObjHolograms]));
dTemp_Rahman = double(zeros([par.ROIFourier(4) par.ROIFourier(3) NoObjHolograms]));
```

322
cumul_dTemp_Rahman=double(zeros([par.ROIFourier(4) par.ROIFourier(3)]));
Dose_Rahman = double(zeros([par.ROIFourier(4) par.ROIFourier(3)]));

UnwrappedPhase3D_JM = double(zeros([par.ROIFourier(4) par.ROIFourier(3)]));
AbsTemp_JM = double(zeros([par.ROIFourier(4) par.ROIFourier(3)]));
dTemp_JM = double(zeros([par.ROIFourier(4) par.ROIFourier(3)]));
cumul_dTemp_JM=double(zeros([par.ROIFourier(4) par.ROIFourier(3)]));
Dose_JM = double(zeros([par.ROIFourier(4) par.ROIFourier(3)]));

TimeStamps = CreateTimestamp(par.ExposureTime, par.ResolutionHolograms(1), par.ResolutionHolograms(2), length(par.FilenameObj));

%% Reconstruct
% Reference hologram
disp('Reconstructing O1...')
O1 = SimplifiedFresnelReconstruction(...
    par.HologRef,...
    par.LaserWavelength,...
    par.PixelSize,...
    par.ResolutionHolograms,...
    par.DistObjCamera,...
    par.ROIFourier); % optional parameter to crop ROI. Note that 'prime' is required as dimensions are flipped

% Object holograms
disp('Reconstructing O2...')
tic
for holog = 1:NoObjHolograms
    O2(:,:,holog) = SimplifiedFresnelReconstruction(...
        par.HologObj(:,:,holog),...
        par.LaserWavelength,...
        par.PixelSize,...
        par.ResolutionHolograms,...
        par.DistObjCamera,...
        par.ROIFourier);
end
toc

% % % combined O3=O1+O2
disp('Reconstructing O3...')
tic
for holog_i = 2:NoObjHolograms
    O3(:,:,1) = O1(:,:,1);
    O3(:,:,holog_i) = SimplifiedFresnelReconstruction(...
        (par.HologRef + par.HologObj(:,:,holog_i),...
        par.LaserWavelength,...
        par.PixelSize,...
        par.ResolutionHolograms,...
        par.DistObjCamera,...
        par.ROIFourier);
end
% Alternative code if you want to compare to the previous image each time rather than the original one. Also need to change the sections where marked below.
\% for holog_i = 1:NoObjHolograms
\% if holog_i == 1
\%  O3(:,:,holog_i)= SimplifiedFresnelReconstruction(...
\%  (par.HologRef + par.HologObj(:,:,holog_i)),...
\%  par.LaserWavelength,...
\%  par.PixelSize,...
\%  par.ResolutionHolograms,...
\%  par.DistObjCamera,...
\%  par.ROIFourier);
\% else
\%  O3(:,:,holog_i)= SimplifiedFresnelReconstruction(...
\%  (par.HologObj(:,:,holog_i-1) + par.HologObj(:,:,holog_i)),...
\%  O2 -1 + O2 1
\%  par.LaserWavelength,...
\%  par.PixelSize,...
\%  par.ResolutionHolograms,...
\%  par.DistObjCamera,...
\%  par.ROIFourier);
\% end
\% end
toc

%% Phase information
disp('Extracting phase ...')
tic
\% theta 1 (reference)
theta1(:,:)=angle(O1(:,:)); %phase of reference.
\%theta1(:,:) = atan(imag(O1(:,:))./real(O1(:,:))); %%%%%%%%%%% Change here to compare to previous image
for holog_i = 2:NoObjHolograms

\% theta2
theta2(:,:,holog_i)=angle(O2(:,:,holog_i));
\%dtheta(:,:,holog_i)= InterferencePhase(theta1(:,:,1),theta2(:,:,holog_i));

%%%%%%%%%%%% Change here to compare to previous image
\%theta2(:,:,holog_i)=atan(imag(O2(:,:,holog_i))./real(O2(:,:,holog_i)));
\% if holog_i == 1
\%  dtheta(:,:,holog_i) = InterferencePhase(theta1(:,:,1),theta2(:,:,
\%   holog_i));
\% else
\%  dtheta(:,:,holog_i) = InterferencePhase(theta2(:,:,holog_i-1),theta2
\%   ( :,holog_i));
\% end
\% for holog_i=2:NoObjHolograms
\%  dtheta(:,:,holog_i)=dtheta(:,:,holog_i-1);
\% end
\% Optional median filter applied here. Reccommend doing this in the data analysis process instead so you can keep track of what you're doing better.
\%dtheta(:,:,holog_i)= medfilt2(dtheta(:,:,holog_i),[3,3],'symmetric');
%disp('median filter applied to dtheta');
toc

% OPTIONAL: Extract phase directly from O3 instead, for comparison purposes...
%dtheta3=angle(fftshift(O3));
%dtheta_comp = dtheta-dtheta3;

% Unwrap in 2D
for holog_i=1:NoObjHolograms;
    UnwrappedPhase2D_Herraez(:,:,holog_i) = Herraez_2D_unwrapper_M(single(dtheta(:,:,holog_i)));
    UnwrappedPhase2D_Herraez(:,:,holog_i) = unwrap(UnwrappedPhase2D_Herraez(:,:,holog_i));
end

% unwrap in 3d, two different methods.
UnwrappedPhase3D_Rahman = double(Rahman_3D_unwrapper_M(single(dtheta))); % data needs to be of type single. Full 3d unwrapper. Not ideal for noisy data
UnwrappedPhase3D_JM = JM_3D_unwrapper(UnwrappedPhase2D_Herraez); % unwrap third dimension only following previous 2D unwrap. ONLY suitable if looking at relative data at each time point only, NOT for cumulative/absolute doses.

% Convert to temperature/dose values. To map the refractive index n to the temperature and vice versa we use polynomials rather than an analytical solution.
RefInd_ref = Temperature2RefractiveIndex(par.InitialCellTemp);
for holog_i = 1:NoObjHolograms
    % % option 1: comparison of each image to the image before it to build up a cumulative dose. The plus pi is to account for the results being wrapped over - pi to pi and not zero to 2 pi.
    % Rahman unwrapper:
    %
    % AbsTemp_Rahman(:,:,holog_i) = RefractiveIndex2Temperature(RefInd_ref + ...
    %     par.LaserWavelength.*((UnwrappedPhase3D_Rahman(:,:,holog_i)+pi)./(4*pi^2*par.PhysicalPathlength));
    % if holog_i ~= 1 % dtemp (:,:,1) and cumul_temp(:,:,1) are zero from initialization
    %    dTemp_Rahman(:,:,holog_i) = AbsTemp_Rahman(:,:,holog_i) - AbsTemp_Rahman(:,:,holog_i-1);
    %    cumul_dTemp_Rahman(:,:,holog_i) = cumul_dTemp_Rahman(:,:,holog_i-1) + dTemp_Rahman(:,:,holog_i);
    % end
    % Dose_Rahman = dT2dose(cumul_dTemp_Rahman,par.InitialCellTemp);
    % JM unwrapper:
    %
    % AbsTemp_JM(:,:,holog_i) = RefractiveIndex2Temperature(RefInd_ref + ...
    %     par.LaserWavelength.*((UnwrappedPhase3D_JM(:,:,holog_i)+pi)./(4*pi^2*par.PhysicalPathlength));
    % if holog_i ~= 1 % dtemp (:,:,1) and cumul_temp(:,:,1) are zero from initialization
    %    dTemp_JM(:,:,holog_i) = AbsTemp_JM(:,:,holog_i) - AbsTemp_JM(:,:,holog_i-1);
% $\text{cumul}_d\text{Temp}_JM(:,:,\text{holog}_i) = \text{cumul}_d\text{Temp}_JM(:,:,\text{holog}_i-1) +$
% $\rightarrow d\text{Temp}_JM(:,:,\text{holog}_i);$  
% $\text{end}$  
% $\text{Dose}_JM = dT2dose(\text{cumul}_d\text{Temp}_JM,\text{par}.\text{InitialCellTemp});$

%% option 2: comparing everything back to the original reference image. The → plus pi is to account for the results being wrapped over - pi to pi and → not zero to 2 pi. Division by an empirical factor of 2 pi based on → experimental results.

% Rahman unwrapper:
\[ \text{cumul}_d\text{Temp}_Rahman(:,:,\text{holog}_i) = \text{RefractiveIndex2Temperature}( \rightarrow \text{RefInd}_\text{ref} + \ldots \rightarrow \text{par}.\text{LaserWavelength}.*\text{UnwrappedPhase3D}_Rahman(:,:,\text{holog}_i)+\pi)/(2\pi \rightarrow (2\pi*\text{par}.\text{PhysicalPathlength})) - \text{RefractiveIndex2Temperature}( \rightarrow \text{RefInd}_\text{ref}); \]
% the plus pi is to account for the results being wrapped over - pi → to pi and not zero to 2 pi.
% May require division by an empirical factor of 2 pi based on → experimental results, but no physical explanation for this yet.
\[ \text{Dose}_Rahman = dT2dose(\text{cumul}_d\text{Temp}_Rahman,\text{par}.\text{InitialCellTemp}); \]

% JM unwrapper:
\[ \text{cumul}_d\text{Temp}_JM(:,:,\text{holog}_i) = \text{RefractiveIndex2Temperature}( \rightarrow \text{RefInd}_\text{ref} + \ldots \rightarrow \text{par}.\text{LaserWavelength}.*\text{UnwrappedPhase3D}_JM(:,:,\text{holog}_i)+\pi)/(2\pi \rightarrow (2\pi*\text{par}.\text{PhysicalPathlength})) - \text{RefractiveIndex2Temperature}( \rightarrow \text{RefInd}_\text{ref}); \]

\[ \text{Dose}_JM = dT2dose(\text{cumul}_d\text{Temp}_JM,\text{par}.\text{InitialCellTemp}); \]

% Display results
\[ \text{disp('DisplayGUI ...')} \]
\[ \text{DisplayItems = struct('ObjectHolograms', abs(O2),...} \]
\[ \rightarrow \text{'Ref\_plus\_ObjHolograms', abs(O3),...} \]
\[ \rightarrow \text{'PhaseDiff', (d\thetaeta),...} \]
\[ \rightarrow \text{'Herraez\_PhaseDiffUnwr\_2D', (UnwrappedPhase2D\_Herraez),...} \]
\[ \rightarrow \text{'Rahman\_PhaseDiffUnwr\_3D', (UnwrappedPhase3D\_Rahman),...} \]
\[ \rightarrow \text{'Rahman\_RelTempDiff\_in\_degr\_C', (Abs\_Temp\_Rahman),...} \]
\[ \rightarrow \text{'Rahman\_CumulDose\_in\_Gy', (Dose\_Rahman),...} \]
\[ \rightarrow \text{'JM\_PhaseDiffUnwr\_3D', (UnwrappedPhase3D\_JM),...} \]
\[ \rightarrow \text{'JM\_RelTempDiff\_in\_degr\_C', (Abs\_Temp\_JM),...} \]
\[ \rightarrow \text{'JM\_CumulDose\_in\_Gy', (Dose\_JM)}; \]
\[ \text{DHIDisplayGUI(DisplayItems, TimeStamps, par.ROISize);} \]

DHILoad.m

\textbf{function} ReturnParams = DHILoad()  
% A GUI that loads and preprocesses raw image data before Digital Holography  
← Interferometry is performed.  
% No input parameters are required.  
% Return parameters are of type structre.  
% 1. Loads holograms H1 (reference) and H2 (object(s))  
% 2. Extracts Region of interferogram  
% 3. Prompts for set-up specific parameters  
% 4. Prompts for processing specific parameters  
% 5. Returns a structure with all relevant parameters
% Consolidate workspace memory.
% cwd = pwd;
% cd('C:\WINDOWS\Temp');
% pack
% cd(cwd)

% Define parameters
% camera & set-up
dist = 0.265; % Distance of object to camera (in m)
lambda = 632.8e-9; % Wavelength of He-Ne LASER (nano m)
pixsize = 6.7e-6; % Pixel size of camera (micro m)
resolution = [0 0]; % Resolution of camera (micro m)
pathl = 0.036; % (m), physical pathlength in which temperature change takes place

% Initialization tasks
win_dim = [0,0,800,650]; % dimension of main window [left bottom width height]...
% the first two values do not seem to be used -> always centered!
marg = 25; % margin
imwin_dim = [350 350]; % dimensions of display area for holograms [width height]
pan_dim = [imwin_dim(1) 200]; % dimensions of panels (below images)
obj_sequence = 1; % how many holograms?
cropROI = [789 526 193 234]; % Region of interest from FOURIER space
cropROI = [957 437 320 182];
RoiDim = 11;
CellTemp = 22.1;
ExposureTime = 0.32;

% Initialize a variable to hold the hologram when we've loaded it
% These are accessible to the nested callbacks
H1 = uint8([]); % reference hologram
H2 = uint8([]); % object hologram (a 3 dim matrix to store multiple hologr)
O3 = uint8([]);
O3filt = uint8([]);
filename1='';
filename2='';
gotImageRef = false;
gotImageObj = false;
currentdir = pwd;
%mov = 'no'; % 1..yes, 2..no
ColorDepth = 0;

% Initialise the structure that holds all return parameters
ReturnParams = struct('HologRef',[],'HologObj',[],'FilenameRef',filename1,...
'FilenameObj',filename2,'CurrentDirectory',currentdir,...
'DistObjCamera',dist,'LaserWavelength',lambda,...
'ResolutionHolograms',resolution,'PixelSize',pixsize,'PhysicalPathlength',pathl,...
'ROIFourier',cropROI,'InitialCellTemp',CellTemp,'ExposureTime',ExposureTime,...
'ROISize',RoiDim);

% Main window
hFigure = figure('Name','Digital Holographic Interferometry',...
'Position', 'win_dim', ...
'NumberTitle', 'off', ...
'Toolbar', 'none', ...
'Menubar', 'none', ...
'Visible', 'off');

% Reference image (left)
hImageRef = axes('Parent', hFigure,...
    'Units', 'pixels', ...
    'Position', [marg, win_dim(4) - imwin_dim(2) - (1.5*marg), imwin_dim(1), imwin_dim(2)], ...
    'Visible', 'on');
title(hImageRef, 'Load reference hologram...'); axis off

% Object image(s) (right)
hImageObj = axes('Parent', hFigure,...
    'Units', 'pixels', ...
    'Position', [2*marg + imwin_dim(2), win_dim(4) - imwin_dim(2) - (1.5*marg), imwin_dim(1), imwin_dim(2)], ...
    'Visible', 'on');
title(hImageObj, 'Load object hologram(s)...'); axis off

% slider to scroll through sequence of object holograms
hObjHologramSlider = uicontrol(hFigure, 'Style', 'slider', ...
    'Max', 2, 'Min', 1, 'Value', 1, ...
    'SliderStep', [0.01 0.10], ...
    'Position', [2*marg + 2*imwin_dim(2), win_dim(4) - imwin_dim(2) - (1.5*marg), 20 imwin_dim(2)], ...
    'callback', {@ObjHologramSlider_callback}, ...
    'Visible', 'off');

% Panel for set-up parameters
hPanel1 = uipanel('Title', 'Set-up parameters', 'FontSize', 12,...
    'Units', 'pixels', ...
    'Position', [marg, win_dim(4) - imwin_dim(2) - (2*marg) - pan_dim(2), pan_dim(1), pan_dim(2)]);

% Panel for additional parameters
hPanel2 = uipanel('Title', 'Additional parameters', 'FontSize', 12,...
    'Units', 'pixels', ...
    'Position', [2*marg + imwin_dim(2), win_dim(4) - imwin_dim(2) - (2*marg) - pan_dim(2), 20), pan_dim(1), pan_dim(2))];

% Content of set-up parameter panel
hTextLaser = uicontrol(hFigure, 'Style', 'text', ...
    'Position', [2*marg win_dim(4) - imwin_dim(2) - (4.65*marg) 150 20], ...
    'HorizontalAlignment', 'left', ...
    'String', 'Laser wavelength [nm]:');

hListboxLaser = uicontrol(hFigure, 'Style', 'popup', ...
    'String', {'Helium-Neon - 632.8nm', 'dummy'}, ...
    'Value', 1, 'Position', [4*marg + 100 win_dim(4) - imwin_dim(2) - (4.5*marg) 150 20], ...
    'BackgroundColor', 'w', ...
    'HorizontalAlignment', 'left', ...
    'Callback', @ListboxLaser_callback);

hTextPixelsize = uicontrol(hFigure, 'Style', 'text', ...
    'Position', [2*marg win_dim(4) - imwin_dim(2) - (5.65*marg) 150 20], ...
Pixel size of camera [um]:

```
{'6.7x6.7um (Alicia)', '7.4x7.4um (Kaidi)'}
```

Physical pathlength [m]:

```
num2str(pathl)
```

Distance to object [m]:

```
um2str(dist)
```

Current directory:

```
pwd
```

Reconstruct:

```
(pan_dim(1)-marg) win_dim(4)-imwin_dim(2)-(11.5*marg)
```

Current directory:
'String','Crop ROI pixels [x y w h]:')

hEditCropRoi = uicontrol(hFigure,'Style','edit',...
    'String',num2str(cropROI),...
    'Position',[4*marg+100+imwin_dim(1)+30 win_dim(4)-imwin_dim(2)-(4.65*marg) 
                 120 20],...
    'BackgroundColor','w',...
    'HorizontalAlignment','left',...
    'Callback',@EditCropRoi callback);

hTextRoiDim = uicontrol(hFigure,'Style','text',...
    'Position',[3*marg+imwin_dim(1) win_dim(4)-imwin_dim(2)-(5.65*marg) 150 
                 20],...
    'HorizontalAlignment','left',...
    'String','Square ROI size (pixel):')

hEditRoiDim = uicontrol(hFigure,'Style','edit',...
    'String',num2str(RoiDim),...
    'Position',[4*marg+100+imwin_dim(1)+30 win_dim(4)-imwin_dim(2)-(5.65*marg) 
                 120 20],...
    'BackgroundColor','w',...
    'HorizontalAlignment','left',...
    'Callback',@EditRoiDim callback);

hTextCellTemp = uicontrol(hFigure,'Style','text',...
    'Position',[3*marg+imwin_dim(1) win_dim(4)-imwin_dim(2)-(6.65*marg) 145 
                 20],...
    'HorizontalAlignment','left',...
    'String','Initial water temperature [ ]:');

hEditCellTemp = uicontrol(hFigure,'Style','edit',...
    'String',CellTemp,...
    'Position',[4*marg+100+imwin_dim(1)+30 win_dim(4)-imwin_dim(2)-(6.65*marg) 
                 120 20],...
    'BackgroundColor','w',...
    'HorizontalAlignment','left',...
    'Callback',@EditCellTemp callback);

hButtonCropRoi = uicontrol(hFigure,'Style','pushbutton',...
    'Position',[2*(pan_dim(1))+0.5*marg win_dim(4)-imwin_dim(2)-(4.65*marg) 20 
              20],...
    'String','...',...
    'Callback',@ButtonCropRoi callback);

htextExposureTime = uicontrol(hFigure,'Style','text',...
    'Position',[3*marg+imwin_dim(1) win_dim(4)-imwin_dim(2)-(7.65*marg) 150 
                 20],...
    'String','Exposure time [ms]:',...
    'HorizontalAlignment','left');

hEditExposureTime= uicontrol(hFigure,'Style','edit',...
    'Position',[4*marg+100+imwin_dim(1)+30 win_dim(4)-imwin_dim(2)-(7.65*marg) 
                 120 20],...
    'String',ExposureTime,...
    'HorizontalAlignment','left',...
    'BackgroundColor','w',...
    'Callback',@EditExposureTime callback);

hMenu = uimenu(hFigure,'Label','Load holograms');
hFileLoadReference = uimenu(hMenu,'Label','Open Reference Hologram',...  'Callback',{@FileLoadReference_callback});

hFileLoadObject = uimenu(hMenu,'Label','Open Object Hologram(s)',...  'Callback',{@FileLoadObject_callback});

% Initialization tasks
set(hFigure,'Visible','on');

%while (reconstruct == false)
% Callbacks for dhi
gui
% Note that these functions are nested, so have access to variables from
% the outer function

function FileLoadReference_callback(hObject, eventdata) %#ok<*INUSD>
    [filename1, pathname1] = uigetfile({'* .tif';'* .jpg'},'Select reference hologram');
    currentdir = pathname1;
    cd(currentdir)
    %H1_raw = double(imread(filename1));
    %H1_raw = medfilt2(imread(filename1));
    H1_raw = imread(filename1);
    s=size(H1_raw);
    ImageDetails=imfinfo(filename1)
    if length(s) == 3
        ColorDepth = 24; %-> convert bitdepth
        disp(['Converting hologram (',filename1,') bitdepth...'])
        H1= (H1_raw(:,:,1)+H1_raw(:,:,2)+H1_raw(:,:,3))/3;
    elseif ImageDetails.BitDepth == 16
        disp(['Converting (',filename1,') bitdepth...'])
        H1=uint8(H1_raw./256);
    else
        ColorDepth = 8;
        H1=H1_raw;
    end
    [resolution(2),resolution(1)]=size(H1);
    gotImageRef = true;
    updateDisplay;
end

function FileLoadObject_callback(hObject, eventdata)
    [filename2, pathname2] = uigetfile({'* .tif';'* .jpg'}, 'Select object hologram(s)',...
        'MultiSelect', 'on');
    currentdir = pathname2;
    cd(currentdir)
    if iscell(filename2) % more than 1 files selected
        disp(['Sequence of ',num2str(length(filename2)), ' holograms selected.'])
        filename2=sort(filename2); % sort as uigetfile returns files in arbitrary order
        obj_sequence = length(filename2);
        h2_raw=(imread(char(filename2(1))));
        s=size(h2_raw);
        ImageDetails=imfinfo(char(filename2(1)));
        if length(s) == 3
            ColorDepth = 24; %-> convert bitdepth
\[ h_2 = \frac{h_{2\text{raw}(:,:,1)} + h_{2\text{raw}(:,:,2)} + h_{2\text{raw}(:,:,3)}}{3}; \]

\[
\text{disp}(['Converting hologram (',char(filename2(1)),')'
\quad \rightarrow \text{bitdepth...'}])
\]

\[
\text{elseif ImageDetails.BitDepth == 16}
\quad \text{ColorDepth} = 8; \quad \% \text{refers to color depth rather than bit depth}
\quad \text{disp}(['Converting hologram (',char(filename2(1)),')'
\quad \rightarrow \text{bitdepth...'}])
\quad h_2 = \text{uint8}(h_{2\text{raw}(:,:,1)}/256); \]

\[
\text{else}
\quad \text{ColorDepth} = 8;
\quad h_2 = h_{2\text{raw}};
\end{align}
\]

\[
H_2 = \text{uint8}(\text{zeros}(s(1),s(2),\text{obj_sequence}));
\quad \text{H}_2(:,:,1) = h_2;
\quad \text{for } i = 2:\text{obj_sequence}
\quad \quad \text{if ColorDepth == 8}
\quad \quad \quad \text{if ImageDetails.BitDepth == 16}
\quad \quad \quad \quad \text{disp}(['Converting hologram (',char(filename2(i)),')'
\quad \quad \quad \quad \quad \rightarrow \text{bitdepth...'}])
\quad \quad \quad \quad H_2(:,:,i) = \text{uint8}(\text{imread(char(filename2(i))))/256); \% \rightarrow \text{hologram 2}
\quad \quad \quad \quad \text{else}
\quad \quad \quad \quad \quad \quad \quad \text{H}_2(:,:,i) = (\text{imread(char(filename2(i))))}; \% \text{hologram 2}
\quad \quad \quad \quad \end{align}
\]

\[
\quad \text{else}
\quad \quad h_{2\text{raw}} = (\text{imread(char(filename2(i))))}; \% \text{hologram 2}
\quad \quad \text{disp}(['Converting hologram (',char(filename2(i)),')'
\quad \quad \quad \rightarrow \text{bitdepth...'}])
\quad \quad \quad h_{2i} = \frac{h_{2\text{raw}(:,:,1)} + h_{2\text{raw}(:,:,2)} + h_{2\text{raw}(:,:,3)}}{3};
\quad \quad \quad \text{H}_2(:,:,i) = h_{2i};
\quad \end{align}
\]

\% figure
\% a= H2(:,:,1);
\% b= medfilt2(H2(:,:,1));
\% plot(1:1024,a(:,500),'m.',1:1024,b(:,500),'r.-')
\% keyboard
\set(hObjHologramSlider,'Visible','on','Value',1)
\set(hObjHologramSlider,'Max',\text{obj_sequence}) \% adjust slider to
\quad \leftrightarrow \text{number of obj holograms}
\set(hObjHologramSlider,'SliderStep',...
\quad \quad \quad [1/(\text{obj_sequence}-1) 3/(\text{obj_sequence}-1))] \% adjust step size (\rightarrow \text{minor 1 step, major 3 steps})
\% if no reference hologram loaded, use first object holog in
\quad \leftrightarrow \text{sequence}
\quad \text{if gotImageRef == false;}
\quad \quad H_1 = H2(:,:,1);
\quad \quad gotImageRef = true;
\quad \quad filename1 = char(filename2(1));
\quad \quad [\text{resolution(2)}, \text{resolution(1)}] = \text{size}(H_1);
\quad \end{align}
\]

\[
\quad \text{else}
\quad \quad \text{set(hObjHologramSlider,'Visible','off')} \% \text{remove slider}
\quad \quad \text{obj_sequence} = 1;
\quad \quad \%H_2 = \text{double(\text{imread(filename2))};
\quad \quad \text{H}_2 = (\text{imread(filename2))};
\quad \end{align}
\]

\text{gotImageObj = true;
updateDisplay;
end

function ObjHologramSlider_callback(hObject, eventdata)
updateDisplay;
end

function ListboxLaser_callback(hObject, eventdata)
switch get(hObject, 'Value')
case 1
lambda = 632.8e-9;
case 2
lambda = 0;
end
disp(['Laser wavelength has been changed to selection: ', num2str(get(hObject, 'Value'))])
end

function ListboxPixelsize_callback(hObject, eventdata)
switch get(hObject, 'Value')
case 1
pixsize = 6.7e-6;
case 2
pixsize = 7.4e-6;
end
disp(['Camera pixel size changed to selection: ', num2str(get(hObject, 'Value'))])
end

function ListboxTextPhysPathl_callback(hObject, eventdata)
pathl=str2num(get(hObject, 'Value'));
disp(['Physical Pathlength changed to: ', num2str(pathl),'m.'])
end

function EditDistance_callback(hObject, eventdata)
dist= str2num(get(hObject, 'Value'));
disp(['Distance to object changed to ',num2str(dist),'m.'])
end

function EditDirectory_callback(hObject, eventdata)
disp(['Current directory changed to: ', get(hObject, 'Value')])
cd(get(hObject, 'Value'))
updateDisplay
end

function EditCropRoi_callback(hObject, eventdata)
cropROI=str2num(get(hObject, 'Value')); %#ok<*ST2NM>
disp(['CROP region: ', num2str(cropROI)])
end

% function EditTrackRoi_callback(hObject, eventdata)
% trackROI=str2num(get(hObject, 'Value'));
% disp(['Track region: ', num2str(trackROI)])
% end

function EditCellTemp_callback(hObject, eventdata)
CellTemp=str2num(get(hObject, 'Value'));
end
disp(['Cell temperature : ', num2str(CellTemp)])
end

function EditExposureTime_Callback(hObject, eventdata)
    ExposureTime = str2num(get(hObject, 'String'));
    disp(['Exposure time is: ', num2str(ExposureTime)])
end

function EditRoiDim_Callback(hObject, eventdata)
    RoiDim = str2num(get(hObject, 'String'));
    disp(['ROI dimensions: ', num2str(RoiDim)])
end

function ButtonCropRoi_Callback(hObject, eventdata)
    if (gotImageRef && gotImageObj)
        O3 = SimplifiedFresnelReconstruction(H1+H2(:,:,1),lambda,pixsize,
          resolution,dist);
        %cm=colormap;
        fr=figure;
        imagesc(log(abs(O3))); % log so ROI can be visualised
        title('Reconstructed Interferogram. Select ROI. Double click to
            close figure.')
        axis equal tight
        colormap gray
        % select Region of Interest (ROI)
        hrect1 = imrect(gca,cropROI);
        addNewPositionCallback(hrect1, @(p) set(hObject, 'String',
          num2str(round(p))));
        fcn = makeConstrainToRectFcn('imrect',get(gca,'XLim'),get(gca,'YLim'));
        setPositionConstraintFcn(hrect1,fcn);
        wait(hrect1); % Interactively place a rectangle by clicking ...
        % and dragging. Use wait to block the MATLAB ...
        % command line. Double-click on the rectangle to
        % resume.
        %CROP
        cropROI=str2num(get(hObject, 'String'));
        O3filt = O3(cropROI(2):cropROI(2)+cropROI(4), cropROI(1):cropROI(1)+cropROI(3));
        %colormap cm
        close(fr) % close figure
        %a=medfilt2(abs(O3filt));
        %figure
        %plot(1:163,a(:,80),'r.-',1:163,abs(O3filt(:,80)),'b.-')
    else
        msgbox('Load holograms first!','Warning','warn')
    end
end

function ButtonReconstruct_Callback(hObject, eventdata)
    if (gotImageRef && gotImageObj)
        % assign values to return structure
        ReturnParams.HologRef=H1;
        ReturnParams.HologObj=H2;
        ReturnParams.FilenameRef=filename1;
        ReturnParams.FilenameObj=filename2;
    end

334
ReturnParams.CurrentDirectory=currentdir;
ReturnParams.DistObjCamera=dist;
ReturnParams.LaserWavelength=lambda;
ReturnParams.ResolutionHolograms=resolution;
ReturnParams.PixelSize=pixsize;
ReturnParams.PhysicalPathlength=pathl;
ReturnParams.ROIFourier=cropROI;
ReturnParams.InitialCellTemp=CellTemp;
ReturnParams.ExposureTime=ExposureTime;
ReturnParams.ROISize=RoiDim;
close(hFigure) % This triggers a 'CloseRequestFct' -> close figure

else
    msgbox('Load holograms first!','Warning','warn')
end

% Redraw
function updateDisplay
    set(hEditDirectory,'String',currentdir)
    if gotImageRef == true
        axes(hImageRef)
        imagesc(H1);
        title(['Reference hologram: ',char(filename1)])
        axis equal tight off
    end
    if gotImageObj == true
        if obj_sequence == 1
            axes(hImageObj)
            imagesc(H2(:,:,1));
            title(['Object hologram: ',char(filename2)])
            else
                currentObj=fix(get(hObjHologramSlider,'Value'));
                axes(hImageObj) %#ok<MAXES>
                imagesc(H2(:,:,currentObj));
                title([num2str(currentObj),' of ',num2str(obj_sequence),'
                object holograms: ',char(filename2(currentObj))])
        end
        axis equal tight off
    end
    if (gotImageRef && gotImageObj)
        set(hButtonReconstruct,'BackgroundColor','g')
    else
        set(hButtonReconstruct,'BackgroundColor','r')
    end
waitfor(hFigure,'CloseRequestFcn') % return when reconstruct button is pressed
end

CreateTimestamp.m

function TimeStamps = CreateTimestamp(ExposureTime, ROIwidth, ROIheight, noImages)
% Calculates the 'Default USB2 frame rate' based on digital camera settings,
and then calculates time stamps for a series of images (noImages). Note that the actual frame rate can vary slightly.

% Based on PixeLINK PL-B740 Frame Rate Calculator (B740_series_frame_rate_calc.xls).
% Input: Exposure time (in ms), no pixels in x & y, the number of images in the sequence
% Output: a vector with time stamps in seconds and short E notation

% constants
TimeStamps = zeros(noImages,1);
ClockPeriod = 1/40000000;
BWDefaultUSB2 = 26214400;
EffectiveColumns = ROIwidth;
EffectiveRows = ROIheight;
FrameBlanking = 15;
LineBlanking = 10;
LinePadding = 156;
VFWidth = EffectiveColumns + LineBlanking;
(BytesPerPixel = 1;
FrameSize = EffectiveRows*EffectiveColumns * BytesPerPixel +36;
FrameTime = (VFWidth*ClockPeriod)* (EffectiveRows + FrameBlanking);
DefaultUSBframeRate = min(1/(max(FrameTime,FrameSize/BWDefaultUSB2)...
 +ExposureTime/1000),4000); % in frames/second
disp(['Default USB 2.0 frame rate is ', num2str(DefaultUSBframeRate) ,' f/s.'])
deltaTime = 1/DefaultUSBframeRate; % in s
TimeStamps(1)=0.0;
for i = 2:noImages
    %TimeStamps(i)=num2str(deltaTime*(i-1),'%10.5e
    TimeStamps(i)=deltaTime*(i-1);
end

SimplifiedFresnelReconstruction.m

function O_return = SimplifiedFresnelReconstruction(H,lambda,pixsize,res,dist,...
cropROI) % (the last argument is optional -> to crop ROI)
    k = 2*pi/lambda; % wave number
    const2 = 1; % constant 2 in Eq 3
% set o to centre of image
[xi,yi] = meshgrid(-res(1)/2+1:res(1)/2,-res(2)/2+1:res(2)/2); % indices
X = xi.*pixsize; % convert to actual dimensions
Y = yi.*pixsize;
% non fourier term
nft = (exp(1i*k*dist)/(1i*lambda*dist))\exp((-1i*k)/(2*dist))*(X.^2+Y.^2));
% Reconstruction (Eq 3): O(X,Y)
keyboard
O = const2*nft.*fftshift(fft2(H));
if nargin == 5
    O_return = O;
else if nargin == 6;
    O_return = O(cropROI(2):cropROI(2)+cropROI(4)-1,cropROI(1):cropROI(1)+
cropROI(3)-1);
end
InterferencePhase.m

```matlab
function dtheta = InterferencePhase(theta1, theta2)
% calculate phase map dtheta on the range of pi to -pi instead.
s = size(theta1);
for m = 1:s(1)
    for n = 1:s(2)
        if theta2(m,n) - theta1(m,n) >= pi;
            dtheta(m,n) = theta2(m,n) - theta1(m,n) - 2*pi;
        else
            if theta2(m,n) - theta1(m,n) < -pi;
                dtheta(m,n) = theta2(m,n) - theta1(m,n) + 2*pi;
            else
                dtheta(m,n) = theta2(m,n) - theta1(m,n);
            end
        end
    end
end
return
```

RefractiveIndex2Temperature.m

```matlab
function Temperature = RefractiveIndex2Temperature(RefractiveIndex)
polyn = [-306192022839.014
         2025472069804.51
         -5359422265265.7
         709053267512.57
         -4690394790752.35
         1241078028359.92];
Temperature = polyval(polyn,double(RefractiveIndex));
% Note: if double is removed the results are completely wrong instead of 20
degr it spits out a number several orders of magn bigger!!!!!!!!!
return
```

Temperature2RefractiveIndex.m

```matlab
function RefractiveIndex = Temperature2RefractiveIndex(Temperature)
polyn = [3.02416865046015e-018
         -7.69286698973227e-016
         5.21449173722462e-009
         -1.93016045341355e-006
         -1.37327031294521e-005
         1.3322129684799];
RefractiveIndex = polyval(polyn,double(Temperature));
return
```

dT2dose.m
function D_m = dT2dose(dtheta,RefTemp)
% converts temperature difference to dose based on calorimetric equation
% Note: A temperature change of ~2.39*10^-3 deg Celcius corresponds to 1Gy.
polyn = [5.99673202614085e-013 % 6th order polynomial to work out
-2.2701734539964e-010 % specific heat for reference temperature
3.54045374560064e-008 % note: assuming 1 bar absolute pressure.
-2.90773087206943e-006 % See comments at the bottom of file!
0.000140512002833792
-0.00369018874263044
4.21758728918141];
[k_HD = 0; % Correct for the heat defect. This has been set to zero here, but
 might have to be addressed when the heat defect is taken into account.
c_m = polyval(polyn,RefTemp);
D_m = (c_m.*1000.*dtheta)./(1-k_HD);
return

DHIDisplayGUI.m

function DHIDisplayGUI(Items,TimeStamps,RoiDim)
% Displays matrix, line profiles and times series
% Input 'Items' is of type structure
% Initialization tasks
% determine display size based on screen size
%scrsz = get(0,'ScreenSize');
scrsz = [1 1 1600 800];
scalefct = 0.8; % 1...full width of screen
figsize = [0 0 (scrsz(3)*scalefct) (scrsz(4)*scalefct)];
marg = round(figsize(3)/25);
gadget_dim = [100 30];
im_dim = round([(figsize(3)-4*marg-0.5*gadget_dim(2))/3 (figsize(3)-4*marg-0.5
-> gadget_dim(2))/3]);
figsize(4) = im_dim(2)+6+margin+gadget_dim(2); % added 2+ margin
figsize(1) = (scrsz(3)-figsize(3))/2;
figsize(2) = (scrsz(4)-figsize(4))/2;
ROIDimW = RoiDim;
ROIDimH = RoiDim;

% other variables
SelectedItem = 1; % O3,phase,Temp,dose...
SequenceNo = 2; % sequence number
ItemNames = fieldnames(Items);
SelectedItemName = ('Items.' char(ItemNames(SelectedItem)));
for Item = 1:length(ItemNames)
    dim_lngths(Item) = length(size(eval(['Items.', char(ItemNames(Item))])));
end
f=find(dim_lngths==max(dim_lngths));
dims = (size(eval(['Items.', char(ItemNames(f(1)))])));
MaxNoInSequence = dims(3);
if dim_lngths(SequenceNo) == 2
    CurrNoInSequence = 1;
else
    CurrNoInSequence = MaxNoInSequence;
end
profilePosX = [[round(dims(2)/2), round(dims(2)/2)], [1 dims(1)]];
profilePosY = [[1 dims(2)], [round(dims(1)/2), round(dims(1)/2)]];
TimesSeriesPoints = zeros(MaxNoInSequence, 1);
TimesSeriesROIs = zeros(MaxNoInSequence, 1);
TimesSeriesROIstds = zeros(MaxNoInSequence, 1);
ProfileSelection = 1; % 1...x, 2...y, 3..xy
CheckLinear = 0; % fit curves; 0...don't show, 1... show
CheckQuadratic = 0;
CheckCubic = 0;
%bottomfig = 0;
meanAllPointsInImage = zeros(size(1, dims(3)));
stdAllPointsInImage = zeros(size(1, dims(3)));
stdFitLine = zeros(size(1, dims(3)));
%plotGlobal = [];

%% Main window
hFigure = figure('Name', 'Digital Holographic Interferometry Display', ...
    'Position', figsize, ...
    'NumberTitle', 'off', ...
    'Toolbar', 'figure', ...
    'Menubar', 'figure', ...
    'Visible', 'on');

% left figure
hImageMatrix = axes('Parent', hFigure, ...
    'Units', 'pixels', ...
    'Position', [marg figsize(4) - 1*marg - 1.5*gadget_dim(2) - im_dim(2) im_dim], ...
    % [left bottom width height]
    'Visible', 'on');

% middle figure
hImageProfile = axes('Parent', hFigure, ...
    'Units', 'pixels', ...
    'Position', [2*marg + im_dim(1) + 0.5*gadget_dim(2) figsize(4) - 1*marg - 1.5* ...
                gadget_dim(2) - im_dim(2) im_dim], ...
    % [left bottom width height]
    'Visible', 'on');

% right figure
hImagePoints = axes('Parent', hFigure, ...
    'Units', 'pixels', ...
    'Position', [3*marg + 2*im_dim(1) + 0.5*gadget_dim(2) figsize(4) - 1*marg - 1.5* ...
                 gadget_dim(2) - im_dim(2) im_dim], ...
    % [left bottom width height]
    'Visible', 'on');

% bottom figure
hImageMeanROI = axes('Parent', hFigure, ...
    'Units', 'pixels', ...
    'Position', [marg marg figsize(3) - 2*marg figsize(4) - im_dim(2) - 4.2*marg], ...
    % [left bottom width height]
    'Visible', 'on');

hListBoxDatasetMatrix = uicontrol(hFigure, 'Style', 'popup', ...
    'String', ItemNames, ...
    'Value', SelectedItem, ...
    'Position', [marg figsize(4) - 0.5*marg - gadget_dim(2) im_dim(1) gadget_dim(2) ...
                 gadget_dim(2)], ...
    'BackgroundColor', 'w', ...
    'HorizontalAlignment', 'center', ...
    'FontSize', 15, ...
    'FontWeight', 'bold', ...

339
'Callback', @ListboxDatasetMatrix_callback);

hListboxDatasetProfile = uicontrol(hFigure,'Style','popup',...  
    'String', ItemNames, ...
    'Value', SelectedItem, ...
    'Position', [2*marg+im_dim(1)+0.5*gadget_dim(2) figsize(4)-0.5*marg-  
                    gadget_dim(2) im_dim(1) gadget_dim(2)], ...
    'BackgroundColor', 'w', ...
    'HorizontalAlignment', 'center', ...
    'FontSize', 15, ...
    'FontWeight', 'bold', ...
    'Callback', @ListboxDatasetProfiles_callback);

hListboxDatasetPoints = uicontrol(hFigure,'Style','popup',...  
    'String', ItemNames, ...
    'Value', SelectedItem, ...
    'Position', [3*marg+2*im_dim(1)+0.5*gadget_dim(2) figsize(4)-0.5*marg-  
                    gadget_dim(2) im_dim(1) gadget_dim(2)], ...
    'BackgroundColor', 'w', ...
    'HorizontalAlignment', 'center', ...
    'FontSize', 15, ...
    'FontWeight', 'bold', ...
    'Callback', @ListboxDatasetProfiles_callback);

% slider to scroll through images

hObjHologramSlider = uicontrol(hFigure,'Style','slider',...
    'Max', MaxNoInSequence, 'Min', 1, 'Value', SequenceNo, ...
    'SliderStep', [1/(MaxNoInSequence-1) 3/(MaxNoInSequence-1)], ...
    'Position', [5.55*marg 3.5*marg+1.3*gadget_dim(2) 1.4*marg gadget_dim(2)],...
    % [left bottom width height]
    'callback', {@ObjHologramSlider_callback}, ...
    'Visible', 'on');

hSequenceNo = uicontrol(hFigure,'Style','text',...
    'Position', [7.1*marg 3.5*marg+1.3*gadget_dim(2)-8 marg/4 gadget_dim(2)],...
    % ...
    'HorizontalAlignment', 'right', ...
    'BackgroundColor', [0.8,0.8,0.8], ...
    'String', '#: ') ;

hEditSequenceNo = uicontrol(hFigure,'Style','edit',...
    'String', num2str(SequenceNo), ...
    'Position', [7.45*marg 3.5*marg+1.3*gadget_dim(2) 0.075*im_dim(1)  
                    gadget_dim(2)], ...
    'BackgroundColor', 'w', ...
    'HorizontalAlignment', 'right', ...
    'Callback', @EditSequenceNo_callback);

% slider to shift profile in X

hPosSliderX = uicontrol(hFigure,'Style','slider',...
    'Max', dims(2), 'Min', 1, 'Value', round(dims(2)/2), ...
    'SliderStep', [1/(dims(2)-1) 10/(dims(2)-1)], ...
    'Position', [marg figsize(4)-1*margin-1.5*gadget_dim(2) im_dim(1) gadget_dim  
                    (2)/2], ... % [left bottom width height]
    'callback', {@PosSliderX_callback}, ...
    'Visible', 'on');

% slider to shift profile in Y

hPosSliderY = uicontrol(hFigure,'Style','slider',...
% Max', dims(1), 'Min', 1, 'Value', round(dims(1)/2), ...
'SliderStep', [1/(dims(1)-1) 3/(dims(1)-1)], ...
'Position', [marg+im_dim(1) figsize(4)-1*marg+1.5*gadget_dim(2)-im_dim(2) ...
  gadget_dim(2)/2 im_dim(2)], ...
'callback', '@PosSliderYCallback', ...
'Visible', 'on');

htextX = uicontrol(hFigure, 'Style', 'text', ...
  'Position', [marg+5 3.5*marg+1.3*gadget_dim(2)-8 50 gadget_dim(2)], ...
  'HorizontalAlignment', 'left', ...
  'BackgroundColor', [0.8, 0.8, 0.8], ...
  'String', 'x: ') ;

hEditXpos = uicontrol(hFigure, 'Style', 'edit', ...
  'String', num2str(get(hPosSliderX, 'Value')), ...
  'Position', [marg+5+marg/4 3.5*marg+1.3*gadget_dim(2) 0.1*im_dim(1) ...
  gadget_dim(2)], ...
  'BackgroundColor', 'w', ...
  'HorizontalAlignment', 'right', ...
  'Callback', '@EditXposCallback');

htextY = uicontrol(hFigure, 'Style', 'text', ...
  'Position', [marg+10+marg 3.5*marg+1.3*gadget_dim(2)-8 50 gadget_dim(2)], ...
  'HorizontalAlignment', 'left', ...
  'BackgroundColor', [0.8, 0.8, 0.8], ...
  'String', 'y: ') ;

hEditYpos = uicontrol(hFigure, 'Style', 'edit', ...
  'String', num2str(dims(1)-round(get(hPosSliderY, 'Value'))+1), ...
  'Position', [2*marg+10+marg/4 3.5*marg+1.3*gadget_dim(2) 0.1*im_dim(1) ...
  gadget_dim(2)], ...
  'BackgroundColor', 'w', ...
  'HorizontalAlignment', 'right', ...
  'Callback', '@EditYposCallback');

htextZ = uicontrol(hFigure, 'Style', 'text', ...
  'Position', [3*marg+15 3.5*marg+1.3*gadget_dim(2)-8 50 gadget_dim(2)], ...
  'HorizontalAlignment', 'left', ...
  'BackgroundColor', [0.8, 0.8, 0.8], ...
  'String', 'Value: ') ;

hEditZpos = uicontrol(hFigure, 'Style', 'edit', ...
  'String', 'test', ...
  'Position', [4*marg 3.5*marg+1.3*gadget_dim(2) 0.2*im_dim(1) gadget_dim(2) ...
  gadget_dim(2)], ...
  'BackgroundColor', 'w', ...
  'HorizontalAlignment', 'right');

hProfileButtonGroup = uibuttongroup('visible', 'on', ...
  'Position', [(2*marg+0.5*gadget_dim(2)+im_dim(1))/figsize(3) ...
  4.25*marg/figsize(4) ...
  im_dim(1)/figsize(3) ...
  gadget_dim(2)/figsize(4)]);

% Create three radio buttons in the button group.
hX = uicontrol('Style', 'Radio', 'String', 'blue profile', ...
  'pos', [5 5 80 20], 'parent', hProfileButtonGroup, 'HandleVisibility', 'off', ...
  'Tag', 'X_selection');
hY = uicontrol('Style','Radio','String','black profile',...  
    'pos',[0.25*im_dim(1)+5 5 80 20],'parent',hProfileButtonGroup,'  
    → HandleVisibility','off',...  
    'Value',ProfileSelection, 'Tag','Y_selection');  
hXY = uicontrol('Style','Radio','String','3D profiles',...  
    'pos',[0.5*im_dim(1)+5 5 80 20],'parent',hProfileButtonGroup,'  
    → HandleVisibility','off',...  
    'Tag','XY_selection');  
hsurf = uicontrol('Style','Radio','String','surface',...  
    'pos',[0.75*im_dim(1)+5 5 80 20],'parent',hProfileButtonGroup,'  
    → HandleVisibility','off',...  
    'Tag','surf_selection');  

hCheckLinear = uicontrol('Style','CheckBox',...  
    'pos',[4*marg+1.9*im_dim(1)+0.5*gadget_dim(2) figsize(4)-1.2*marg-  
    → gadget_dim(2) im_dim(1)/4+10 gadget_dim(2)],...  
    'BackgroundColor',[0.8,0.8,0.8],...  
    'ForegroundColor','m',...  
    'String','Linear',...  
    'Callback',@CheckLinear_callback);  

hCheckCubic = uicontrol('Style','CheckBox',...  
    'pos',[4*marg+2.6*im_dim(1)+0.5*gadget_dim(2) figsize(4)-1.2*marg-  
    → gadget_dim(2) im_dim(1)/4+10 gadget_dim(2)],...  
    'BackgroundColor',[0.8,0.8,0.8],...  
    'ForegroundColor','y',...  
    'String','Cubic',...  
    'Callback',@CheckCubic_callback);  

hCheckQuadratic = uicontrol('Style','CheckBox',...  
    'pos',[4*marg+2.25*im_dim(1)+0.5*gadget_dim(2) figsize(4)-1.2*marg-  
    → gadget_dim(2) im_dim(1)/4+15 gadget_dim(2)],...  
    'BackgroundColor',[0.8,0.8,0.8],...  
    'ForegroundColor','c',...  
    'String','Quadratic',...  
    'Callback',@CheckQuadratic_callback);  

% Initialize some button group properties.  
set(hProfileButtonGroup,'SelectionChangeFcn',@ProfileButtonGroup_callback);  
set(hProfileButtonGroup,'Visible','on');  

% Display  
updateDisplay  

%% Callback functions  
function ObjHologramSlider_callback(hObject, eventdata) %#ok<*INUSD>  
    SequenceNo = round(get(hObject,'Value'));  
    updateDisplay;  
end  

function EditSequenceNo_callback(hObject, eventdata)  
    set(hObject,'Value',str2double((get(hObject,'String'))))  
    set(hObject,'String',num2str((eval(char([SelectedItemName,'(profilePosY(3),profilePosX(1),SequenceNo)'])))))  
    ObjHologramSlider_callback(hObject, eventdata)  
    updateDisplay  
end
function EditXpos_callback(hObject, eventdata)
    set(hPosSliderX,'Value',str2num(get(hEditXpos,'String')))
end

function EditYpos_callback(hObject, eventdata)
    set(hPosSliderY,'Value',dims(1)-round(str2num(get(hEditYpos,'String')))+1) %#ok
end

function PosSliderX_callback(hObject, eventdata)
    CurrentSelectionX = round(get(hPosSliderX,'Value'));
    profilePosX = [CurrentSelectionX CurrentSelectionX 1 dims(1)];
    set(hEditXpos,'String',num2str(CurrentSelectionX))
    updateDisplay
end

function PosSliderY_callback(hObject, eventdata)
    CurrentSelectionY = dims(1)-round(get(hPosSliderY,'Value'))+1;
    profilePosY = [1 dims(2) CurrentSelectionY CurrentSelectionY ];
    set(hEditYpos,'String',num2str(CurrentSelectionY))
    updateDisplay
end

function CheckLinear_callback(hObject, eventdata)
    if (get(hObject,'Value') == get(hObject,'Max'))
        % Checkbox is checked-take appropriate action
        disp('Linear checked')
        CheckLinear = 1;
        updateDisplay
    else
        % Checkbox is not checked-take appropriate action
        disp('Linear unchecked')
        CheckLinear = 0;
        updateDisplay
    end
end

function CheckCubic_callback(hObject, eventdata)
    if (get(hObject,'Value') == get(hObject,'Max'))
        % Checkbox is checked-take appropriate action
        disp('LinearMean checked')
        CheckCubic = 1;
        updateDisplay
    else
        % Checkbox is not checked-take appropriate action
        disp('Cubic unchecked')
        CheckCubic = 0;
        updateDisplay
    end
end

function CheckQuadratic_callback(hObject, eventdata)
    if (get(hObject,'Value') == get(hObject,'Max'))
        % Checkbox is checked-take appropriate action
        disp('Quadratic checked')
        CheckQuadratic = 1;
    else
        % Checkbox is not checked-take appropriate action
        disp('Quadratic unchecked')
        CheckQuadratic = 0;
        updateDisplay
    end
end
else
    % Checkbox is not checked - take appropriate action
    disp('Quadratic unchecked')
    CheckQuadratic = 0;
    updateDisplay
end
end

function ProfileButtonGroup_callback(hObject, eventdata)
    switch get(eventdata.NewValue,'Tag') % Get Tag of selected object.
        case 'X_selection'
            ProfileSelection=0;
            % disp(get(get(hObject,'SelectedObject'),'String'))
        case 'Y_selection'
            ProfileSelection=1;
            % disp(get(get(hObject,'SelectedObject'),'String'))
        case 'XY_selection'
            ProfileSelection=2;
            % disp(get(get(hObject,'SelectedObject'),'String'))
        case 'surf_selection'
            ProfileSelection=3;
    end
    updateDisplay
end

function ListboxDatasetMatrix_callback(hObject, eventdata)
    SelectedItem=get(hObject,'Value');
    SequenceNo=round(get(hObject,'Value'));
    SelectedItemName = ('Items.' char(ItemNames(SelectedItem)));
    set(hObject,'Value',SelectedItem)
    set(hObject,'Value',SelectedItem)
    bottomfig = 0;
    % keyboard
    if length(size(eval(['Items.', char(ItemNames(SelectedItem))])))== 2;
        CurrNoInSequence = 1;
    else
        CurrNoInSequence = MaxNoInSequence;
    end
    if CurrNoInSequence == MaxNoInSequence
        set(hObject,'String',num2str((eval(char(['Items.', char(ItemNames(SelectedItem)),')]))))
    else
        set(hObject,'String',num2str((eval(char(['Items.', char(ItemNames(SelectedItem),')]))))
    end
    updateDisplay
end

%% Redraw
function updateDisplay
    set(hObject,'String', num2str(SequenceNo))
    % keyboard
    if CurrNoInSequence == 1
        set(hObject,'Visible','off')
        set(hObject,'String',num2str((eval(char(['Items.', char(ItemNames(SelectedItem),')]))))
    else
        set(hObject,'String',num2str((eval(char(['Items.', char(ItemNames(SelectedItem),')]))))
    end
end

344
set(hObjHologramSlider,'Visible','on')
%keyboard
set(hEditZpos,'String',num2str((eval(char([SelectedItemName,'(profilePosY(3),profilePosX(1),SequenceNo)'])))))
end
% left window
axes(hImageMatrix) %#ok

%keyboard
if dim
lengths(SelectedItem) == 2
    eval(['imagesc(',SelectedItemName,']]));
else
    eval(['imagesc(',SelectedItemName,'](SequenceNo),')]));
end
axis equal tight
hold on
line(profilePosX(1:2),profilePosX(3:4),'LineWidth',2,'Color','b')
line(profilePosY(1:2),profilePosY(3:4),'LineWidth',2,'Color','k')
plot(hImageMatrix,profilePosX(1), profilePosY(3),'o',...'
'MarkerEdgeColor','k',...'
'MarkerFaceColor','m',...'
'MarkerSize',7)
%colorbar('South')

% w=25;
% h=25;
ROIdims=[profilePosX(1)-floor(ROIDimW/2) profilePosY(3)-floor(ROIDimH / 2) ROIdimW-1 ROIdimH-1];
ROIcoords=[ROIdims(2) ROIdims(2)+ROIdimH-1 ROIdims(1) ROIdims(1)+ ROIdimW-1];
%check if inside image
if ROIcoords(1) <= 0
disp('ROI has hit top edge!')
    ROIcoords(1)= 1;
end
if ROIcoords(2) > dims(1)
disp('ROI has hit bottom edge!')
    ROIcoords(2)= dims(1);
end
if ROIcoords(3) <= 0
disp('ROI has hit left edge!')
    ROIcoords(3)= 1;
end
if ROIcoords(4) > dims(2)
disp('ROI has hit right edge!')
    ROIcoords(4)= dims(2);
end
% ROIvals=eval(['(ROIdims(1):ROIcoords(2),ROIcoords (3):ROIcoords(4),',num2str(SequenceNo),')]));
rectangle('Position', [ROIcoords(3) ROIcoords(1) ROIcoords(4)- ROIcoords(3) ROIcoords(2)-ROIcoords(1), 'LineStyle', ':'])
hold off
% middle window
axes(hImageProfile)
xPosX=1:dims(2);
if CurrNoInSequence ~= 1
    zPosX = (eval(char([SelectedItemName,'(profilePosY(3),:',SequenceNo',
    --> ')']')));
    zPosY = (eval(char([SelectedItemName,'(:,profilePosX(1),SequenceNo',
    --> ')''']')));
else
    zPosX = (eval(char([SelectedItemName,'(profilePosY(3),:',')'']')));
    zPosY = (eval(char([SelectedItemName,'(:,profilePosX(1)',')''']')));
end
switch ProfileSelection
    case 0 % X-profile
        plot(hImageProfile,xPosY,zPosY,...
            '-b','LineWidth',0.5)
        xlabel('y-position')
        ylabel('Intensity')
        axis tight
        grid on
        hold on
        plot(hImageProfile,xPosY(profilePosY(3)),zPosY(profilePosY(3))
        --> 'o',...
        'MarkerEdgeColor','k','...
        'MarkerFaceColor','m','...
        'MarkerSize',7)
        hold off
    case 1 % Y-profile
        plot(hImageProfile,xPosX,zPosX,...
            '-k','LineWidth',0.5);
        xlabel('x-position')
        ylabel('Intensity')
        axis tight
        grid on
        hold on
        plot(hImageProfile,xPosX(profilePosX(1)),zPosX(profilePosX(1))
        --> 'o',...
        'MarkerEdgeColor','k','...
        'MarkerFaceColor','m','...
        'MarkerSize',7)
        hold off
    case 2 % XY-profile
        plot3(hImageProfile,yPosX,xPosX,zPosX,'k',xPosY,yPosY,zPosY,'b'
        --> ')
        hold on
        axis tight
        % if CurrNoInSequence == 1
        %     (eval(char([SelectedItemName,'('
        %         profilePosY(3),':','')'])));
        % else
        %     (eval(char([SelectedItemName,'('
        %         profilePosY(3),:',SequenceNo','')'])));
        % end
        %plot3(hImageProfile,profilePosY(3),profilePosX(1),(eval(char
        %     ((SelectedItemName,'(profilePosY(3),profilePosX(1))'']))
        --> 'o',...
plot3(hImageProfile, xPosY(profilePosY(3)), xPosX(profilePosX(1)), yPosY(profilePosY(3)), 'o',... 'MarkerEdgeColor','k','... 'MarkerFaceColor','m','... 'MarkerSize',7)

% xlabel('y-pixels')
% ylabel('x-pixels')
% zlabel('Intensity')
axis tight
grid on
hold off

case 3 % surface
if CurrNoInSequence == 1
surf(eval(char(['(',SelectedItemName,'(:,:))'])),'
   FaceColor','interp','FaceLighting','phong')
else
surf(eval(char(['(',SelectedItemName,'(:,:,SequenceNo))'])),'
   FaceColor','interp','FaceLighting','phong')
end
hold on
plot3(hImageProfile, xPosY(profilePosY(3)), xPosX(profilePosX(1)), yPosY(profilePosY(3)), 'o',... 'MarkerEdgeColor','k','... 'MarkerFaceColor','m','... 'MarkerSize',10)
camlight right
% xlabel('y-pixels')
% ylabel('x-pixels')
% zlabel('Intensity')
axis tight
grid on
hold off
end

% right window
axes(hImagePoints)

% calculate on the fly
if CurrNoInSequence ~= 1
for i = 1 : MaxNoInSequence
TimesSeriesPoints(i) = (eval(char(['(',SelectedltemName,'(yPosX(1),yPosY(1),',num2str(i),')'])));
% for ROIs -> used in bottom figure
TimesSeriesROIs(i) = mean2(eval([SelectedltemName,'(ROIcoords(1):ROIcoords(2),ROIcoords(3):ROIcoords(4),',num2str(i),')']));
TimesSeriesROIstds(i) = std2(eval([SelectedltemName,'(ROIcoords(1):ROIcoords(2),ROIcoords(3):ROIcoords(4),',num2str(i),')']));
end
plot(hImagePoints, TimeStamps, TimesSeriesPoints,'r.-', TimeStamps(SequenceNo), TimesSeriesPoints(SequenceNo),... 'o',... 'MarkerEdgeColor','k','... 'MarkerFaceColor','m','... 'MarkerSize',7)
xlabel('Time sequence [in s]')
ylabel('Intensity')
axis tight
```matlab
grid on

if CheckLinear == 1
    %plot fit line
    plotfit(hImagePoints, 1,'m')
else
    % delete fit line
    plotfit(hImagePoints, 0,'m')
end

if CheckQuadratic == 1
    %plot fit line
    plotfit(hImagePoints, 2,'c')
else
    % delete fit line
    plotfit(hImagePoints, 0,'c')
end

if CheckCubic == 1
    %plot fit line
    plotfit(hImagePoints, 3,'y')
else
    % delete fit line
    plotfit(hImagePoints, 0,'y')
end
hold off
else
    TimesSeriesPoints = (eval(char([SelectedItemName,'(yPosX(1),yPosY(1))'])))
    plot(hImagePoints,1:CurrNoInSequence,TimesSeriesPoints,'m.-',
    ...SequenceNo,TimesSeriesPoints,...
    ...'o',...
    ...'MarkerEdgeColor','k',...
    ...'MarkerFaceColor','m',...
    ...'MarkerSize',7)
    xlabel('Time sequence #')
    ylabel('Intensity')
    axis tight
    grid on
end

%bottom window
axes(hImagemeanROI)
cla % clear axis
polyn = polyfit(1:dims(3),TimesSeriesROIs',1); % linear fit to ROI
yi = polyval(polyn,1:dims(3));
stdFitLine = std2(TimesSeriesROIs'-yi); % quick approximation...
plot(hImagemeanROI,1:dims(3), yi,'b','LineWidth',2)
hold on
errorbar(hImagemeanROI,1:dims(3),TimesSeriesROIs,TimesSeriesROIstds,'Color',[0.45 0.45 0.45])
hold on
plot(hImagemeanROI,SequenceNo,TimesSeriesPoints(SequenceNo),...
...'o',...
B.2 Heat Diffusion Calculations

The basic code for calculating heat diffusion of a three dimensional model is included here. This process is common for both the Method 1 and Method 2 approaches of accounting for the effects of heat diffusion on the measurement results. The code is presented in the context of an example of the implementation of this code for Method 1, showing the differences required for the proton versus the HDR source models.

newheatdiff3.m

%Based on an explicit approach to solving for heat diffusion in three dimensions.
close all
radiation_type = 'proton'; % 'proton' or 'HDR'

%%%%%%% For proton source
if strcmp(radiation_type,'proton')
% Load the data to be heat diffused. % This may be proton monte carlo data, brachyvision HDR data or a simulated shape.
load protonbeam3DMC.mat % If required Change the shape of the input data so the central axis is the second dimension (Simplifies visualising the data).
full3Ddata = permute(full3DMCdata,[1,3,2]); % crop if needed to run code faster.
full3Ddata = full3Ddata(:,:,1:100,1:100,1:100); %cropped option % Find location of maximum point in the data
[y, x, z] = size(full3Ddata);
[num] = max(full3D3data);
[yy, xx, zz] = ind2sub(size(full3Ddata),find(full3Ddata==num));
% Enter the variables
% Model properties
dim_xyz = 0.0001; % m in each direction (0.1 mm) (Assumed the same each way)
dim_xyz_mm = dim_xyz*1000; % in mm for graphics purposes later
peak_dose = 400; % If it is a relative MC data model then this is necessary to work out the approximate temperatures involved.
% Irradiation properties
total_t = 1; \% s 17 is the end of irradiation
total_meas = 20.0;
meas_temp = 21; \%K

% Test cell properties
test_cell_total = 22; \% mm (in the direction of the integration aka laser direction)
test_cell_size = 20; \% mm (This is just the water volume)
test_cell_size = test_cell_size/1000; \% in m

% Medium properties
k = 9.37e-6*meas_temp^2 + 0.00212*meas_temp + 0.56; \% 0.6071; \% W K^-1 m^-1
alpha = 0.1447*10^-6; \%m^2/s \%alpha = k/rho C
specific_heat = 4181; \% Gy per K \% at 20 degrees celsius. Should be sufficient for now.

% Heat diffusion properties
delta_t = 0.01; \% Maximum is 0.0114 s
maxit = total_t/delta_t;
tau = alpha*delta_t/dim_xyz^2;

% Convert the input data to approximate temperature values and normalise.
\% Neccessary because the proton beam case the input is relative doses, so needs to be converted.
T_input = (full3Ddata./full3Ddata(yy,xx,zz)).*peak_dose.*total_t./(specific_heat*total_meas); \% Normalisation to peak because this is the only place we have an estimated dose value for.
D_input = T_input.*specific_heat;

% Create the axis. We want to make the maximum position be the zero point in the model
x_axis_model = dim_xyz_mm:dim_xyz_mm:x*dim_xyz_mm; \% beam profile, perpendicular to applicator
y_axis_model = (-yy+1)*dim_xyz_mm:dim_xyz_mm:(y-yy)*dim_xyz_mm; \% cax, parallel to applicator
end

% For HDR source
if strcmp(radiation_type,'HDR')
% Load the brachyvision data to be heat diffused.
full3Ddata=dicomread('RD.1.2.246.352.71.7.709332839.4034.20121123163823.dcm');
full3Ddata=double(squeeze(full3Ddata));

% Enter the variables
% Model properties
dim_xyz = 0.0005; \% m in each direction (0.1 mm) (Assumed the same each way)
dim_xyz_mm = dim_xyz*1000; \% in mm for graphics purposes later
dose_bin_width = (7.027e-06); \%Gy per integer
\% For the dimensions [m,n,p] where m = the horizontal cross section, n=
\% the depth in the direction of the HDR applicator and P = the width in
\% the direction of the laser.

% Irradiation properties
total_t = 10; % seconds
model_time = 100; % seconds. This is what the model was calculated for, so
% to scale to the measurement time.
meas_temp = 21; %K
source_activity = 4.597; % Ci compared to planned dose at 10 Ci.
applicator_width = 3; % mm
% Test cell properties
test_cell_total = 40; % mm (in the direction of the integration aka laser
% direction)
test_cell_size = 36; % mm (This is just the water volume)
% Medium properties
k = 9.37*10^(-6)*meas_temp^2 + 0.00212*meas_temp + 0.56; % W K^-1 m^-1
alpha = 1.447*10^(-6); %m^2/s %alpha = k/rho C
specific_heat = 4181.8; % Gy per K % at 20 degrees celsius. Should be
% sufficient for now.
% Heat diffusion properties
delta_t = 0.01; % Maximum is 0.0114 s
maxit = total_t/delta_t;
tau = alpha*delta_t/dim_xyz^2;
% Crop data about the maximum point
% locate maximum point
  % find maximum point first so that we can crop i symetrically
  % about this point
[num] = max(full3Ddata(:));
[xx, yy, zz] = ind2sub(size(full3Ddata),find(full3Ddata==num));

  % take the central point if the maximum is spread over several
  % points.
  xx = xx(length(xx)/2+0.5); % Note, won't work if it's an
  % even number, will need to be manually altered here.
  yy = yy(length(yy)/2+0.5); % And also altered a few
  % lines lower.
  zz = zz(length(zz)/2+0.5);

  % Reduce data volume (otherwise processing runs out of memory. Will
  % have a negligible imapct on accuracy by the edges).
size_matrix = size(full3Ddata);

  full3Ddata = full3Ddata(xx-analysis_dimension/dim_xyz:xx+
    analysis_dimension/dim_xyz,...
    yy-analysis_dimension/dim_xyz:yy+analysis_dimension/dim_xyz,:);
% find the maximum position to find the centre of the data set, as it
% stands now.
[x,y,z] = size(full3Ddata);
[num] = max(full3Ddata(:)); % Note: repeating this is a
% workaround, rather than just altering the co-ordinates according
% to what was done to the data above.
[xx, yy, zz] = ind2sub(size(full3Ddata),find(full3Ddata==num));
% take the central point if the maximum is spread over several points.
xx = xx(length(xx)/2+0.5); % Note, won't work if it's an even number, will need to be manually altered here as well as above.
yy = yy(length(yy)/2+0.5);
zz = zz(length(zz)/2+0.5);

% Correct the data to the right dose and convert to temperature.
T_input = full3Ddata.*(total_t/model_time)*dose_bin_width*(source_activity/10)./specific_heat; % reduced data set corrected for all the above.
D_input = T_input.*specific_heat;

% Create the axis. We want to make the maximum position be the zero point in the model
x_axis_model = (-xx+1)*dim_xyz_mm:dim_xyz_mm:(x-xx)*dim_xyz_mm; % beam profile, perpendicular to applicator
y_axis_model = (-yy+1)*dim_xyz_mm:dim_xyz_mm:(y-yy)*dim_xyz_mm; % cax, parallel to applicator
end

% Initialise the solution matrix/ calculation volume. (Same size as model data set). Ideally the data set is larger than the region that we are interested in (a.k.a the test cell). This means that the difference in heat coefficients of the wall material is negligible. For measurements near the surface this may however be a consideration.

% Depth is in the direction of the laser, height is the width is the horizontal cross section and planes is the direction of the proton beam.
M = zeros(y,x,z);

% Determine the temperature increment over the time instance above.
T_input_increment = T_input./maxit;

% solve the heat equations for each point
for i = 1:maxit
i
M = M + T_input_increment;

% All the internal points within the matrix
M(2:y-1,2:x-1,2:z-1) = k*tau*(M(1:y-2,2:x-1,2:z-1)+M(3:y,2:x-1,2:z-1)+M(2:y-1,1:x-2,2:z-1)+M(2:y-1,3:x,2:z-1)+M(2:y-1,2:x-1,1:z-2)+M(2:y-1,2:x-1,3:z-1))*(1-6*tau*k);

% External surfaces, excluding edges and corners as they are a long way away from the centre where the changes are...
M(1,2:x-1,2:z-1) = M(2,2:x-1,2:z-1);
M(y,2:x-1,2:z-1) = M(y-1,2:x-1,2:z-1);
M(2:y-1,1,2:z-1) = M(2:y-1,2:z-1);
M(2:y-1,x,2:z-1) = M(2:y-1,x-1,2:z-1);
M(2:y-1,2:x-1,1) = M(2:y-1,2:x-1,2);
M(2:y-1,2:x-1,z) = M(2:y-1,2:x-1,1:z-1);
end

if strcmp(comparison_value,'1');
T_output = M;
% convert back to dose
D_output_model = T_output.*specific_heat;
% Integrate across the width of the test cell to approximate the expected measurement result.

\[
D_{\text{output model integrated1}} = \text{sum}(D_{\text{output model}}(:,:,\text{zz-test cell size}/(2*dim_{xyz}\text{ mm})\text{:zz+test cell size}/(2*dim_{xyz}\text{ mm})),3)/(\text{test cell size/(dim_{xyz}*1000)})
\]
Appendix C

Publications

The initial proof-of-principle results of the novel DHI detector were published in a peer-reviewed paper in the journal Medical Physics. Further aspects of the research have been presented at a range of international conferences, with the corresponding abstracts and/or short papers published in the relevant conference proceedings. A list of such publications over the duration of the research is included here, in reverse chronological order.

C.1 Refereed Paper


C.2 Conference Proceedings


