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Digital Imaging Based Screening and Detection of Breast Cancer - The DIET Concept

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Liege
Christchurch, NZ

Outline

- The Problem → The DIET Concept

- Inverse Elastographic Reconstruction
  - Simulation based proof of concept and very 1st experiments
  - If we can measure can we do it?

- Imaging and Image Processing – Tracking 1000's of points at 50-100Hz
  - Since we can do it, can we actually measure?

- Putting It All Together
  - Silicone phantom studies and experimental proof of concept
  - Does it work (for real)?

- Conclusions and the Future

The Problem

- Breast cancer was the most common cause of female cancer death in 1999

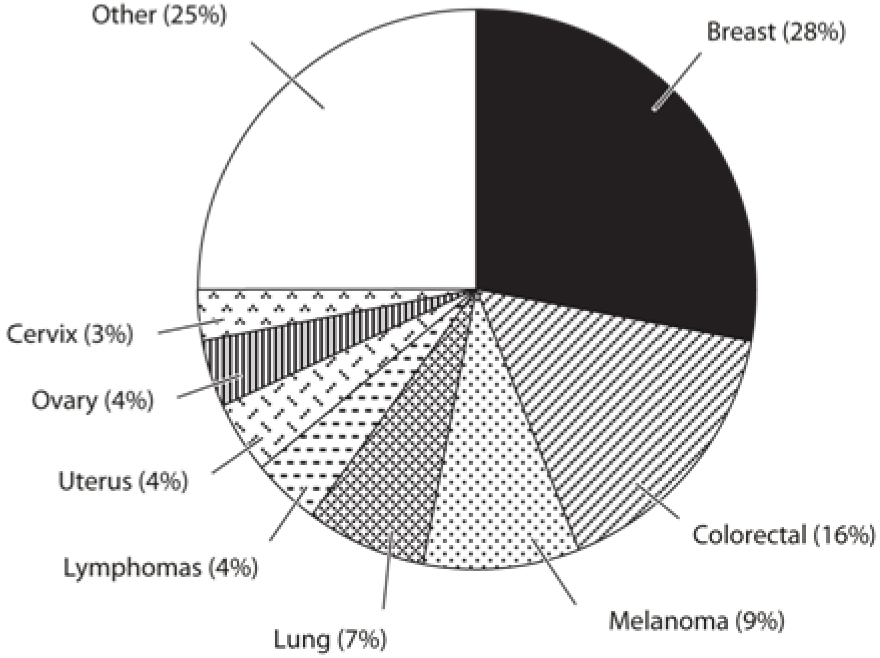
- Over the period 1972 to 1997, the annual number of breast cancer deaths increased from 427 to 643[1]

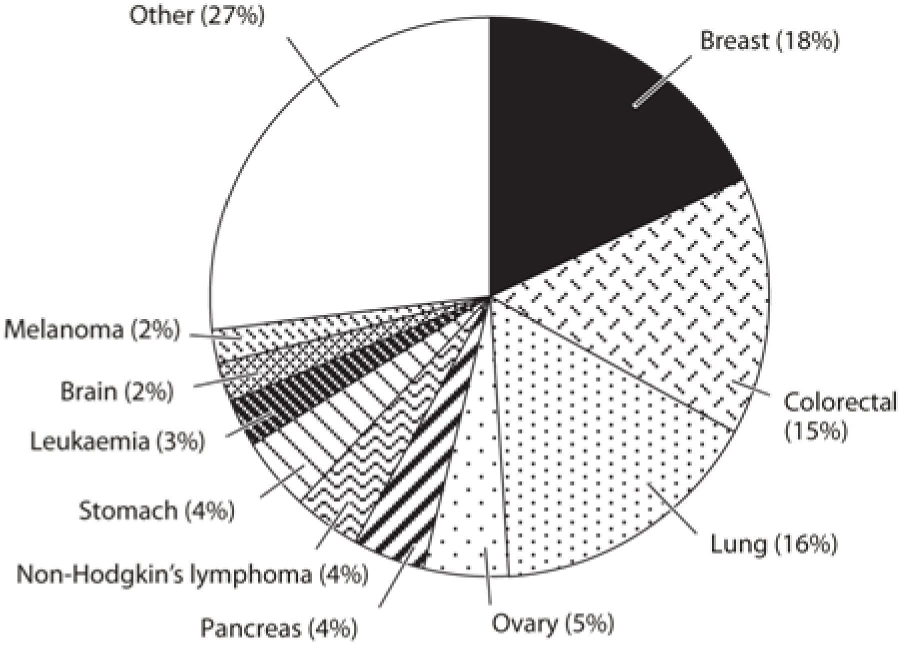
- Breast cancer is over represented among Maori (in NZ) and other ethnic groups worldwide

[1] NZ Ministry of Health, 2002

Breast Cancer as a Public Health Issue (NZHIS, 2002)

- New Zealand Health Information Service (2002)



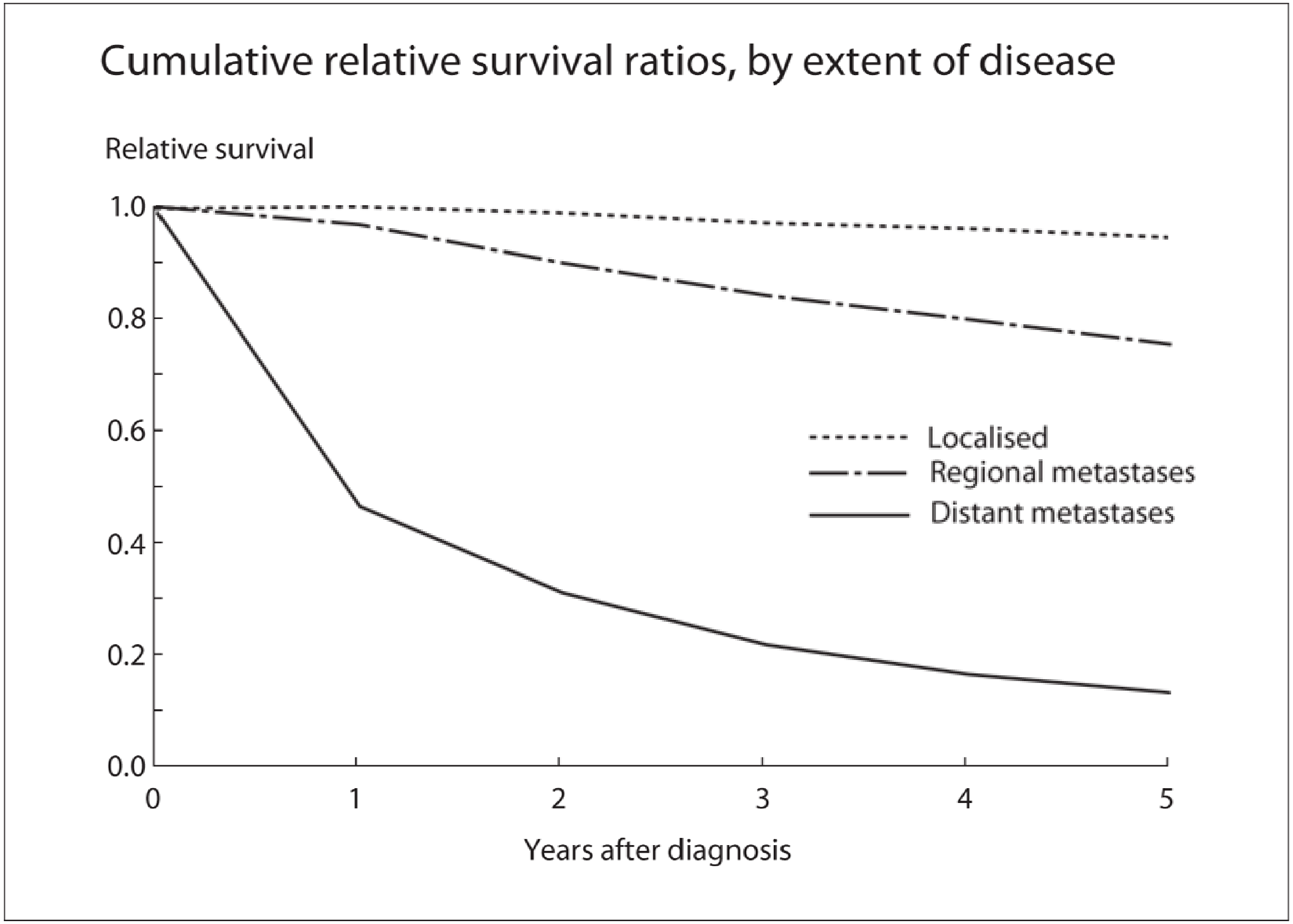


- Female cancer registration sites
  - 1999

- Causes of female cancer death
  - 1999

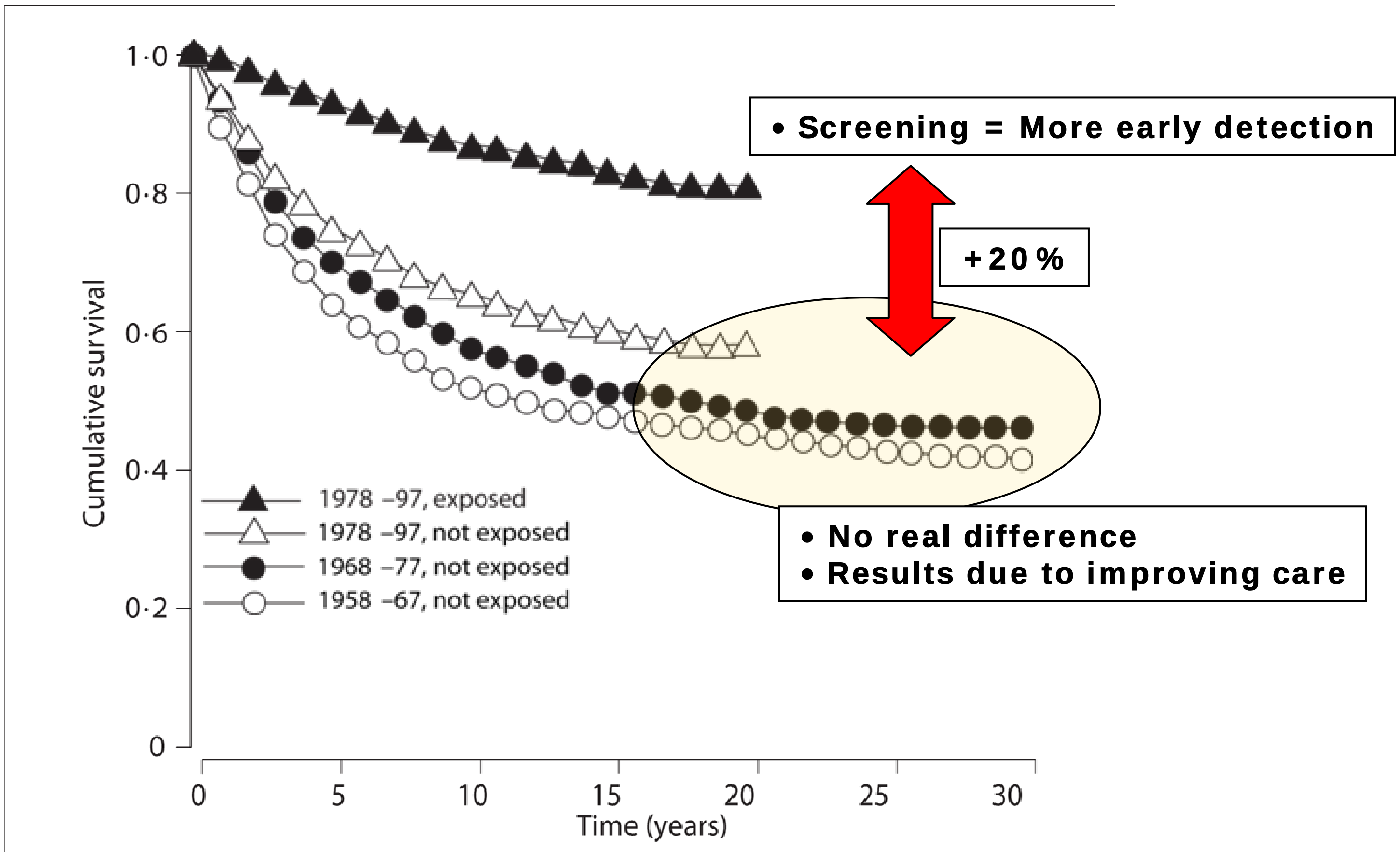
- **Not dissimilar elsewhere**

The Importance of Early Detection (NZHIS, 2006)



NZHIS (2006)

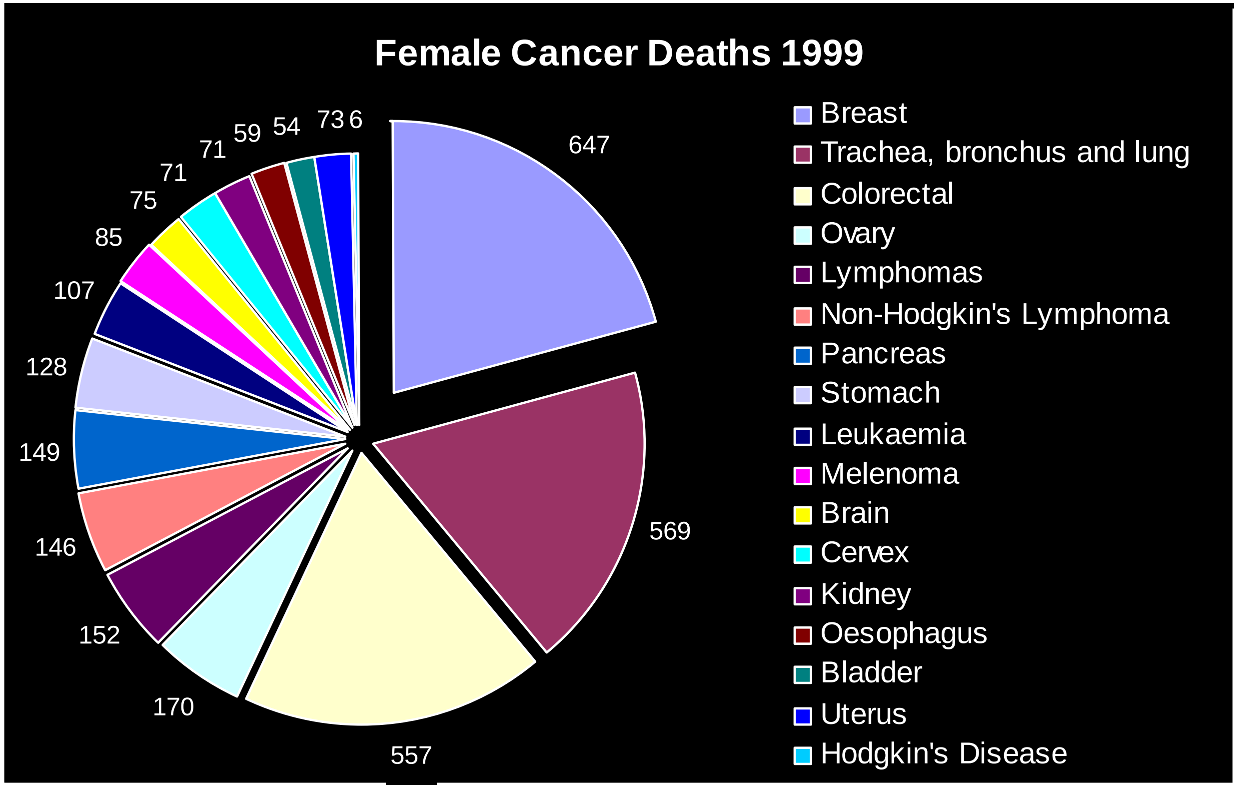
Breast Cancer Screening Reduces Mortality (Tabar et al, 2003)



Cumulative survival of breast cancer patients aged 40–69 years at diagnosis

Tabar *et al.* (2003)

647 in New Zealand and Public Policy



- **<u>In Comparison</u>:**
  - Drink driving caused 141 deaths in 2003.
  - In 1989, 329 deaths were caused by drink driving. The most in the last 24 years.
  - In the 12 months to the end of September 2004, 439 people were killed on New Zealand roads.
  - $10.5 million is spent per year on road safety campaigns.

New Zealand = Ineffective

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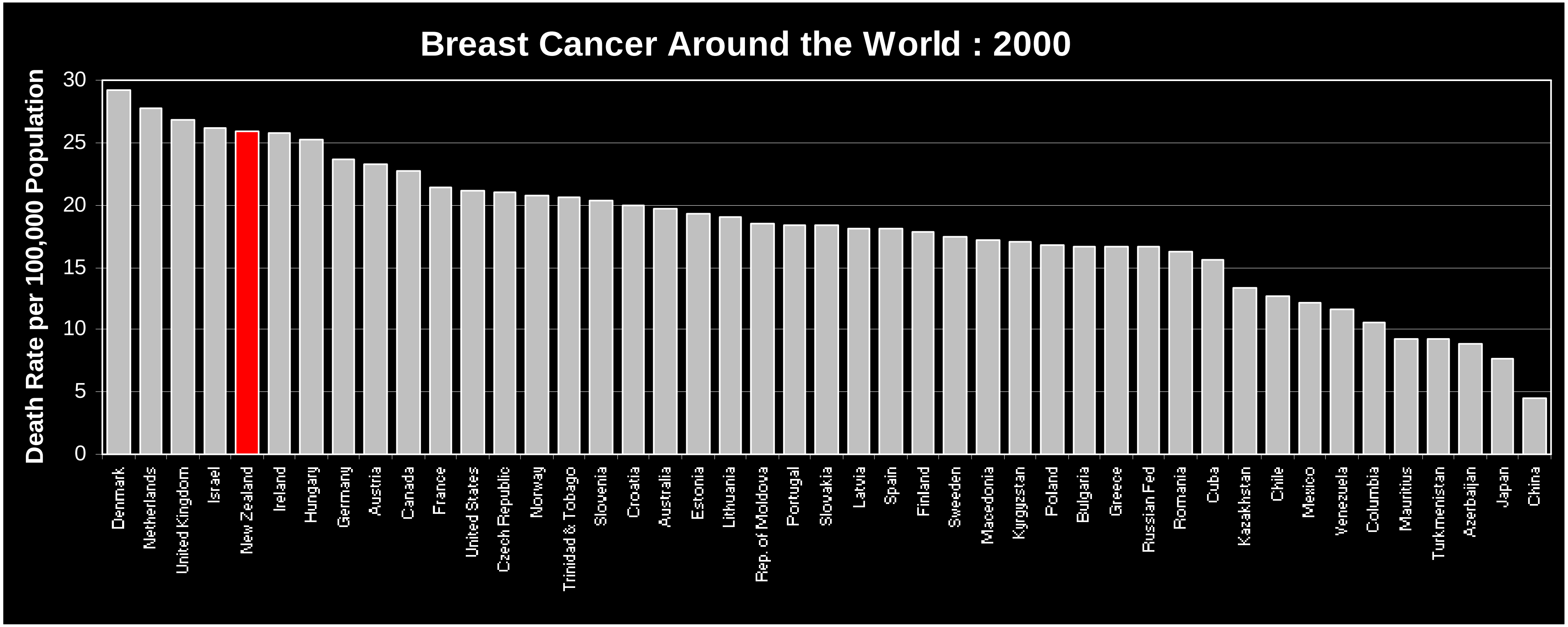

Why?
Low Compliance & Access

	2003/4	2004/5	2005/6	2008/9
Eligible Population	318,625	544,710	561,285	612,495
Screened Volume	104,526	141,812	152,152	181,058
Coverage	32.8%	26.0%	27.1%	29.6%

What you don't see can kill you!

- Predominant compliance rates in the US and EU range from 50-80% based on many factors
- Eligible populations (over 50 years) are growing demographically for next 10-20 years
- Certain sub-groups have very low screening rates and thus much higher mortality
    - Occurrence rates don't seem to particularly favor any group

Current Screening Techniques

- Mammography
- Ultrasound
- Magnetic Resonance (MR) Scanning

- Early diagnosis increases survival rate to over 95% [2]

- **Spending 100% more on screening cuts <u>total</u> costs by 33% [3]**

This only looks fun because it's a marketing photo! And, she's way too young!

[2] American Cancer Society, 2004

[3] US Insurance Industry Study, 2000

Problems with Existing Techniques

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- Currently, predominant breast cancer screening methods are:
  - Uncomfortable
  - Subject the patient to doses of radiation
  - Require expensive, location specific equipment and clinical staff.
    - They thus have relatively limited throughput (not enough capacity)

- They are also **low contrast** as cancerous tissue density varies only ~5-10% from healthy tissue

- Coupled with resulting low compliance rates the average tumour size detected is **1cm = 10x larger than possible**

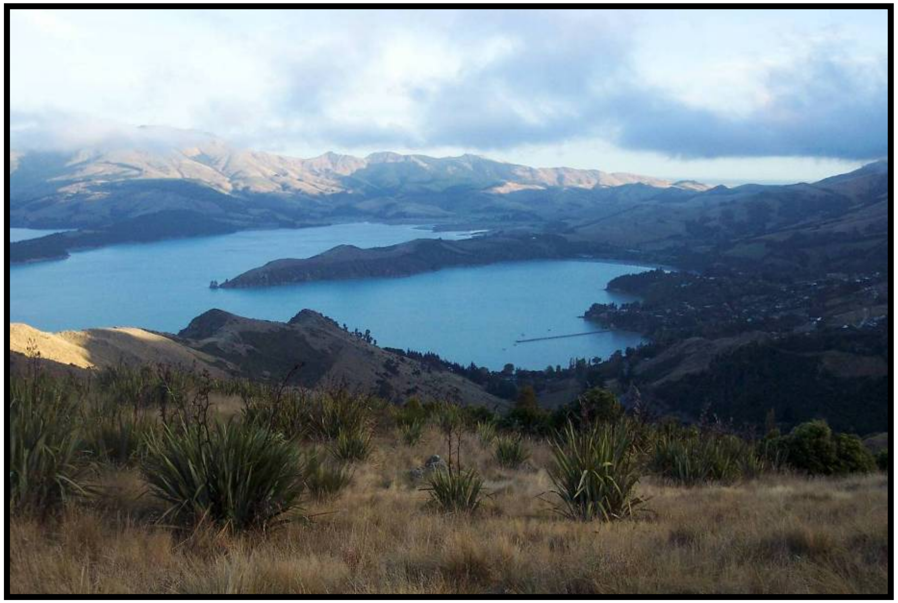
What's Needed?

- An all new approach
  - Must be clinically and commercially feasible
  - Must address compliance (w/ screening) issues
  - Must offer high throughput in terms of speed to test and access

- An ideal design list would include:
  - Low cost equipment with no need for specialist technician
  - Portable
  - No X-Ray dose
  - Equal efficacy (1cm detection) compared to mammography
  - Greater comfort (no compression)

The DIET Concept

- **DIET** = **D**igital **I**maging-based **E**lasto-**T**omography
- Can we meet all these needs?



Governors Bay, Christchurch

Sunset over Southern Alps, Christchurch

Digital Image Elasto-Tomography or DIET

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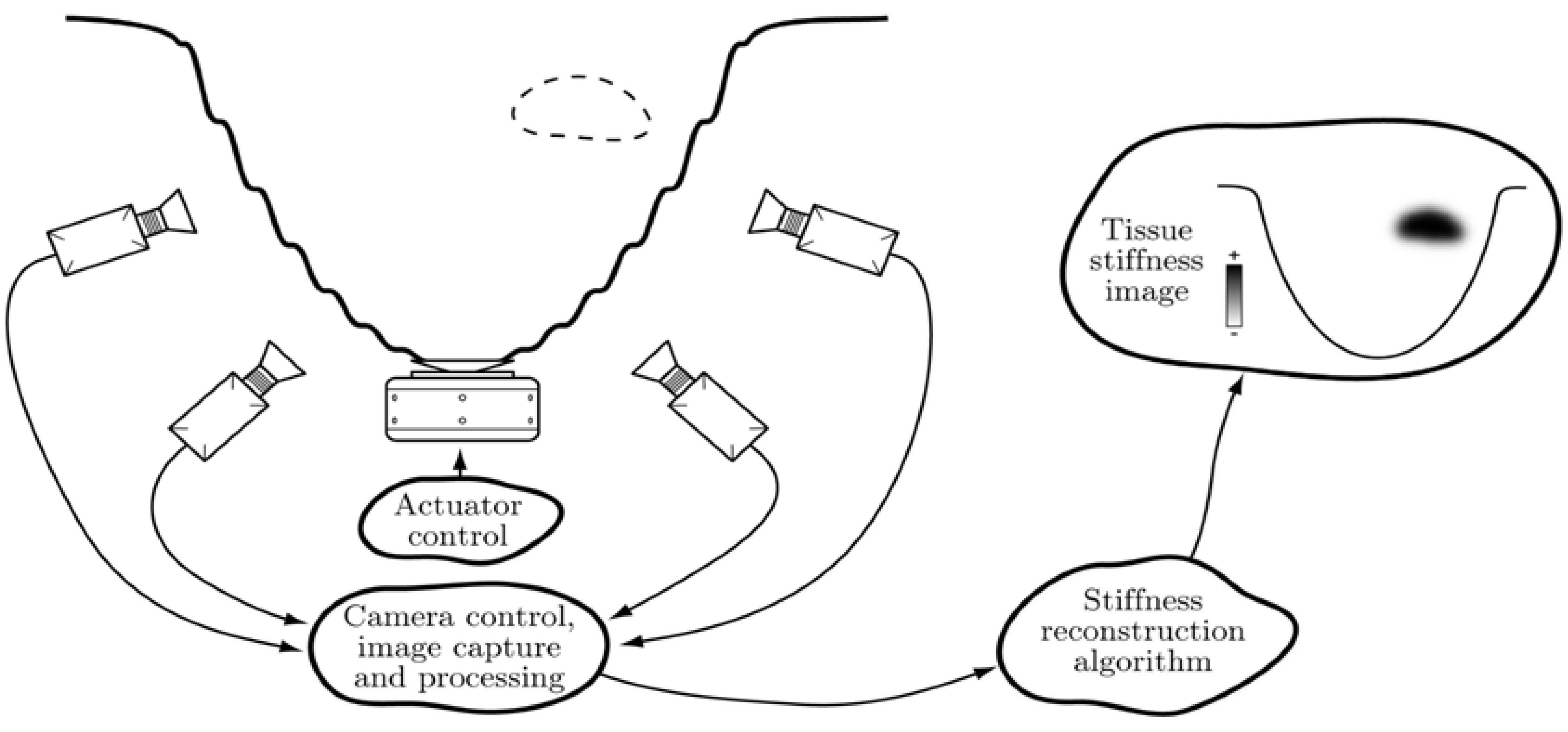
- DIET is intended to be a full-volume elastographic imaging system for breast cancer screening.
  - Initial goal = pre-screening system in a hierarchy of tests
- The system will utilize only surface motion, avoiding the use of potentially harmful x-rays.
- The elastic property contrast measured by DIET is higher than the contrast measured with a screen-film mammogram.
  - 500-1000% vs only 5-10% for mammography
- DIET imaging hardware is intended to be inexpensive and compact, with the potential for mobile screening in remote areas.
  - Distance is a reported major cause of poor screening compliance.

The DIET System Concept



DIET system overview

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4 fundamental steps:

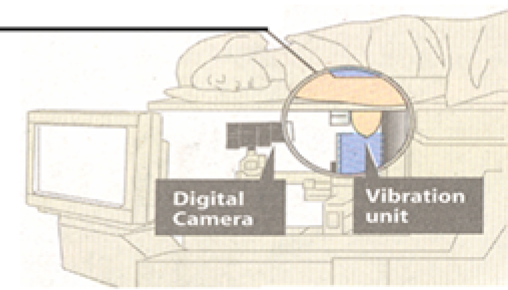
(1) Actuation

(2) Image Capture

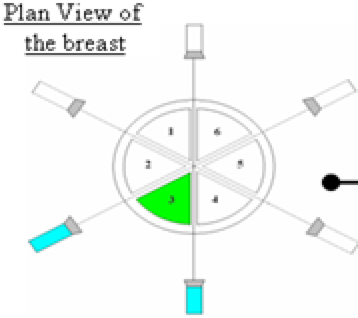
(3) Motion tracking and measurement

(4) Tissue stiffness reconstruction

1. A woman's breast is vibrated by an actuator and imaged with high-resolution digital cameras.

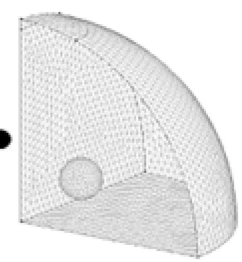


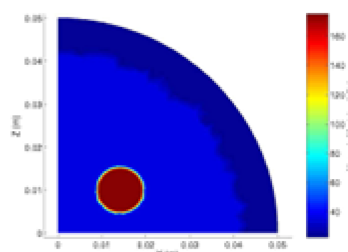
Plan View of the breast



2. Spatially calibrated digital cameras combined with a motion sensor measures the surface motion of the breast.

3. Finite Element method converts the measured breast surface motion into a 3-D stiffness distribution, where regions of high stiffness suggest cancer.





Advantages of the DIET Concept

- Screening from a younger age (no radiation dose)
- Possible to build a history (every year!)
- Less painful alternative (equals higher compliance)
- Accuracy (initial target 1cm)
- Portability and ease of use (no specialised technician and no loss of compliance due to travel)
- Scalability (will improve as silicon technology used improves)
- Should be low cost (low-cost technologies used)

Elastographic Reconstruction & Initial Proof of Concept

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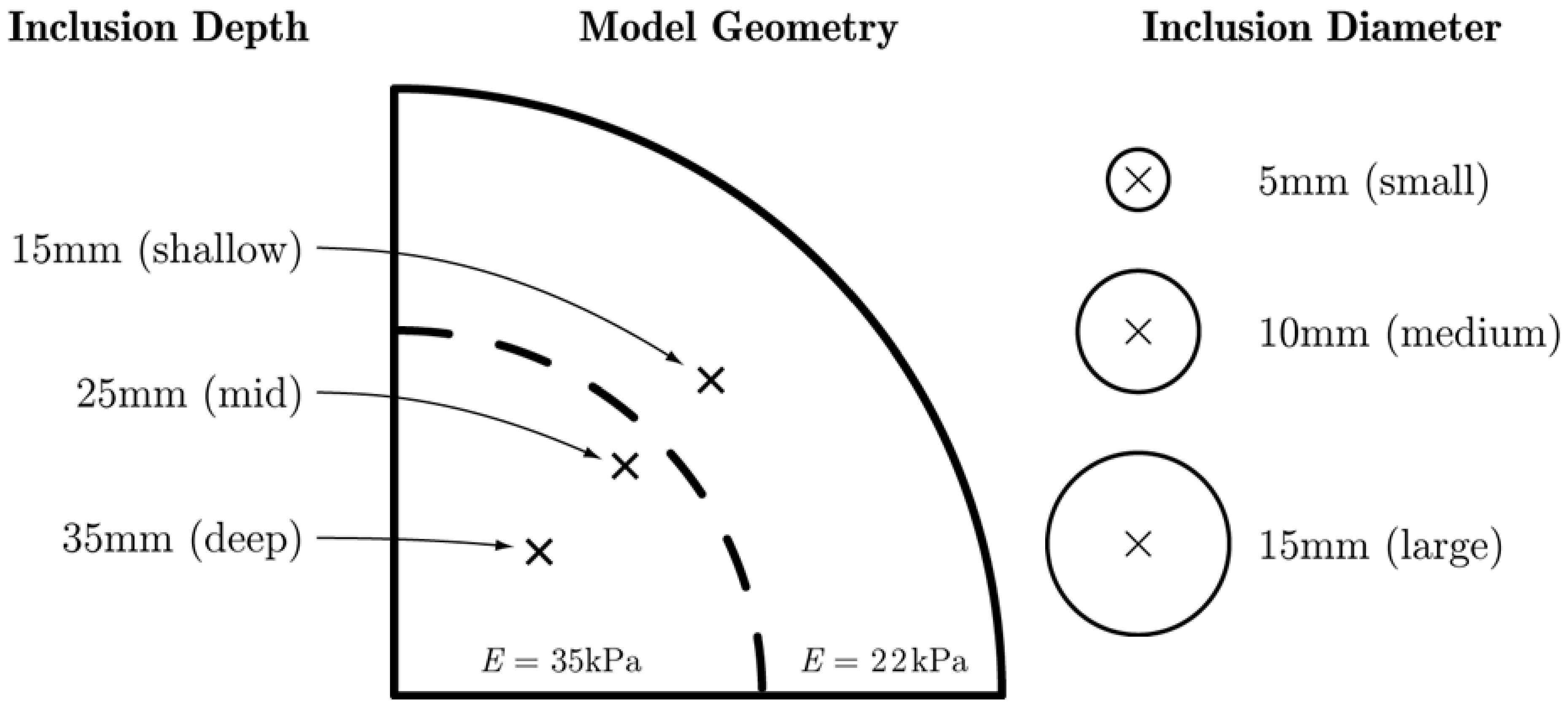
- If we could measure surface motions could we do the reconstruction to detect cancerous lesions, from surface data only?

Lake Mathieson, Mirror Lakes
West Coast of S. Island

Lindis Pass and into Wanaka
Cental Otago, S. Island

Proof of Concept Study:

Could we do this if we could measure the motion?

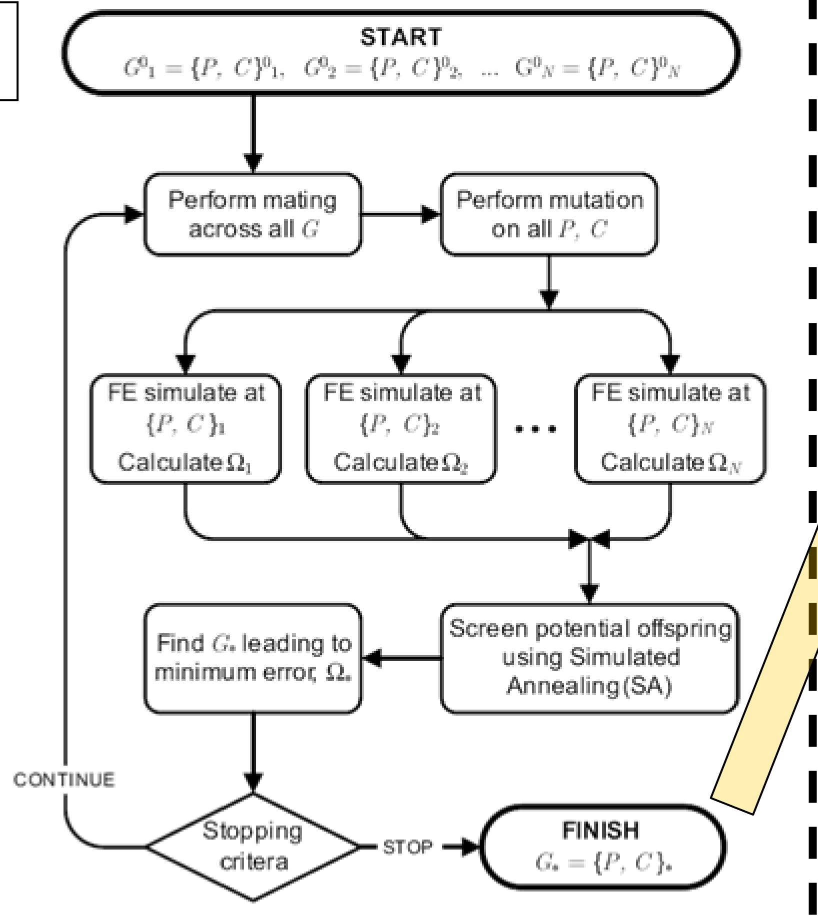


¼ Hemisphere FEA Model – Inclusions on primary axis

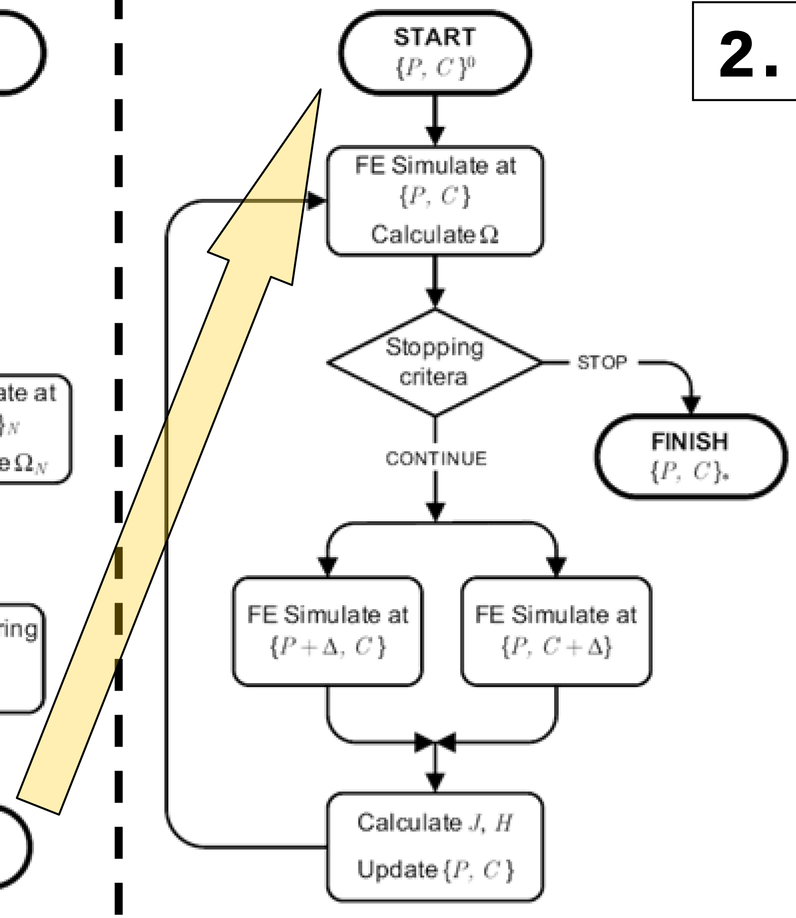
Hybrid Reconstruction: GA + GD:

A good starting point is hard to beat!

1. GA

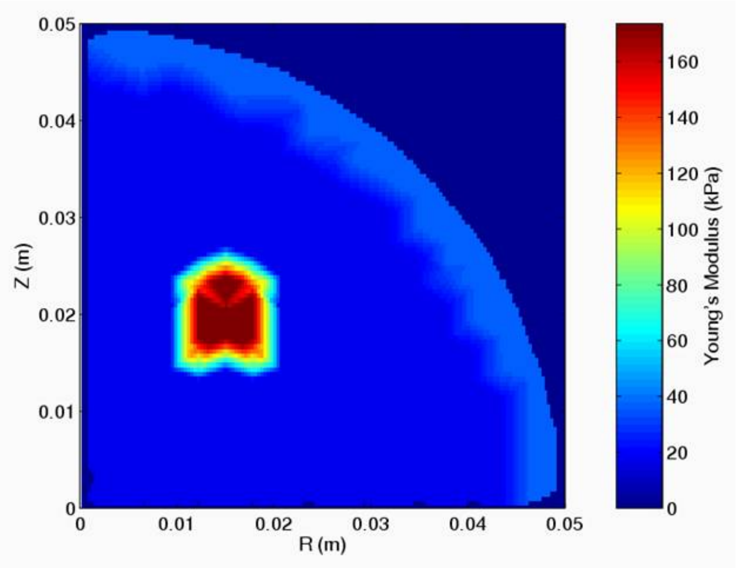


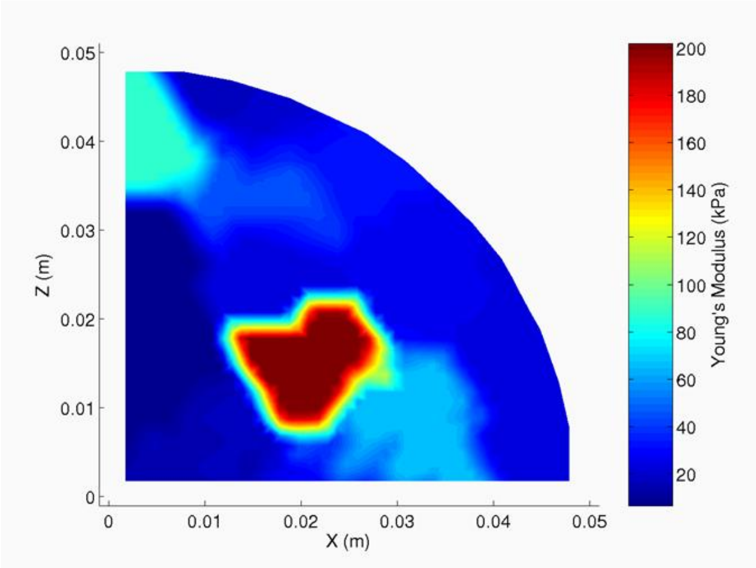
2. GD



Proof of Concept: Simulation Studies

- *Simulated* motion with added noise based on imaging tests
- Gradient-descent based reconstruction techniques for first try





- Proved the concept, though several issues required further investigation[1]

[1] Peters et. al, JSME Int. Journal, (2004)

Proof of Concept Study Results

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Answer = Maybe!

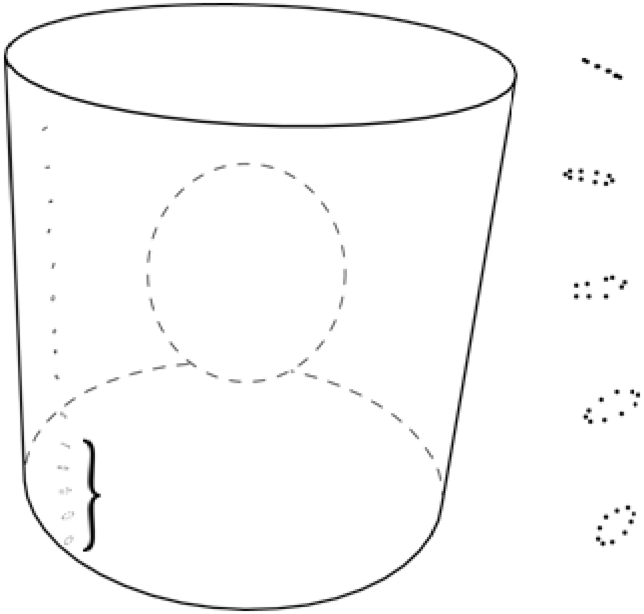
Inclusion Diameter and Stiffness Contrast

Inclusion Position	5mm Diameter			10mm Diameter			15mm Diameter		
	5x	10x	100x	5x	10x	100x	5x	10x	100x
Shallow	✗	✓	✓	✓	✓	✓	✗	?	?
Middle	✓	✓	✓	✓	✓	✓	?	✗	✗
Deep	✓	✗	✓	✓	✓	✓	✓	✗	✗

Many issues with GD algorithms as used → GA + GD for further work

Proof of Concept:

Simple Phantom Studies



- Only 4x contrast in Silicone materials utilised
- Base Silicone has 20kPa modulus similar to healthy tissue
- Initially measuring only a line of dots – symmetricity assumed for ease

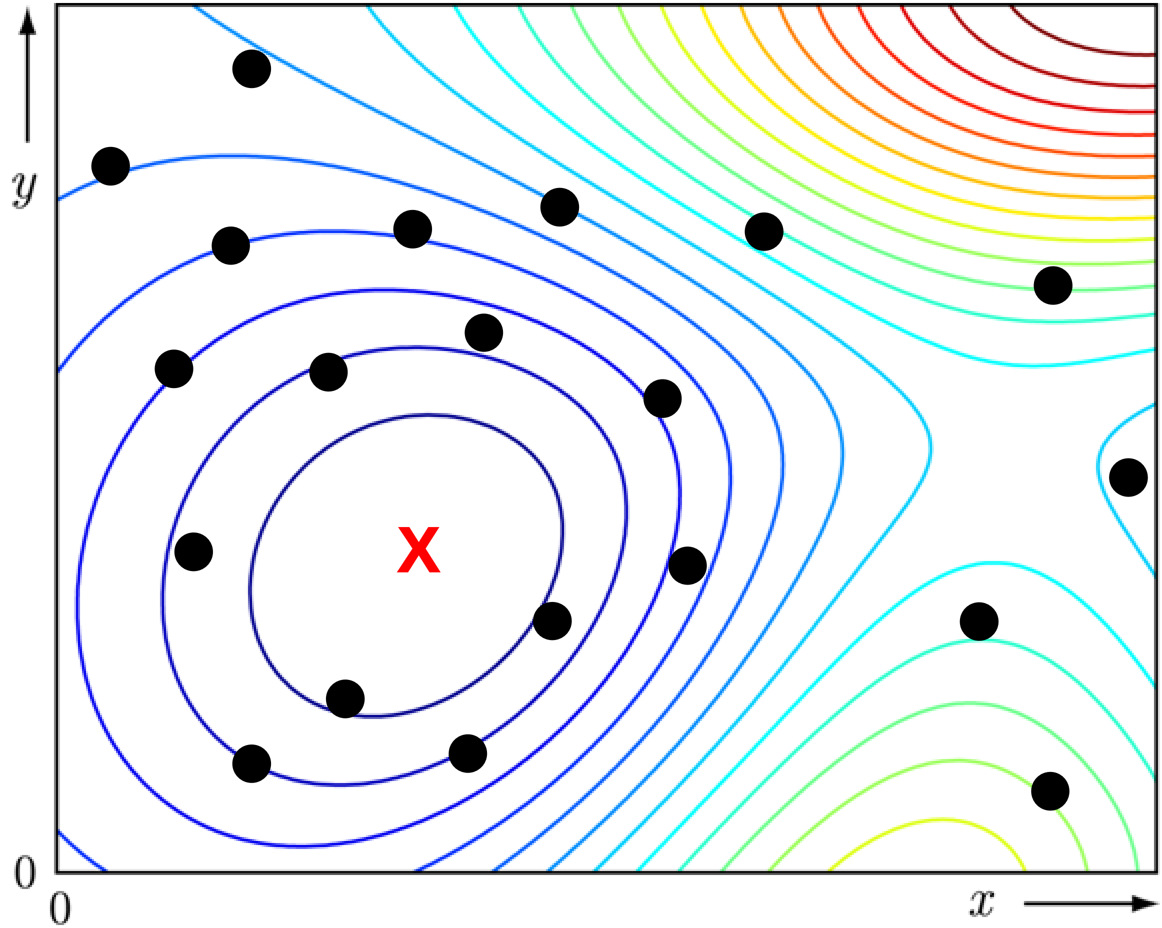
Non-linear Reconstruction: Affect of using a GA first

- Error map is non-convex
- X marks the spot
- 2 parameter problem
  a. location of inclusion
  b. if any …

- Same holds true with more variables

- GD alone finds local minima w/o good start points

- Resulting algorithm:
  a. 10-100 generation GA
  b. 10-100 steps GD

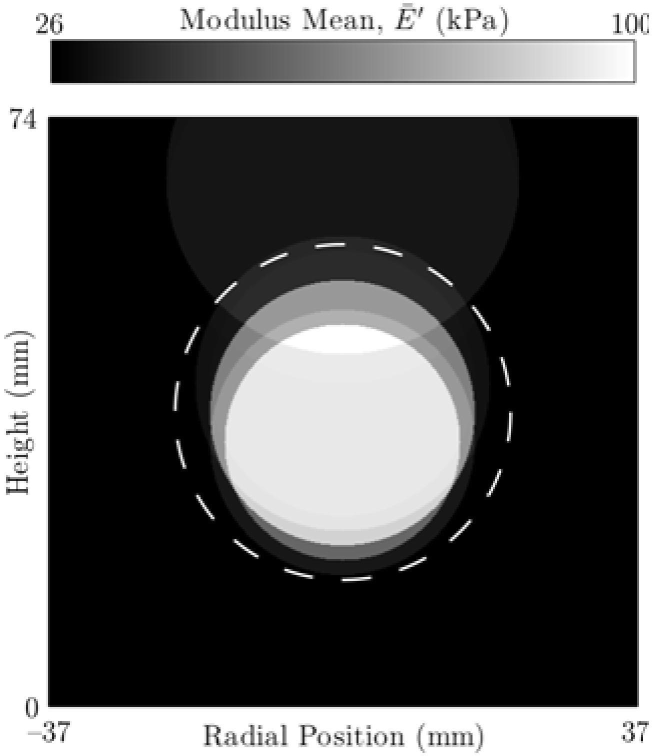


▪ Combinatorial optimization (CO) algorithm

Phantom Study Results in Brief

- Spherical inclusion found at 4x contrast expected
- Slight error towards top of phantom due to no measurements made there
- Excellent outcome for very few measurements and many assumptions made
- Similar results for other symmetric phantoms and no inclusion case

- **Outcome: Improve imaging and move on to far more realistic phantom studies**



Imaging and Image Processing

- Can we measure to sub 0.1mm?
- Can we measure 1000s of points moving <1.0mm at 50-100Hz?
- This all seems very hard!

Lake Wanaka, Central Otago, S. Island

Imaging in 3 Big Steps

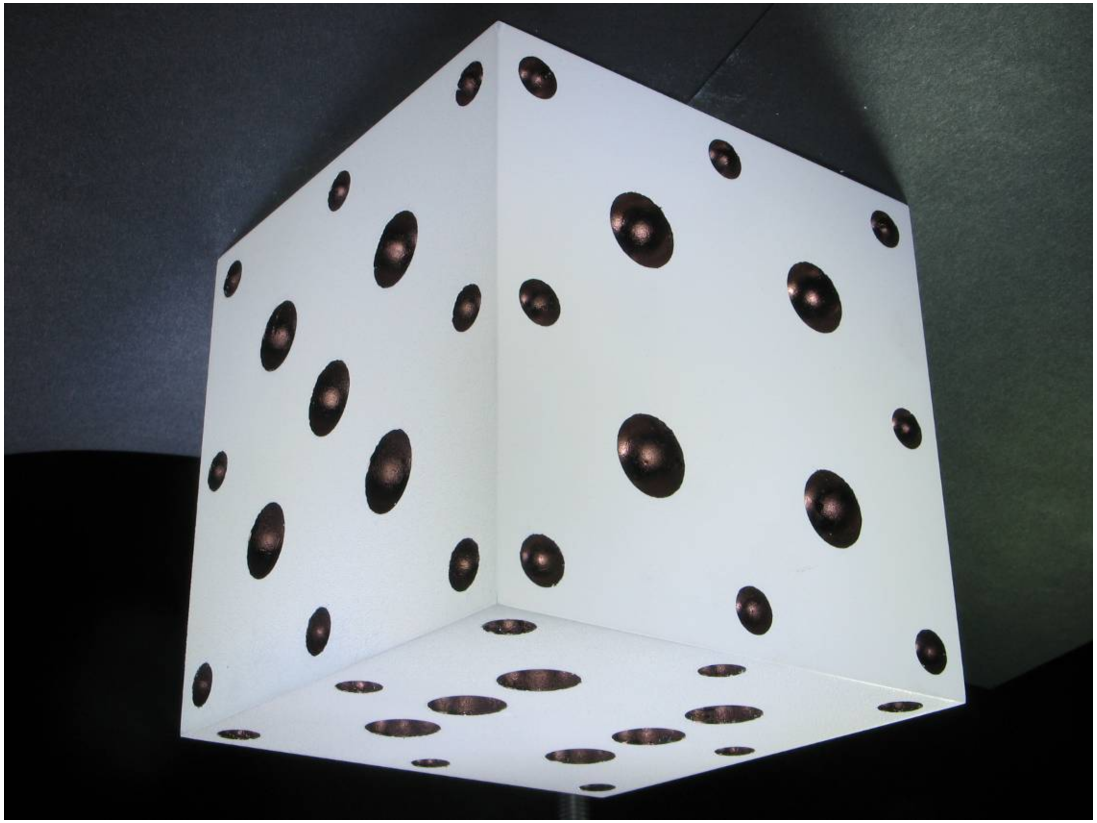
- **Calibration** – must be robust and provide high accuracy to results
- **Motion tracking** within an image
  - Must track a large number of points
  - Must be computationally efficient
- **Combination** of 2+ image plane motions into 3D
  - Must be fast and accurate and efficient
- Would like to do all three steps local to cameras or system

1. Camera Calibration

- Essential that cameras are accurately calibrated, otherwise 3D reconstruction is not accurate

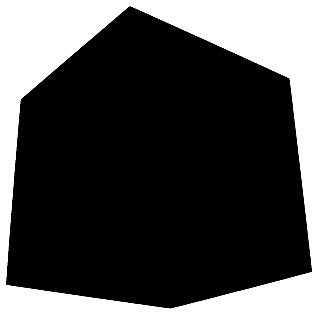
- Calibration gives
  - Position and orientation of each camera in 3D
  - Internal camera parameters (e.g. focal length, etc)

Calibration Cube

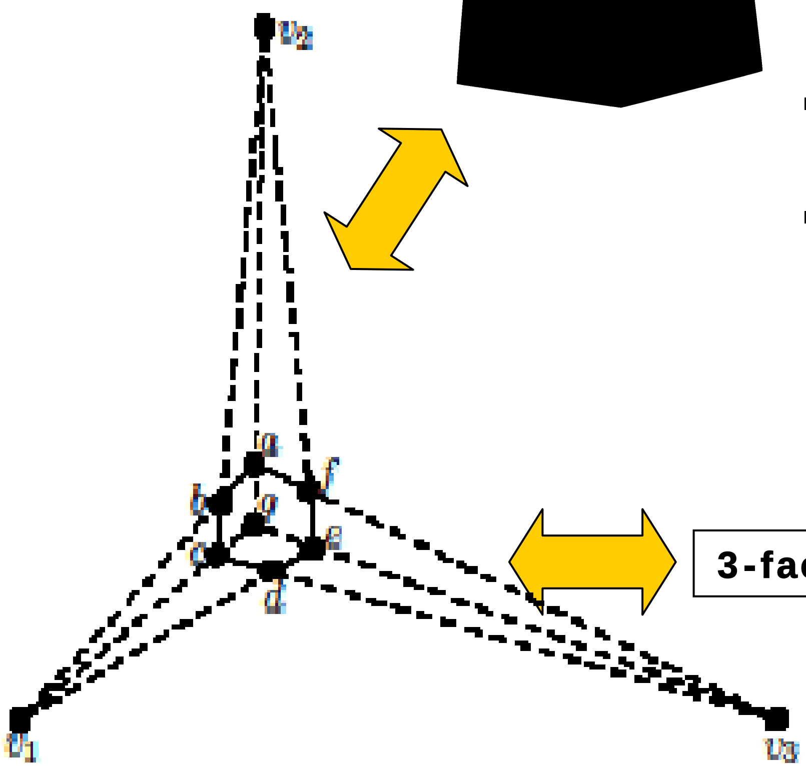


- Die face pattern for unique face identification
- CNC machined to sub-0.1mm accuracy
- Circular features for accurate centre location
- Overall approach relies on matching face boundaries from image and <u>not corners or lines</u>

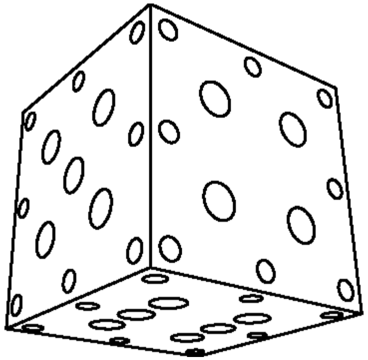
Face Boundary Extraction and Elliptical Feature Fitting



- Cube faces are partitioned by finding face boundaries from silhouettes by geometric construction, based on vanishing points
- Can be done for either two or three faces of the cube visible
- Individual faces found by ellipsoid/circle pattern
- Ellipses found by least squares fit to thresholded feature boundaries



3-faces visible case



Face and feature identification

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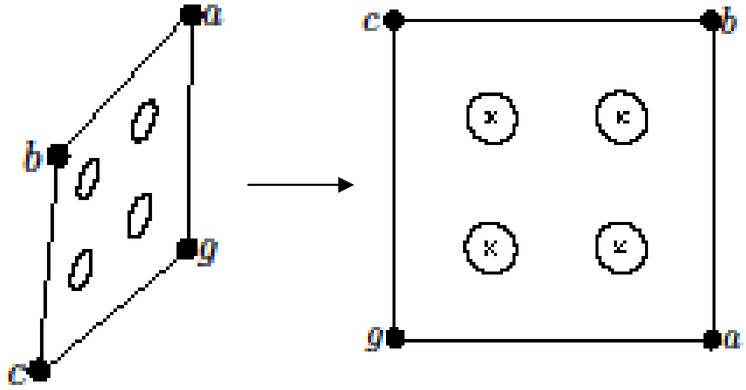

$$Q \mapsto H^{-T} Q H^{-1}$$

- Faces are mapped by a homography H to a reference square
- Ellipses (as matrix quadratic forms in homogeneous coordinates) are mapped to circles (if no error)
- Mapped point locations in the reference square are used to determine which face is present
- Once all three (or two) visible faces are identified, image points can be uniquely matched to known world coordinates

Calibration and Resection

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- Once image-world correspondences are known, the 3x4 camera projection matrix $\boldsymbol{P}$ is estimated by nonlinear least squares, minimising:

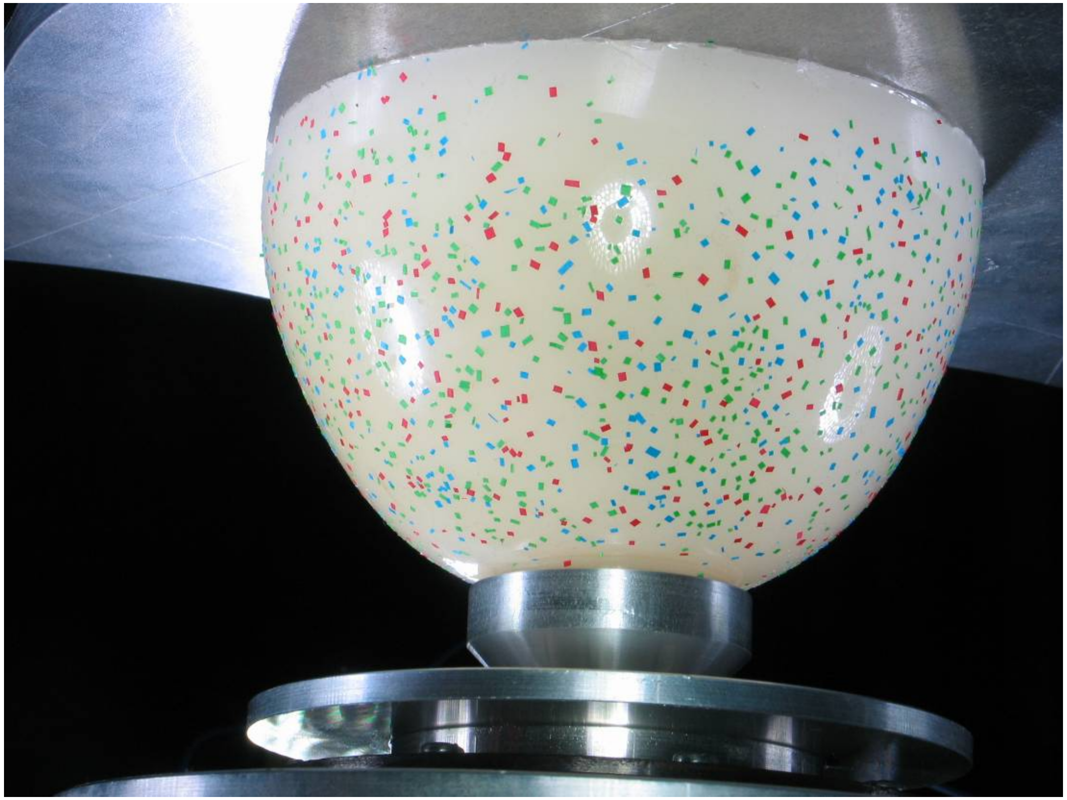
$$\sum_i d(\mathbf{x}_i, P\mathbf{X}_i)^2$$

- This is a standard approach in the field, given that the cube has been identified and correspondences made.

2. Feature Tracking

- Features are artificially applied coloured dots in three colours, red, green, and blue

- Features are tracked from frame to frame by either nearest neighbour matching, if the motion is small, **or** by matching geometric invariants of the feature configuration



Euclidean-Invariant for Sets of 3 Points

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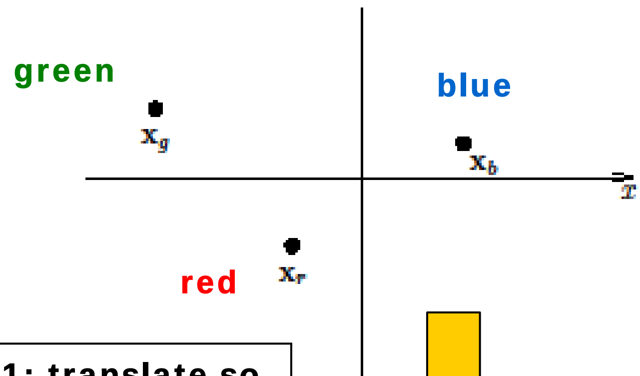
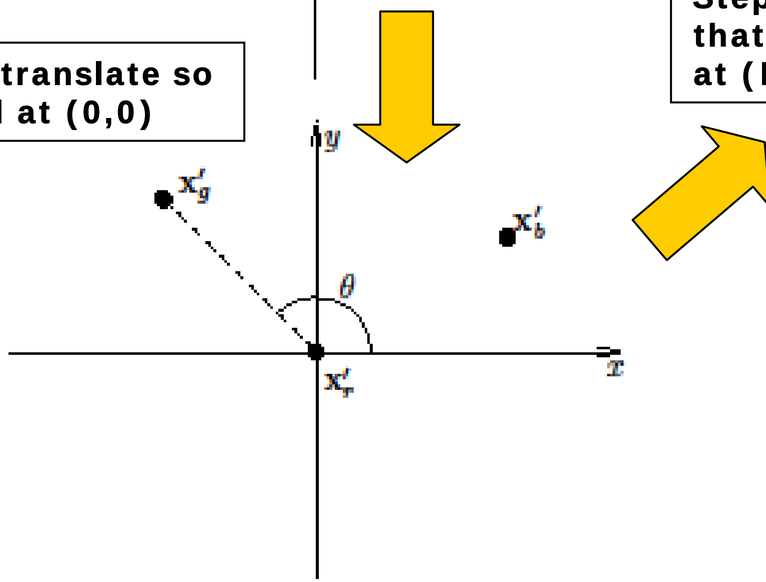
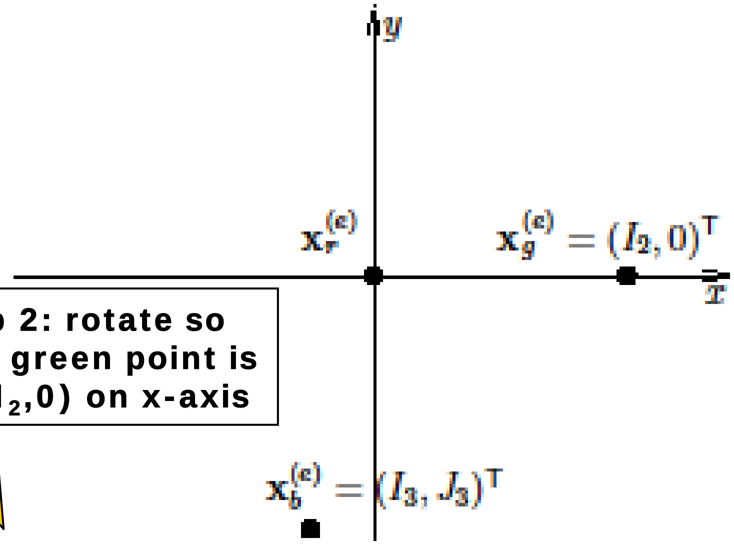
Red point w/ closest green + blue neighbors



Step 1: translate so that red at (0,0)



Step 2: rotate so that green point is at $(I_2,0)$ on x-axis



The remaining components of the blue point (I_3, J_3) and x-coord of green (I_2) are invariant to Euclidean transformation.

Thus, if you rotate+translate those 3 points anywhere else you will get same triple

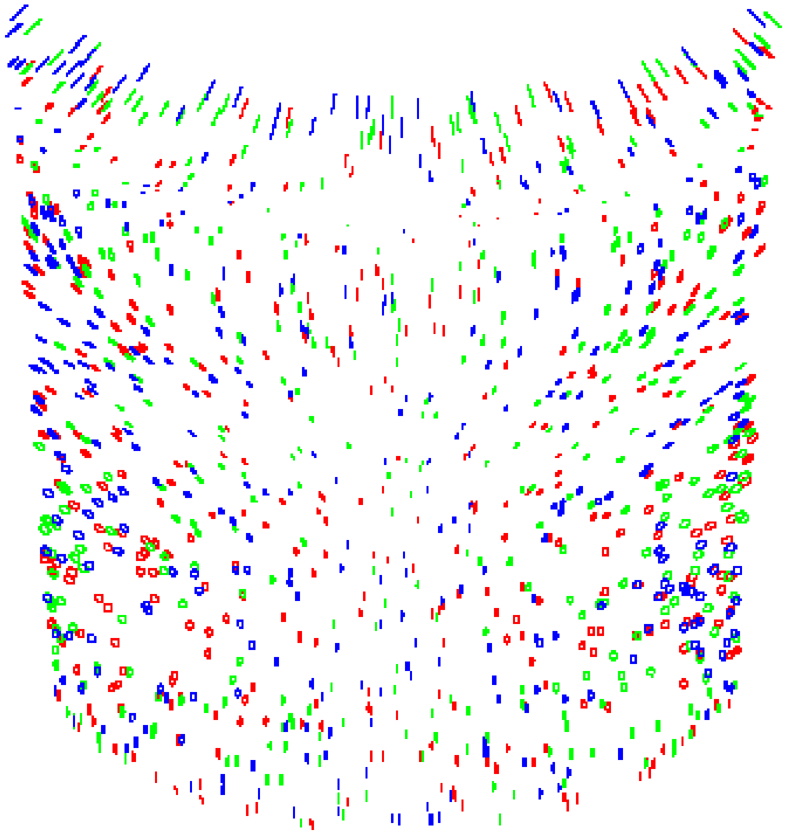
Assumes: in this usage that image-to-image motion is Euclidean (enough)

Feature Tracking Using Invariants

- Given a red point **R** in the first frame, its invariant is computed, and compared with the invariants of all the red points within a certain radius of **R** in the second frame

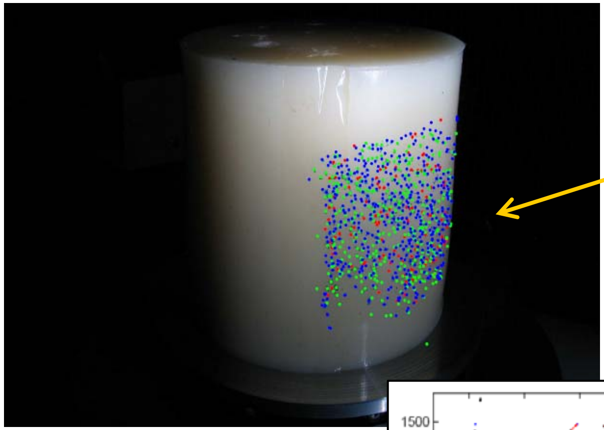
- The invariant which matches best is the match for **R**

- The remaining points are tracked by interpolating the motion of the red points



Result for a cylindrical phantom actuated at 1mm and 50Hz

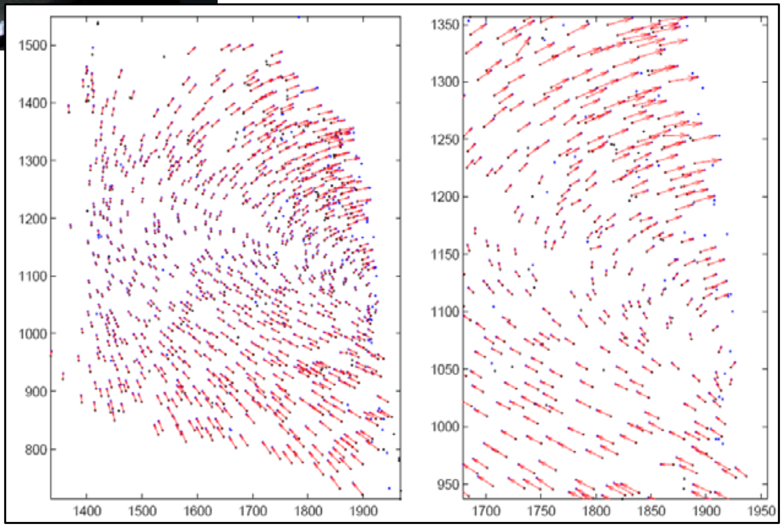
Gel Phantom simulation



Colours and points successfully detected

- ~750 coloured fiducial marks
- Frequency=50Hz, 1mm peak to peak (0.5mm ampl)
- 20 images (18 degrees of phase)

- 90% of fiducial marks tracked successfully by point tracking method (<u>thru all 20 images over whole cycle, i.e. last matches first</u>)
- NB: can use fact that last point of 20 doesn't match first (0 and 2π radians) to discard false tracking results over cycle



(a) whole set (b) Subset (zoomed in)

Tracking Procedure

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1) Extract all red, green, and blue point locations from images

2) Find nearest blue and green neighbours to each red point to form the point triples

3) Compute motion invariant signature for each red point

4) Match triples by matching their signatures in signature space

   - discard any matched red points > upper bound on expected motion

5) Match remaining unmatched points by interpolating motion between matched points

3. SEER: Algorithm for 3D Reconstruction Using Epipolar Constraints

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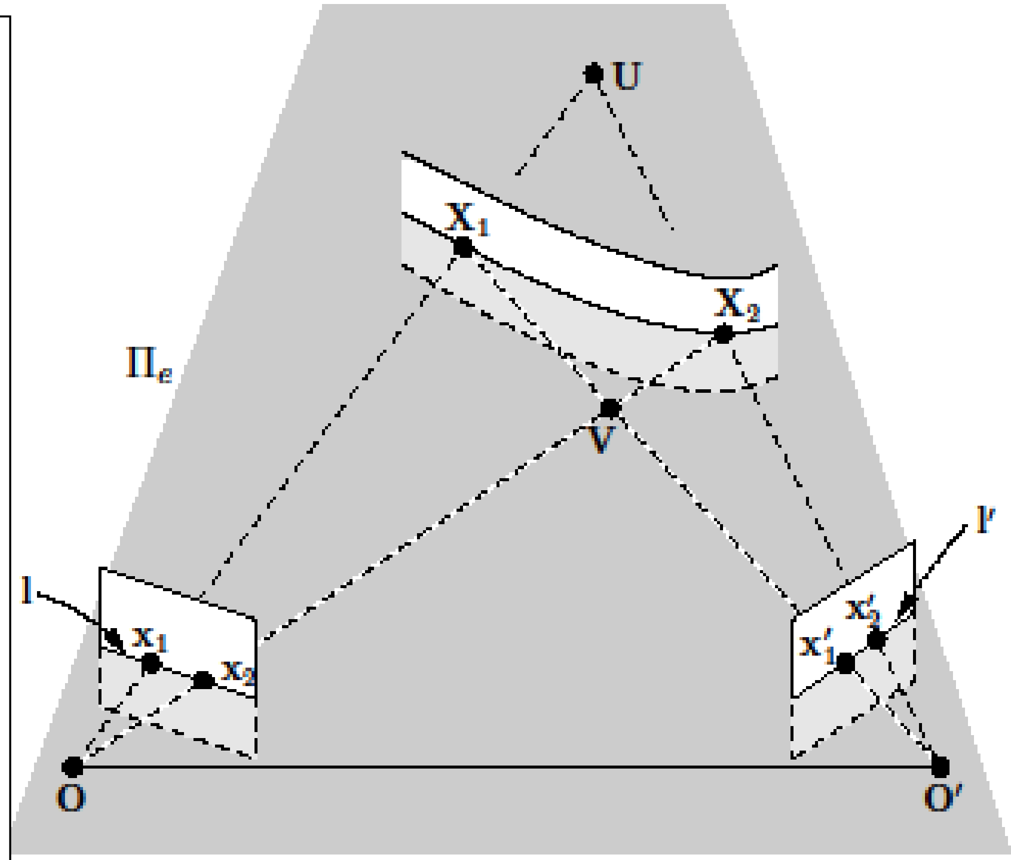
- All points on matching epipolar lines (computed from the two camera projection matrices) satisfy the epipolar constraint
- All points satisfying the constraint are reconstructed in 3D
- 2 points→ 4 reconstructed
  - 2 are not true surface points and must be eliminated
  - Given density used in this study may have several more epipolar matches (than 2).



Point Clouds from Epipolar Constraint: All possible matches

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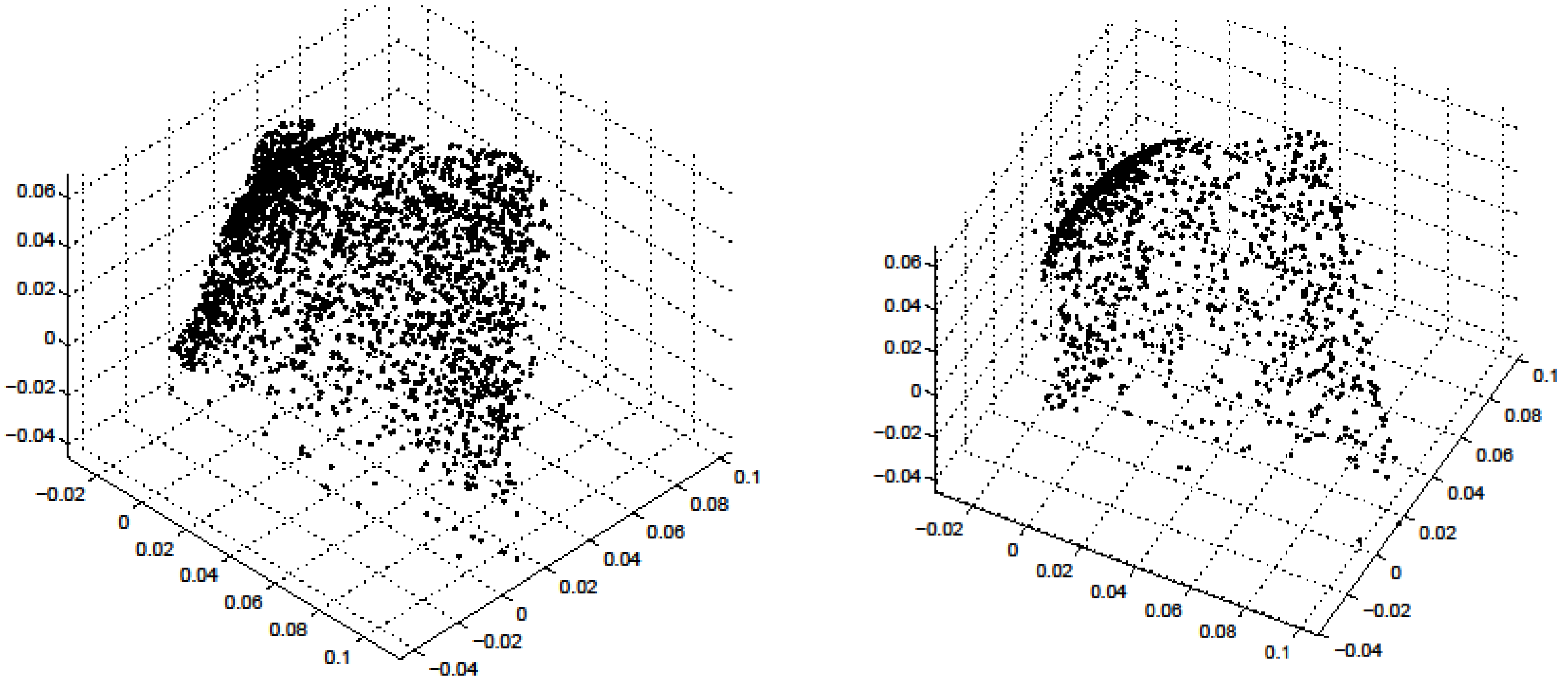
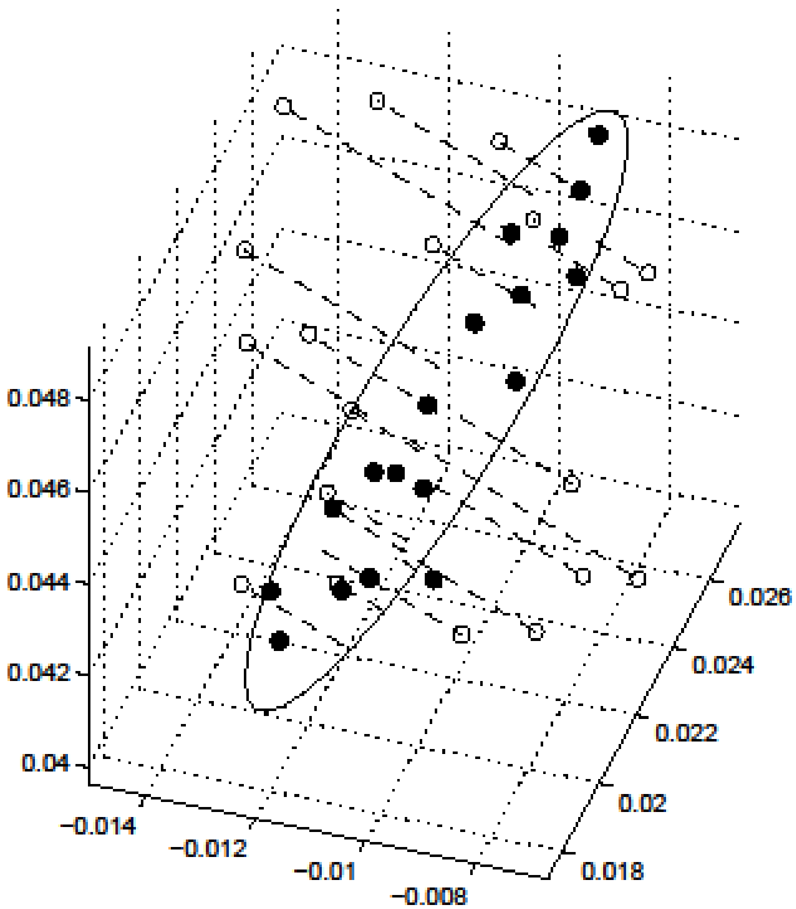


- Point cloud where colours are not used (left) and where colours are used (right) to constrain epipolar matches
- The hemispherical surface can be seen in the point cloud
- This cloud is from a single camera frame from 2 cameras

Extracting the True Surface from the Point Cloud



- Planes are fitted robustly to neighbour -hoods of each point using RANSAC
- Points are marked as *adjacent* in a graph G if:
  - They are inliers to a plane fitted with that point at center
  - The normal to each plane differs only by a small angle, for near neighbouring points
  - Thus, nearby points should have parallel planes (or very nearly so)
- Surface points are thus chosen to be the largest connected component of a graph G.
  - I.e. Parallel near neighbours connect all points (the most points) → answer!

3D Motion Reconstruction Process

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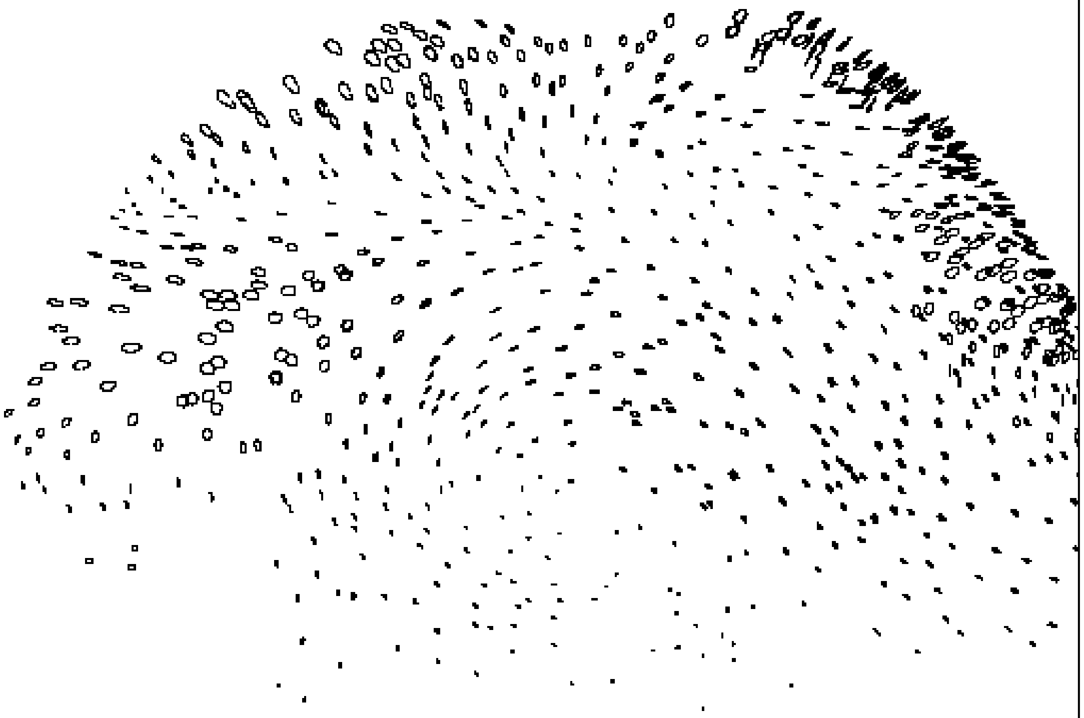


Portion (2 camera view) of hemispherical example

- 3D points are reconstructed from pairs of adjacent cameras, and combined
- Each 3D point is constructed from 2x2D points from 2 adjacent cameras, or more!
- Thus, the 3D trajectory of each point is reconstructed from each frame of a tracked sequence of the 2D points

Putting It All Together!

- Can we detect a small inclusion of ~10-20mm in a phantom?
  - With low contrast (4x)?
- 1st experimental studies on a pre-pre- … -pre prototype

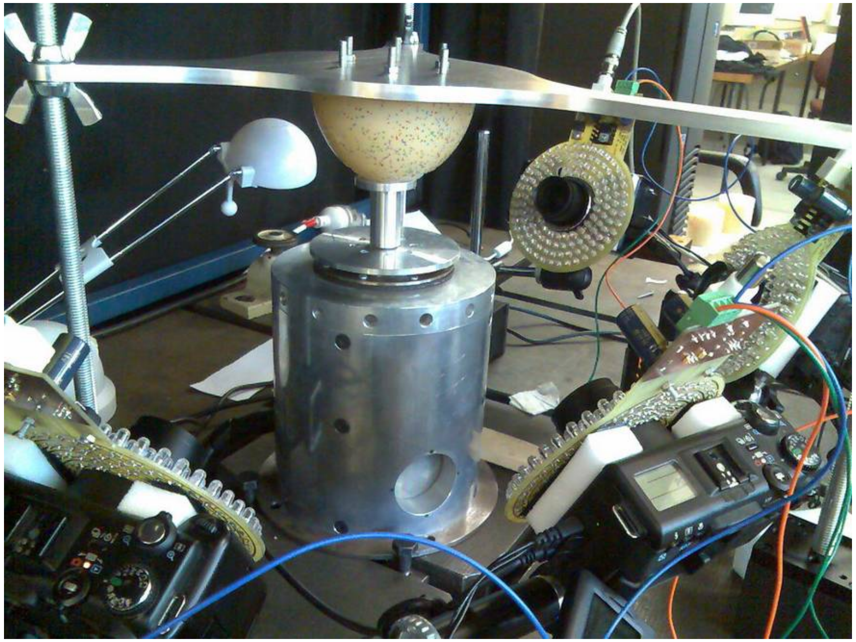
Canterbury Plains, Hamner, S. Island

Mitre Peak, Milford Sound, S. Island

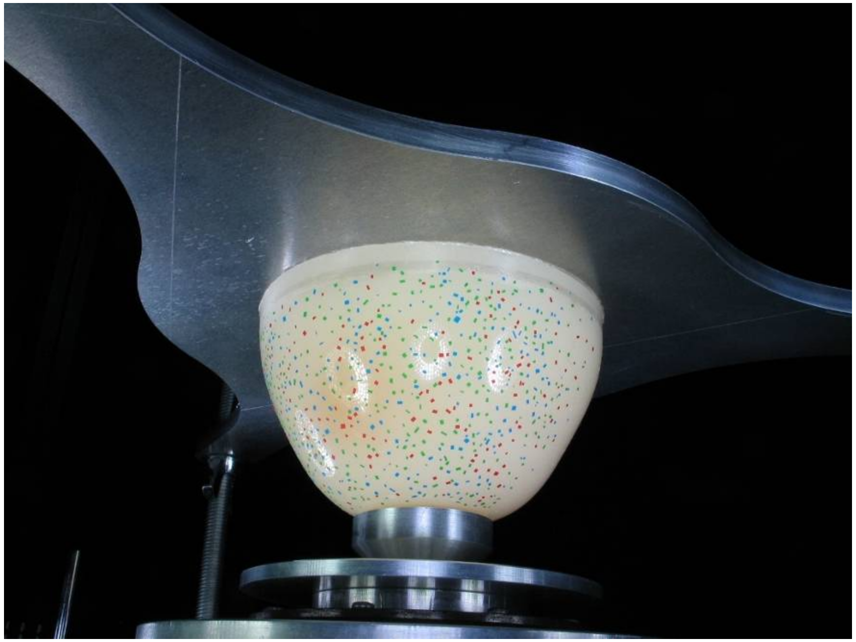
(Pre)^y Prototype Proof of Concept

($y \in$ Integers$^+$ > 3) – it's very early days!

Breast shaped phantom with "chest wall" – Actuated at 50Hz and 0.5mm Ampl.

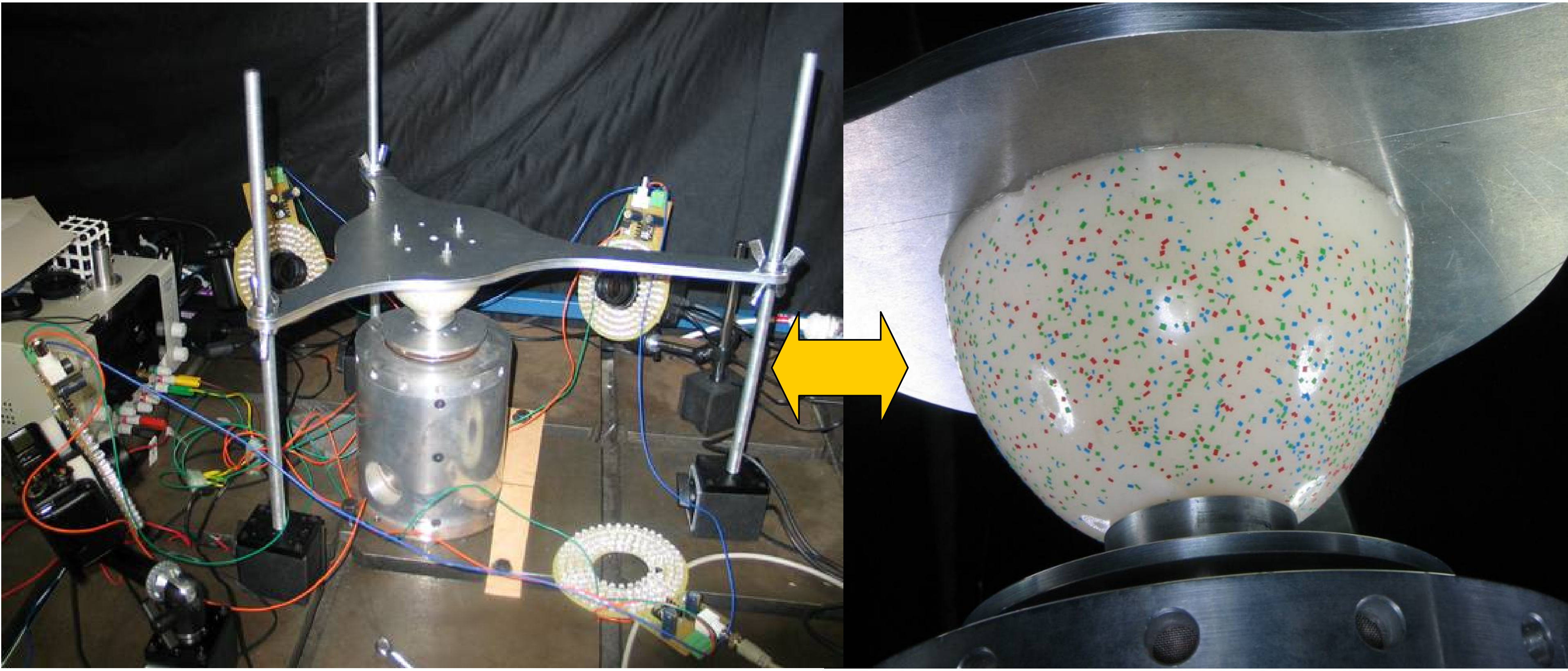


Experimental setup: Actuator, gel phantom, and 4-5 cameras fitted with LED ring flashes



Silicon phantom under actuation with coloured dots applied

Experimental Setup: 5 cameras



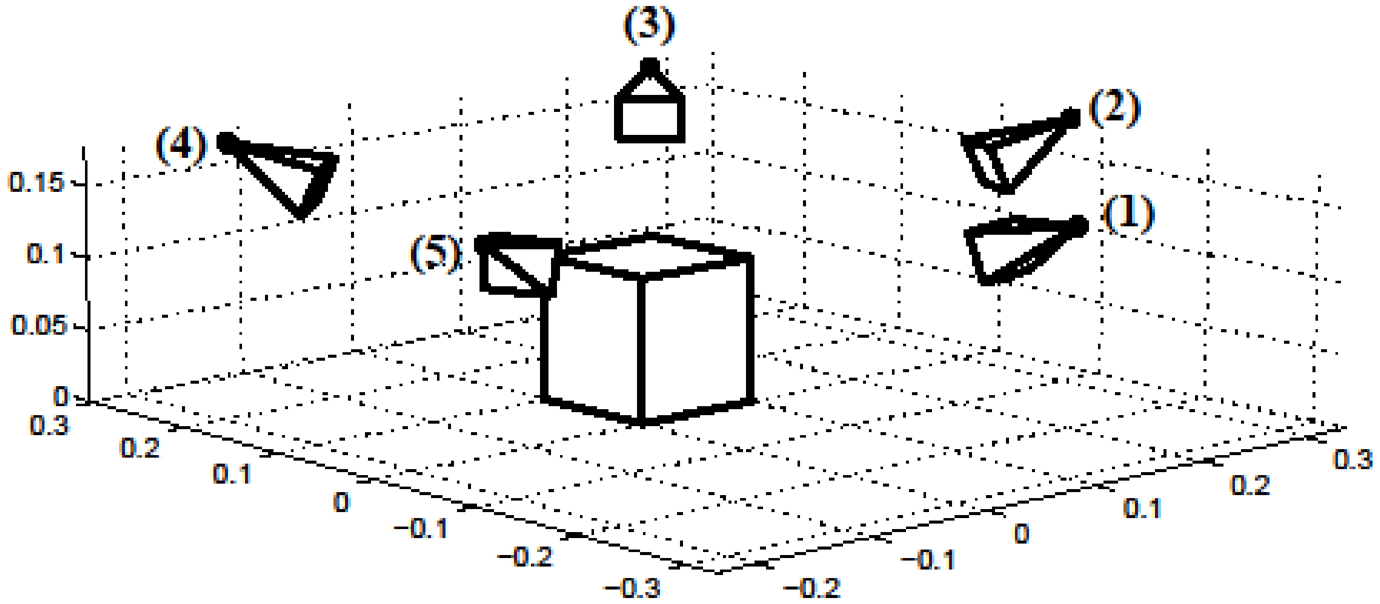
3 Cases Tested

- Three cases + homogeneous (no inclusion case) being tested
  - ~10-15 mm inclusion
  - ~20 mm inclusion
  - ~30 mm inclusion

- All inclusions are placed ~10mm from surface of phantom
  - Phantom is ~100mm diameter at base and ~70mm deep
  - Typical placement near or just under less stiff breast surface tissue.

- Actuation at 50-100 Hz and 1.0-2.0 mm (peak-peak) sinusoidal motion in several combinations

Calibration Results



- Reconstructed camera positions and orientations with respect to cube
- Reconstruction of 3D cube features from image measurements was accurate to within 0.1mm (typically less than 0.02 mm)

3D Surface Reconstruction: One frame typical result

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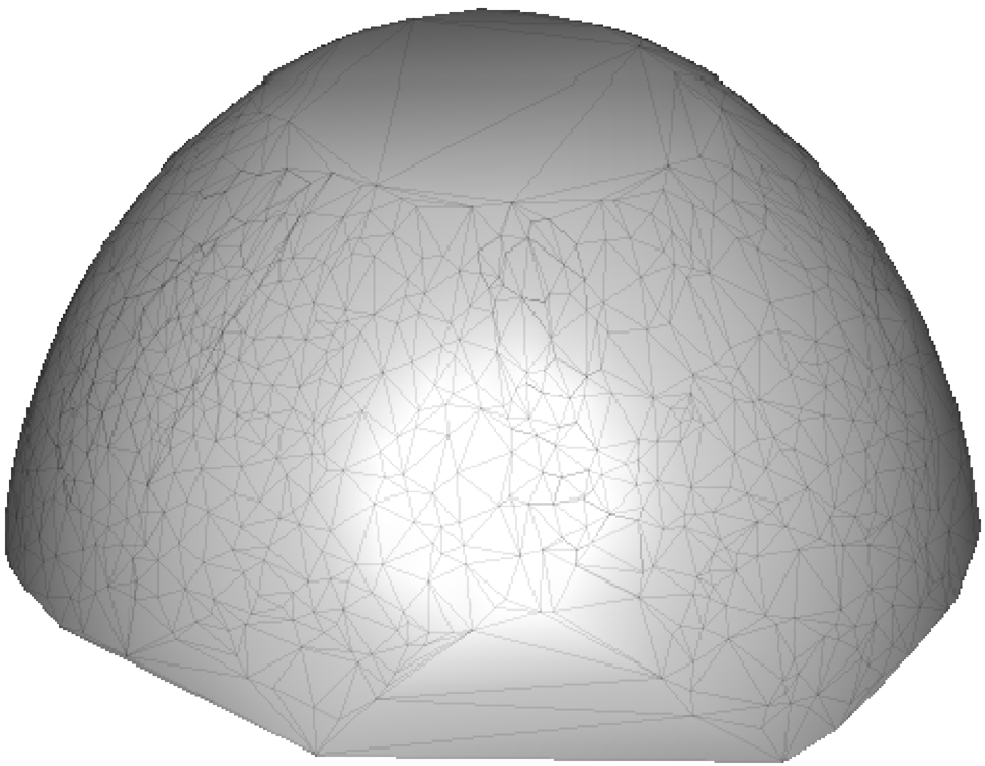
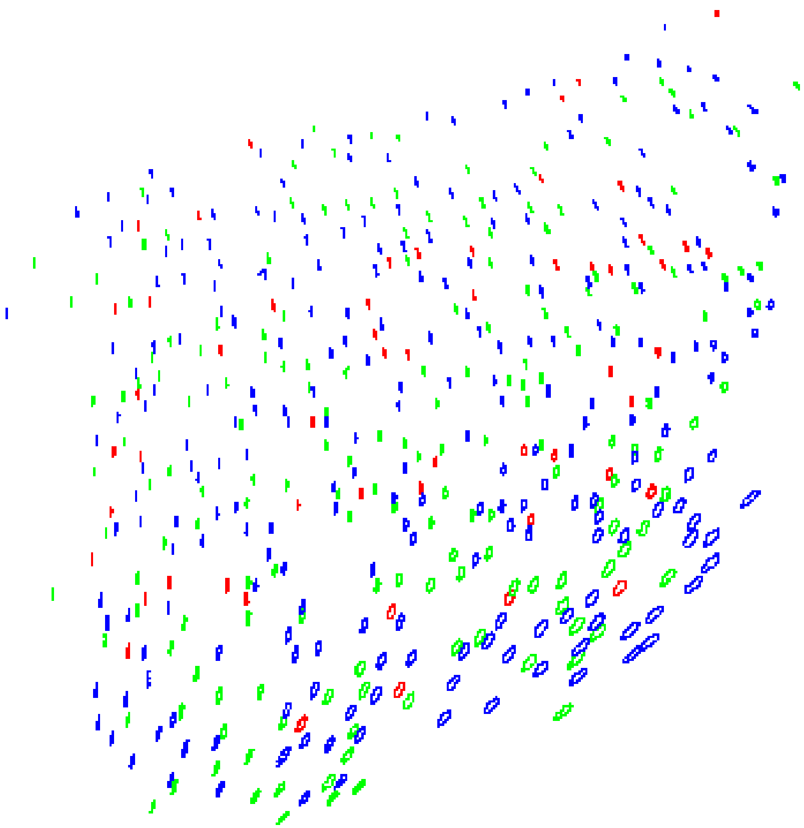


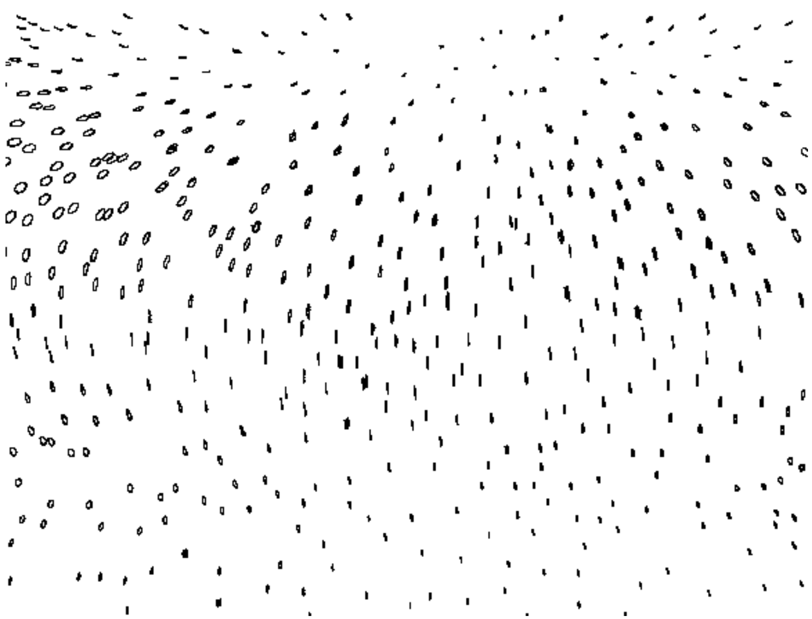
Image Motion



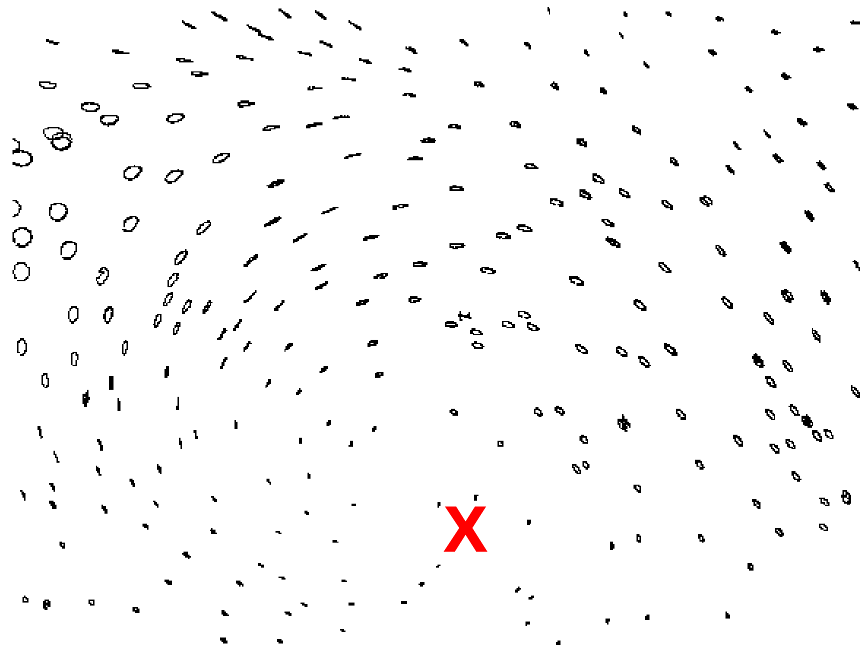
- Coloured points tracked using Euclidean-invariant
- Points are tracked around 20 frames, and then back to the first.
- Incorrectly tracked (non-elliptical) trajectories are thus able to be eliminated (last ≠ first)
- Multiple colours used but not required

3D Motion Reconstruction: One pair of cameras example

No Inclusion

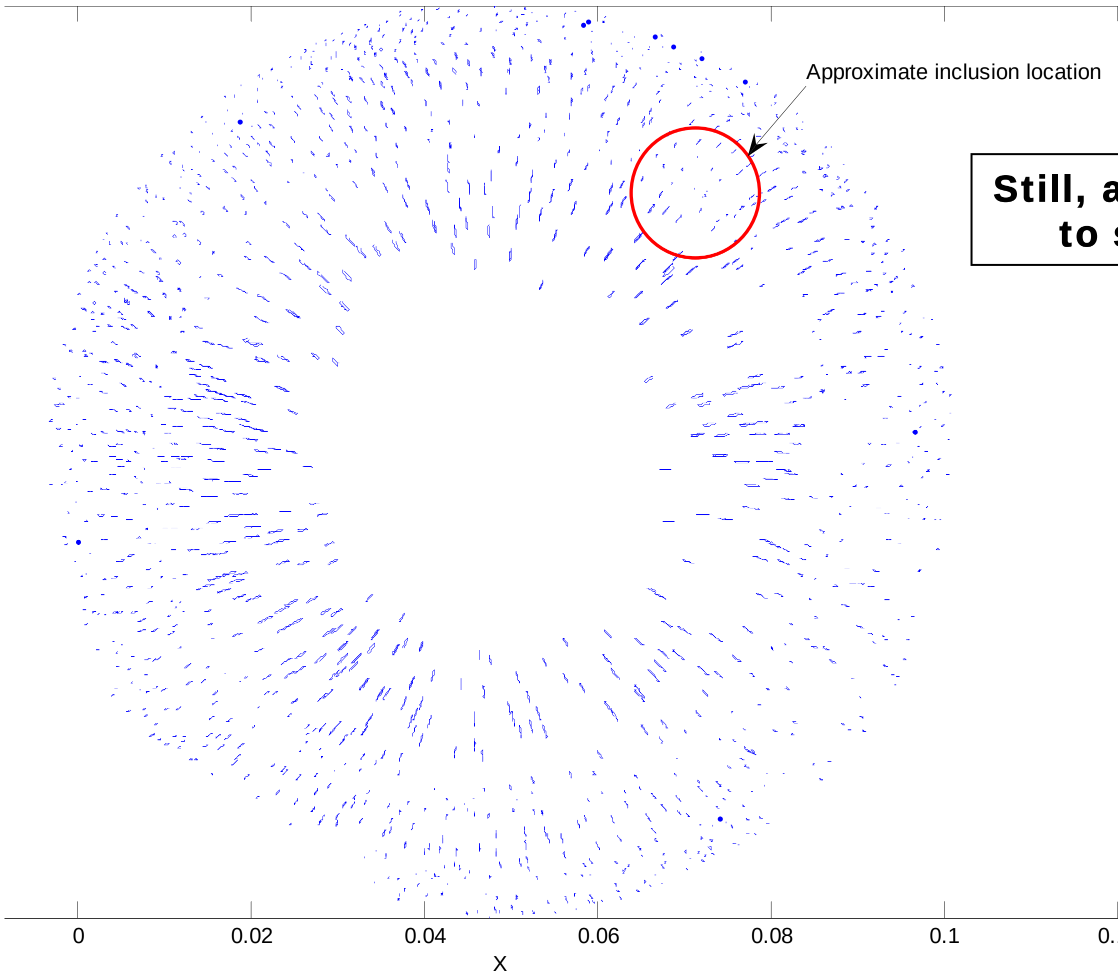


~10mm Inclusion



- Motion trajectories can be seen circling the location of the hard inclusion (right image) which has very little motion (high stiffness)
- Left image has no inclusion, motion is vertical (apparent curves are curvature of the surface as flattened in this image)

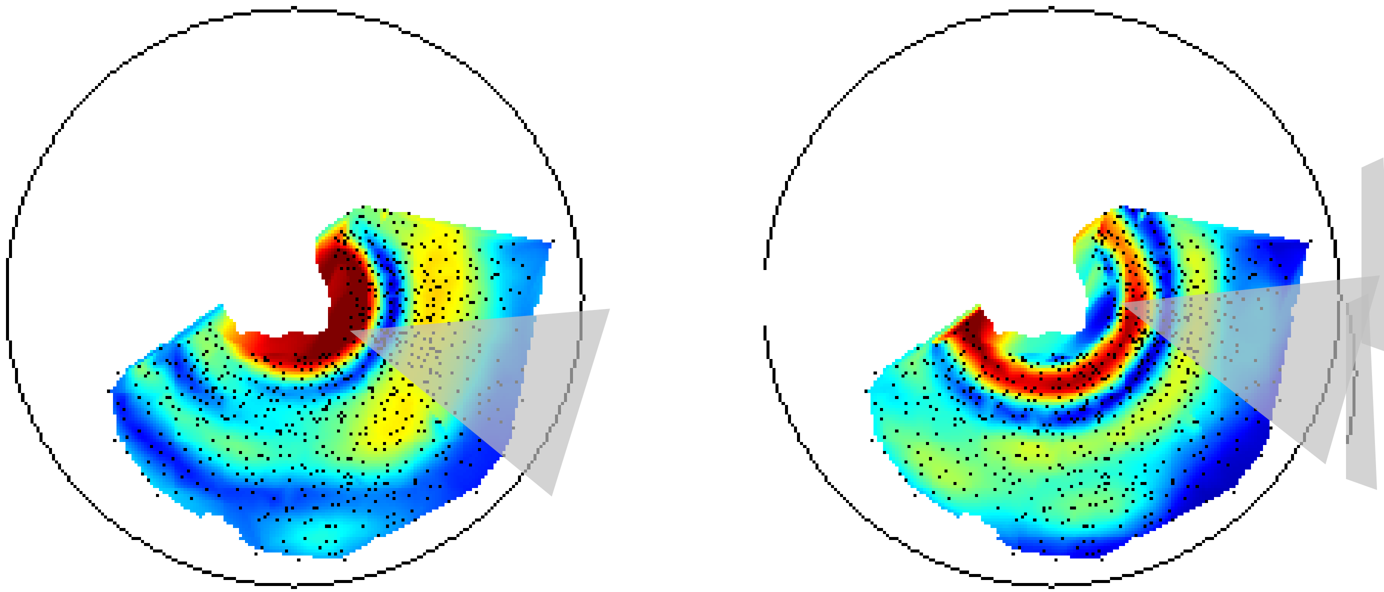
Full Motion Field



Still, a little hard to see here

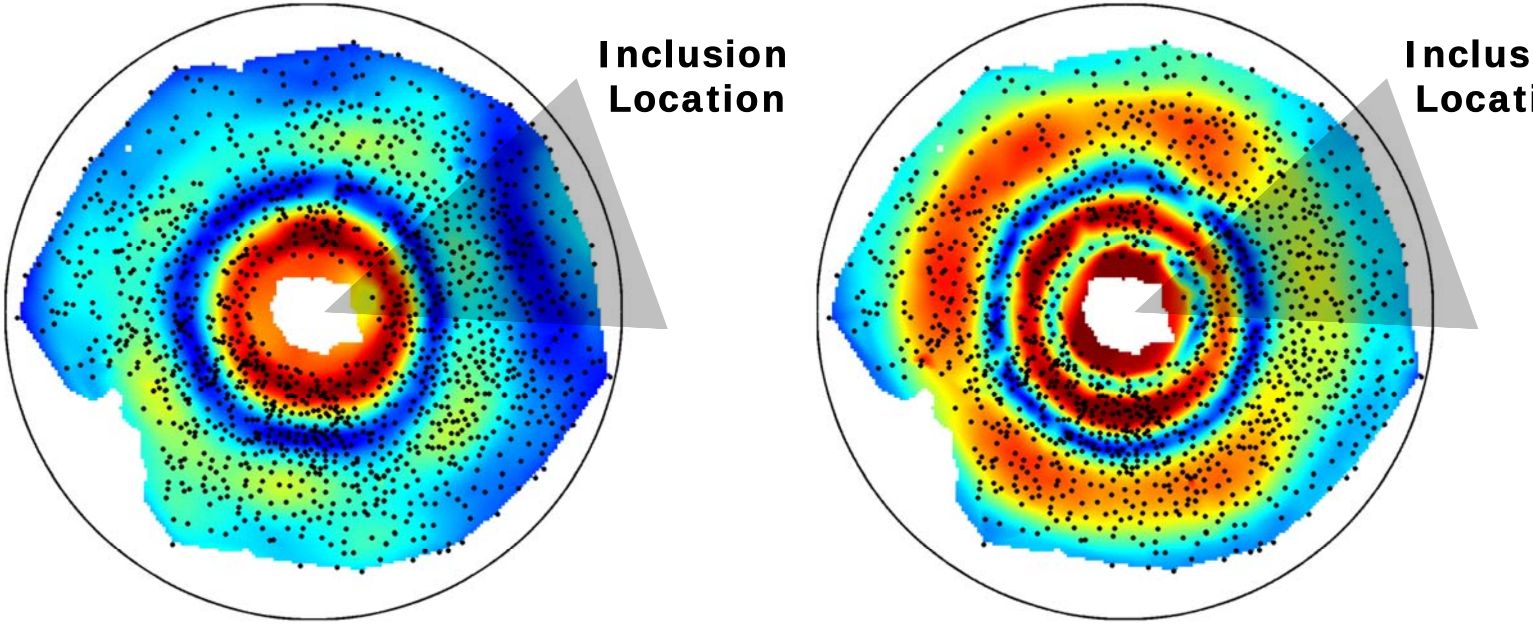
Several Experimental Motion Results: Harmonic motion in Re + Im parts

- Continual improvement and refinement of data collection techniques
- **Left**: Amplitude of Real Part **Right**: Amplitude of Imag Part



27_breast-small_80hz_0,75mm.png

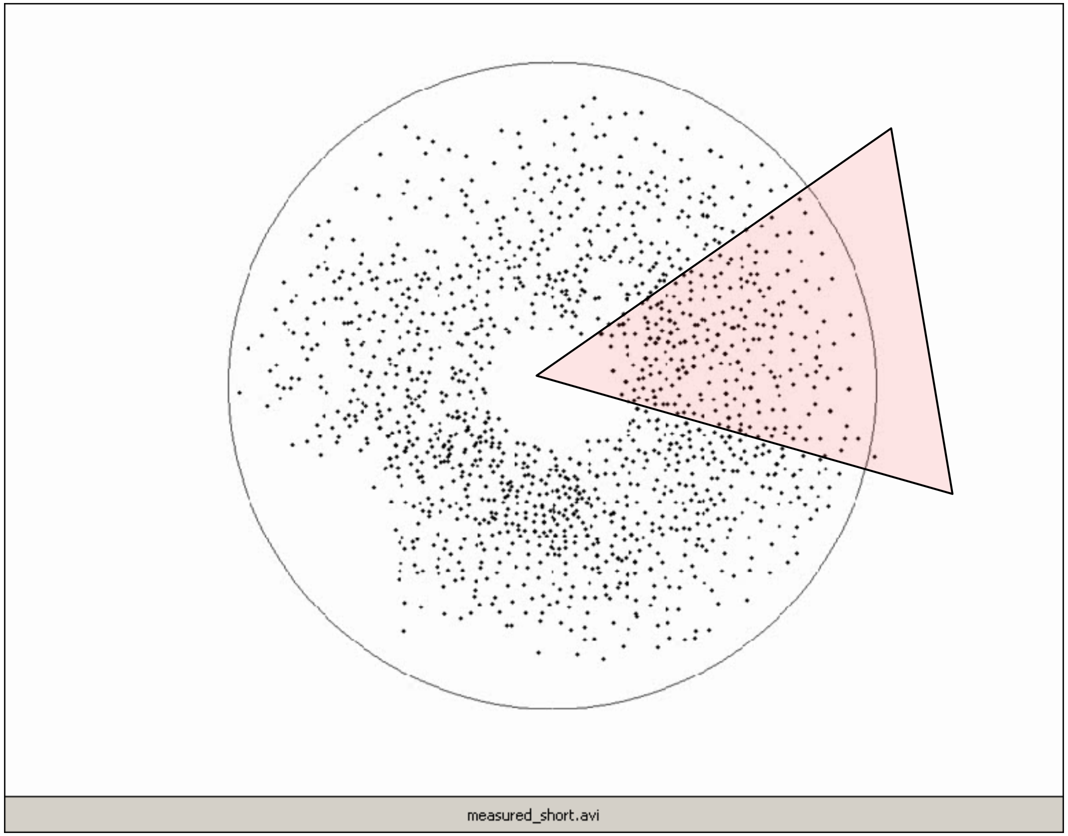
Full Motion Field:
A better view and clearer result



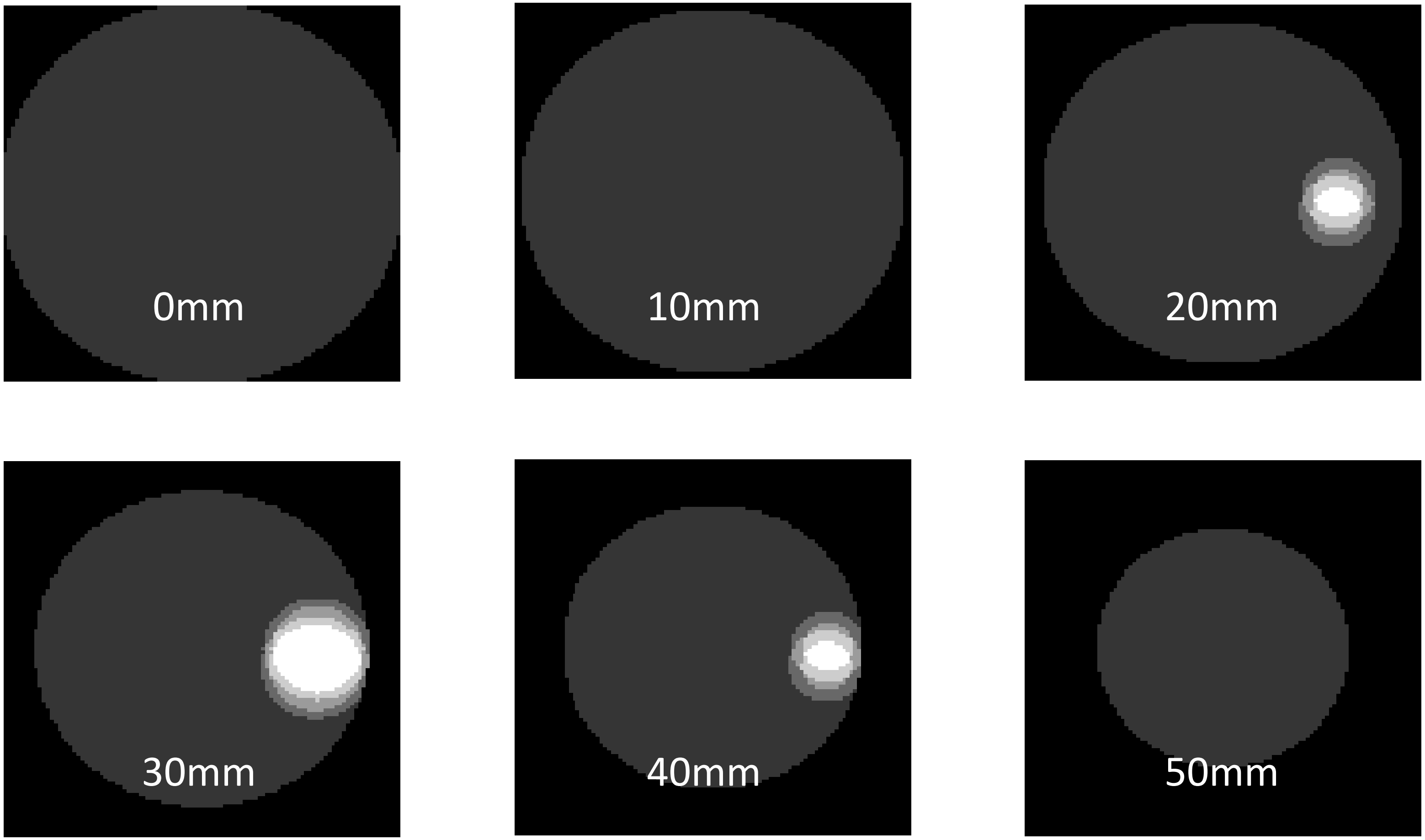
- Significant differences in motion field due to inclusion – More would be expected at higher contrast in stiffness (bigger "rock in the water")
- Very evident in Imag part means Phase shift is very discontinuous around inclusion
- **Provides the idea that initial screening might be made online and without reconstruction based only on surface motion – A first screen (of 2)**

Can we see the motion?

- If the movie works you can see the different phase around the inclusion as smaller motions similar to last slide



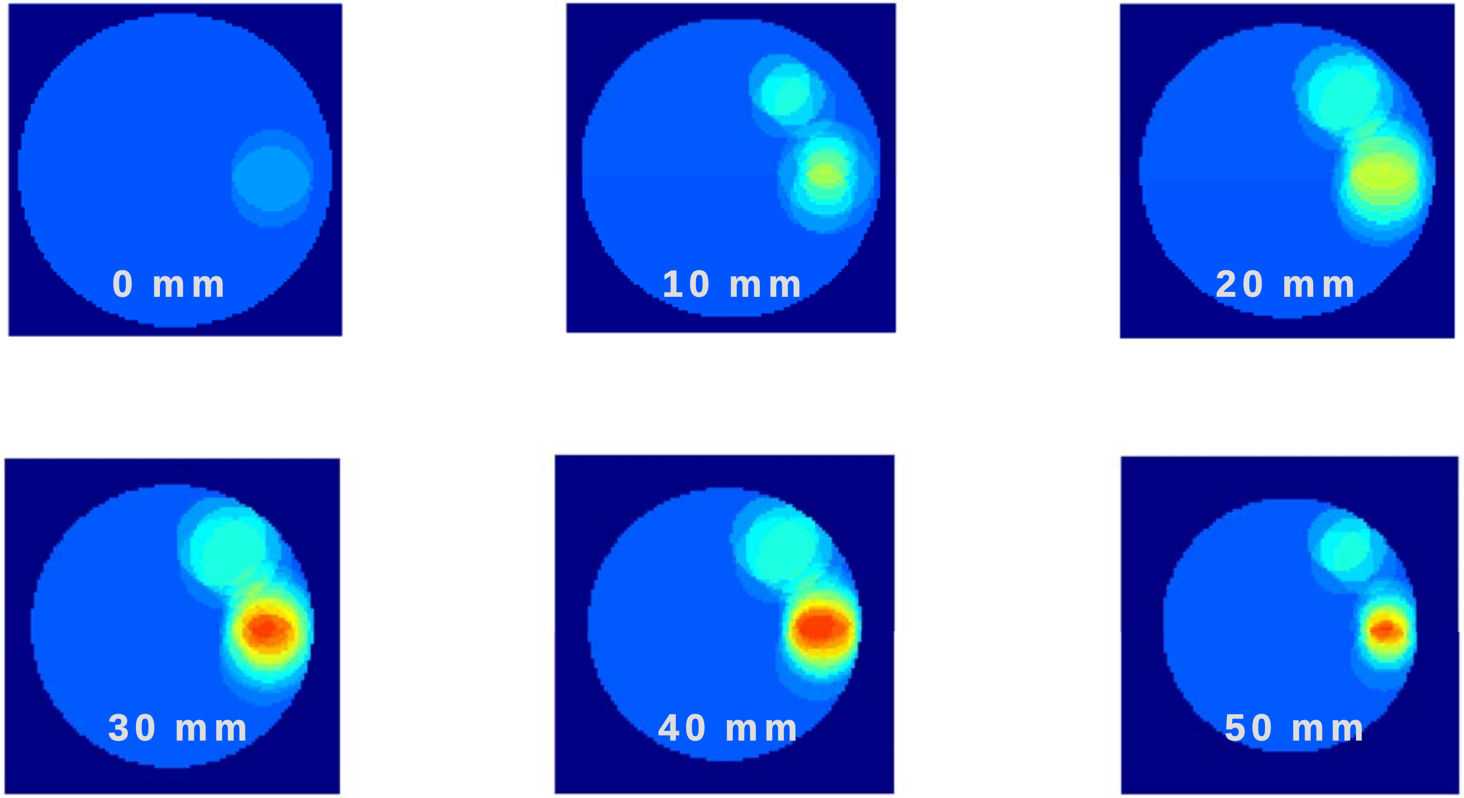
Reconstruction:
An even better view and clearer result



Another Case w/ Similar Result

(Hot off the press)

- Small inclusion actuated at 80 Hz and 0.5mm amplitude



Many Questions … and Final Thoughts

- Did we meet our goals? How might this be used? The Future!?
- Overall conclusions ..

Arthurs Pass, Canterbury, S. Island

New Brighton Beach and Pier, Christchurch

So, it seems to work....
But, did we meet our goals? … Yes!

- System = low-cost precision actuator + DSP chips + digital CCDs
  - All off the shelf
  - All very low cost
  - Would expect system components to cost $500-1000 or less
  - All silicon technologies that will scale/improve over time (for free)
- No X-Ray or radiation dose → earlier and more frequent screening
- No compression = “comfort” = should improve compliance
- Current system could fit into 1-2 suitcases = Portable
  - Portable screening might improve compliance rates
- We do experiments in <5 mins → High throughput for large numbers

First Uses: Our view

- A pre-screening tool at 0.5-1.5 cm accuracy
  - Screen yearly from any age onward
  - Abnormal test would mandate mammogram for 1-3 years at any age
- Improved compliance and portability will:
  - Target underserved populations (ethnic and distant)
  - In a hierarchy of screening, result in greater earlier detection and survival
- Low cost system and running cost means:
  - Screening cost estimated at 10% or less of mammography
  - Could screen widely for very large groups thus improving detection
- **Overall, a potential for improving screening rates *and* reducing costs, while increasing detection and survival → win, win, win scenario**

A Brief Summary

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- DIET is an all new approach to breast cancer screening that offers several potential advantages over current methods
- Initial simulation and experimental proof of concept studies showed that it might be possible to achieve realistic screening (~1cm inclusion size detection)
- The main imaging and reconstruction steps are technologically challenging
- Initial proof of concept experiments on silicone phantoms have been successful in identifying inclusions both via reconstruction and from disturbances in surface motion

The Future!
In the order we may see it…

- Use of boundary element methods in reconstruction (now)
- Extending phantom studies (this year)
  - More realistic shapes (from castings)
  - Greater inclusion contrast if possible with silicone
- Initial "ergonomic" clinical studies (this year?)
  - Can we build a simple prototype anyone would even remotely trust themselves to try?!?
- Eventual simple (known case) clinical tests on a pre^{x} (where x<y) prototype (the further future)

LIEGE IMAGE DAYS
March 12-13, 2008
Liège, Belgium
MEDICAL IMAGING

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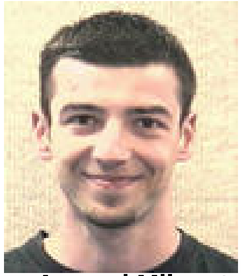
Acknowledgements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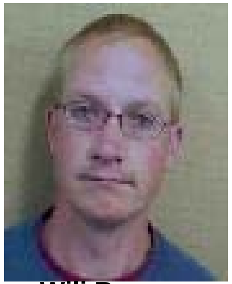
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Fabrice Jandet


Edouard Ravni


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Stefan Wortmann


DIET Project Team 2004


DIET Project Team 2005


Shig Kinoshita


Dr. Eli Van Houten


Dr. Chris Hann

BOUNDARY lifesciences


Questions?