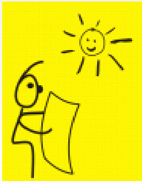
Medical Imaging and Processing.

Quantitive Medical Imaging to Extract Clinical Knowledge



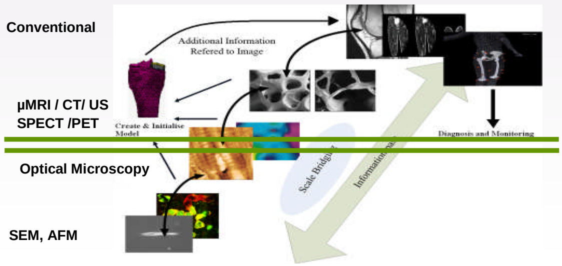
SSIP 2008

Andrew Todd-Pokropek
University College London,
Medical Physics and Bioengineering
[INSERM U678 UPMC]
A.Todd@ucl.ac.uk

Sub-topic

Multiscale Imaging

- Model relates underlying structure to clinical image



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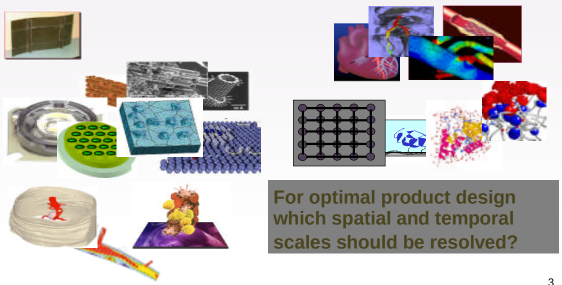
Multiple Spatial and Temporal Scales

The Challenge

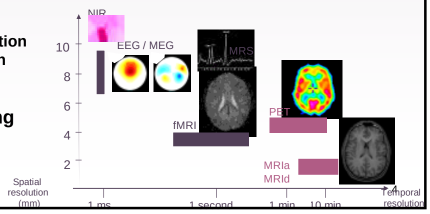


For optimal product design which spatial and temporal scales should be resolved?

3

Overview (roadmap)

- Some tools
  - Detection
  - Segmentation and measurement
  - Registration and fusion
  - Quantification
  - Modelling,
- Some issues
  - Intelligent acquisition
  - Artefact correction
  - Partial Volume
  - Towards Therapy
- Multi-scale imaging
  - Bone
  - Cartilage
  - 3DAH



Acknowledgements

Colleagues and Collaborators:
CMIC (in particular Derek Hill and Dave Hawkes), CS,
Medical Physics and Bioengineering
MIAS IRC (UCL, Oxford, Imperial, Manchester)
INSERM U494 /U678
Harvard, Georgetown, Leuven, INRIA,
EPSRC, MRC, Welcome, Siemens, Philips, GSK,
and many others.

Why do we want Quantify?

- A description without numbers is a very poor things [Lord Kelvin]
- To determine limits e.g. normal/ abnormal
- To determine progress e.g. increasing/decreasing
- For research e.g. new classes/ phenomena

- Note difference between absolute and relative quantitation
  - Different regions/ times
  - MBq /ml

But we have been waiting for a long time

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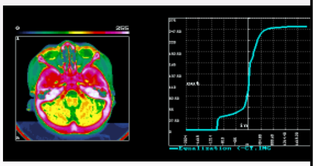
Image Processing in General



Histogram Equalization

- Aims of image processing
  - Detection
  - Measurement
  - Description
- What is special about medical images
- Many different types of data
  - MR, CT, NM, US ....
- Pre-Processing Manipulation Assessment

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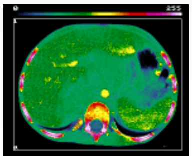
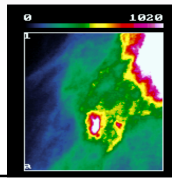
Some Examples

- Tumour staging
  - Detection
    - segmentation
  - Measurement
    - volume
  - Description
    - staging
    - diagnostic strategy
- Microcalcifications
  - Detection
    - matched filter
  - Measurement
    - how many
    - shape
  - Description
    - benign/ malignant





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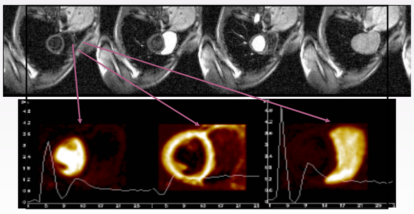
Models
Physical, Mathematical
Physiological

Processing
(Quantification)

Management



Manipulation of
Associated Data

Evaluation

Interpretation

Ack U494/U678

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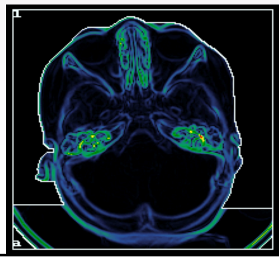
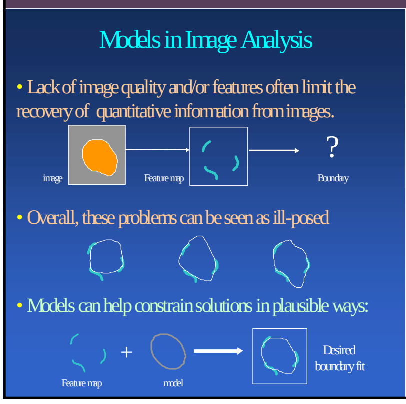
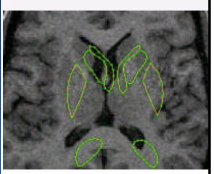
Segmentation

- Classic ‘edge detection’ methods
  - Gradient (Sobel etc), zero crossings of Laplacian
  - Canny
  - Marr Hildreth
- Phase congruency
- Model based
  - Medial axis MREP
  - Active shape
- Clustering
  - Split merge
  - K-Means
  - Affinity
- etc



10





Ack Taylor

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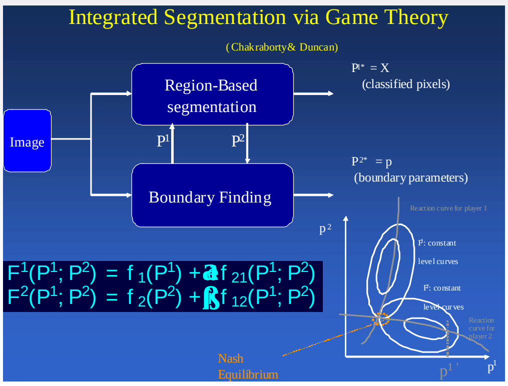

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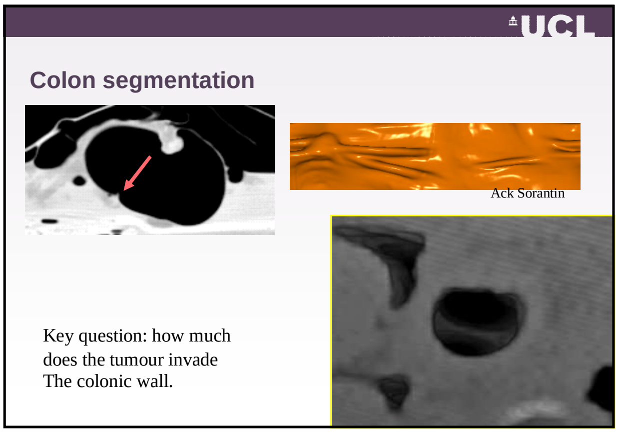
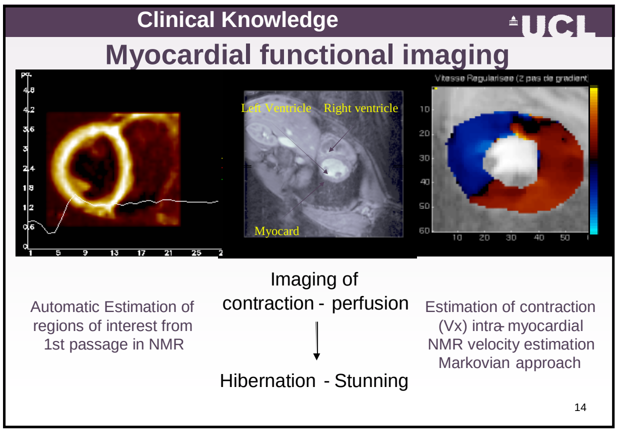
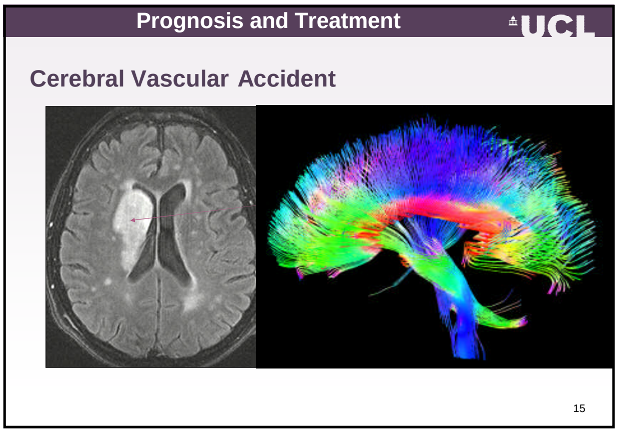
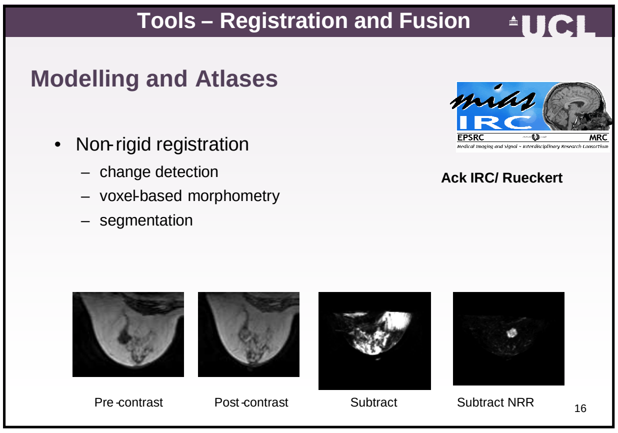
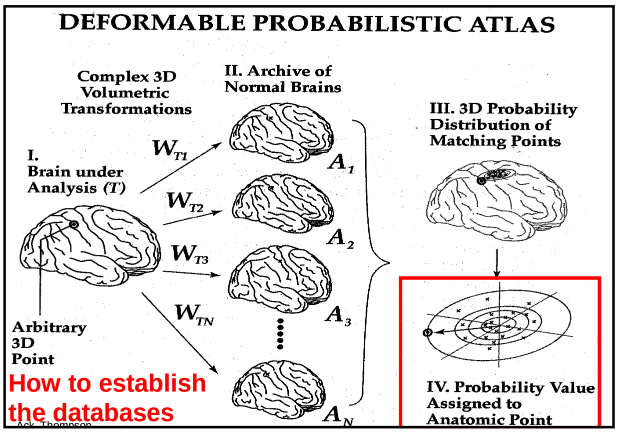
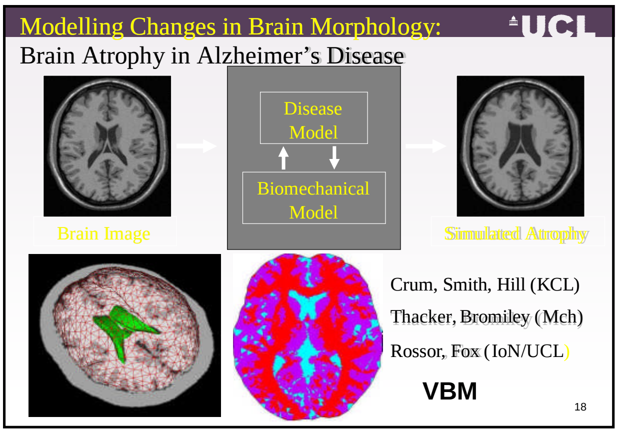

UCL
Colon segmentation
Ack Sorantin
Key question: how much
does the tumour invade
The colonic wall.


Clinical Knowledge
UCL
Myocardial functional imaging
Left Ventricle
Right ventricle
Myocard
Automatic Estimation of
regions of interest from
1st passage in NMR
Imaging of
contraction - perfusion
Hibernation - Stunning
Estimation of contraction
(Vx) intra-myocardial
NMR velocity estimation
Markovian approach
14


Prognosis and Treatment
UCL
Cerebral Vascular Accident
15


Tools – Registration and Fusion
UCL
Modelling and Atlases
Non-rigid registration
– change detection
– voxel-based morphometry
– segmentation
IRC
EPSRC
MRC
Ack IRC/ Rueckert
Pre-contrast
Post-contrast
Subtract
Subtract NRR
16


DEFORMABLE PROBABILISTIC ATLAS
Complex 3D
Volumetric
Transformations
II. Archive of
Normal Brains
III. 3D Probability
Distribution of
Matching Points
I.
Brain under
Analysis (T)
W_T1
W_T2
W_T3
W_TN
A_1
A_2
A_3
A_N
Arbitrary
3D
Point
IV. Probability Value
Assigned to
Anatomic Point
How to establish
the databases


Modelling Changes in Brain Morphology:
UCL
Brain Atrophy in Alzheimer's Disease
Disease
Model
Biomechanical
Model
Brain Image
Simulated Atrophy
Crum, Smith, Hill (KCL)
Thacker, Bromiley (Mch)
Rossor, Fox (IoN/UCL)
VBM
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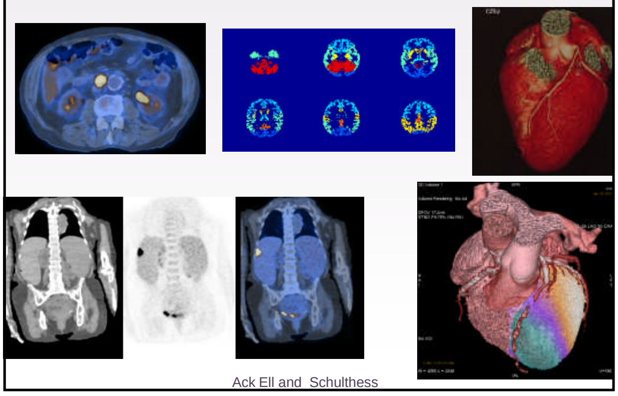
Quantitation in PET/CT



Ack Ell and Schulthess

Some Problems

1) **Bandwidth**

- Adequate spatial resolution
- Adequate temporal resolution
- Smart acquisition

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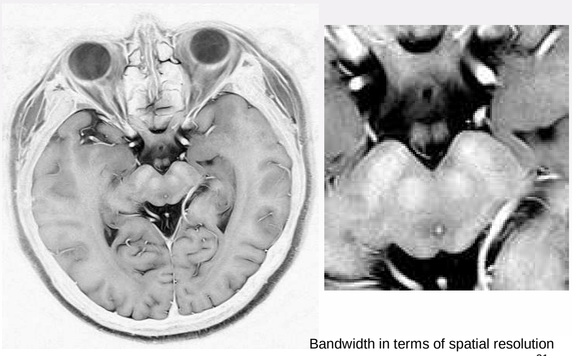
MRI



Bandwidth in terms of spatial resolution

Bandwidth v. SNR/ Field of View

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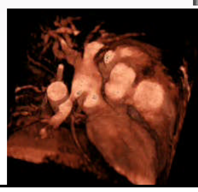
3D + Time (+ channel)

Cardiac acquisition (and registration)



Bandwidth in terms of temporal resolution

Ack U494/U678

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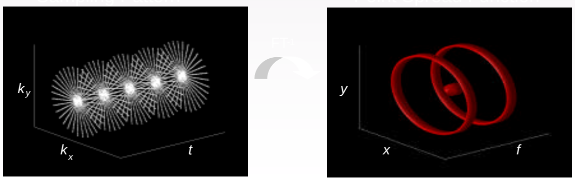
Pushing the temporal resolution boundary:

- There are relevant applications where lattice sampling is not possible:



Michael Hansen, et al, ISMRM 2006

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Dealing with motion

Respiratory motion

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Problems

2) Partial volume effects

- Correction and estimation
- Super-resolution
- Towards multi-scale imaging

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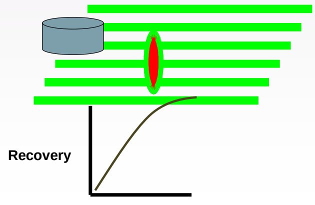
Partial volume effects

- When slice is not fully occupied
- When object is comparable to resolution in slice
- Spatially variant
- Dependent on object shape
- Probably the key limitation with respect to quantification



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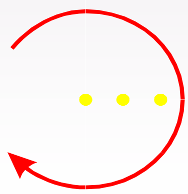
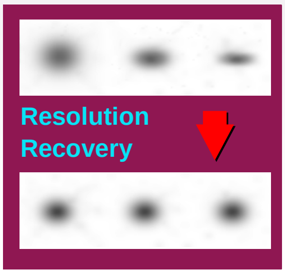
Tomographic Reconstruction

Depth Dependent Resolution Recovery

3 Point Sources





Ack. O'Connor

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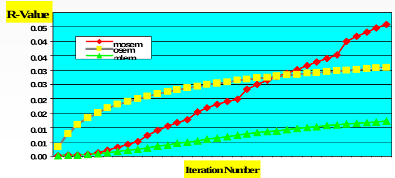
- Iterative Tomographic Reconstruction
- (Non-Quadratic) Penalty Functions

$$\phi(\theta, \overline{Y}(\theta)) = L(\theta, \overline{Y}(\theta)) - R(\theta)$$

$$R(\theta) = \sum_j \frac{1}{2} \sum_k \omega_{jk} \psi(\theta_j - \theta_k)$$



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Partial Volume Correction

ROI based operations

- Generate ROIs
- Create a mixture matrix
  - ROIs v. Compartments
  - Solve for components
  - Corrects for PVE
- Does NOT enhance resolution

$$\begin{bmatrix} C1 \\ C2 \\ \vdots \\ Cn \end{bmatrix} = \begin{bmatrix} M11 & M12 & & Mn1 \\ M12 & & & \\ & & & \\ M1n & & & Mnn \end{bmatrix} \begin{bmatrix} R1 \\ R2 \\ R3 \\ Rn \end{bmatrix}$$

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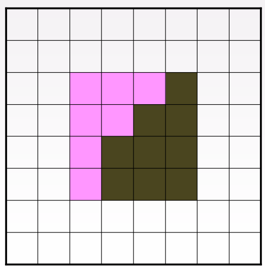
Sub-voxel operations

- Label on sub-pixel are defined from higher resolution image
- Higher resolution image resolution downgraded to SPECT/PT pixel size
- PVE defined if no. of compartments (labels) is fixed.



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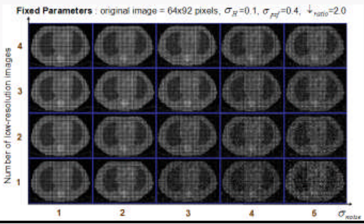
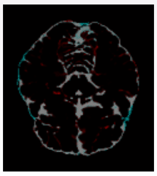
PVE corrections

- PVElab (FP6 project)

[1] Meltzer CC. J Cereb Blood Flow Metab 1996;16:650-8
[2] Muller-Gartner HW, et al. J Cereb Blood Flow Metab 1992;12:571-83
[3] Rousset OG, et al. J Nucl Med 1998;39:904-11
[4] Prinster A, et al, HBM2002,S20183





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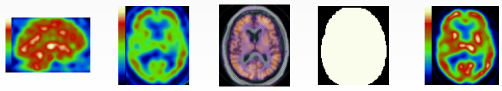
The use of higher resolution data (CT…) to correct for Attenuation and partial volume

Patient projections → *Scatter correction (Generalized Linear Multi-window)* → *reconstruction (OSEM)* → *Registration (MRI, SPECT)* → *Generation of attenuation And PV map* → *Attenuation & detector response corrections + Reconstruction (OSEM)*



G El Fakhri et al. Absolute activity quantitation in simultaneous I-123/Tc-99m brain SPECT. *J Nucl Med* 2001; 42 : 300-308.

Molecular Imaging

- Viewing physiological processes
  - Direct uptake of tracers
  - Indirectly via activated receptors
  - Major applications
    - Oncology
    - Cardiology
    - Neurology
  - Impact on gene expression and therapy

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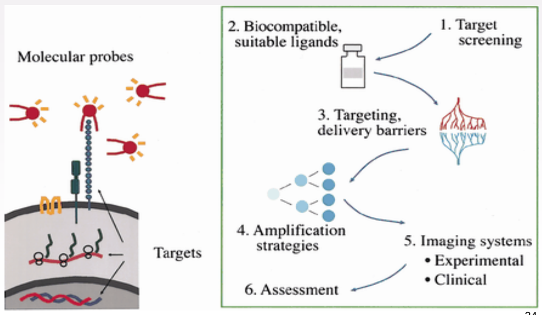
The process



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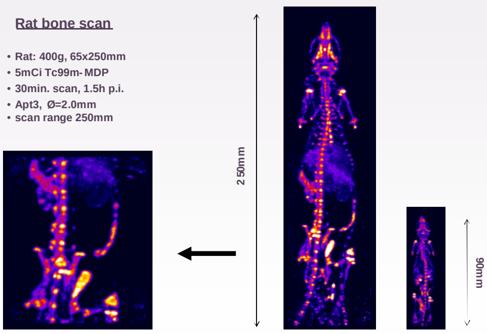
Drug discovery and small animal scanners

Rat bone scan

- Rat: 400g, 65x250mm
- 5mCi Tc99m-MDP
- 30min. scan, 1.5h p.i.
- Apt3, Ø=2.0mm
- scan range 250mm



zoom of rat spine — 400g rat — 30g mouse

μ imaging 20-400μm

Ack Schramm

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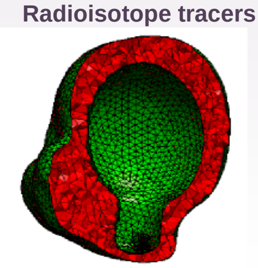
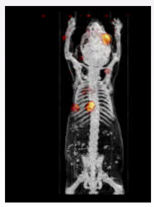
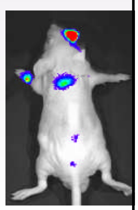
Combining Biomedical Optics and Radioisotope tracers




PET


Optical

Using a priori information

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3) From Diagnosis toward therapy

- PET/CT (Fusion)
- Surgical Planning
- Image guided intervention
- Evaluation

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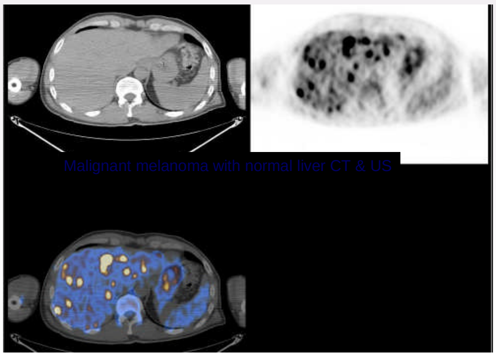
PET / CT - Fusion

Courtesy of: Liselotte Højgaard,MD DMSc, Annika Eigtved, MD ph.d, Anne Kiil Berthelsen, MD. PET & Cyclotron Unit, Dept. Nuclear Medicine, Rigshospitalet, University of Copenhagen.



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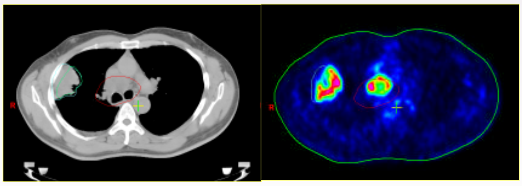
PET/CT improving cancer treatment

[A different type of quantification]



Tracers- F18- FDG tumour cell volume
IUDR tumour growth MISO hypoxia

Courtesy of Holy Name Hospital

Dizendorf, Univ. of Zurich: Diagnostic Imaging – PET/CT Fusion Proves Its Worth

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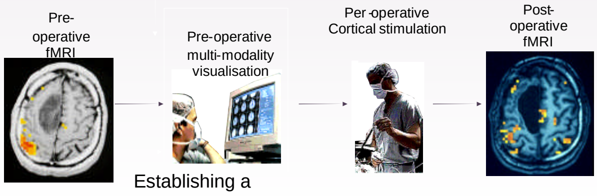
Towards Therapy

A Project –

Ack Unité 494 INSERM, LENA UPR 640 CNRS, Unité 483 INSERM, Centre MEG, Service de Neuroradiologie, Hôpital Pitié-Salpêtrière



Establishing a clincal interface
Integrating statistical models *

How to make it practical/ routine

•in collaboration with existing projects

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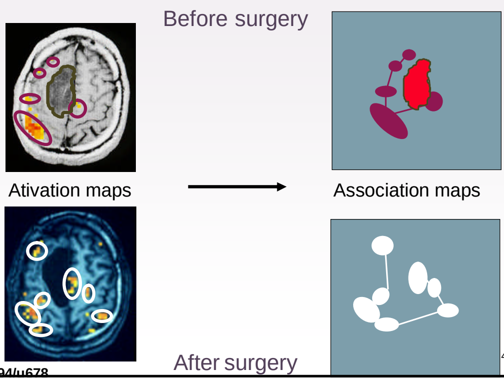
Functional images and surgery



Ack U494/u678

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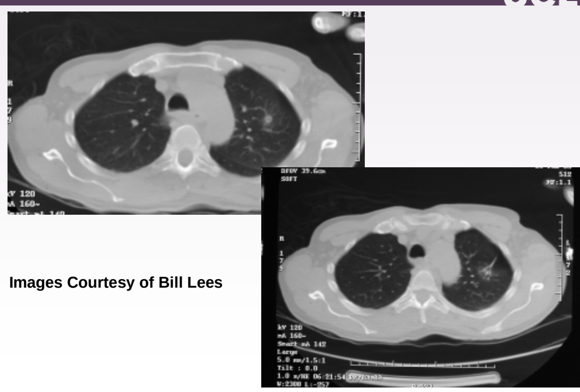
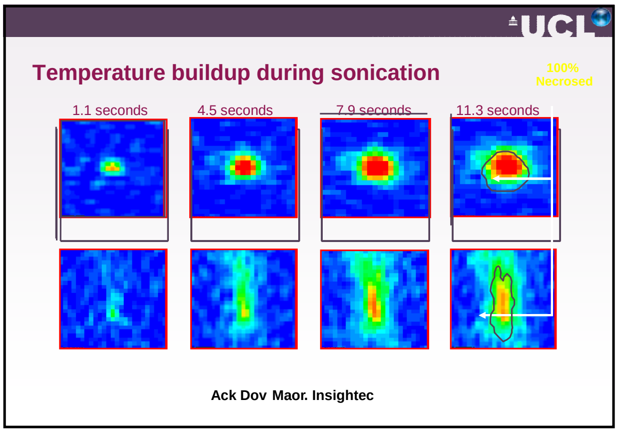
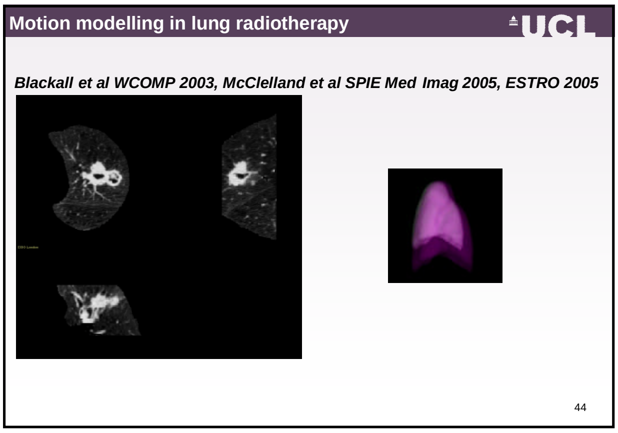
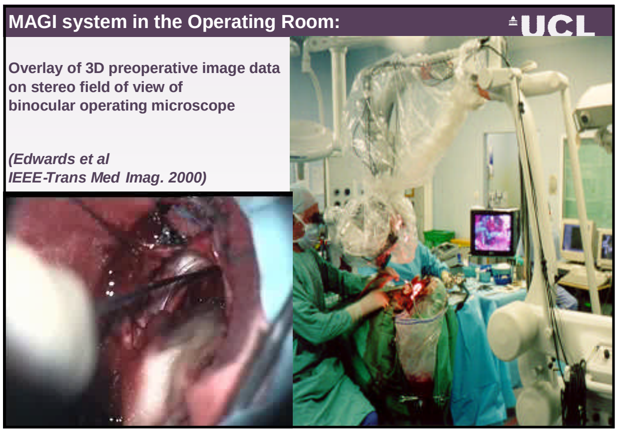
RF Ablation of Lung Tumours

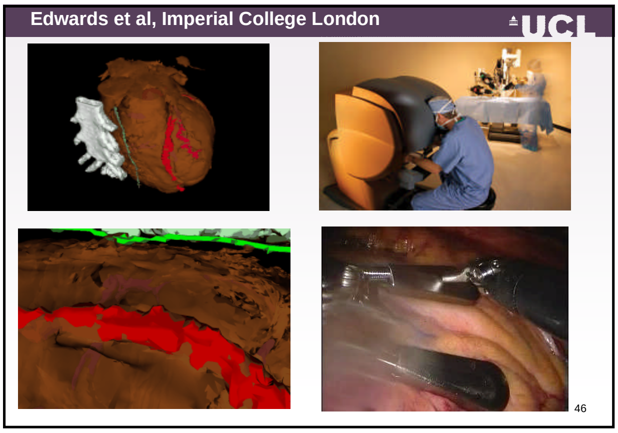


Images Courtesy of Bill Lees


UCL
Temperature buildup during sonication
100%
Necrosed
1.1 seconds
4.5 seconds
7.9 seconds
11.3 seconds
Ack Dov Maor. Insightec


Motion modelling in lung radiotherapy
UCL
Blackall et al WCOMP 2003, McClelland et al SPIE Med Imag 2005, ESTRO 2005
44


MAGI system in the Operating Room:
UCL
Overlay of 3D preoperative image data on stereo field of view of binocular operating microscope
(Edwards et al
IEEE-Trans Med Imag. 2000)


Edwards et al, Imperial College London
UCL
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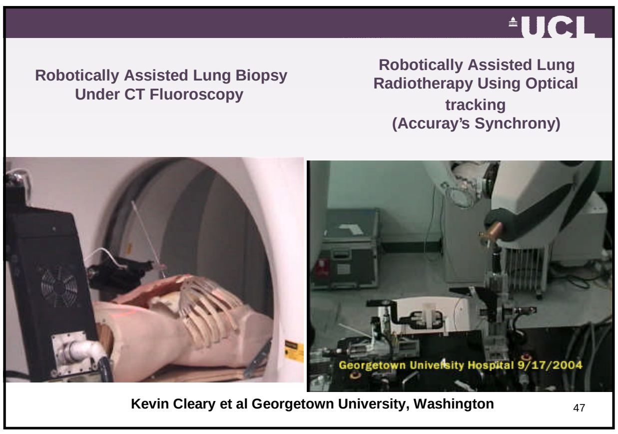
UCL
Robotically Assisted Lung Biopsy Under CT Fluoroscopy
Robotically Assisted Lung Radiotherapy Using Optical tracking
(Accuray's Synchrony)
Georgetown University Hospital 9/17/2004
Kevin Cleary et al Georgetown University, Washington
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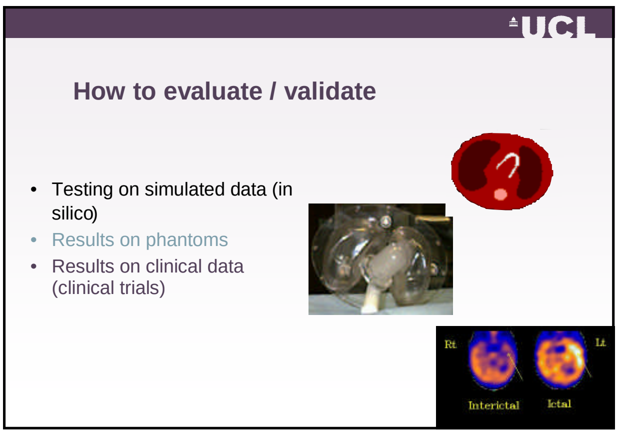
UCL
How to evaluate / validate
• Testing on simulated data (in silico)
• Results on phantoms
• Results on clinical data (clinical trials)
Rt
Lt
Interictal
Ictal

How do you evaluate- measures and statistics?

- True positive and false positive rates
- Probabilistic distances
  - Hausdorf distance (largest difference)
- Volume and volume overlap
- Interclass correlation coefficient
  - Williams (modified) index
- ??? How to measure false negatives???

- Valmet software www.ia.unc.edu.public.valmet

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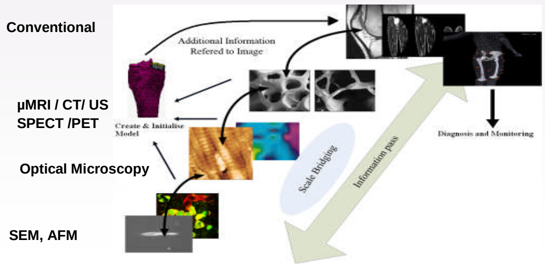
Back to Sub-topic

Multiscale Imaging

- Model relates underlying structure to clinical image



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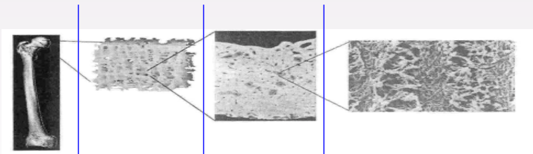
Levels of Structural Organization



Whole Bone Level
- The structural organization is determined by the bone external and internal geometry, the bone density distribution and the bone anisotropy

Trabecular Bone Level
-Trabecular architecture
- Length scale of trabecular thickness 100 μ m

Bone Tissue Level
-Structure is merely determined by the porosity of the bone due to Haversian cannals, lacunae, and canliculi

Bone UltrastructuralLevel
-The structure is determined by the organization of the apatite and collagen that form the constituents of the bone tissue, (figure taken from Marotti G 1996, Ital. J. Anat. Embryol. 101 25-79

Ack, Bert van Rietbergen, Finite Element Modeling, The Physical Measurement of Bone, 475-510

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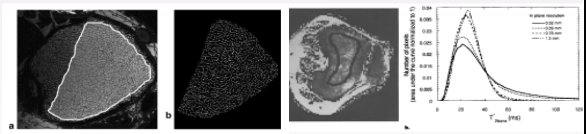
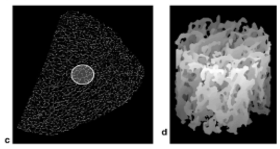
Quantitative MRI for Bone





- **Direct method is to measure the microstructure directly from the images**
- **Indirect method is to measure the relaxation time of T_2***

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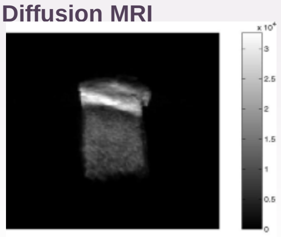
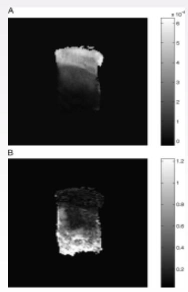
Diffusion MRI



T_2 weighted image of an axial slice of a portion of bovine epiphysis extracted by a bovine femur covered by a layer of fat

C. Rossi et al. / Magnetic Resonance Imaging 23 (2005) 245-248



MD and FA maps of an axial slice of a portion of epiphysis covered by a layer of fat

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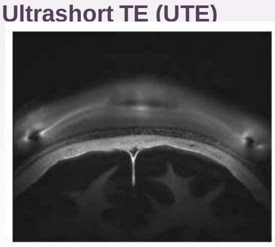
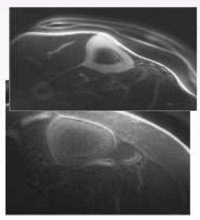
Ultrashort TE (UTE)



Trabecular bone (IR 500/0.08 minus 4.5/200msec at 1.5T, resolution 512 512, FOV 14 cm). Difference UTE image of the skull. Trabecular bone can be seen between the inner and outer tables.



Normal

Osteoporosis

Ack Bydder

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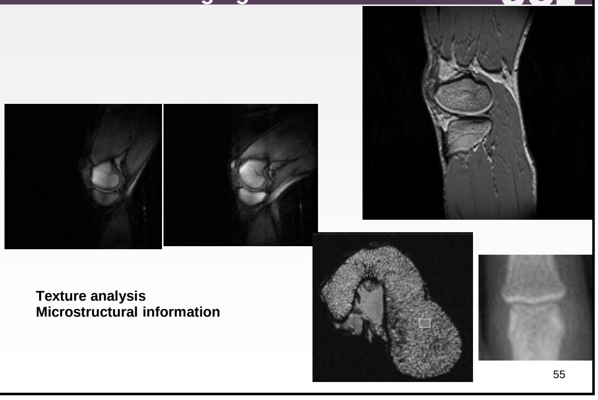
Multi-scale Imaging



Texture analysis
Microstructural information

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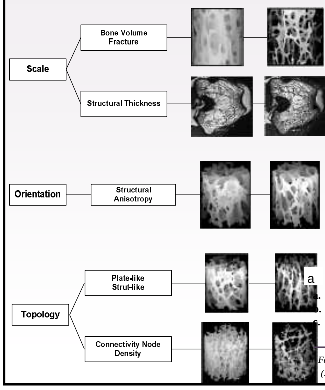
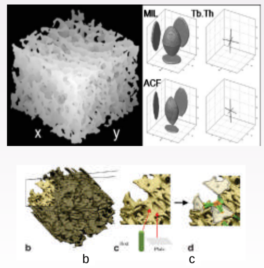
Parameters for Structure Analysis





a. 3D rendition of TB core
b. Cubic sub-region of (a)
c. Skeleton representation and topological assignment using the colour coding in (a)

Felix W. Wehrli, Ph.D, JOURNAL OF MAG RES IMA 25:390-409 (2007)

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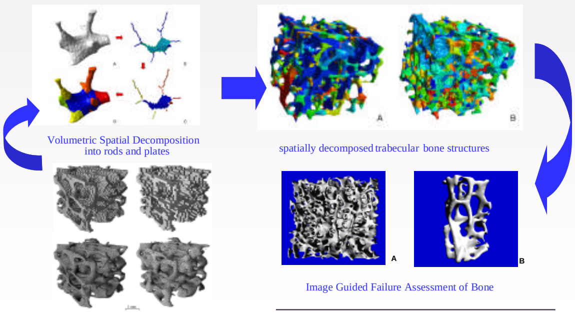
Finite Element Methods



Ack R. Muller et al

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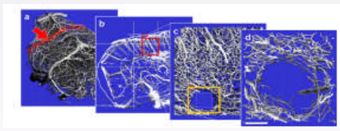
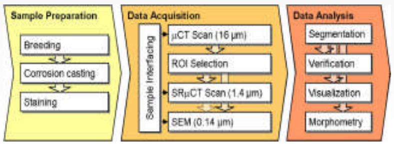
A multiscale method





Framework of hierarchical imaging

S. Heinzer et al. / NeuroImage 32 (2006) 626 – 636

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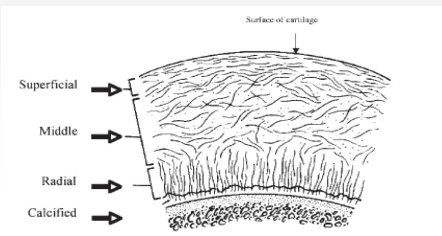
Structure of Articular Cartilage

- Zonal orientation of collagen



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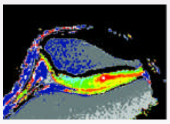
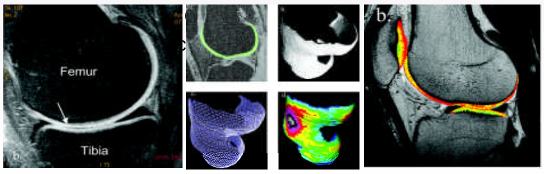
Articular Cartilage

- Imaging cartilage is challenging
- Thin (<4mm), leads to significant partial volume effect
- Osteoarthritis (OA) common cartilage disease, significant area of current research interest
- Early detection of OA – changes to structure
- Monitor potential treatments
  - Disease slowing drugs?
  - Disease altering drugs?
- Intervention
  - Knee Replacement
  - Graft

MRI of Cartilage

- Imaging cartilage





Burstein 2003

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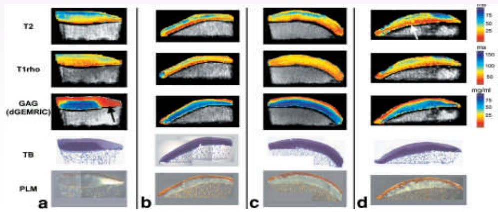
Imaging Matrix Constituents

- T2 and T1rho mapping
- Comparison to histology



Menezes 2004

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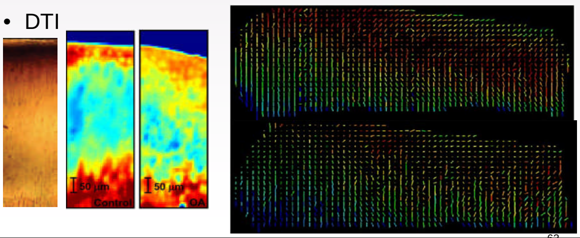
Imaging Matrix Constituents

- DTI



Bi 2007, Deng 2007

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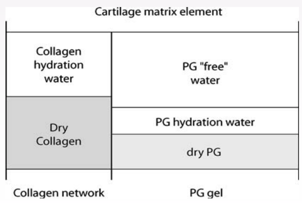
Modelling Articular Cartilage

- A number of models have been created to describe the mechanics of cartilage
- Model parameters to describe cartilage



Quinn 2007

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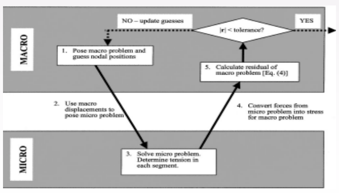
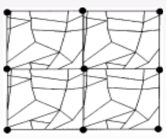
Modelling Articular Cartilage

- Multiscale methods provide a better fit to the data than single scale equivalents



Multiscale modelling flowchart, applied to a mechanical model of cartilage



Multiscale finite element methods.

Agoram 2001

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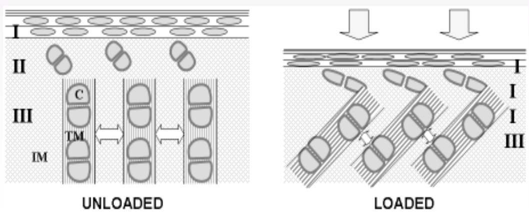
Modelling Mouse AC

- Model can be tuned to describe composition of mouse articular cartilage through data obtained with histology



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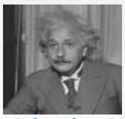
Adaptive Multiscale Modeling

The Vision of Einstein



Einstein: *"The model used should be the simplest one possible, but not simpler."*

Adaptive Multiscale Modeling: "Start with a ***simpler model***, based on a single scale and uncoupled physical processes, and then adaptively introduce additional scales to permit coupled multiscale-multiphysics considerations, whenever and wherever these are needed, until the ***simplest possible model*** is obtained."

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Adaptive Multiscale Modeling

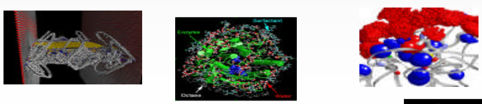
- Model transition schemes
  - Pollution errors at the interface for continuous-continuous and continuous-discrete transitions
  - Mathematically consistent discrete-continuum transition

Is stochastic modeling required?

- Probability error estimators
- Multiscale sensitivity analysis

Stochastic Nature of Multiscale Problem

- Physical uncertainties (loads, domain, material properties)
- Statistical uncertainties (amount of data available, probability fields such as correlations)
- Model uncertainties (mathematical modeling of physical behavior)



Other related topics

- Brain autoregulation modelling
- Cardiac Modelling
- 3D Anatomical Human
- Physiological Human

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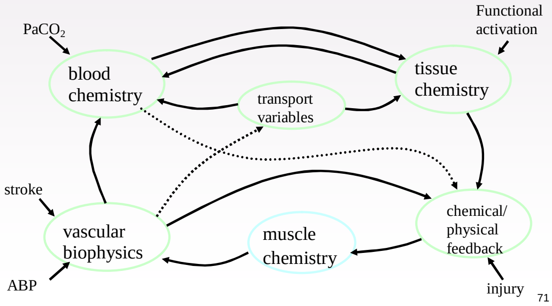
Autoregulation in brain: multiscale modelling



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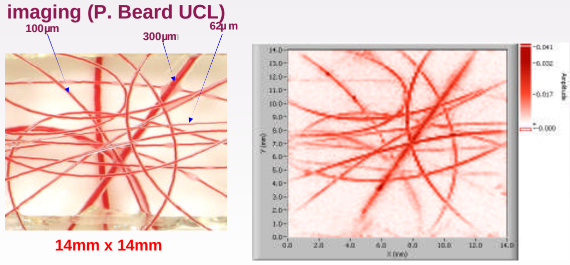
Imaging of blood filled tubes in intralipid by photoacoustic imaging (P. Beard UCL)



- Excitation: 800nm (6.7mJ/cm^2); pulse duration=8ns
- Lateral scanning step-size: 140μm

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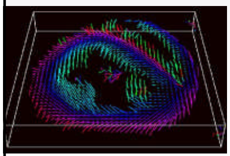
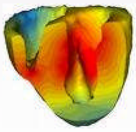
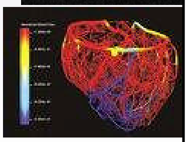
Cardiac Modelling



Ack Harvard



Ack INRIA



Ack Noble/ Hunter

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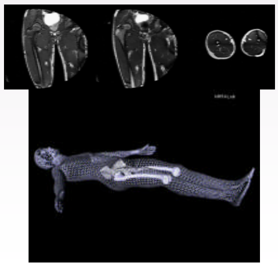
Models

Virtual Human
NLM

3DAnatomical Human->
Physiological Human



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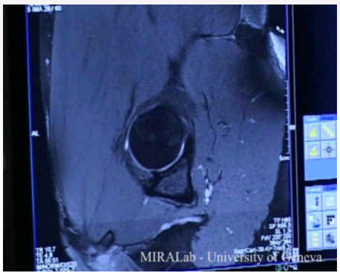
3D Anatomical Human
Physiological Human



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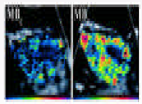
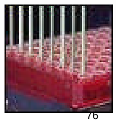
The Future of Medicine?

- Preventive medicine
  - Including environment
- Personalised Medicine
  - Using the –omics (genomics/ proteomics …)
- Keyhole/ robotic surgery
  - Implanted devices
- Nanotechnology
  - Biolab
  - MEMS (micro electro-mechanical systems)
  - Lab-on-a-chip micro-arrays and diagnosis
  - Drug production
- Complex Systems
  - Mathematical biology
  - Modelling and simulation





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