

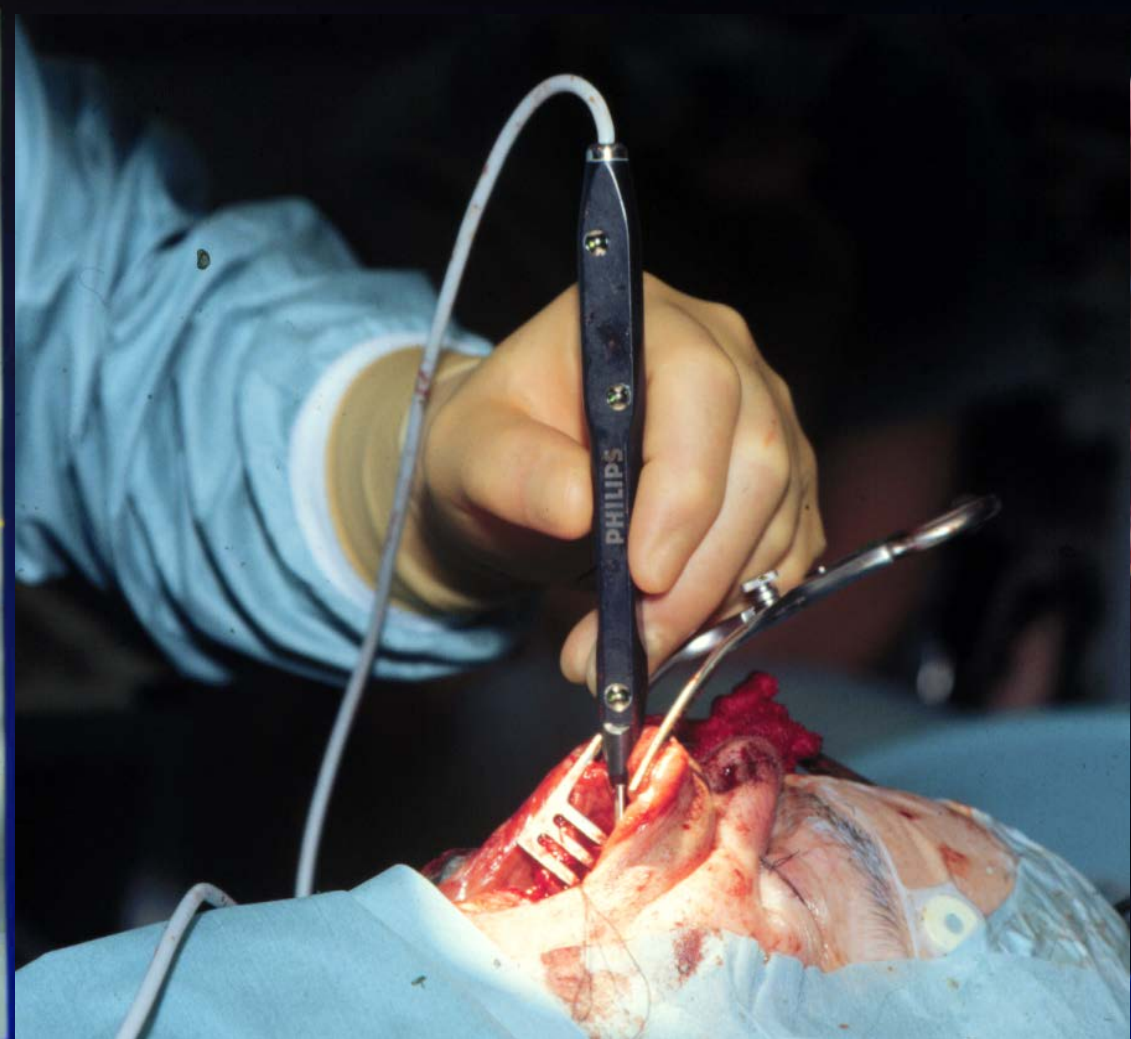
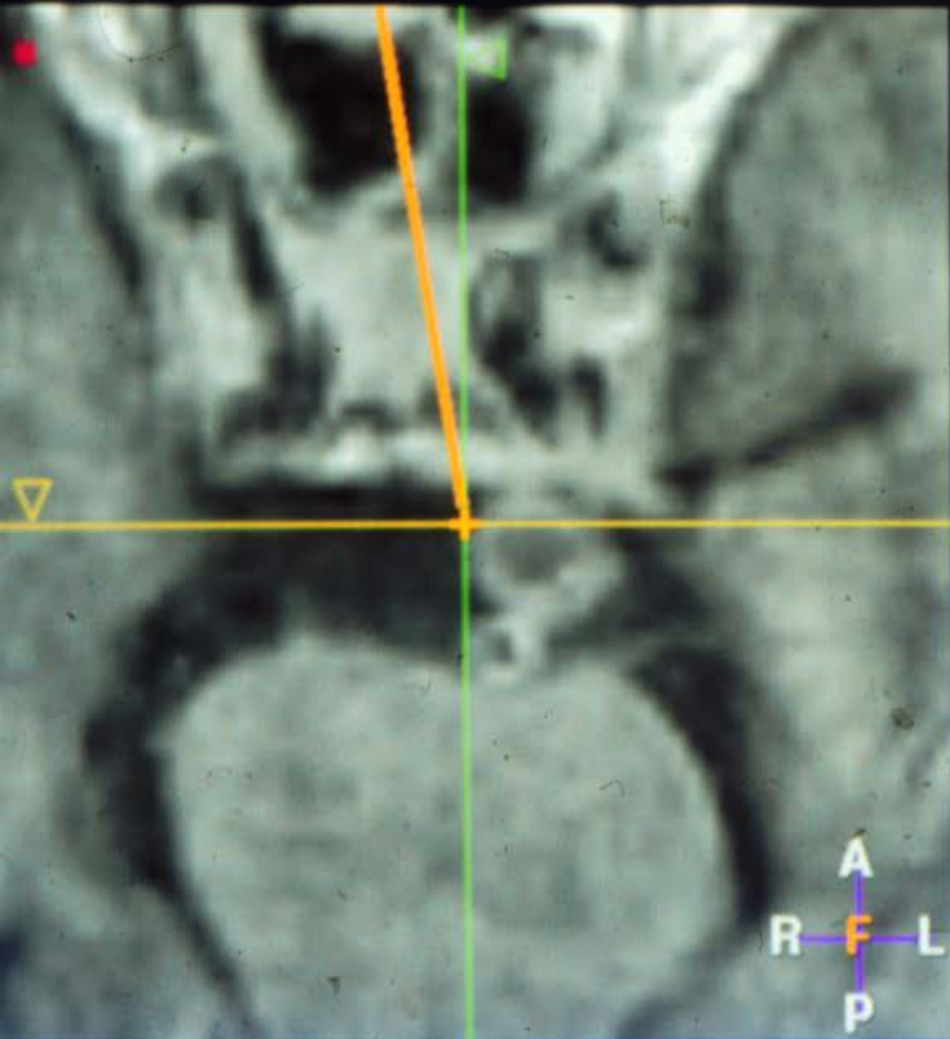
# Multi-Scale Image-Guided Interventions

*Dave Hawkes,*  
*[d.hawkes@ucl.ac.uk](mailto:d.hawkes@ucl.ac.uk)*  
*[www.ucl.ac.uk/cmhc](http://www.ucl.ac.uk/cmhc)*



# Tracked localiser in use during maxillotomy

*Alan Crockard, National Hospital, Queen Square*



Overlay of 3D preoperative image data  
on stereo field of view of  
binocular operating microscope

*(Edwards et al  
IEEE-Trans Med Imag 2000)*



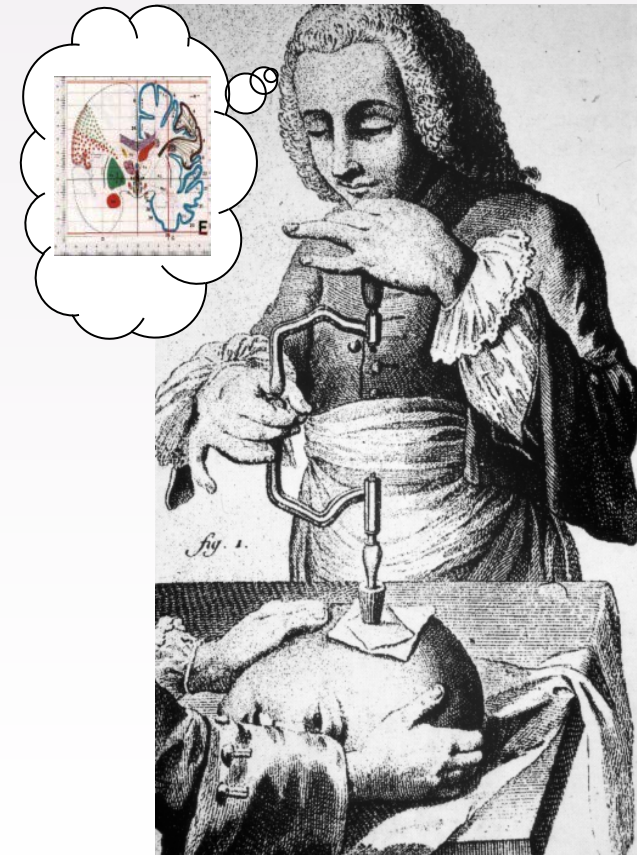
# Multi-scale image guided interventions in cancer treatment

- Target identification
- Target location and verification
- Target destruction with minimal collateral damage



# Spatial correspondence and tissue characterisation in image guided interventions

- Tissue microstructure, pre- and intra-operatively (In-vivo “histology”)
- Maintaining a target accuracy of ~1mm in presence of soft tissue deformation
  - Neurosurgery
  - Patient stratification and focal therapy in prostate and breast cancer
  - Compensation for tissue deformation in the prostate or breast and respiratory motion in the liver and lung.



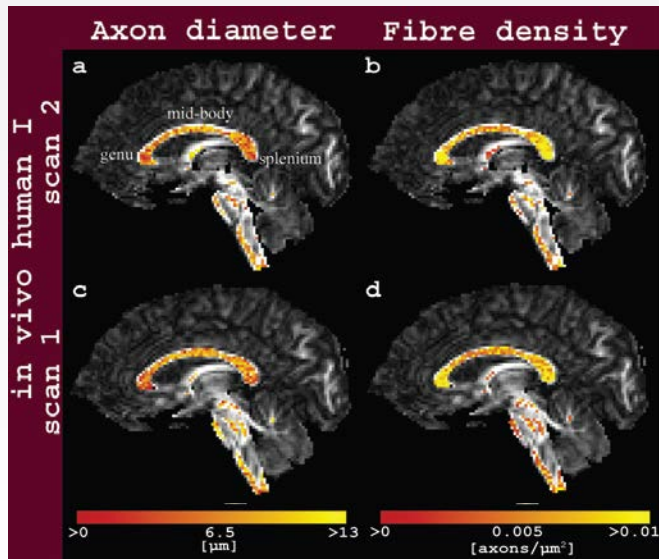
## MR advances in tissue microstructure, physiology and metabolism in cancer

- Glucose CEST (Walker-Samuel et al, Nature Med 2013)
- C-13 Pyruvate etc with Hyperpolarised MR
- Tissue Microstructure with diffusion MRI – VERDICT (Panagiotaki et al Cancer Research 2013)
  - Exploring assessment of the tissue heterogeneity (the phenotype) related to the genetic heterogeneity

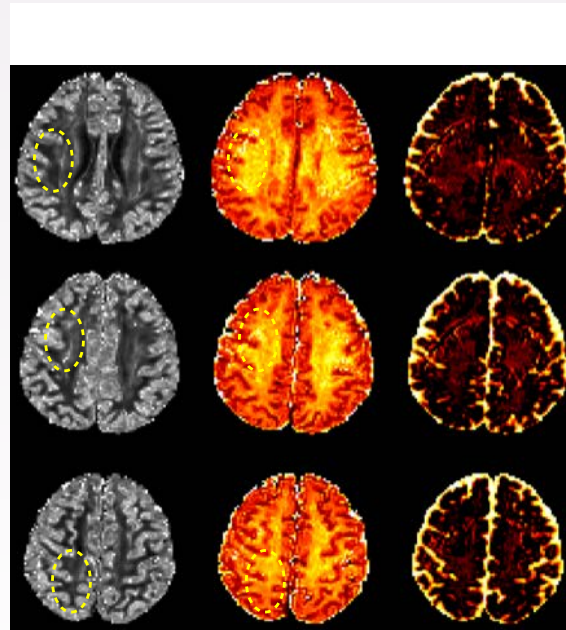
# iMRI facility at NHNN



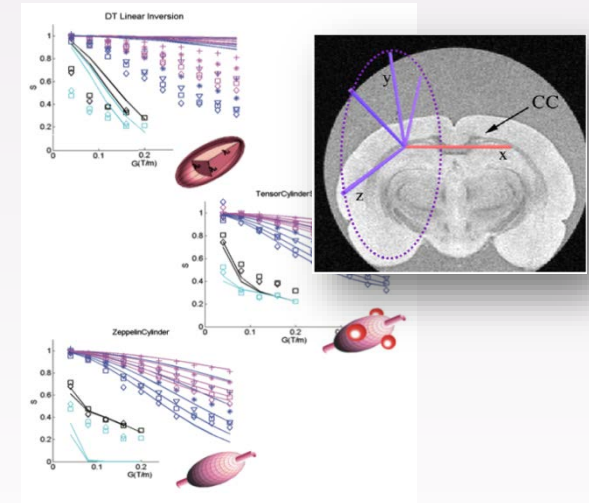
Alexander et al  
NeuroImage 2010



Zhang et al  
NeuroImage 2012



Panagiotaki et al  
NeuroImage 2012



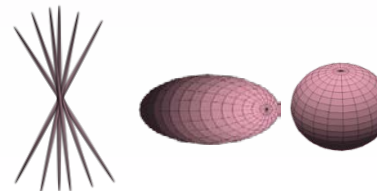
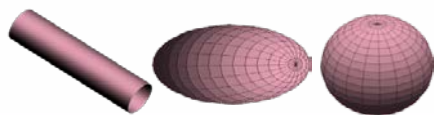
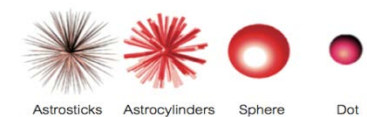
### Intra-axonal compartments



### Extra-axonal compartments



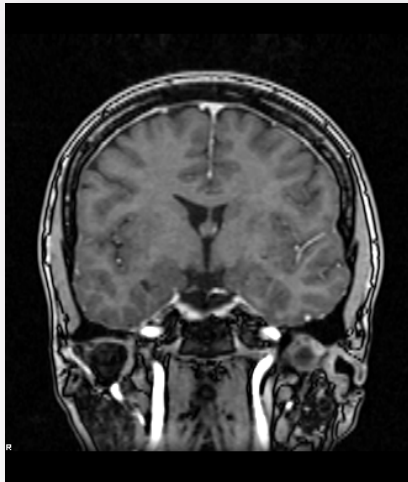
### Isotropic restriction



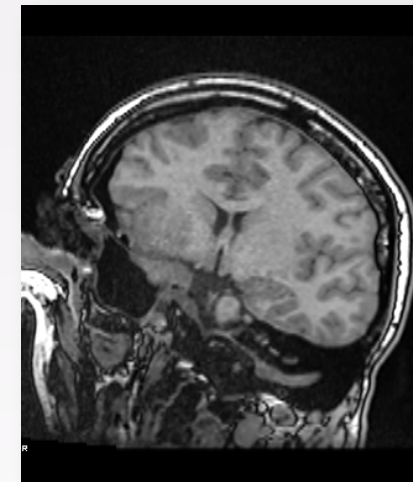
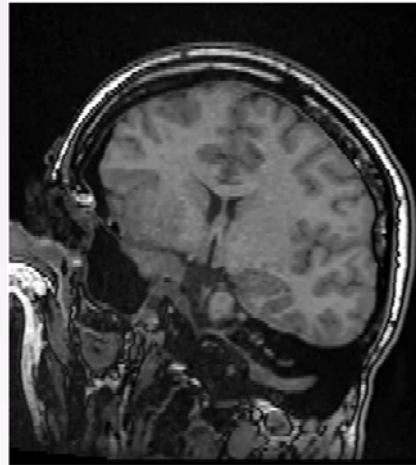


# Planning and guiding avoidance of optic radiation

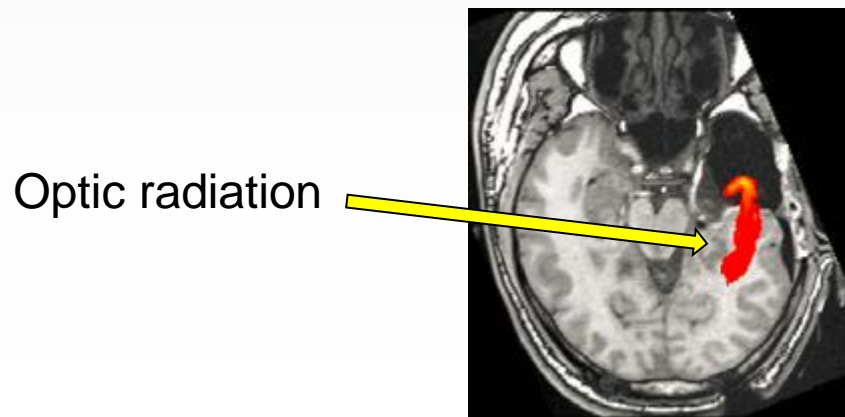
Daga, Duncan, Ourselin et al IEEE TMI 2012



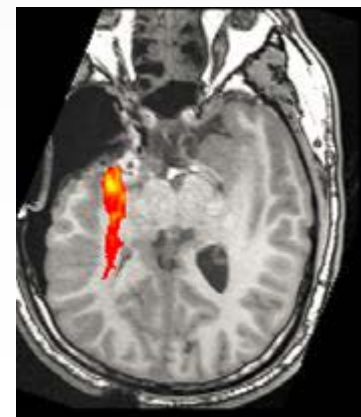
**Pre-operative  
image and plan**



**Intra-operative  
image**



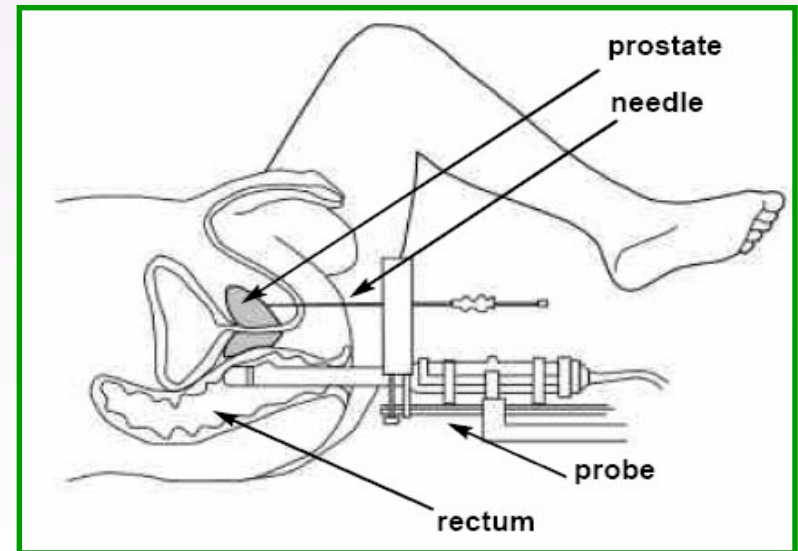
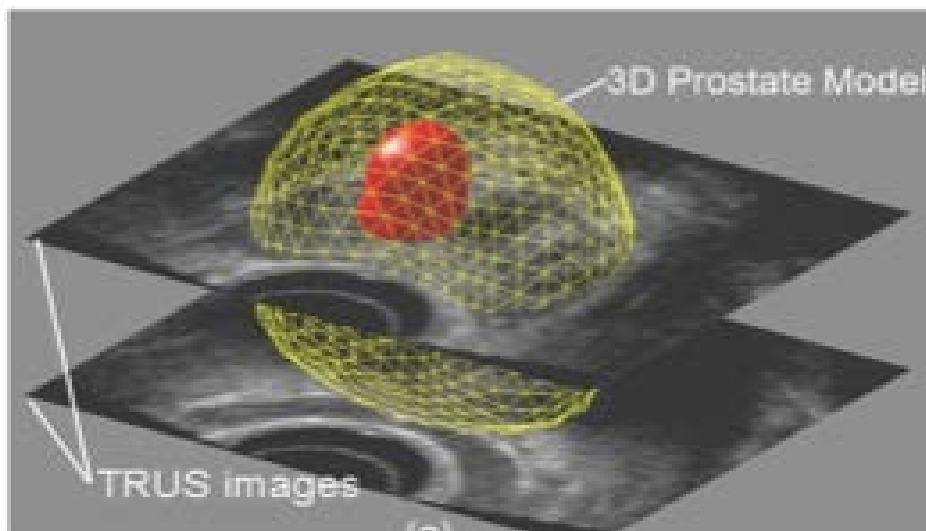
27% visual field loss

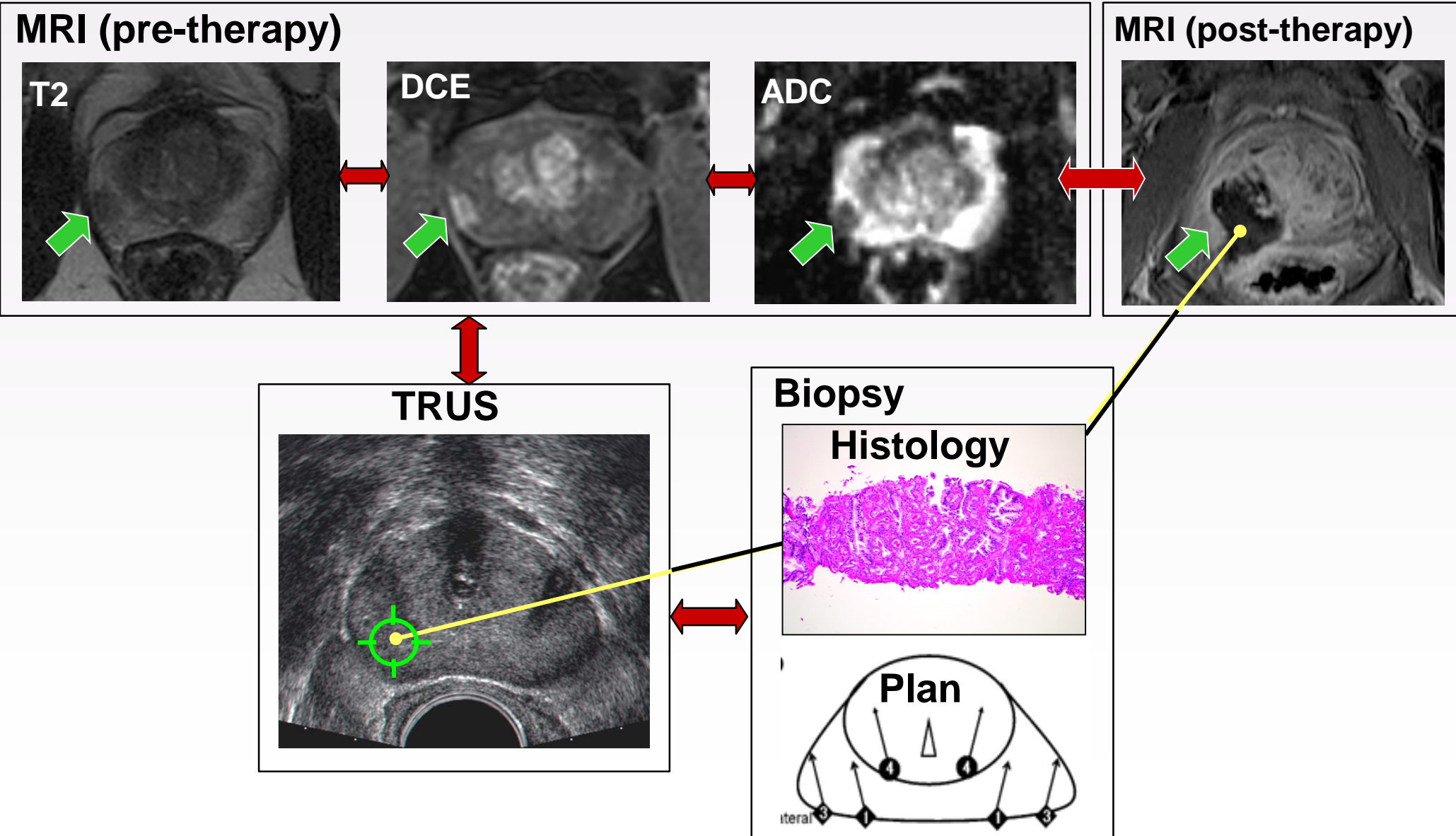


No visual field loss

# Prostate Cancer: Image guided biopsy and focal ablation

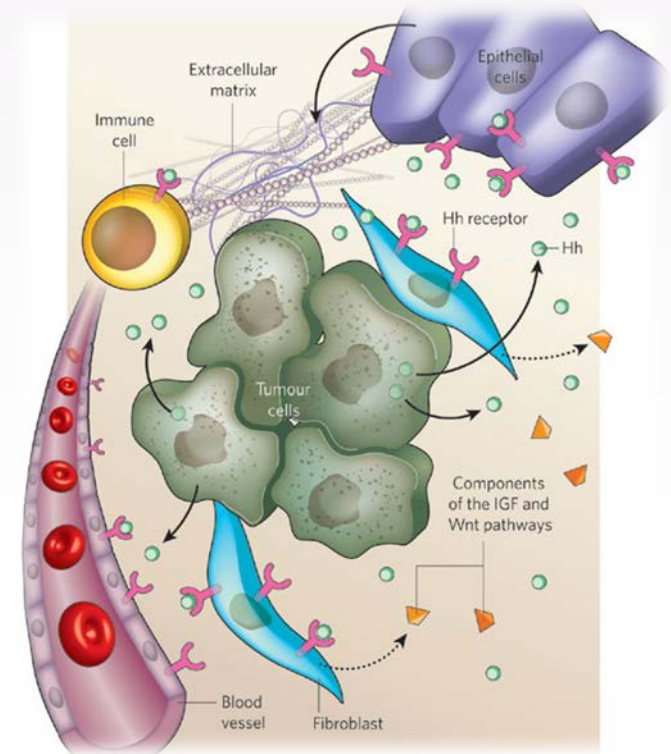
*Mark Emberton, Hash Ahmed, Dean Barratt, Yipeng Hu*





- Signal comes from
  - intracellular water trapped inside cells.
  - extracellular, non-vascular water adjacent to, but outside cells and blood vessels.
  - water in blood undergoing microcirculation in the capillary network.

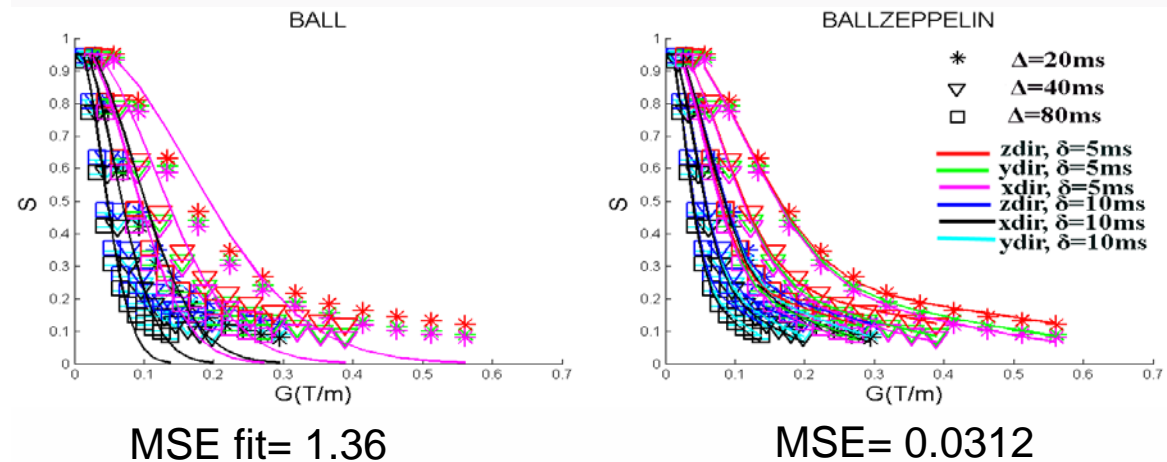
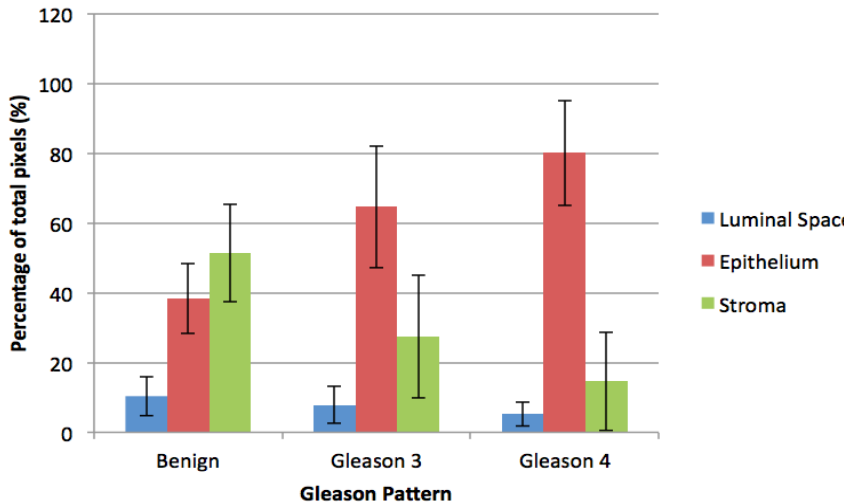
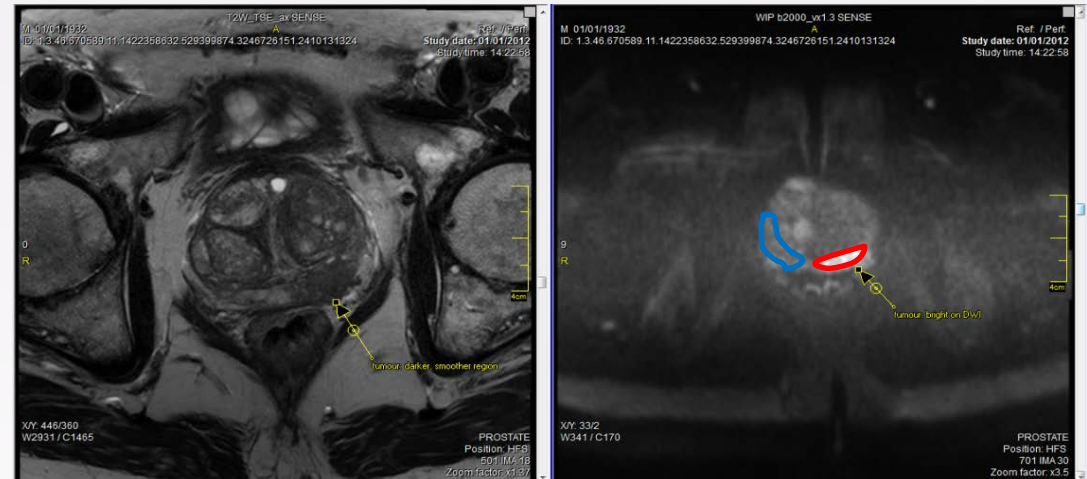
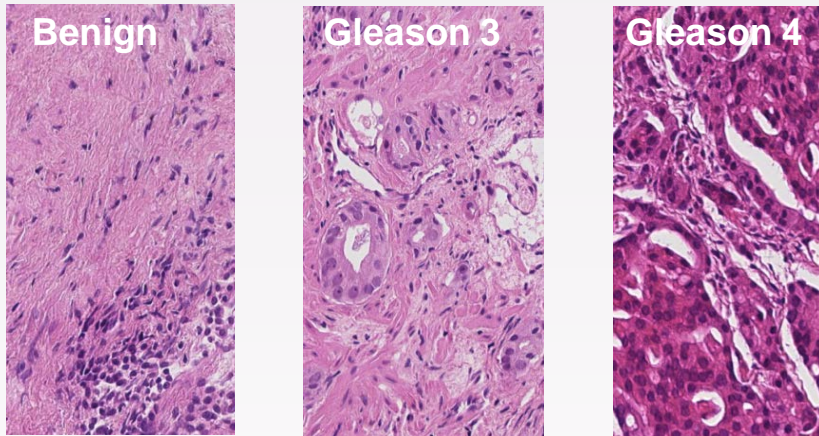
$$S = \sum_{i=1}^3 f_i S_i \quad i, 0 \leq f_i \leq 1, \sum_{i=1}^3 f_i = 1.$$



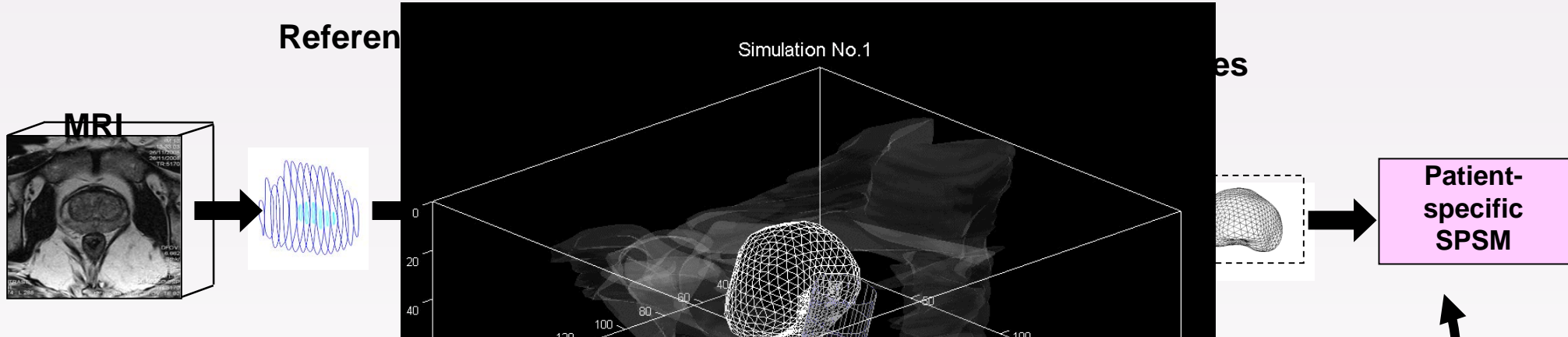
# Microcompartment MRI-DW Imaging and modelling

## Non-invasive Gleason Grading of Prostate Cancer

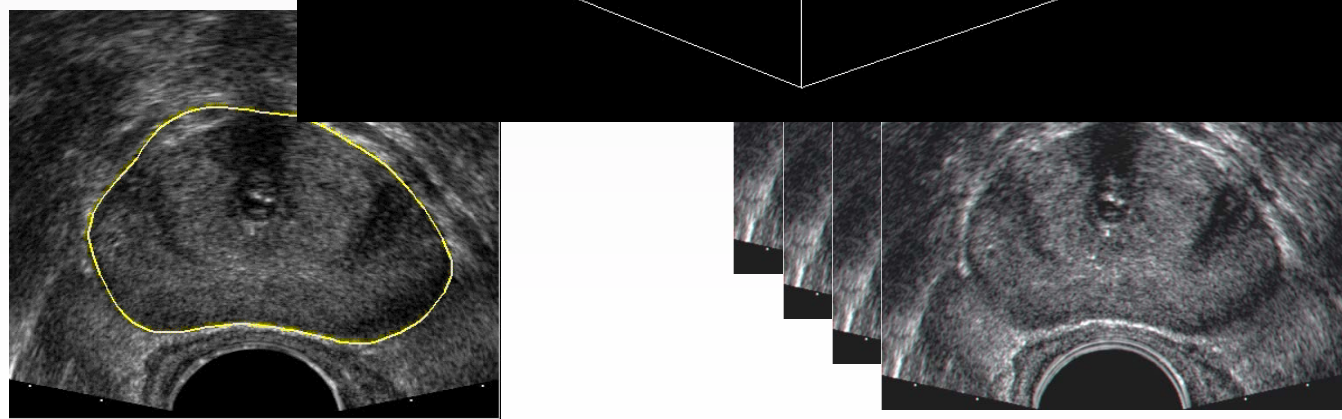
20



## PRE-PROCEDURE

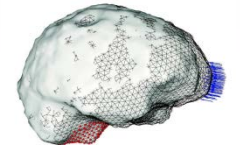


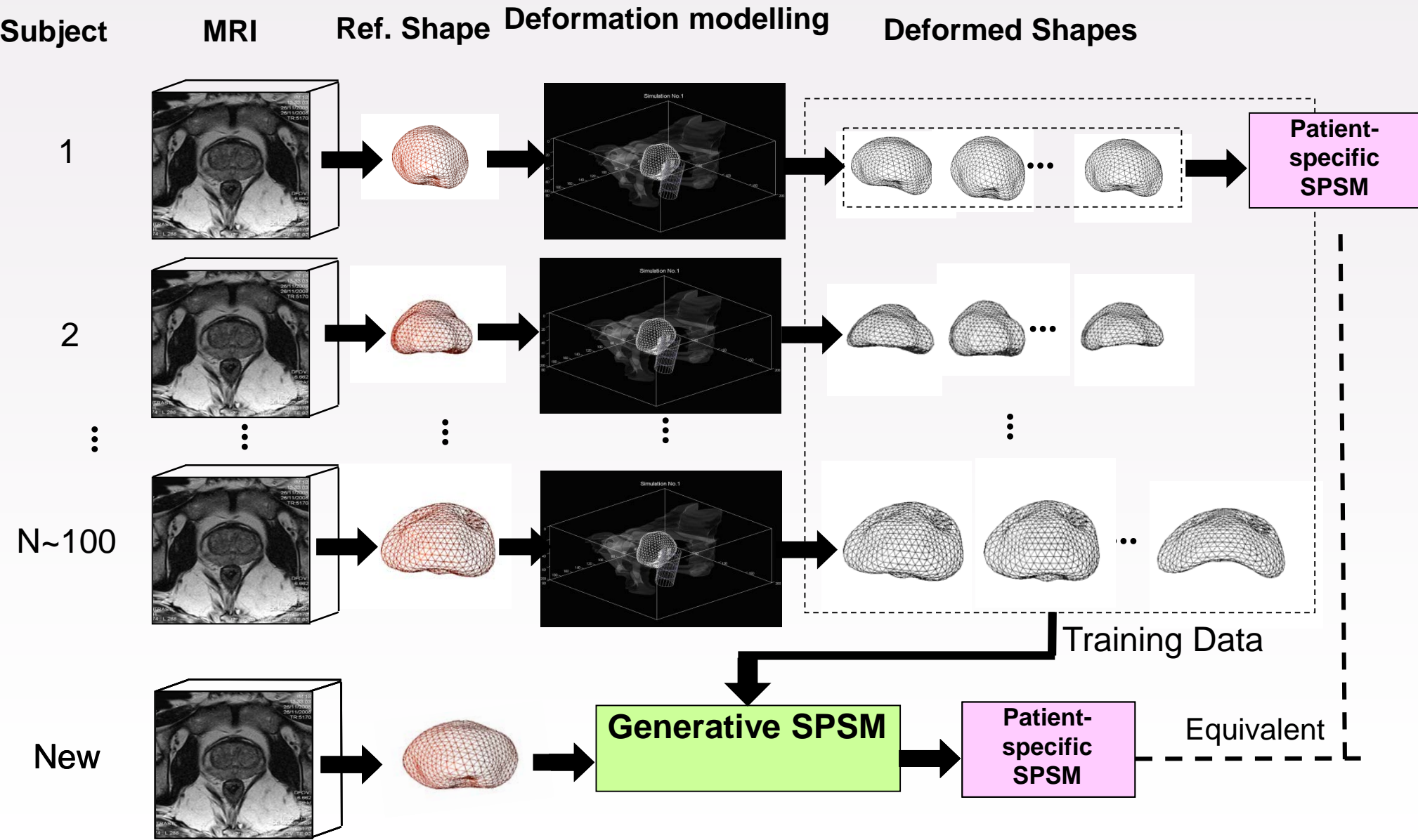
## DURING PROCEDURE



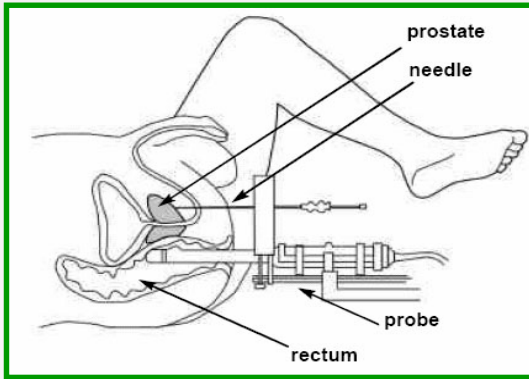
Register

NiftySim

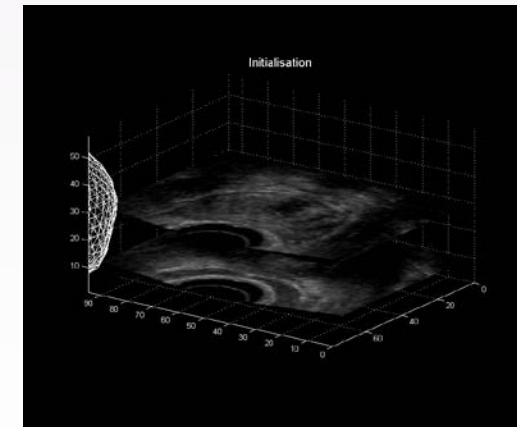
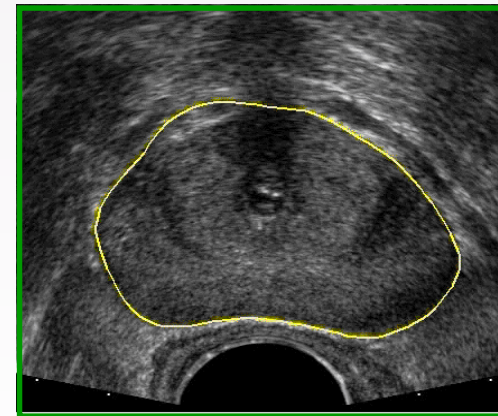
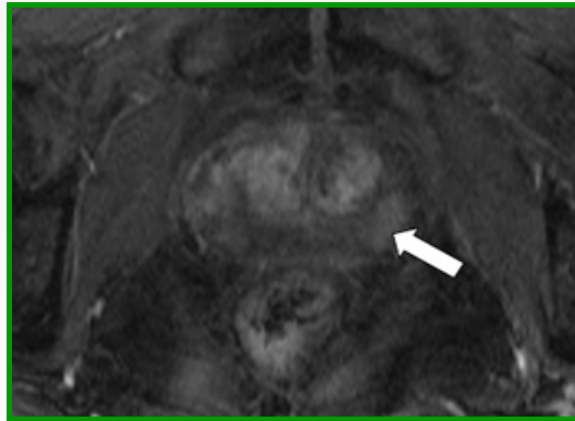




# Image Directed Biopsy and Partial Prostate Ablation



- Multimodal MR, registration and tissue classification used to delineate focal, high grade cancer
- Cancer accurately targeted for biopsy and hence focal therapy (PDT or HIFU) delivered (via needle or transrectally) with transrectal ultrasound guidance
- Critical structures avoided.



**Statistical motion model built from 100's of FEM examples**

Capturing variation in pelvic anatomy, insufflation, mechanical properties

*Hu Y, et al IEEE-tMI, 2011 + patent  
Hu y et al MedIA 2012*

Model based non-rigid registration,  
TRE 5 patients, 48 landmarks  
1.8mm (RMS) +/- 0.7mm

EPSRC, NIHR i4i, Wellcome DoH HICF, clinical trial commenced, > 100 patients



# Screening, diagnosis and treatment of breast cancer



X-ray mammography screening



Diagnostic MRI



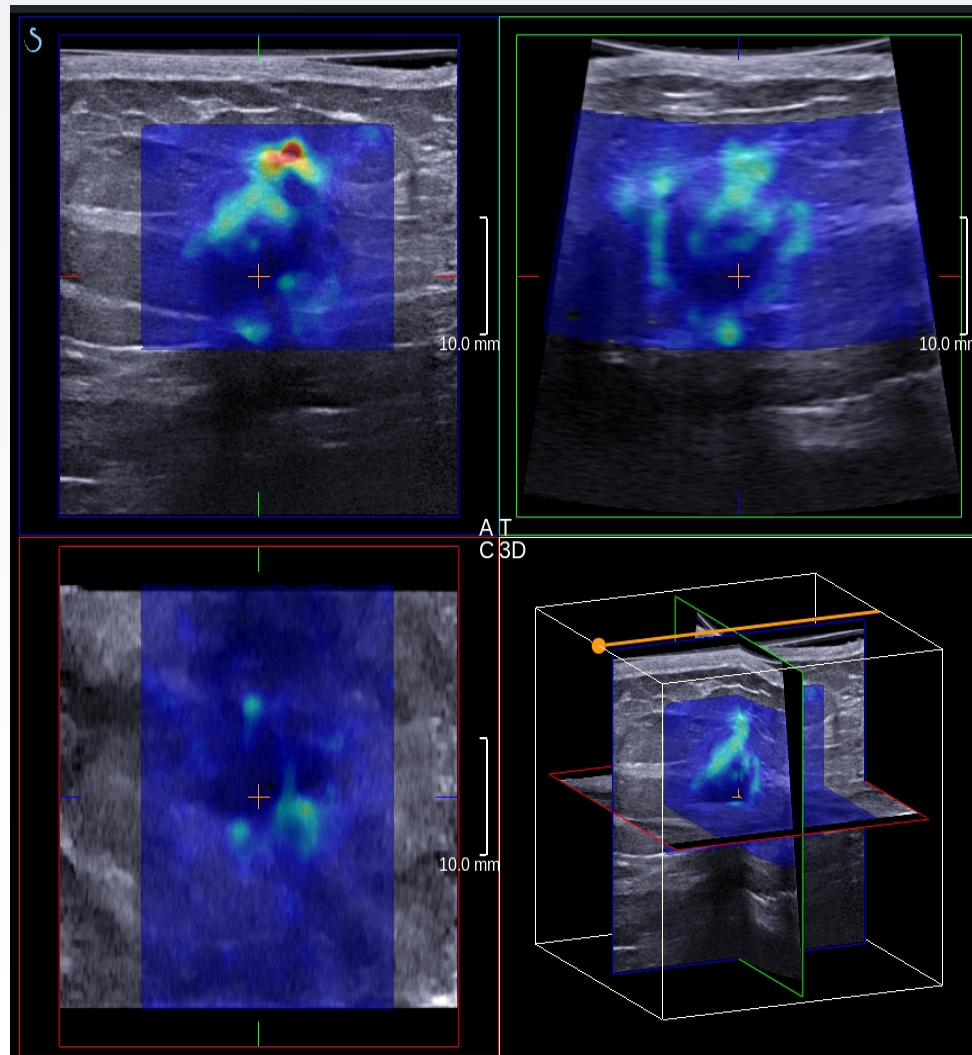
Image guided lumpectomy

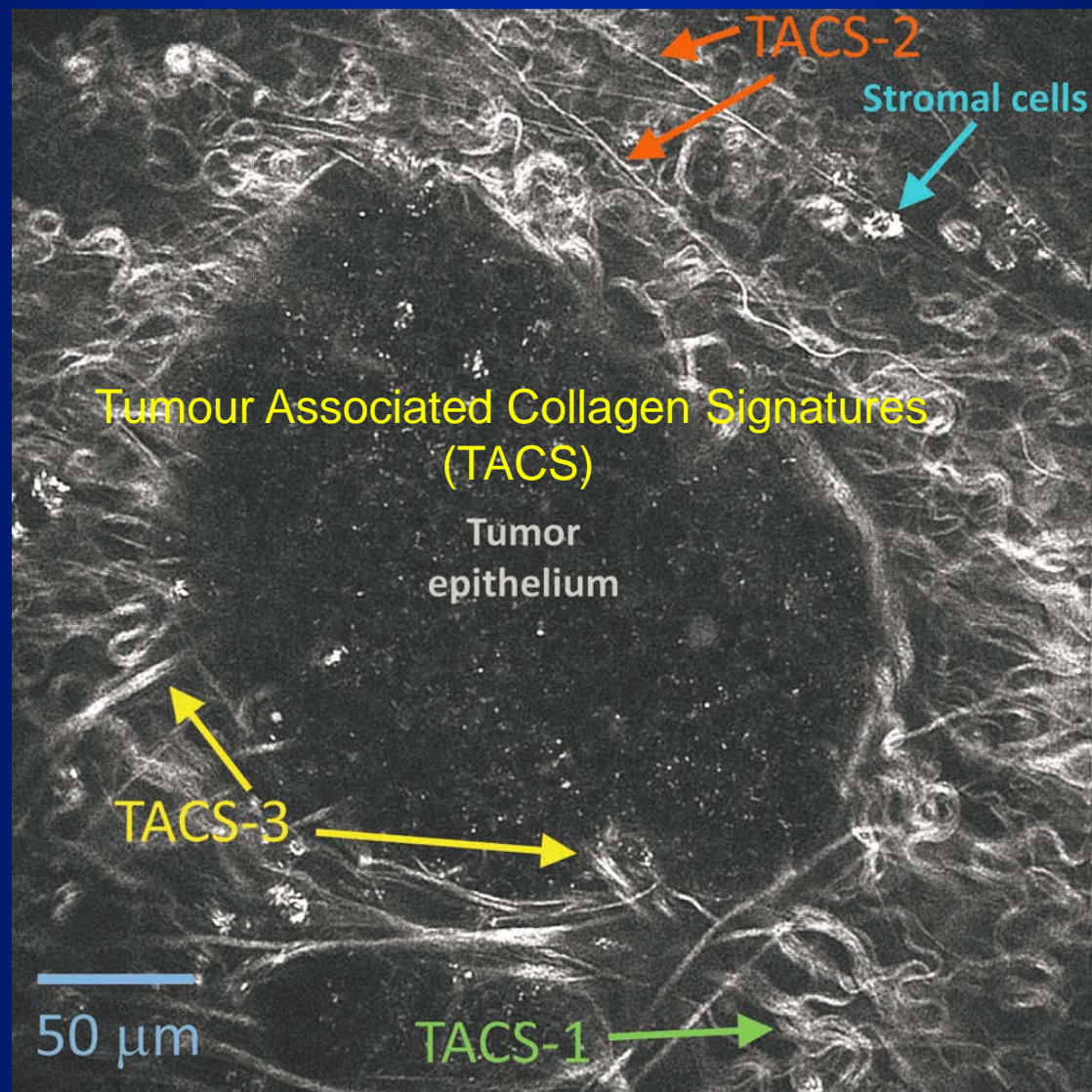
## Over diagnosis of breast cancer

- Wolfe suggests dense breast has 37x greater risk than least dense grade [1976]
- 2 – 6 fold increase in breast cancer risk with breast density (Boyd et al, JNCI, 1995)
- Mammographic density increase associated with increase in cellularity but primarily increase in collagen
- Evidence that in symptomatic patients peritumoral stromal tissue is stiffer (Evans et al 2012)

# 3D ultrasound shearwave

*(Courtesy of Prof Andy Evans, Dundee)*





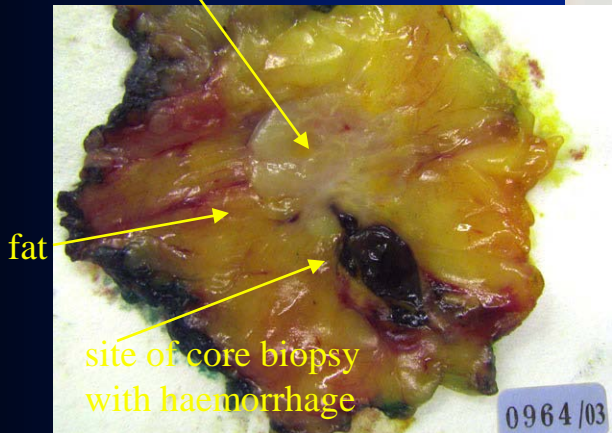
- “Potential for application during surgery and biopsy ... can be performed on fresh, unstained tissue”
- “Changes in tensional forces and extracellular matrix stiffness could be used to define disease progression”

*Conklin and Keeley, Cell Adhesion and Migration(2012), 6:3, 249-260*

invasive breast cancer

x250

invasive carcinoma



fat

site of core biopsy with haemorrhage

0964/03

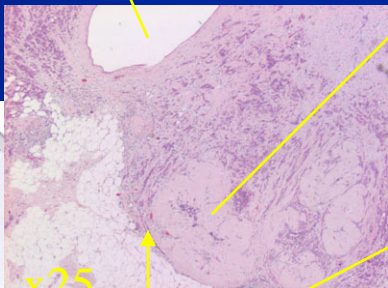
Healey Albana Unit  
Guy's Hospital  
964 G  
2003

benign cyst

x250

fibroadenoma surrounded by carcinoma

x250



central area of fibrosis

x25

fibroblasts & collagen

invasive edge of carcinoma

x25

invasive edge of carcinoma

x25

DCIS

small artery

x250

site of core biopsy granulation tissue and repair

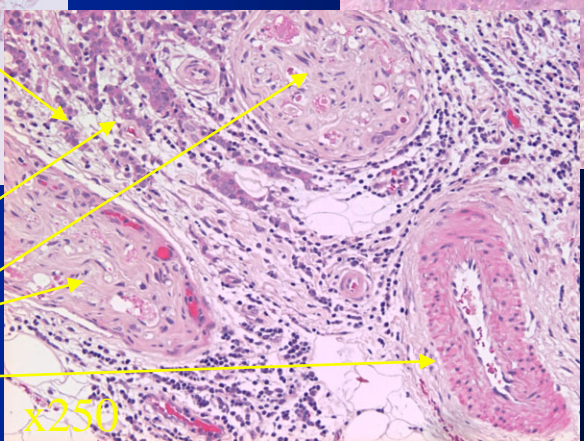
x250

tumor nerves

small artery

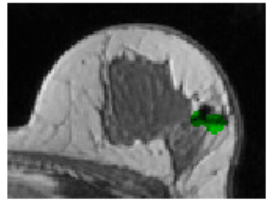
x250

x250



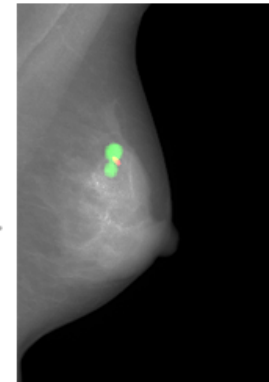
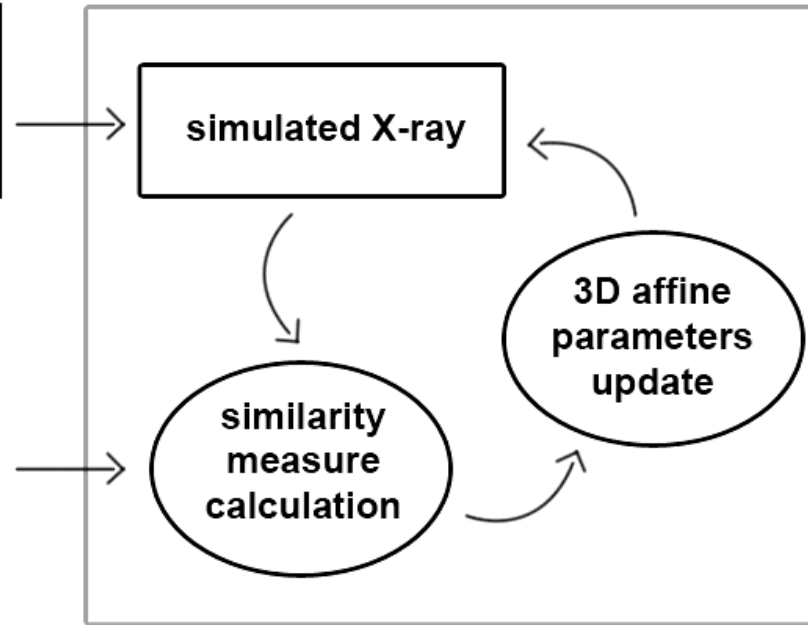
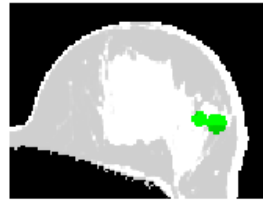
# MRI to X-ray mammography registration and visualisation

pre-contrast MRI



EM-MRF  
segmentation

X-ray attenuation



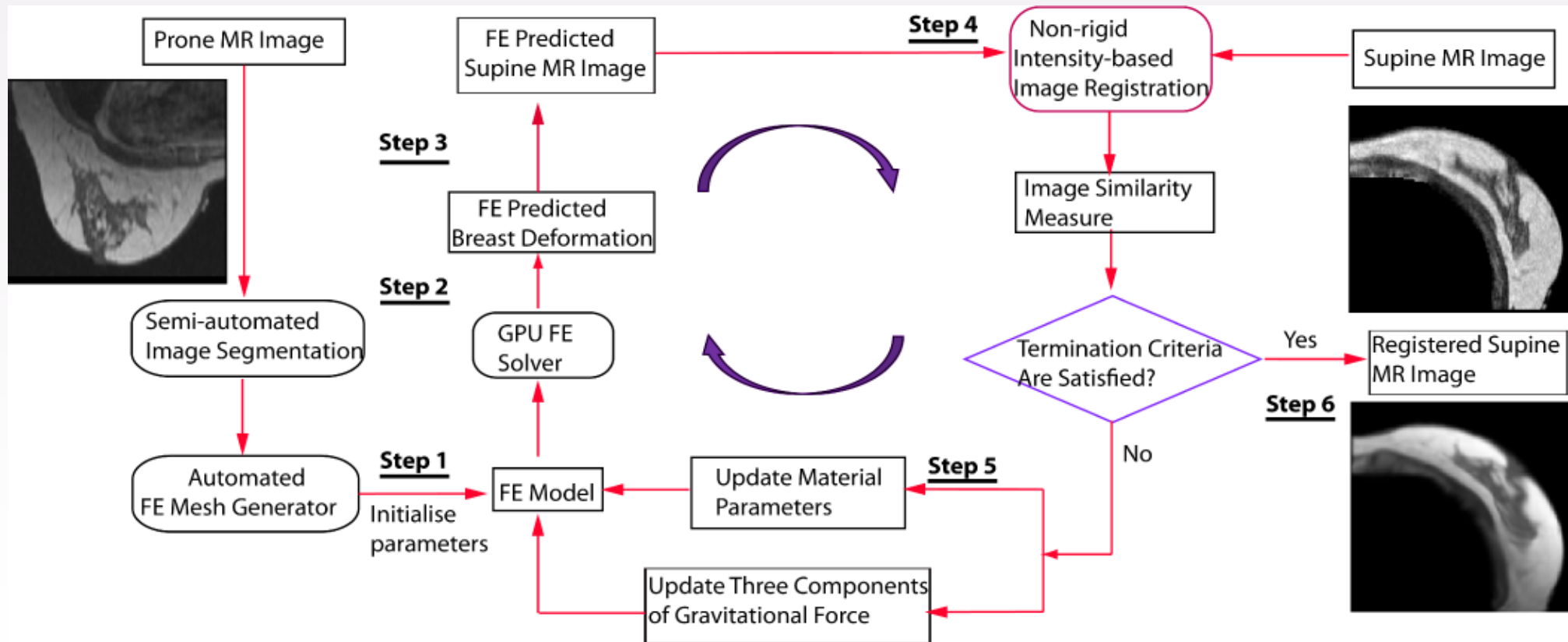
fusion of the MRI and X-ray lesion

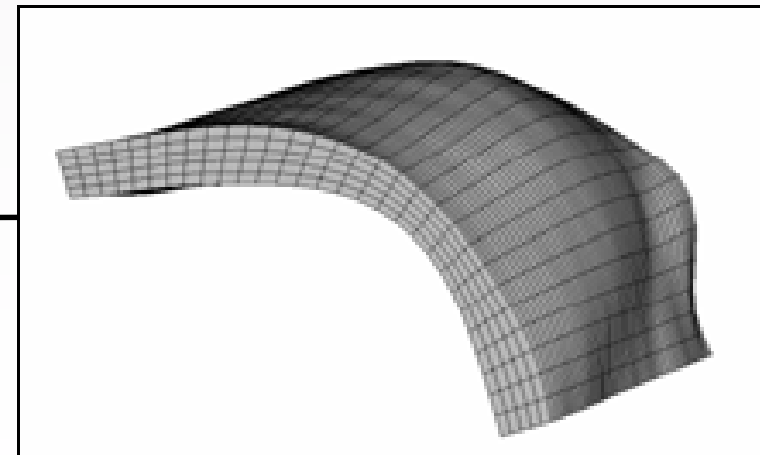
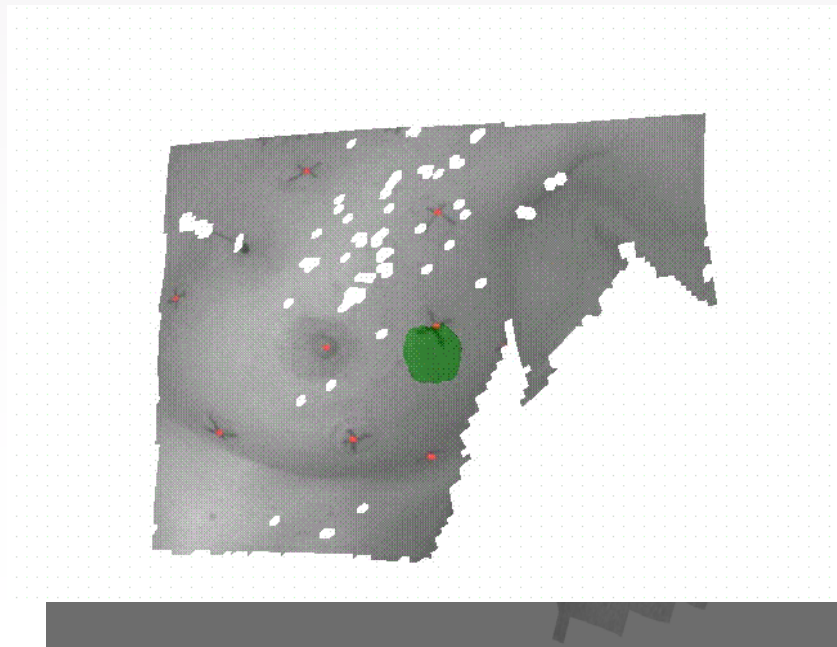
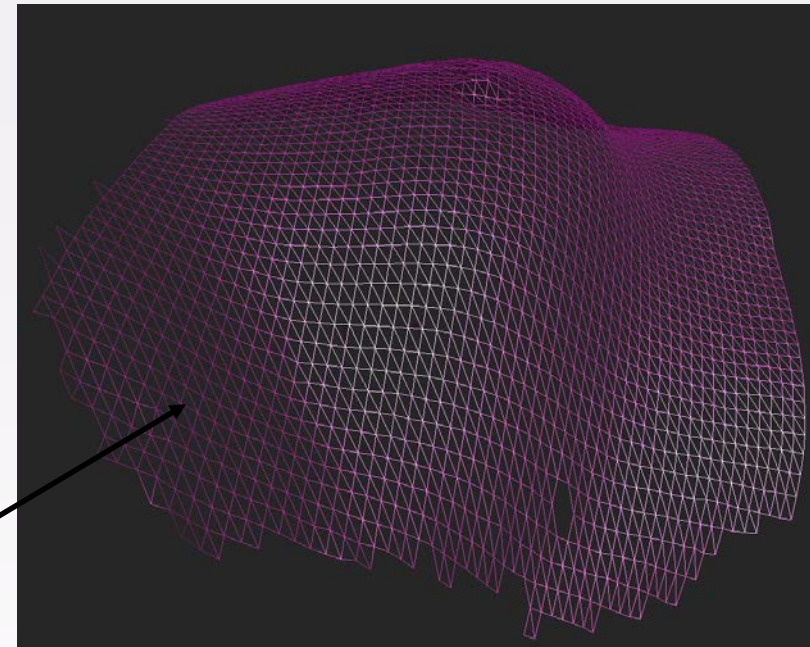
iterative registration loop

X-ray mammogram



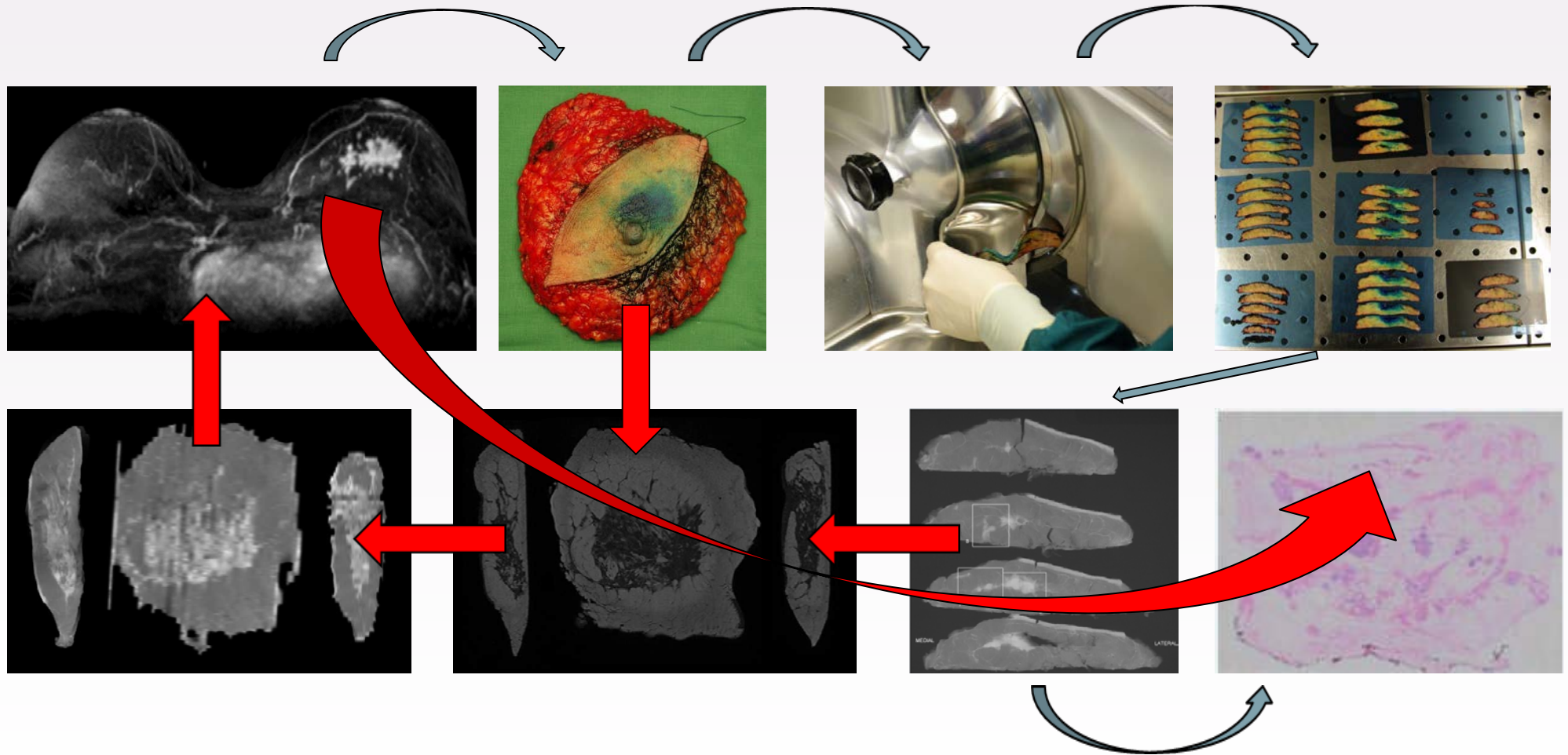
# Correspondence between prone and supine MR images of the breast







# Spatial correlation from radiological image to histology



# **Motion models to improve tissue correspondence in structures moving with the respiratory cycle**

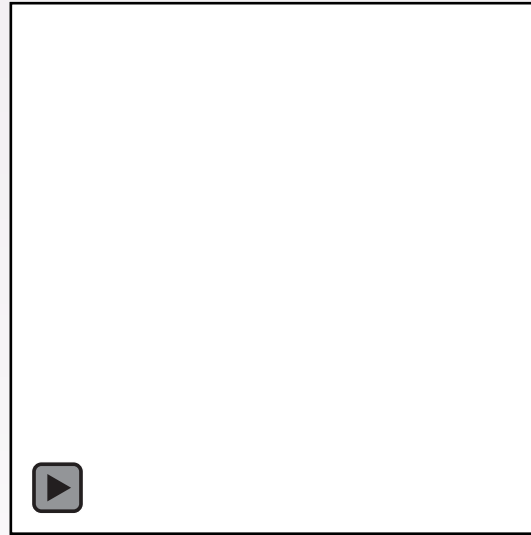
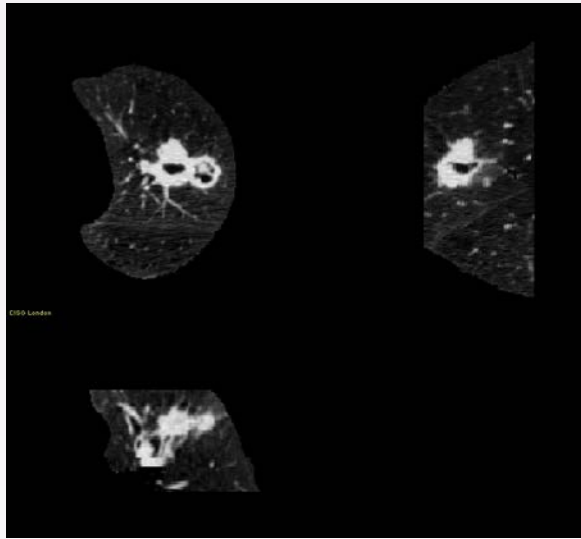
**e.g. Lung and Liver**

# Combining Image Registration, Respiratory Motion Modelling, and Motion Compensated Image Reconstruction

- Deformation of high quality static reference driven by external surrogate
  - But cannot account for changes from one day to next

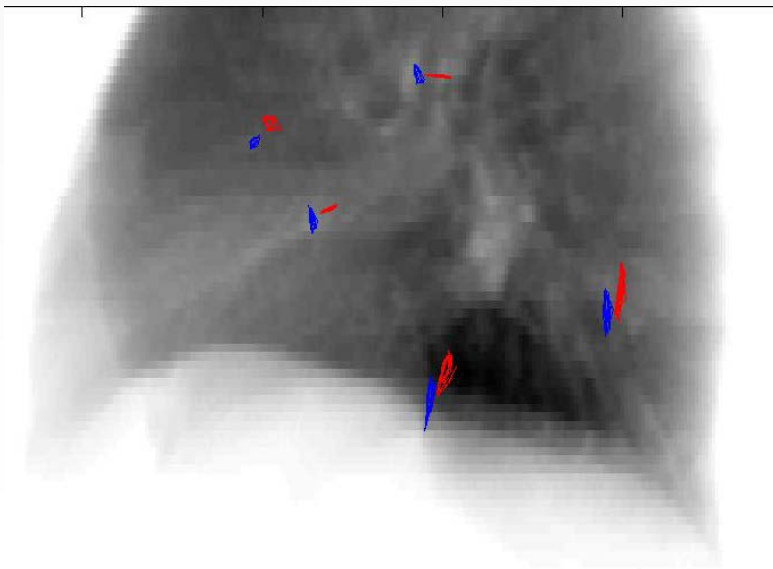
## *New paradigm*

- Simultaneous reconstruction of motion model and static reference
- Synchronisation of motion model driven by real-time partial imaging data (projections, a few slices etc.)



Model error 1.7mm (RMS), slice thickness 1.5mm

*McClelland et al Medical Physics 2006*

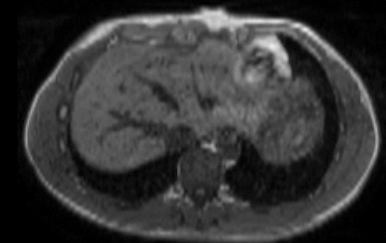
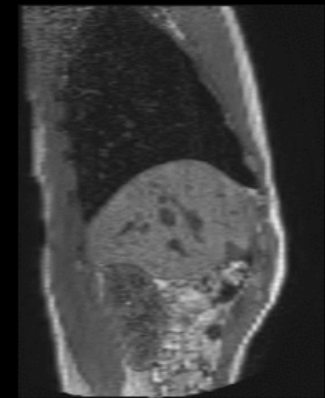
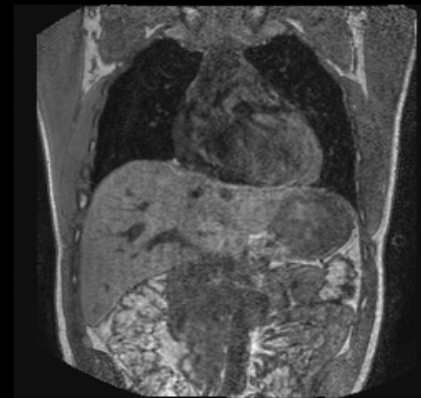
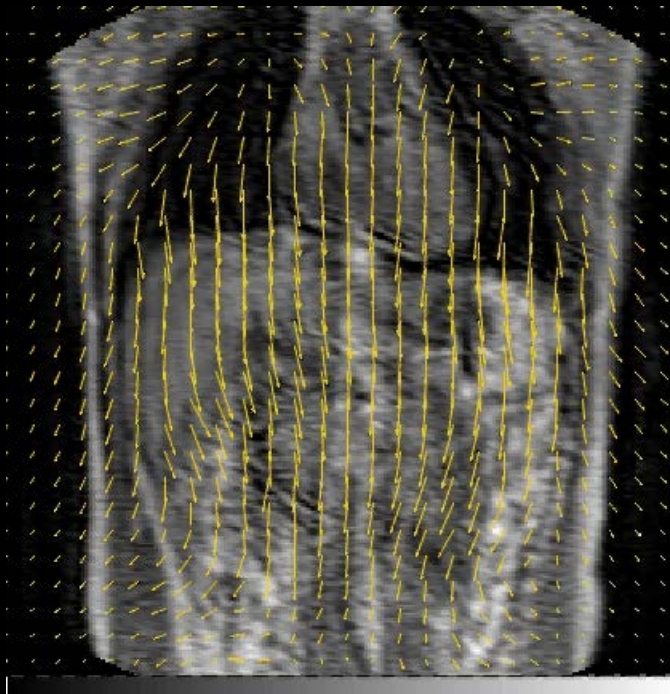


Problem: Significant interfractional variation in breathing patterns

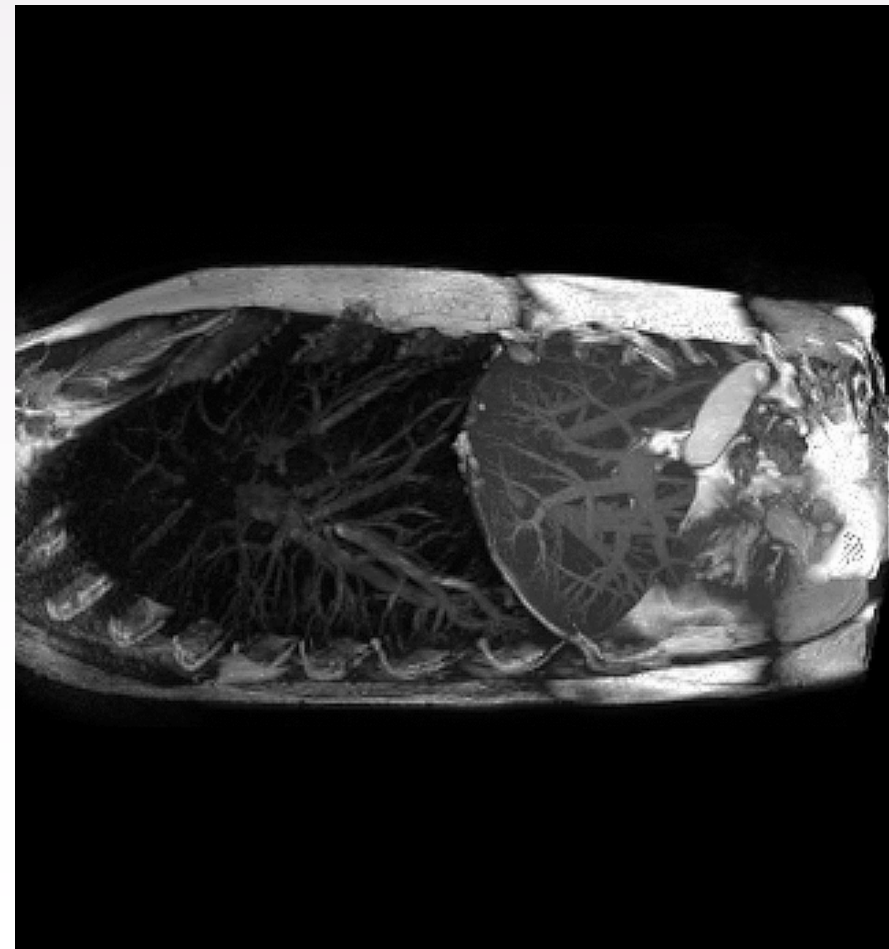
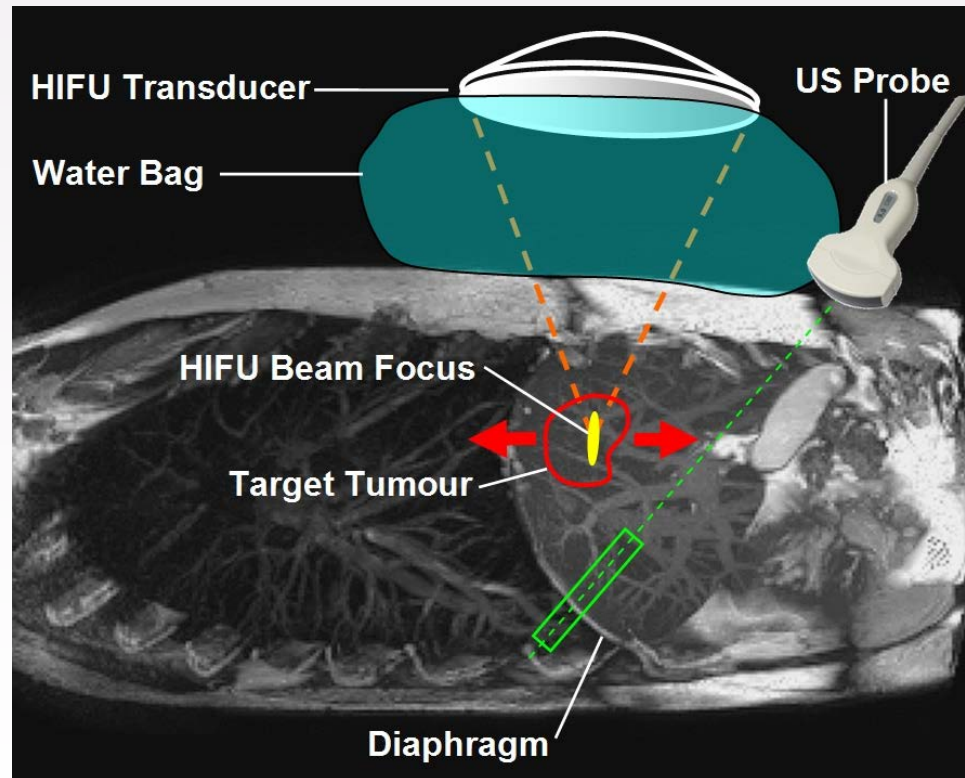
*McClelland et al Phys Med Biol 2011*

# Transcostal High Intensity Focussed Ultrasound of Lesions of the Liver

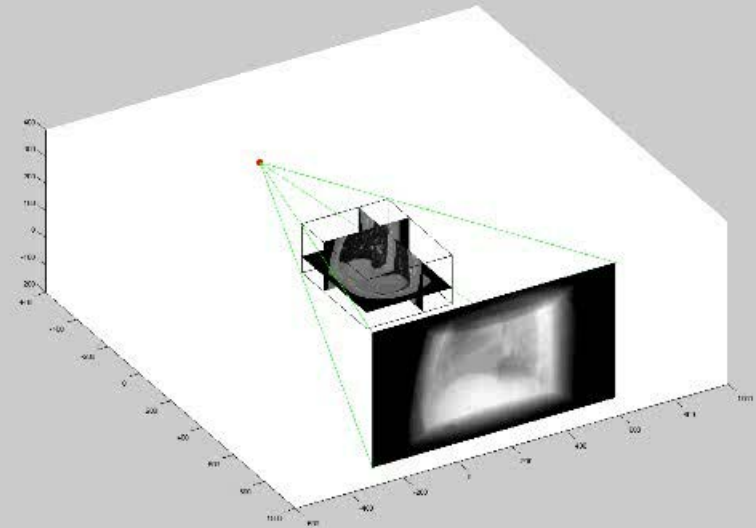
## Breathing Patterns from Real-time MR THRIVE and motion modelling



# Transcostal High Intensity Focussed Ultrasound of Lesions of the Liver



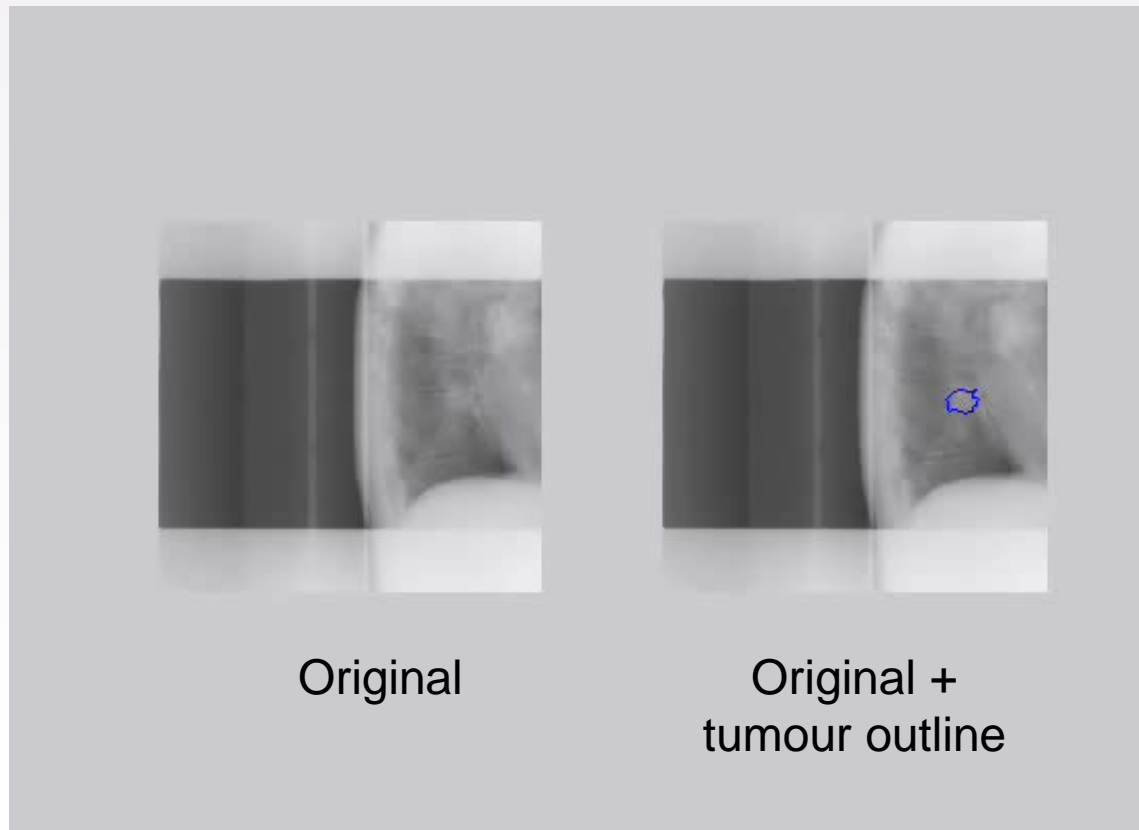
# In-room stereo video, KV and MV imaging with linac



Updated inter-fraction model from  
cone-beam CT

# Simultaneous extraction of motion parameters and motion compensated cone-beam reconstruction

Martin et al Phys Med Biol 2013

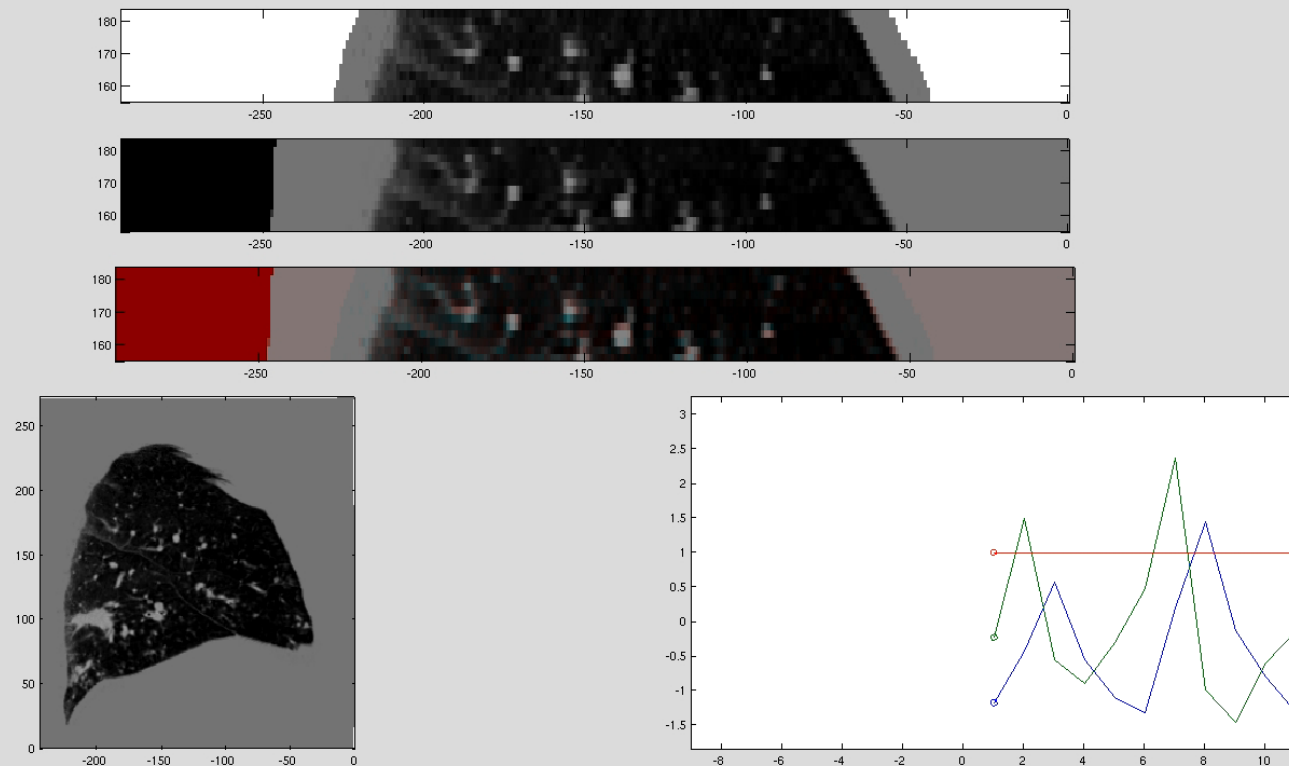


Synchronised in real-time with intra-fraction 4D  
skin surfaces (VisionRT)

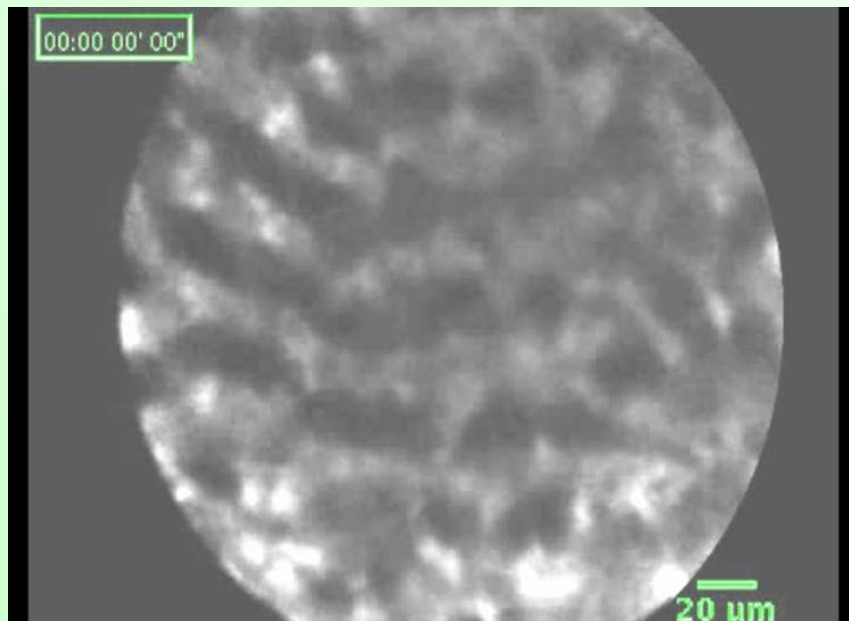


# Preliminary results on real data

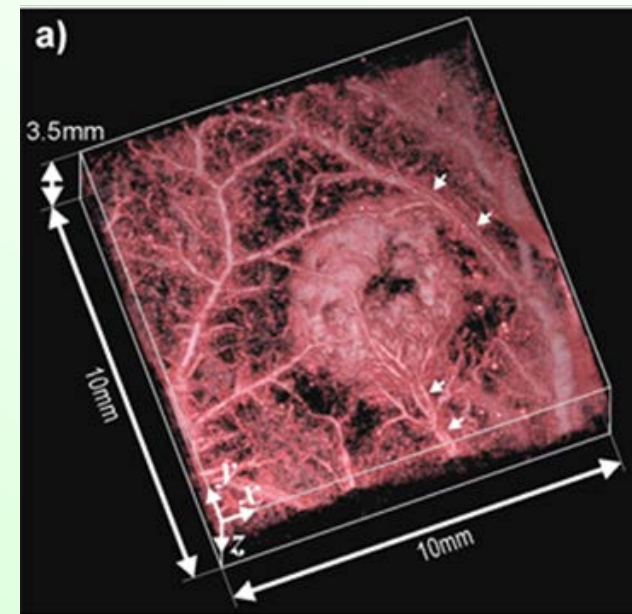
## Cine CT data – BH as static reference



# Integration with novel optical tissue interrogation methods:



Fibred microendoscopy  
(Mauna Kea Technologies)



3D photacoustics  
(Beard, Desjardins et al UCL)

# Healthcare Providers



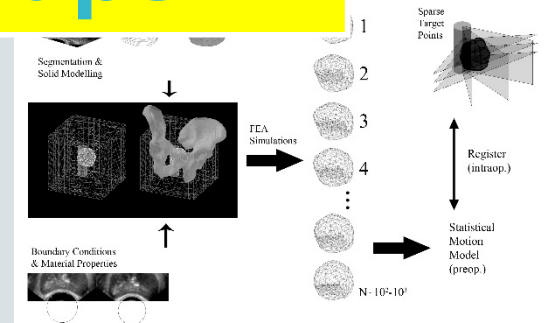
UCL Partners

Med  
Tech

Academic  
Imaging  
Groups



Compliance with regulatory  
environment  
Enabling first-in-man  
and clinical trial



# Acknowledgements

- John Hipwell, Lianghao Han, Thomy Mertzani, Seb Ourselin, Pankaj Daga, Marc Modat, Matt Clarkson, Dean Barratt, Yipeng Hu, Jamie McClelland, James Martin, Laura Panagiotaki, Danny Alexander *CMIC UCL*
- Nico Karssemeijer and the PRISM consortium
- Mark Emberton, Hash Ahmed, Shonit Punwani, *UCLH*
- John Duncan, *IoN*, Mo Keshtgar, *Royal Free Hospital*
- Andy Evans, Sarah Vinnicombe, *Dundee*
- David Landau, *Guy's & St. Thomas'*, Steve Webb, *Institute of Cancer Research*
- *EPSRC, MRC, CR-UK, TSB, NIHR, Wellcome, DoH*
- *VisionRT, Leica, Philips Medical Systems, Elekta*



*Thank you*

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*[www.ucl.ac.uk/cmhc](http://www.ucl.ac.uk/cmhc)*