The Interaction of Light with Skin

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by
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Abstract

The past thirty years have seen many advances in medicine. One of the most significant developments has been in the use of the laser. This instrument has been used in a number of surgical therapies including the removal of vascular lesions and the removal of tattoos.

Lasers for the treatment of vascular lesions have progressed from early devices which ablated the skin surrounding the ectatic vessels and thus caused scarring, to devices which use selective thermolysis and leave the texture of the skin unchanged. Two such devices are the flash-lamp pumped pulsed dye laser and the copper vapour laser.

This thesis investigates what is known about the processes that occur in the skin following the treatment of vascular lesions with these lasers. The purpura-like response of the pulsed dye laser is due to a stationary coagulum of erythrocytes in the treated vessels. The blanching caused by the copper vapour laser is less well understood. We photograph the treatment process, and quantitatively measure the light remitted from the skin. We conclude that blanching is caused by a combination of vasoconstriction, as proposed by Marini et al. (1992), and destruction of epidermal melanin.

It is observed that light coloured vascular lesions blanch faster and require more energy to blanch than dark lesions. These phenomena are related to the smaller size of the ectatic vessels in light coloured lesions.

The use of Q-switched ruby lasers for removal of tattoos has long been established. However such devices are expensive and are unable to remove red pigments. This thesis reports on progress made towards the development of a cheaper flash-lamp based system which might be able to remove all pigment colours.
Chapter 1

Introduction

In recent decades light in the visible and near-visible parts of the electromagnetic spectrum has become an increasingly important weapon in the medical practitioner's armoury. Physiotherapists use infra-red light in the treatment of soft tissue injuries, dermatologists use ultraviolet light to treat psoriasis, and with the invention of the laser many more conditions became open to treatment with light. Ophthalmologists can now treat many eye disorders without the need for invasive surgery, oncologists can use lasers in photodynamic therapy to activate drugs applied to certain tumors. Lasers used as scalpels in other forms of surgery reduce the risk of spreading an infection, may reduce the amount of blood lost around an incision, and may require a smaller incision to achieve the same result as conventional surgery.

Plastic and reconstructive surgeons seek to improve the appearance of their patients. Often this involves the removal of some cutaneous blemish. Such blemishes may be naturally occurring, such as a vascular lesion (for example a port-wine stain, or telangiectasia); or a pigmented lesion (an area of skin with an overabundance of melanin); or self-inflicted, such as a tattoo. Conventional surgical techniques for removing such blemishes invariably involve damaging structures in the skin other than the cause of the problem. Damage to the fibrous structure of the dermis often leads to scarring, a result which may be worse than the original complaint. In Chapter 2 we describe the physiology of human skin. In addition we also describe the structure of vascular lesions and tattooed skin.
Lasers treatment of vascular lesions began in the mid 1960s. Initially carbon dioxide (CO$_2$) and ruby lasers were used. These lasers vaporise skin down to a level in the dermis below the ectatic blood vessels (Ratz and Bailin 1987, Solomon et al. 1968). The resulting wound is similar to that caused by conventional surgical techniques such as dermabrasion, and can lead to scar formation.

These results prompted the use of lasers that cause more specific damage to vasculature, such as the argon and Nd:YAG lasers. Light from these lasers is selectively absorbed by the colour centres (chromophores) in the skin. However, the long illumination times necessary with these lasers still result in conduction of heat to surrounding dermal tissue, causing non-specific coagulation necrosis (Solomon et al. 1968), which again leads to scarring. In addition, damage to the melanin producing cells (melanocytes) in the epidermis can lead to abnormal pigmentation when the skin has healed.

Theoretical modelling (Anderson and Parrish 1981, van Gemert et al. 1982) led to the use of yellow light lasers, particularly the pulsed dye laser which emits 577 nm wavelength light, and the copper vapour laser which emits 578 nm wavelength light. These wavelengths are strongly absorbed by the red haemoglobin but less strongly absorbed by melanin than green or blue wavelengths and so cause more specific damage to ectatic vessels.

Although the yellow light lasers produce good clinical results (Tan 1992, Pickering et al. 1990), they do so by rather different mechanisms. The pulsed dye laser produces a purpura-like response in the skin whilst the copper vapour laser produces a transient whitening (known as blanching) of the skin. Little real understanding exists of either of the mechanisms, due in part to non-standard use of medical terminology. Pickering et al. (1992) expresses the hope that standardisation of reporting results will improve the ability of researchers to interpret each other’s work, and we support that ideal. In Chapter 3 we briefly examine what is understood of the two mechanisms, and describe why animal model and in vitro examinations of the damage processes are of limited clinical value.

In Chapter 4 we present a photographic investigation of the blanching response time of vascular lesions to copper vapour laser treatment. This yet to be
published experiment measures the millisecond timescale changes that occur in skin colour during the clinical treatment.

Measuring the amount of light remitted from the skin during copper vapour laser treatment of vascular lesions has produced corroborative evidence for the effect of vascular structure on the blanching response time. These measurements are presented in Chapter 5.

Chapter 6 is a discussion of the implications of the results of these two experiments to the understanding of the processes which occur in the skin as a result of copper vapour laser illumination.

Lasers began to be used to treat cutaneous pigmented lesions soon after the invention of the ruby laser in 1960. Within three years results of investigations into the effect of the laser beam on the skin were being published (Goldman et al. 1963, Goldman et al. 1965, Goldman et al. 1967). It became obvious that the ruby laser offered a new option in the treatment of various pigmented lesions, especially black and blue tattoos (Laub et al. 1968), since pigment removal was reported with little or no surrounding tissue damage. Since then the Q-switched ruby laser has been the only viable alternative to standard surgical techniques for the removal of black and blue tattoos.

However, Q-switched ruby laser treatment has three main drawbacks. The first, and major, drawback is the high cost of the equipment (about $NZ 300,000). The low efficiency of the ruby laser is partly to blame for the high cost. Ruby has a three energy level system and is less efficient than the four energy level system common in other lasers. In the Q-switched mode of operation the efficiency is typically 0.1% to 0.2%. This, combined with the high sensitivity of the output to operating temperature, requires a complicated cooling system.

The second drawback of the Q-switched ruby laser is that only small treatment areas are possible, due to the difficulty in producing a uniform ruby crystal for a large scale ruby laser. At present most systems have a 5 mm diameter treatment area. This results in long, tedious treatment sessions at high cost and inconvenience to the patient.

The third drawback of Q-switched ruby lasers is their inability to remove red
pigments. This is because the 694.3 nm wavelength ruby laser light is not absorbed by red pigment.

Chapter 7 describes the search for an alternative to ruby laser treatment for tattoo removal. We also present an experimental design of a discharge circuit for a high pressure xenon-filled flash-lamp. This circuit is designed to produce light output of sufficient power to selectively damage pigmented structures of all colours. This would lead to a cheaper, faster, broad spectrum tattoo removal method.

In Chapter 8 we summarise the results of this thesis. First, we support the model of Marini et al. (1992), who proposed that the transient blanching response of vascular lesions to copper vapour laser treatment is caused by vasoconstriction. Second, we add to this model the suggestion that the more persistent blanching is due to the destruction of melanin containing structures in the epidermis. Third, we suggest that rescanning an erythemic vascular lesion will produce an improved result, providing that adequate protection by cooling is given to the epidermis. Fourth, we conclude that a feedback mechanism to control movement of the laser beam during copper vapour laser treatment of vascular lesions is not possible, since remittance from the lesion does not change whilst it is still being illuminated. Fifth, we have measured the rates of blanching of various colours of vascular lesions and conclude that light coloured vascular lesions blanch faster than dark coloured lesions. This has been attributed to the shorter time necessary for the endothelial cells of smaller vessels to swell and occlude the vascular lumen. Sixth, we suggest that the higher fluence required to treat light coloured vascular lesions is caused by less light being absorbed in smaller vessels. This results in insufficient heat being conducted to the endothelial cells to do the required thermal damage. Seventh, we note that the inconsistent use of medical terminology has slowed the progress made towards better laser systems for the treatment of vascular lesions. Eighth, we report on clinical success in removing some tattoo pigment from a professional tattoo using a high-powered flash-lamp. This indicates that, with further development, tattoo removal with high-powered flash-lamps may be an alternative to Q-switched ruby laser treatment.
Chapter 2

Physiology

2.1 Human Skin

Human skin is a complex organ, varying in thickness from 1 mm on the eyelids to 4 mm on the back, palms of the hands, and soles of the feet (Goldsmith 1983). Skin consists of three main layers: the epidermis, the dermis, and the subcutaneous fat (see figure 2.1).

2.1.1 Epidermis

The epidermis is the most superficial layer of the skin and is between 60 μm and 100 μm thick. It is cellular in structure and entirely avascular. The epidermis is composed of four layers; the innermost is the basal layer, followed by the stratum spinosum, the stratum granulosum, and the stratum corneum or keratin layer.

Unlike most other parts of the body, the epidermis continually produces new cells whose main purpose is to be shed. The cells of the basal layer continually divide and migrate outwards towards the stratum granulosum where they die. The cell remnants within the stratum corneum form a protein called keratin which is tough, pliable, and relatively impermeable to substances passing in or out of the body. Eventually the keratin is shed. The entire process from basal cell formation to keratin shedding takes 45 to 75 days, depending on the thickness of the epidermis.
The basal layer is only one cell thick and produces two types of cells: keratinocytes and melanocytes. The keratinocytes produce the cells that form the main structure of the epidermis. The melanocytes produce melanosomes, small (0.3 μm to 1.0 μm) egg-shaped sacks that contain the chromophore melanin. The melanosomes are distributed throughout the keratinocytes by the melanocytes. It is melanin which provides skin with its yellow, brown, or black pigmentation and prevents most ultraviolet and visible radiation penetrating through to the dermis. The amount of light that reaches the dermis may vary by a large fraction between any two sites on the skin of an individual depending on the melanin concentration at each site. Further, the melanin concentration at any site may change over a period of days or weeks depending on the exposure to the sun the skin receives, and also the biological and hormonal stimulation of melanocytes.
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2.1.2 Dermis

The dermis contains the bulk of the skin between the epidermis and the subcutaneous fat, and is normally 1 mm thick. The epidermal basal layer and the top of the dermis form the epidermal/dermal junction which is characterised by undulations which protrude up to 100 μm into the dermis. Between each of these protrusions is the region known as the dermal papilla. The troughs of the protrusions form the arbitrarily defined boundary between the two layers of the dermis. The top layer, the papillary dermis, contains the capillaries that provide nutrients for the epidermis. The lower layer is called the reticular dermis which extends inwards towards the fatty layer, and contains the larger blood vessels. Both layers of the dermis are comprised mainly of fibrous connective tissue called collagen. Collagen has a high tensile strength with each fibril being able to support at least 10 000 times its own mass (Wood and Bladon 1985). This strength, along with the elasticity provided by elastin, creates a network of strong fibres which are able to protect underlying organs from mechanical injury.

2.2 The Cutaneous Vascular System

The cutaneous blood supply serves a dual purpose. First, it provides nourishment to both the surrounding dermis and the avascular epidermis. However the skin has a larger blood supply than is needed to satisfy its oxygen requirements (Wood and Bladon 1985). The large volume of blood which flows through the skin plays an important role in regulating the temperature of the body. On exposure to heat a larger than normal volume of warm blood flows to the peripheral regions of the body through a widely dilated vascular network. In contrast, the rate of blood flow falls upon exposure to cold. The velocity of the blood flow through the circulatory system depends on the cross-sectional area of the blood vessels. In the aorta blood travels at an average velocity of 40 to 50 centimetres per second, whilst in the capillaries the velocity is reduced to less than 1 millimetre per second (Rushmer 1972).
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Figure 2.2: Blood vessels form a tree-like structure in the dermis. It is often capillaries in the sub-papillary and papillary plexi that are ectatic.

2.2.1 Blood Vessel Distribution

The distribution of blood vessels within the dermis can be approximated by a tree-like structure (figure 2.2).

An artery approximately 100 µm in diameter enters the lower dermis through the subcutaneous fat. This artery may divide once or twice before reaching the mid-dermis where the branches are approximately 50 µm in diameter and are now called arterioles. More branching occurs as the arterioles reach upwards until they begin to form one or two plexi (the sub-papillary plexi) of small capillaries that lie approximately parallel to the surface. Extending from these plexi into the dermal papilla are the papillary (or terminal) capillaries. These are vertical loops in the shape of a hair pin (Ryan 1973) which supply the papillae. The papillary capillaries are only 5 µm to 10 µm in diameter and a typical papilla contains only one such vessel. The capillaries drain into venules which lead to larger and larger veins deeper within the dermis.

Capillaries are formed of a single layer of entwined endothelial cells. Unlike
other types of blood vessel, capillaries have no surrounding muscle tissue to control vessel diameter and hence blood flow. Blood flow through capillaries is instead controlled by a pre-capillary sphincter muscle. Only a fraction of the capillaries carry blood at any one time, since there is insufficient blood to fill every blood vessel in the body at the same time (Chaffee and Lytle 1980). According to Professor Boswell of the Pathology Department of the Christchurch Medical School, this fraction has never been determined. The fraction varies throughout the body and also varies with body temperature and emotional state.

The endothelial cells resemble lightly fried eggs rolled over to form a tube (Ryan 1973, Rushmer 1972). The yoke represents the nucleus and may be up to 6 μm thick (Chaffee and Lytle 1980). The egg-white represents the cytoplasm of the cell and may be found in any shape and is only 1 μm thick. The volume enclosed by the endothelial cells is called the vessel’s lumen. Endothelial cells are semi-permeable and permit the escape of water, sugar, sodium chloride and other nutrients from the blood to surrounding tissue (Best and Taylor 1961).

Blood, which is contained within the lumen, is a collection of many components but is mainly, by volume, 55% plasma, 40% erythrocytes (red blood cells), and 5% leukocytes (white blood cells). Erythrocytes are bi-concave discs averaging about 7.7 μm in diameter and are about 3 μm thick (Tortora and Anagnostakos 1984). They move in single file along the capillary, separated by other blood elements (see figure 2.3). In the process the erythrocyte’s outer surface is left in contact with the vessel wall allowing, among other processes, the transfer of oxygen from oxyhaemoglobin (HbO₂) within the cell to the surrounding tissues.

2.3 Vascular Lesions

Vascular lesions are areas of skin with an abnormally red colouration. They vary in size from a few square centimetres to over 10% of the body surface area (approximately 2000 cm²). Skin displaying vascular lesions contains capillaries within the sub-papillary or papillary plexus which are enlarged, or ectatic. Ectatic vessels are irregularly shaped with diameters ranging from 20 μm to in excess of 150 μm.
Figure 2.3: In a normal capillary erythrocytes fill the vessel’s lumen. Vascular lesions have ectatic capillaries which allow erythrocytes to flow in greater numbers.

Barsky et al. (1980) measured the thickness of endothelial cells to be 4 \( \mu \text{m} \) to 6 \( \mu \text{m} \) for all ectatic vessels. The volumes of these vessels are typically 5 to 100 times greater than those of normal vessels, hence the erythrocytes no longer move in single file down the capillary. Since the volume of blood within the sub-papillary plexus determines the redness of the skin colour (Chaffee and Lytle 1980), vascular lesions result.

2.3.1 Telangiectasias

Telangiectasia is the obvious redness of the lower legs, neck, cheeks, and nose that is common in late middle age. It is caused by the loss of papillary capillaries resulting in dilation of vessels in the sub-papillary plexus. Thus the ectatic vessels tend to have diameters at the larger end of the scale but tend to be well separated. This results in a red discoloration which varies little between patients. Often individual vessels may be seen (see figure 2.4).
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2.3.2 Port-Wine Stains

Port-wine stains are salmon pink to purple vascular lesions present in about 0.3% to 0.5% of the population (Carruth and Shakespeare 1986). They tend to be darker and more sharply defined than telangiectasias (see figure 2.5). The ectatic vessels may occur anywhere between the papillary dermis and the lower dermis. Port-wine stains have been classified into four types (Ohmori and Huang 1981): constricted, intermediate, dilated, and deeply located. The first two categories have ectatic vessels in the papillary dermis. The second two categories have larger ectatic vessels lower in the dermis.

Clinically port-wine stains are also classified by colour. They vary in colour between salmon pink and dark purple. Children tend to have lighter coloured lesions than adults, which implies that the colour of a port-wine stain darkens with age. The lighter colour of salmon pink port-wine stains indicates a lower volume of blood present in the lesion.

The cause of the ectasia is largely unknown. There is a small tendency for stains to be hereditary, but no physical reason has been firmly established. However Smoller and Rosen (1986) performed histologies which indicated that ectasia may be caused by a lack of nerves to muscular tissue that controls arteries and arterioles (Rydh et al. 1991). Pickering et al. (1991) noted that lesions tended to involve singular or adjoining regions of the skin, an observation which supports a link to the nervous system.

The physiological reason for the difference in blood volume is not well established. According to Noe et al. (1980) and Barsky et al. (1980), the number of ectatic vessels stays the same but they become progressively dilated due to the surrounding collagen degenerating as the patient ages. They also suggest that more of these dilated vessels become full as the patient ages.

Niechajev and Clodius (1990) disagree, claiming the number of ectatic blood vessels which are full of erythrocytes is an unimportant artifact, since this number varies (see Section 2.2.1). They also claim that vessel diameter does not increase with age. They suggest that colour differences are caused by differences in vessel
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Figure 2.4: A typical telangiectasia. Often individual vessels can be seen.

Figure 2.5: A typical, but extensive, red port-wine stain.
diameter, vessel wall structure, depth of the ectatic vessels in the dermis, and the quality of the overlying skin.

The only agreement between the two histological studies is the importance of vessel diameter to lesion colour. Whilst this is sufficient for most modelling purposes, it does not explain the ageing of lesions. This area needs further research.

2.4 Decorative Tattoos

Decorative tattoos are formed by the deliberate introduction of pigment into the skin. Rather than being uniformly distributed, the pigment tends to accumulate in clusters that are membrane bound, normally in fibroblasts which surround blood vessels. These clusters may be up to 30 μm in diameter (Zhang 1993). Histologically decorative tattoos may be divided into two categories: professional tattoos, and amateur tattoos.

2.4.1 Professional Tattoos

Professional tattoos are applied by a cluster of needles mounted on an electric vibrator. The needles penetrate an even distance into the skin and when they retract leave behind the tattoo dye. This results in an uniform distribution of pigment clusters superficially within the dermis (Apfelberg et al. 1980) with, on average, 70% of clusters occurring between 5 μm and 15 μm below the dermal/epidermal junction (Zhang 1993). The method of application also results in even pigment concentration between clusters. Professional tattoos tend to be sharply delineated with little blurring at the edges.

2.4.2 Amateur Tattoos

Amateur tattoos are applied by the penetration of sharp objects (for example, needles and pens) to a nonuniform depth into the skin (Taylor et al. 1990). As a result the pigment varies in concentration from cluster to cluster, and the clusters themselves vary in size. The pigment is often distributed nonuniformly throughout
the epidermis, dermis, and the subcutaneous fat, but as a rule is deeper than pigment in professional tattoos. The combination of these factors gives amateur tattoos less distinct, more blurred lines than professional tattoos (Apfelberg et al. 1980).

2.4.3 Tattoo Dyes

Nearly one hundred coloured commercial tattoo dyes are available in the major American catalogue (Spaulding & Rogers catalogue 1988, 1989-1990, 1991-1992), and many more are available from other sources. Coloured tattoo dyes traditionally contain metals, such as mercury, iron, aluminium, cobalt, copper, titanium, chromium, lead, and magnesium. These help to make tattoos vivid and more resistant to fading (Loewenthal 1960, Agris 1977, Slater and Durrant 1984). More recent coloured dyes are organic, but tattooists are reluctant to provide precise details.

Indian ink is used for blue and black amateur tattoos. This is made from candle-black and a binding agent such as gelatin or glue (Hanks 1988). Coloured organic pigments may be made from the following process. Organic dyes are dissolved in water, absorbed onto aluminium hydroxide, forming an aluminium hydroxide hydrate. This is then heated to form aluminium oxide and ground into a powder. The pigment adheres to, or is trapped inside, the aluminium oxide granules (Zhang 1993).

Tattoos fade after a number of years. Black tattoos fade to light blue over 20 to 50 years and also become less sharply defined. This is caused by the diffusion of the pigment in the dermis as a result of flexing of the skin. In areas of the skin where the skin is frequently flexed (such as the wrists and knuckles) a black tattoo may fade over 5 to 6 years. Coloured tattoos are generally less resilient than black tattoos and tend to disappear completely after 50 years.
Chapter 3

Treatment of Vascular Lesions

3.1 History

Before 1975 no cosmetically acceptable treatment for vascular lesions existed. The usual remedy for those who wanted to conceal their lesion was to hide it beneath dense theatrical makeup. Several medical and surgical techniques had been tried: tattooing with white pigment, dermabrasion, carbon dioxide laser vaporisation, skin grafts, x-ray bombardment, infrared heating, ruby laser heating, and cryotherapy being the main procedures. However, all of these treatments cause damage to healthy, normal tissue. This can cause scarring and the end result may be no improvement over, or far worse than, the original lesion.

A method which selectively damages the ectatic vessel without excessively harming adjacent tissue is direct heating of the erythrocytes contained in the vessel itself. This process is called selective thermolysis. Direct heating of erythrocytes can be achieved since HbO₂, like melanin, absorbs visible light. Hence by selecting light of an appropriate wavelength, the erythrocytes containing HbO₂ can be heated causing damage to the endothelial cells of the blood vessel.

The argon laser was the preferred laser for treatment of vascular lesions for a number of years. This laser has been used both untuned (488 nm to 514.5 nm) and tuned (usually to 514.5 nm). However the long exposures necessary with this laser to sufficiently damage the ectatic vessels allows conduction of heat from vascular to non-
vascular cutaneous structures. Damage to these structures may lead to hypertrophic scarring. In addition, argon laser light is absorbed by melanin in the epidermis. Excessive damage to the melanocytes can cause hypopigmentation of the treated lesion.

### 3.2 Yellow Light Lasers

Theoretical modelling proposed that 577 nm would be an ideal wavelength for the treatment of vascular lesions (Anderson and Parrish 1981). This yellow light is at an absorption peak of HbO$_2$ and is minimally absorbed by melanin and other non-vascular tissue. Two different types of yellow light laser are currently in use: the flash-lamp pumped pulsed dye laser (FPDL) and the copper vapour laser (CVL). These lasers have characteristically different beams, and are used in almost totally different ways. Both, however, have the ability to significantly reduce, or even remove, vascular lesions (Garden *et al.* 1988, Nelson 1991, Walker *et al.* 1989, Pickering *et al.* 1990).

#### 3.2.1 Pulsed Dye Lasers

Flash-lamp pumped pulsed dye lasers produce short pulses of light (normally with 577 nm wavelength) at a low repetition rate determined by the flash-lamp that is used to provide the energy for the pulse. When treating vascular lesions, pulse lengths of between 300 ns and 450 $\mu$s (Anderson and Parrish 1981, Garden *et al.* 1986) have been used and beam diameters between 0.1 mm and 5 mm (Scheibner and Wheeland 1989, Tan and Stafford 1992).

The shorter pulse lengths (<100 $\mu$s) were used to deposit the energy of the pulse in a time shorter than the thermal relaxation time of the targeted vessel. The thermal relaxation time is arbitrarily defined as the time required for 50% of the heat produced by the absorbed light to conduct out of the blood vessel into adjacent tissues (Anderson and Parrish 1983). This criterion was used with the aim of reducing the radius of thermally damaged tissue around the treated blood vessel (Tan *et al.*
However, it does not specify that there must be sufficient heat conducted to the endothelial cells to cause necrosis. Greenwald et al. (1981) and Hulsbergen-Henning et al. (1984) observed that the vessels treated with these short pulses were torn by the pressure wave generated by steam formation. Hulsbergen-Henning et al. (1984) also observed that these vessels healed rapidly following treatment and concluded that this mechanical injury caused insufficient damage to ectatic vessels to reduce the severity of the port-wine stain.

Longer pulse lengths allow more heat conduction to endothelial cells causing thermal rather than mechanical damage (Garden et al. 1986). There is no rupture of endothelial cells and hence no extravasation of erythrocytes. Vessels treated with longer pulses are thermally necrosed and within a few days of treatment are replaced by normal dermal tissue and normal blood vessels resulting in the reduction of the severity of the vascular lesion (Tan et al. 1986).

The clinical response of vascular lesions to pulsed dye laser treatment is usually described as purpura appearing seconds to one minute after exposure. The traditional medical definition of purpura is extravasation of erythrocytes (Miller and Keane 1987) and appears as a blue/grey colour within the skin. It is clear that only short pulse lengths produce classic purpura. Another mechanism must produce the clinical response to long flash-lamp pumped pulsed dye laser pulses. Garden et al. (1986) and Tan et al. (1986) claimed that the discolouration (still called purpura) was caused by necrosed erythrocytes forming an intravascular coagulum.

However some workers persisted with short pulse pulsed dye lasers (Bandoh et al. 1990), and as a result a large fraction (approximately 19%) of their patients show no improvement, compared to near 100% success rates of other workers who use longer pulse lengths (Tan et al. 1989b, Tan 1992). It is possible that this loose use of medical terminology has delayed the understanding that suitable necrosis of the vessel wall, rather than mechanical rupture, is required for optimal improvement.
CHAPTER 3. TREATMENT OF VASCULAR LESIONS

3.2.2 Copper Vapour Lasers

Copper vapour lasers emit light at two wavelengths: 511 nm and 578 nm. For the treatment of vascular lesions only the 578 nm wavelength is used, the other being removed by a filter. The copper vapour laser used during research for this thesis produces light in short pulses that last 50 ns, with an interval between pulses of 67 μs, giving a repetition rate of 14.9 kHz. This effectively makes the copper vapour laser a continuous wave device (since the inter-pulse duration is short in comparison to the total illumination time and to the time over which a blood vessel will lose a significant quantity of heat (Pickering 1990b)). Thus it is possible to produce illumination times within the range of 1 ms to 10 ms predicted by thermal models (van Gemert et al. 1986, Pickering et al. 1989).

The clinical response of vascular lesions to copper vapour illumination is whitening of the skin, or blanching. Transient blanching, defined as the illumination necessary to just whiten the lesion but followed by erythema within seconds, is used by the workers at St. George’s Hospital as the clinical endpoint of copper vapour laser treatment. Arndt (1984) attributed the whitening of the skin to protein coagulation in the endothelial cells through a process similar to the whitening of egg white when cooked. Gourgouliatos et al. (1992) stated that this process is too fast to be a coagulation according to the classic medical definition which requires several seconds to minutes. The blanching of port-wine stains was reported to occur in a period of the order of tens of milliseconds (Marini et al. 1992). Marini et al. (1992) proposed that the blanching occurs because the damaged endothelial cells of the capillary wall absorb blood plasma constituents and expand towards the centre of the capillary, removing the blood from the treated area.

It is difficult to determine the actual processes that occur in the skin during copper vapour illumination. Several workers have performed skin flap experiments on animals (Flock et al. 1992, Gourgouliatos et al. 1992). These involved inserting glass windows into the skins of small animals to replace the epidermis. Lasers were then used to illuminate large vessels beneath the window. Neither set of workers observed vascular coagulation. Both however observed vascular constriction and
CHAPTER 3. TREATMENT OF VASCULAR LESIONS

an embolised coagulum (again different from the classical definition) of erythrocytes flowing rapidly away from the treated area. These observations would tend to support the vasoconstriction model of Marini et al. (1992).

Unfortunately certain difficulties exist in the application of results obtained from animal models and histology. Considering animal models, the blood vessels treated are not the same as human ectatic capillaries. They are normal blood vessels, often arterioles which may have surrounding muscular sheaths. It is not obvious that these animal vessels will behave the same way under copper vapour laser illumination as human ectatic capillaries. Histology presents a different problem. Samples take several minutes to prepare, far longer than the blanching processes take to occur, and thus cannot be used to investigate such short time scale processes. In addition, in vitro experiments involving excised port-wine stained skin cannot be relied upon to provide meaningful results since the main component of a port-wine stain, blood, is not flowing normally. Thus evidence obtained from these sources must be confirmed by observations conducted during the clinical treatment of vascular lesions.

The major portion of my research was devoted to developing, conducting, and interpreting two such experimental procedures: real-time photography of the treatment process, and measurement of the light remitted from port-wine stains during the treatment process.
Chapter 4

Camera Flash-Lamp System

4.1 Preliminary Investigations

The exact rate at which port-wine stained skin responds to copper vapour laser treatment has never been reported. However, several investigations into the rate of blanching have been undertaken by this Department, which have given bounds on the rate. Marini et al. (1992) observed that blanching appeared to occur immediately, certainly no longer than a few tens of milliseconds after illumination. Initial testing of a system designed to measure the light remitted from the skin during treatment using a fast photodiode (see Chapter 5) also confirmed that the skin blanched on this time scale, but was unable to determine the exact blanching rate.

My preliminary investigation (Mehrtens 1993) of this rate using a video camera supported these conclusions, but I was unable to measure the rate more precisely due to the limited resoulution available. Two major problems were encountered.

First, the laser beam was too bright for the video camera and hence appeared to 'bloom' on the video tape. The 'blooming' hid any unblanched interval of skin behind the laser spot. This could not be reduced by filtering as too much colour information would be lost. Second, the resolution of the video information following frame-grabbing was insufficient. This process introduced noise to the image which blurred the image of the blanched areas of skin.
4.2 Experimental Requirements

Any successful investigation of the blanching time had to overcome these problems. In addition, consideration had to be given to the clinical treatment session. The experiment could not excessively disrupt the treatment. As previously discussed (section 3.2.2) any interference with the treatment before the measurements are taken could affect the results.

Not all patients in any given treatment session would be involved in the experiment. Thus the laser and scanner had to be usable at all times, whether or not the experiment was in progress. The equipment also had to be safe, not only for the operators, but also for the patient and those nearby who could not reasonably be expected to be familiar with the safety requirements of any apparatus used.

Finally, the equipment used had to be capable of recording information very quickly. Since the processes involved reportedly occurred in only a few milliseconds, we needed to take a photograph that would be exposed only for a few microseconds, and yet not end up with the grainy prints associated with high speed film.

An experiment was designed which satisfied all of these requirements.

4.3 Photography

4.3.1 Laser and Scanner

The laser used is a modified Quentron™ QM91C copper vapour laser. This is a quasi-continuous wave device with a repetition rate of 14.9 kHz, each pulse of light being 50 ns long. The laser produces an average of 5 W of yellow (578 nm) light, but the average power of each pulse is 7000 W which makes it considerably brighter than the ambient light level.

The laser light is directed onto the lesion with the computer controlled scanner described by Smithies et al. (1991). This system allows the laser spot to be stepped at a very uniform and controlled rate across the lesion or kept stationary for a predetermined period of time. Under normal conditions the 0.3 mm spot is
scanned in a raster-scan pattern over the vascular lesion. Normal illumination times vary between 3.5 ms (fluence 9.72 J/cm²) and 4.5 ms (fluence 12.5 J/cm²) depending on the response of the lesion to treatment.

4.3.2 Camera and Film

The camera used to photograph the treatment was a Pentax® Pino 35J. This camera has a 'behind-the-lens' leaf-type shutter which exposes the entire negative for 8 ms. This shutter arrangement is necessary to avoid different parts of the negative being exposed at different times, as happens with a single lens reflex camera. Such a process would complicate any temporal resolution in the photograph.

I made several modifications to the camera to make it compatible with the design requirements. The camera's built-in flash was disabled. Camera flash units produce light in a pulse that is at least 2 ms long. Exposing the negative for this length of time would also reduce the temporal resolution of the photograph since changes in the skin were predicted to occur on this time scale.

A set of magnifying lenses was attached to the camera to enable close-up photography. The overall focal length of the lens system was 12.5 cm. A mounting frame was designed and built to mount the camera at the focal length with the laser beam moving parallel to the face of the camera to avoid parallax errors (see figure 4.1).

A miniature infra-red opto-switch was placed inside the camera so that it detected shutter movement. The opening of the shutter was used as a signal to commence the experiment and all the timing in the experiment is referenced to this point.

Kodak™ Ektar™ 25ASA ultra high definition 35 mm colour film was used since it is slow to expose and thus will not be exposed by background light. The fine grain of this film means that good quality prints can be obtained even after extreme enlargement. A Kodak™ colour strip was included in the photographs to provide scale and to allow colour matching during processing.
4.3.3 The Xenon Flash-Lamp

A high powered Xenon flash-lamp was used as a light source. The system consists of a Micropulse power supply (model 457A), a xenon flash-lamp (both manufactured by Xenon Corp. U.S.A.), and a reflector. This Micropulser and flash-lamp produced pulses of 20 μs duration. In combination with the 'slow' film this meant that photographs could be taken in 20 μs. Hence rapid changes in the colour of the skin during laser treatment could be recorded.

The unit has a capacitive discharge circuit (figure 4.2). The charging resistor, r, limits the current of the charge circuit. The storage capacitor, C (7.5 μF), has a maximum charge potential of 10 kV, and hence the maximum electrical input energy is 375 J.

The xenon-filled flash-lamp used had the following specifications (Table 4.1).

The expected lifetime of a flash-lamp cannot be exactly determined due to the lack of standardised operating conditions. However, for any given application an
approximate lifetime can be calculated and is a function of bore size, arc length, input energy, and pulse duration. The maximum input energy a flash-lamp can sustain is referred to as the explosion energy, the energy at which the tube is likely to fracture. Empirical studies have suggested that the explosion energy for a given flash-lamp is given by

\[ U_{\text{ex}} = kd\sqrt{t}\]

where

- \( U_{\text{ex}} \) = explosion energy in joules
- \( k = 90 \)
- \( d = \) bore size in mm
The expected useful lifetime of the flashlamp is then (to within an order of magnitude)

$$\text{lifetime} = \left( \frac{U_{in}}{U_{ex}} \right)^{-8.5}$$

where $U_{in}$ is the input electrical energy.

The explosion energy of the flash-lamp used for exposing the photographs was 360 J. To achieve a good exposure within the constraints of the experimental apparatus, 135 J input energy was required. Thus the lifetime of the flash-lamp was approximately 4000 shots and the tube was very unlikely to fail explosively during the clinical experiment. At approximately 50% of the explosion energy, failure is more likely to be due to cathode splutter obscuring part of the quartz wall, contamination of the fill gas, or failure of electrode seals. Since the flash-lamp was mounted only 30 cm away from the patient and even closer to some theatre staff, the tube was encased in a PVC pipe so that all electrically live regions of the tube were covered and only the light emitting section of the tube was visible. As a precaution against hearing damage due to the loud 'crack' made when the flash-lamp was fired, the patient, and anyone else close to the tube, had ear protection to deaden the sound.

4.3.4 Timing Circuit

The output of the infra-red opto-switch is used to trigger a circuit which controls the timing of the equipment (see figure 4.3). This circuit was designed to my specifications by the Physics and Astronomy Department's Electronics Workshop. Once the opto-switch detects movement of the shutter mechanism, the circuit interrupts the output of the laser's thyatron firing circuit by means of a TTL signal to open an electronic relay, which has been substituted for a physical connection on the thyatron firing circuit. This stops light output from the laser before the camera aperture opens. A fibre-optic cable is used for this connection to eliminate the transmission of electrical noise from the laser via a wire acting as an antenna.
is necessary to turn off the laser output to prevent the bright light from the laser obscuring detail on the skin.

Once the shutter has had time to fully open (approximately 4 ms), the electronic relay is closed briefly to enable the laser to emit one pulse of light. This pulse is used to mark the position of the laser spot on the lesion. Given this information and the known speed of the spot across the skin, the interval between the spot and a previous point on its path can be determined.

Simultaneously with the laser pulse the Xenon flash-lamp is triggered to emit white light to expose the film. Once the camera shutter is closed the laser is enabled and the treatment continues. A photograph of the arrangement of the equipment is included as figure 4.4.

4.3.5 Laser Output

Although electronically this timing is possible, it became apparent that in practice the laser could not be relied upon to give the desired output. During early trials the system seemed to perform reliably. However, when the system was used
to obtain photographs of patients undergoing treatment, some photographs had no laser pulse visible. It is possible that the cause of the problem was the decay, over the time of the experiment, of the gas temperatures in the laser tube.

The copper vapour laser operates by using direct current pulses of 11 kV, 1000 A to excite electrons from copper atoms. Neon gas and copper vapour form the media through which the discharge is passed. The excitation produces a population inversion in the energy levels of the copper electrons and laser emission results.

The discharge current is switched by a thyratron at a frequency of 14.9 kHz, in 50 ns pulses. Thus the current is on for 50 ns then off for 67 μs. The laser could conceivably be operated at 1 kHz, resulting in 1 ms between current pulses. During the time that the current is switched off the relative temperatures of the electrons, ions, and neutrals change.

By switching the current off for a period of the order of 4 ms we allowed the gas conditions to change beyond the point where they could be relied upon to produce immediately stable output if the current was switched back on. Thus the single
current pulse could generate either no light, or more light than expected, depending on the state of the gas temperatures. Thus certain photographs had no visible laser pulse, whilst others had the output of more than one pulse. Figures 4.5 and 4.6 show two photodiode (see Chapter 5) records of the output of the laser under the controls of the photographic system. In both cases the timing of the pulse is the same but it is of variable intensity and length. Notice also the 30 ms after the laser is finally switched on. The light output ramps up to 50% higher than normal, then settles down. Thus even when the current is turned on and left on, the light output is still unstable for a considerable time.

Fortunately the brightness of the laser pulse was not vital to the experiment, provided it did not obscure any detail. Nor was the length of the pulse excessively important since timing could be taken from the point of first impact of the laser spot if it was not so bright that it ‘bloomed’. Only its timing was important. As this was consistent throughout all the photodiode records, any photographs with suitable laser pulses could be used to obtain measurements.

The experiments described here result in a gap of a few millimetres in a treated line left unblanched on a patient. This untreated patch is clinically insignificant.

4.3.6 Blanching Time Calculation

The calculation of the time taken for a particular lesion to blanch after laser illumination is straightforward. Based on the assumption that blanching takes longer than 4 ms to occur, the camera shutter was opened 4 ms after the laser was switched off. 8 ms later the laser illuminated the lesion at the point where the laser spot would have been had the laser not been turned off (since the stepper motors had continued moving). The time, $t$, that the lesion takes to blanch (i.e. the time taken for the laser spot to move from the point at the end of the visible blanching to the point where the photograph was taken) is given by

$$ t = \frac{d}{v} - 8 \text{ ms} $$
CHAPTER 4. CAMERA FLASH-LAMP SYSTEM

Figure 4.5: Photodiode recording of the output of the camera/flash-lamp system. Here the marking laser pulse is very intense and the photograph may be unsuitable for analysis.

Figure 4.6: Photodiode recording of the output of the camera/flash-lamp system. Here the marking laser pulse is less intense and thus the photograph should be suitable for analysis. Note the consistency of the timing of the laser output.
where

- $d$ is the distance between the end of the visible blanching after 4 ms and the point marked on the lesion after 12 ms,
- $v$ is the velocity of the laser spot (Smithies et al. 1991).

However the distance $d$ has been scaled by the photography. Thus

\[ d = ad' \]

where

- $a$ is the magnification of the photograph,
- $d'$ is the distance between the end of the visible blanching on the photograph and the point marked on the lesion by the laser.

Thus, from the photograph, the time that the lesion takes to blanch is

\[ t = \frac{ad'}{v} - 8 \text{ ms} \]

The distance $d'$ was measured from the photographs, and the magnification calculated from the known size of the colour chart. Magnification of the photographs was often necessary. This was achieved either by photographic enlargement, or the use of a magnifying lens.

### 4.4 Results

Photographs taken with the camera/flash-lamp system reveal that blanching is visible as white lines following the path taken by the laser beam. The width of these lines is approximately the same as the diameter of the laser spot. Figure 4.7 shows blanching on a red port-wine stain. The blanching is uneven due to the patient moving slightly earlier in the treatment. The unevenness does not persist once the erythema set in, seconds after treatment. We note that the patient was only lightly anaesthetised, and was motionless while the photograph was taken.
Figure 4.7: Copper vapour laser induced blanching on a red port-wine stain (fluence 12.5 J/cm²). Some early blanching is uneven due to the patient moving. This unevenness disappears in the minutes following treatment.

Photographs of salmon pink (figure 4.8), and purple (figure 4.9) port-wine stains were also taken.

Not all photographs taken were able to be analysed. Out of the 55 photographs taken with the system, 16 were unusable due to poor positioning of the camera or flash-lamp. Of the remaining 39, only 11 were suitable for analysis. The remainder either had no blanching visible or no laser spot visible as a reference point (see section 4.3.5). Analysis of the photographs yielded the data contained in table 4.2.

Analysis of the photographic data reveals that light port-wine stains blanch faster than darker stains. The three photographs of salmon pink lesions showed blanching over a range of 7 ms to 10 ms, with a mean of 8.3 ms (standard deviation 1.5 ms). Four photographs showed red lesions took between 15 ms and 23 ms to blanch (mean 19.5 ms, standard deviation 4.0 ms), and four photographs showed that purple lesions take longest to blanch, taking between 31 ms and 33 ms (mean 31.5 ms,
CHAPTER 4. CAMERA FLASH-LAMP SYSTEM

Figure 4.8: Copper vapour laser induced blanching on a salmon pink port-wine stain (fluence 12.5 J/cm²). Note the evenness of the result.

Figure 4.9: Copper vapour laser induced blanching on a purple port-wine stain (fluence 11.5 J/cm²).
CHAPTER 4. CAMERA FLASH-LAMP SYSTEM

Table 4.2: Results of the photographic experiment

<table>
<thead>
<tr>
<th>Lesion Number</th>
<th>Photograph Number</th>
<th>Colour</th>
<th>Fluence, J/cm²</th>
<th>Time, ms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>pink</td>
<td>12.5</td>
<td>7</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>pink</td>
<td>12.0</td>
<td>8</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>pink</td>
<td>12.5</td>
<td>10</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>red</td>
<td>10.8</td>
<td>15</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>red</td>
<td>10.8</td>
<td>17</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>red</td>
<td>10.8</td>
<td>23</td>
</tr>
<tr>
<td>7</td>
<td>1</td>
<td>red</td>
<td>10.5</td>
<td>23</td>
</tr>
<tr>
<td>8</td>
<td>1</td>
<td>purple</td>
<td>10.2</td>
<td>30</td>
</tr>
<tr>
<td>9</td>
<td>1</td>
<td>purple</td>
<td>10.2</td>
<td>31</td>
</tr>
<tr>
<td>9</td>
<td>2</td>
<td>purple</td>
<td>10.2</td>
<td>32</td>
</tr>
<tr>
<td>9</td>
<td>3</td>
<td>purple</td>
<td>10.2</td>
<td>33</td>
</tr>
</tbody>
</table>

standard deviation 1.3 ms). However, it is often necessary to use a slightly higher fluence to treat pink lesions. It is not possible to tell from this investigation whether or not the trend is a result of the higher fluence. We return to this issue in Chapter 5.

4.5 Injection Sclerotherapy

Telangiectasia which had just received injection sclerotherapy also received laser treatment. Sclerotherapy involves injecting an irritant into an ectatic vessel causing the endothelial cells to swell, blocking the vessel’s lumen. As a result, red blood cells become trapped inside those capillaries whose associated arterioles and venules have been sclerosed. Following laser treatment these capillaries turn dark red or purple since the heated red blood cells form a stationary coagulum, a result similar to the purpura-like effect obtained using short illumination time pulsed dye lasers (see figure 4.10).
Figure 4.10: Photograph showing the purpura-like response of sclerosed capillaries after copper vapour laser treatment.
Chapter 5

Photodiode Measurement of Remitted Light

It had been noted previously that, while using the computer controlled scanner described in Smithies et al. (1991), light remitted from port-wine stains undergoing laser treatment was observable on the ceiling of the operating theatre. It was also observed that the intensity of this light varies and considerable flickering is present. This light is a combination of the light reflected from the surface of the skin and the light scattered from within the skin. An increase in the amount of light re-emitted from the skin indicates that less light is being absorbed in the skin and hence that blanching has occurred.

In 1992 Mr Derek Smities, a fellow student, constructed a light recording system in an attempt to measure the time that lesions take to blanch. The aim was to determine the feasibility of a feedback system for the computer controlled scanner which would automatically adjust the speed of the laser spot.

This system is based around a fast photodiode (MRD500, 5 ns rise time) mounted vertically above the treatment area, and a recording computer (Amiga 2000). The recording computer recorded the amount of light remitted from the port-wine stain, and also the times at which move pulses are sent from the computer which controls the scanner to the scanner’s stepper motors. This information is then converted into Postscript for viewing and analysis. The response of the system was tested and
found to be linear. A 1% variation in output was noted due to analogue to digital conversion noise.

Unfortunately, the original photodiode system was unable to determine the precise time taken for lesions to blanch (see section 5.2.1). However by modifying the system slightly it was possible to use it to verify the results obtained using the camera/flash-lamp system, and also to investigate the possibility that the quicker blanching of light port-wine stains (as noted in the section 4.4) is caused by higher fluences being used in their treatment. I spent some time working on the testing and analysis phases of this experiment.

5.1 Testing

The laser beam was scanned over a series of black and white lines. The pattern left on the paper is shown in figure 5.1.

A portion of the photodiode recording of this event is shown in figure 5.2. It can be seen that light remittance data can be correlated to movement of the laser beam. The peaks correspond to white paper and the troughs to black ink lines. The considerable variation in the troughs is due to ink being burnt off, leaving a lighter spot on the paper (figure 5.1) The large number of vertical lines in a row at the bottom of the graph are the times that a horizontal move pulse is sent to the stepper motors. The two sets of two short vertical lines above this row give the times that a vertical move pulse is sent to the stepper motors. These marks allow correlation

Figure 5.1: Laser scanned black and white lines. The laser burns off ink leaving a lighter spot on the paper.
Photodiode data: large and extra large black lines. 3.4ms 10.5W

1012ms elapsed

Figure 5.2: Remittance data when laser scanned over black and white lines. The narrow trough just before half way through the data is caused by absorption by the thin line on figure 5.1. The laser was moving from left to right across the lines when this data was gathered.
between laser beam movement and changes in light remittance.

Over longer samples there is an oscillation observable in the data. This was expected and is due to the laser beam moving away from a vertical orientation. This causes less light to be reflected vertically into the photodiode.

Figure 5.3: Remittance data when laser scanned over a patient's nose. The 5 high peaks correspond to light being incident on the bridge of the nose, and the 5 lesser peaks to light being incident on the cheeks.

Similar results were obtained when the light is scanned horizontally across the bridge of a patient's nose (figure 5.3). The 5 maxima mid-way between vertical move pulses correspond to the laser beam being incident on the bridge of the patient's nose. The 5 lesser peaks correspond to the laser beam being incident on the cheeks of the patient. Here the near horizontal skin causes an increase in reflected light levels following the steeply angled sides of the nose. There is some variation in the output, due in part to the 1% noise to which reference has already been made. The main cause, however, is the non-uniform nature of the skin. Some regions contain higher or lower volumes of blood than the average for a particular patient and thus absorption (and hence reflection) can be expected to vary. Skin texture will also
CHAPTER 5. PHOTODIODE MEASUREMENT OF REMITTED LIGHT

Figure 5.4: Remittance data when laser scanned over a light pink port-wine stain. No periodic fluctuation in the level of remitted light can be related to the beam movement as shown at the bottom of the graph.

cause non-uniformity in the angle of incidence of the beam on the skin. This will also cause a fluctuation in the results. The photodiode system is thus shown to work in a clinical environment and provides results consistent with expectation.

5.2 Results

5.2.1 Normal Scanning

Figure 5.4 shows the results for scanning a light pink port-wine stain. The illumination time is 4.5 ms. Close examination of the data does not show any periodic fluctuation of the level of remitted light that could be related to the movement of the laser spot. It appears from this data that either light pink port-wine stains do not blanch in less than 4.5 ms, or that blanching does occur but is hidden by noise in the recorded data. Similar negative results were obtained for darker port-wine stains.
5.2.2 Spot Treatment

If the photodiode system is to record the port-wine stain blanching, a different scanning technique is needed. The software was altered so that the laser spot is held stationary for 50 ms and then moved quickly to a point 5 mm away. This process is repeated so that the port-wine stain is treated in a lattice pattern. This results in a series of blanched spots on the skin. The port-wine stain is then rescanned using the normal treatment method to provide an even, clinically acceptable result.

The data was analysed by approximating both the change in remitted light level when the laser beam was moving between spots (the level changes since the angle of incidence of the laser beam changes), and the increase due to blanching, as linear and placing lines of best fit on the data. Where these two lines intersected was taken to be the point at which blanching began. One millisecond was subtracted from the interval between the last move pulse and the intersection to correct for the delay between the move pulse and the laser beam coming to rest. In figure 5.5, data for one spot on a dark red port-wine stain is shown. The point 1 ms after the final move pulse is labelled 0 ms and the point where blanching begins is also shown. The delay between the two points is 12 ms.

Three patients were treated with this procedure. They were selected because their lesions were even in colour, and large enough to allow at least fifteen spots to be recorded (i.e. at least 2.25 cm²). One lesion was treated on each patient. Patient 1 had an extensive pink port-wine stain on the face which allowed data from 147 spots to be recorded. Patient 2 had a 5 cm² dark red port-wine stain on the face, data from 19 spots was recorded from this patient. Patient 3 had a similar sized dark purple port-wine stain on the face which allowed data from 18 spots to be recorded. A summary of the results obtained is shown in table 5.1. The data from these patients is shown in figures 5.6, 5.7, and 5.8.
Figure 5.5: Remittance data from one laser spot on a dark red port-wine stain. The time before blanching occurs is 12 ms.
Table 5.1: Results of the photodiode experiment

<table>
<thead>
<tr>
<th>Time (ms)</th>
<th>Patient 1, pink frequency</th>
<th>Patient 2, dark red frequency</th>
<th>Patient 3, purple frequency</th>
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</thead>
<tbody>
<tr>
<td>0</td>
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<td></td>
<td></td>
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CHAPTER 5. PHOTODIODE MEASUREMENT OF REMITTED LIGHT

Figure 5.6: Remittance data when laser spot-scanned over a very light pink port-wine stain. The average time before blanching occurs is 4.0 ms.

Figure 5.7: Remittance data when laser spot-scanned over a dark red port-wine stain. The average time before blanching occurs is 11.5 ms.
It should be noted that the blanching times generated by this spot scanning technique are predictably shorter than those times obtained from the photographs. By continuing to supply energy for two to three times longer than normal we would expect the skin to change significantly faster than normal. However, even with this overexposure, darker port-wine stains took longer to blanch than the normal scanning illumination time range of 3.5 ms to 4.5 ms. This would suggest that an automated scanning system is impractical. The trend for dark port-wine stains to take longer to blanch is still in evidence.
Chapter 6

Discussion of Results and Observations

Examining the results presented in the previous two chapters we can see that, when using transient blanching as a clinical endpoint, blanching at a point on a vascular lesion does not occur whilst the laser spot is still incident on that point. In fact, using normal scanning techniques with illumination times between 3.5 ms and 4.5 ms the skin takes between 7 ms and 33 ms to blanch, depending on the colour of the lesion. This indicates that the scanning system cannot be automated further by the introduction of a feedback mechanism that samples the remitted light levels and moves the laser spot when there is a suitable change in lesion colour. The only means of assessing the suitable transient blanching response is still observation by a trained operator of the equipment.

The observation of the laser treatment of sclerosed vessels provides evidence for the vasoconstriction damage model of Marini et al. (1992). If we force erythrocytes to absorb all the energy incident on a capillary, by preventing them from leaving the capillary, they form a dark coagulum. The absence of this coagulum during normal treatment suggests that blood is indeed forced out of the vessel in response to laser illumination. Normal blood flow rates of 1 mm per second (section 2.2) can not account for this movement.

It would also seem that the conclusions based on the animal models of Gour-
gouliatos et al. (1992) and the observations of Marini et al. (1992) are valid. Their results are consistent with our observations. Hence it is likely that heat conduction from erythrocytes to capillary endothelial cells leads to vasoconstriction.

The dependence of the blanching rate on lesion colour is indicative of the difference in structure between light and dark vascular lesions. The endothelial cells of smaller diameter ectatic vessels, characteristic of light stains, have to swell less to occlude the vascular lumen. Thus we would expect lighter vascular lesions to blanch faster than dark lesions.

It must be noted, however, that the blanching is transient. Most disappears when erythema sets in and blood flow is redirected to other untreated (since they were empty) capillaries. Some blanching persists for longer however. This behaviour is characteristic of melanin whitening (Tan et al. 1991). Even though melanin absorption is low at 578 nm wavelength, some light is still absorbed. This reduces the amount of light available for absorption by HbO₂ and also increases the risk of abnormal pigmentation and scarring after healing has taken place. Thus it can help if the melanin content of the epidermis is reduced prior to laser treatment. This is achieved by the application of a high SPF sunblock for at least two months before treatment. This is particularly relevant for those patients with darker tans.

Currently, an area of vascular lesion is only scanned once per treatment. The temptation to rescan the lesion after erythema has set in is great, as one might expect to be able to treat vessels missed during the first scan. However there is a risk of overheating the epidermis if the lesion is scanned too quickly after the initial treatment, which would result in excessive damage to melanin. Therefore a combination of a delay of the order of several seconds and external cooling of the lesion should allow rescanning. It is important that the cooling method does not put pressure on the lesion as this would force blood away from the lesion, thus reducing the effectiveness of the rescanning.

It has also been observed that light vascular lesions require slightly more energy to be transiently blanched than dark port-wine stains. This is also linked to the size of the vessels. A small vessel contains less blood than a large vessel and therefore will absorb less energy if both are illuminated with the same fluence. As a
result the blood in the smaller vessel may not reach a sufficiently high temperature to cause enough heat to be conducted to the endothelial cells. Thus we would expect to have to supply more energy to constrict the smaller vessel. However, since only the top of a vessel is required to be damaged (since the endothelial cells are rolled over to form a tube), the lower absorption is offset somewhat by the need for a smaller area of the vessel wall to be thermally damaged (Anderson and Parrish 1981, van Gemert et al. 1982, van Gemert et al. 1986, Pickering et al. 1989).
Chapter 7

Tattoo Removal

7.1 The Search for a Cure

Many people who have tattoos wish to have them removed, preferably without leaving behind an unsightly scar as a reminder. Their reasons vary. Some individuals have hypersensitive reactions to the dyes and therefore have medical reasons for removal (Lehmann and Pierchalla 1988). Others desire to change the nature of their employment and find the tattoo a hindrance. Still others wish to distance themselves from a previous imprisonment, or merely regret getting a tattoo in the first place. Whatever the reason for wishing the removal of a tattoo, it has never been easy to accomplish. The major problem is removing the tattoo without damaging adjacent tissue in the process. As has already been noted, damage to tissue including and below the basal layer of the epidermis has a tendency to cause scarring. Unfortunately surgical techniques, such as excision (Lindsay 1989), dermabrasion (Clabaugh 1975), and laser ablation (Brady et al. 1979, Reid and Muller 1980, Apfelberg et al. 1985), invariably involve disruption of this area.

The advent of the ruby laser in the early 1960s seemed to offer hope. For the first time tattoo pigment could be removed by a non-invasive technique. The users of Q-switched ruby lasers claim that the laser removes pigment by shattering the pigment clusters by a photoacoustic mechanism, or by photochemically converting carbon pigment into CO\textsubscript{2} (Reid et al. 1990). Unfortunately the ruby laser cannot
treat red pigments since there is insufficient absorption of 694.3 nm wavelength light by pigments of this colour (Laub et al. 1968).

The cost of treatment is another complication. The need to recover the capital outlay of purchasing a NZ$300,000 ruby laser means that treatment costs are often extremely high, even before adding on the surgeon’s fees for a procedure which is forced to be long, due to the small beam diameter of the ruby laser. It must also be remembered that often people who desire to have tattoos removed will not easily be able to afford expensive medical procedures.

My supervisor became interested in the removal of tattoos when he heard of the effectiveness of the Q-switched ruby laser treatment. His interest was sparked by models of the damage processes which seemed unlikely. For example, if carbon is photochemically converted into CO$_2$, where does the O$_2$ come from? Thus he began the search for some answers, and a possible cheaper, more effective alternative to ruby lasers.

### 7.2 The Xenon Flash-lamp

The search has revolved around a high powered xenon-filled flash-lamp, the brightest non-laser light source available. The theory is based on a calculation which suggested that a short pulse (<100 μs) of white light with energy density 10 J/cm$^2$ would be absorbed by all pigment colours, killing the fibroblasts, damaging a few dermal cells surrounding the pigment clusters, and allowing the body’s natural defence mechanisms to remove the pigment. This process is once again selective thermolysis. Such a system would cost approximately one tenth of the cost of a ruby laser and thus would be a better, cheaper treatment method.

A Xenon Corp. flash-lamp was purchased, the details of which have been presented in section 4.3.3. Clinical trials were conducted with this system by Mrs Huaying Zhang as part of her M.Sc. research.

Using 20 μs pulse length and approximately 2.8 J/cm$^2$ energy density, both an amateur blue tattoo (on yellow asian skin) and a professional coloured tattoo (on pale caucasian skin) were treated. The immediate response to the exposure was the
CHAPTER 7. TATTOO REMOVAL

Skin turning grey/white. A pricking sensation was felt. Very light erythema and oedema persisted for 48 hours. A slightly greater response in areas with dark pigment was noted. The response was greater from the tattoo on caucasian skin, probably due to the lesser melanin concentration in this skin.

However, no lasting improvement was observed by either volunteer, but the results did indicate that light was selectively absorbed by tattoo pigment. They also showed the effect of melanin on the treatment.

Mrs Zhang then modified the discharge circuit to extend the pulse length to 550 μs, which gave an energy density of 8 J/cm². A coloured professional tattoo on pale caucasian skin was treated. The response of the skin was similar to the response reported for successful Q-switched ruby laser treatment of black pigment (Scheibner et al. 1990), but was observed in all pigment colours. This gave hope that that 8 J/cm² was very close to the treatment threshold. Unfortunately there was slight erythemic reaction in non-tattooed skin, indicating that the long pulse length had allowed conduction to non-pigmented areas of the dermis. We are unsure whether this conduction is significant, as little or no scarring has been reported.

Two months after treatment (at the end of Mrs Zhang’s thesis) there was little loss of pigmentation. Recently, however, the volunteer has reported that after several months, pigment in the treated area is significantly reduced, confirming that the energy density was near the damage threshold.

The requirement for a shorter pulse length led to new flash-tubes being specially constructed. This design called for a high fill pressure (3 atmospheres) and thicker walls. The output specifications were 100 μs pulses at 10 J/cm².

7.3 Discharge Circuit Design

These new flash-tubes could not be operated using the existing Micropulser. Hence a high voltage supply and an 8 kV, 115 μF capacitor has been used. It is also necessary to externally trigger the flash-tube with a circuit designed by Mrs Zhang, and brought to an operational level as part of my research. This new discharge circuit was designed to produce 80 μs pulses at 400 J input electrical energy. However the
current pulse at this input energy would be highly peaked (of the order of 7000 amps) and underdamped resulting in possible tube failure (Zhang 1993, ILC Technology 1986).

In order to achieve 400 J input energy without damaging the tube, the current pulse needs to be square. This means that a lower peak current can be maintained for a longer time thus producing the required energy without creating a shock-wave which would shatter the flash-tube.

To produce such a square current pulse two options exist. Either a multi-branch transmission line could be used to modify the pulse shape, or a design incorporating a transformer could be produced. The transmission line concept requires the purchase of a number of high voltage, high capacitance, low effective resistance capacitors. These are expensive (several thousand NZ dollars each) and as part of the aim is to keep the cost of the equipment low it was decided to design and build a transformer-based discharge circuit.

The Micropulse power supply could be used to provide a high voltage to the transformer which in turn supplies a current pulse to the flash-tube. The external trigger system would still be necessary to ionise the xenon gas to form a current path through the tube. It has been decided to utilise a simmer trigger mechanism. This places a small dc current (a few milliamps) through the flash-tube after external triggering to maintain the ionisation until the high flash current is triggered. This improves the conversion efficiency of the flash-lamp and prolongs tube lifetime (Schlesinger 1993). The proposed circuit is presented in figure 7.1.

To design the transformer we need to know the current required to provide the 400 J in 80 μs. This corresponds to an average power over the pulse of 5 megawatts. I designed an experiment to measure the current required to deliver this power over 20 μs using the Micropulser power supply. This shorter time means that a much lower input energy is required. A 1.5 cm x 1.0 cm x 30 μm piece of stainless steel foil was sandwiched between two sets of two copper blocks and used as a resistance foil to measure the current. The resistance of the foil strip is 0.004Ω. Thus even a current of ten thousands amps would only create a potential difference of forty volts across the foil. This was to be measured using a digital storage oscilloscope.
The tube was successfully flashed at the required input energy, but the DSO failed to trigger. Before the DSO trigger level could be adjusted, the discharge capacitor in the Micropulse power supply was accidentally shorted when still charged. This resulted in a very short (and therefore very high powered) current pulse which shattered the flash-tube. No time was left before the completion of this thesis to redo this experiment, or a similar one with a flash-tube of the same design. Thus the transformer circuit is still at the proposal stage.

7.4 The Future

The success reported using 8 J/cm² and 550 μs pulses is encouraging. If it is possible to produce such an energy density in an 80 μs to 100 μs pulse there is a good chance that selective thermolysis can be produced leading to effective pigment removal. The high pressure flash-tube should be able to produce this, especially with the improved efficiency provided by simmer triggering. The recent report of the success of the 550 μs pulses may even indicate that such short pulses are unnecessary. If this is the case then this system represents a viable alternative to the expensive Q-switched ruby laser.
Conclusion

This thesis investigated the results of illuminating the colour absorbers of the skin with light of high energy density. Two fields of research have been investigated: vascular lesion removal, and tattoo removal.

We support the model of the damage process that occurs as a result of copper vapour laser illumination of vascular lesions proposed by Marini et al. (1992). That is, that selective thermolysis of oxyhaemoglobin in the blood heats by conduction the endothelial cells which form the vessel walls. This heating causes thermal damage which allows blood plasma constituents to be absorbed into the cells causing centripetal expansion, and thus lumen occlusion.

We suggest that some of the blanching caused by copper vapour illumination of vascular lesions is caused by the destruction of some of the melanin containing structures in the skin. In order to minimise this effect it is important to reduce the melanin concentration in the skin as much as possible prior to treatment. This procedure is already in use.

Since rescanning a treated lesion once erythema has set in should allow the treatment of previously untreated vessels, we suggest that after suitable cooling has been applied to the lesion the lesion be rescanned. This should improve the clinical response.

The real-time photography of vascular lesions undergoing laser treatment, and the measurement with a photodiode of remitted light levels during treatment,
both show clearly that vascular blanching does not occur whilst the laser is still illuminating the blood vessel under normal transient blanching conditions. Thus we conclude that a feedback system that controls laser beam movement according to the level of blanching is not possible.

Light coloured vascular lesions have been observed to blanch faster than dark lesions. This has been attributed to the shorter time required for the endothelial cells of smaller vessels to swell and occlude the vascular lumen.

An explanation for the need for the higher fluences needed to treat light vascular lesions has been suggested. The smaller vessels contain less blood and therefore absorb insufficient energy to cause the required thermal damage if they are treated with the fluence needed to treat dark lesions. Therefore more energy must be supplied to raise the absorption by oxyhaemoglobin to the required level.

We have noted that the progress made in the development of laser systems to treat vascular lesions has been retarded by inconsistent use of medical terminology, and differences in the reporting of results. Some standardisation in both areas would assist researchers in their quest for better clinical results.

A proposed improved design for a high-powered xenon flashlamp discharge circuit should provide an increase in the energy density of the output and also limit the pulse width to between 80 $\mu$s and 100 $\mu$s. These characteristics are hoped to be sufficient to treat tattoos at least as effectively as the Q-switched ruby laser, but by a different mechanism.
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