



# UCL

# OPEN DAY

Monday April 3rd 2006





# Introduction

In January 2005, Professor David Hawkes, Professor Derek Hill and colleagues moved from King's College London to University College London to form the new Centre for Medical Image Computing (CMIC) as a joint initiative between Medical Physics and Computer Science together with Professor Simon Arridge, Professor Andrew Todd-Pokropek and Dr. Daniel Alexander. The Centre brings together a substantial group of physicists, computer scientists, mathematicians and engineers working on medical image analysis and image processing. Our work encompasses the full range of activity in image formation, image analysis and image guided interventions.

We have pioneered novel, automated and highly accurate methods for combining and comparing image derived information, with application in the neurosciences, cardiovascular sciences, oncology and orthopaedics. Our advances in image registration technologies, image reconstruction and inverse problems, optical tomography, image guided interventions, cardiac MR, structural neuroimaging, diffusion imaging and tractography are widely recognised as world leading. We are now integrating models of physiological function (e.g. electrophysiology of the heart), statistical shape models (e.g. in orthopaedic surgery), and models of repetitive motion (e.g. cardiac imaging, liver interventions, lung radiotherapy, and PET imaging) with image guidance technologies. We are developing models of disease processes to better interpret image-derived information (e.g. in image based monitoring of disease progression in dementia and response to therapy and in analysis of fibre tracts in the brain). We will be developing novel image guidance and therapy monitoring for translating to the clinic the new, targeted therapies based on cellular and molecular processes. We plan to develop methods to combine information across wide ranges of spatial scale from molecular through cellular to whole organ or system imaging.

We work very closely with colleagues in clinical and biomedical research and with the medical imaging industries. We strongly believe that effective clinical solutions in our area require a combination of academic engineering and scientific research, industrial based research and development, and clinical research. We have been successful at building teams of researchers in particular clinical and biomedical areas of research activity that encompass all three groups. We also strongly believe in a supportive, cooperative and collaborative environment to provide our PhD students and RAs with high quality training in the wide range of skills required in this multidisciplinary research area.

This booklet provides a snapshot of all activity currently underway in CMIC. All members of CMIC – academics, research fellows, research assistants and PhD students – were asked to provide a paragraph describing their work and will be giving talks, presenting posters or providing demonstrations of their work. The booklet also lists our clinical collaborators and partners in industry. Our publications since the start of CMIC in January 2005 are listed at the end.

Finally I wish to thank Ron Gaston, CMIC manager, for all his efforts far beyond the call of duty in putting the day together; Robin Saklatvala for all her help in sorting the invitations, making the arrangements for the day, putting the booklet together and bravely attempting to organise me; Stuart Nightingale from UCL Media Resources for laying out this booklet; the whole of CMIC for making this day a success; and all those organisations who funded our research without whose support none of this would have been possible.

David Hawkes – April 3rd, 2006



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# Imaging Brain Structure and Function

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## Daniel Alexander – Principal Investigator

Quantitative MRI techniques, such as functional MRI and diffusion MRI, exploit the sensitivity of the MR signal to microscopic mechanisms, such as Brownian motion or particle exchange, to provide insight into the structure and function of tissue. These techniques rely on computational methods for model fitting, image processing and optimizing acquisition schemes. Researchers at CMIC are actively developing these computational methods, which are key to the success of these imaging techniques. Improved computational methods improve contrast, increase detail and provide new insights into the workings of biological systems such as the human brain. Many of our current activities focus primarily on diffusion MRI, but most are more generally applicable and impact other imaging modalities. This talk will give an overview of current efforts within the general context of imaging brain structure and function.

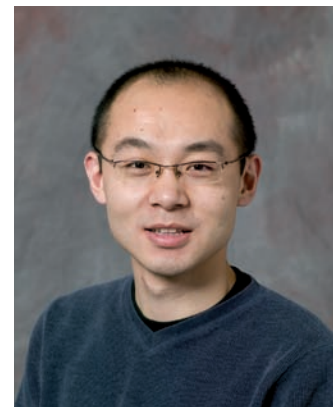


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## Bai, Yu

### Motion Correction in Diffusion Magnetic Resonance Imaging.

In the diffusion tensor (DT) MRI, a number of diffusion-weighted images with different diffusion-weighting gradient directions are taken during scanning. During such a long time, small head movements are not easy to avoid. However, the tensor calculation assumes that each voxel corresponds to the same anatomical location in all the measurements. That means to fit the diffusion tensor, all the measurements need to align properly. A small bulk motion can cause an unmatched measurement value to be used during the tensor fitting. The standard correction scheme uses the non-diffusion weighted image as the reference for registration, but the differences between diffusion-weighted images and the non-diffusion weighted reference image cause mismatching to occur during registration. We propose several alternative methods to improve the motion correction and correct the errors that the standard correction scheme introduces. We test the new approaches on both a reduced-size data set with artificial movement corruption and a full data set. Tests on the reduced-size data confirm efficacy of some variants of the new method. Tests on the full data set reveal advantages of the new methods over the traditional approach.



FA maps overlaid with a hand segmented outline of the corpus callosum from the  $b=0$  image, after (a) standard motion correction and (b) FTSM correction

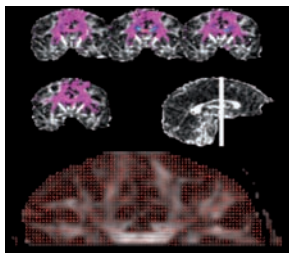
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## Phil Cook

Diffusion MRI is a rapidly evolving research field that has produced a wealth of algorithms for the analysis of white-matter fibre architecture and disorders in the brain. Camino (<http://www.cs.ucl.ac.uk/research/medic/camino>) is an open-source toolkit designed to make a selection of these algorithms, convenient to use and extend for diffusion MRI users and developers. Camino implements a data processing pipeline, providing tools for the manipulation and synthesis of raw data, through to the probabilistic tracking of white matter fibres. The data pipeline approach allows for easy scripting parallel processing and flexible integration with other software.

Camino implements the standard diffusion tensor algorithms and also provides



a range of advanced reconstruction algorithms that can resolve crossing fibres, such as the Persistent Angular Structure (PAS). Spherical harmonic voxel classification detects non-Gaussian diffusion, which is an indication that crossing fibres may be present in a voxel. Camino contains tools to extract statistics such as diffusion anisotropy and estimated fibre orientations from the reconstructed data.

Camino's probabilistic tractography uses the Probabilistic Index of Connectivity (PICO) algorithm with the improvements and refinements. PICO combines standard tracking algorithms with the data synthesis and statistical tools, to visualise the uncertainty in reconstructed fibre paths.

The figure shows a PICO reconstruction of a fibre pathway (top), and fibre orientations reconstructed with the PAS.

**Collaborators:** University of Manchester: Geoff Parker

**Funding:** EPSRC.

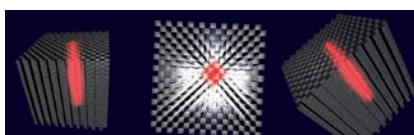


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## Matt Hall

I am interested in Diffusion MR Imaging, in particular the properties of the diffusion process being measured and nonlinear reconstruction algorithms able to resolve complex sub-voxel architecture such as crossing fibres. These are situations in which the traditional diffusion tensor method of image reconstruction is insufficient to correctly resolve the structure present in a voxel and hence new approaches must be used. Several of these approaches exist and it is not clear which techniques perform well under different circumstances.

As part of the Camino project, I have constructed a Monte-Carlo model of diffusing spins in an environment made of permeable membranes which may be arranged to model diffusion in specific situations of interest. The figure shows the positions of diffusing spins in an environment in which diffusion is restricted by a substrate with lanes in a single direction. The model has many applications including constructing test data to compare image reconstruction algorithms and more broadly to calibrate techniques based on diffusion MRI data such as tractography techniques, which are used to reconstruct white matter structures in the brain.



Three different views of a population of diffusing spins on a substrate with "lanes" in one direction that restrict the motion of spins. 100000 spins are shown in red. The diffusion environment is made up of permeable cubic cells whose faces impede the spins' random diffusive motion.

**Collaborators:** St George's, University of London: Dr Thomas Barrick, Dr Nigel Lawes; Institute of Child Health: Dr Chris Clark.

**Funding:** EPSRC.

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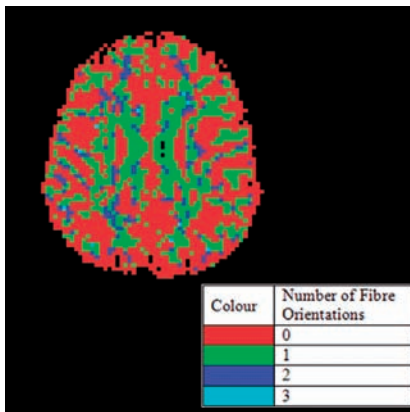


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## Shahrum Nedjati-Gilani

Diffusion MRI provides an insight into the microstructural architecture of tissue by observing the restricted and hindered displacement of water molecules undergoing Brownian motion. Diffusion-Tensor MRI (DT-MRI) is the most common diffusion MRI technique and is often used for mapping fibre orientations. However, DT-MRI is only capable of recovering a single fibre orientation in each voxel, and cannot resolve the orientations of crossing-fibres.

A new generation of reconstruction algorithms such as PAS-MRI, q-ball and spherical deconvolution has appeared that can resolve crossing fibre orientations; however, these more complex algorithms are generally less successful in correctly identifying the orientation of single fibres and are more computationally demanding than DT-MRI. Therefore, it would be useful to know the expected



number of fibre populations present in each voxel in order to choose a suitable reconstruction algorithm. Also, the aforementioned methods cannot distinguish between various fibre configurations such as crossing and kissing fibres.

The aim of my research is to find and evaluate methods for mapping the number of fibre orientations in each voxel of a 3D diffusion MRI acquisition, and to develop methods to discriminate between different fibre microstructure, e.g. differentiating between kissing, crossing and diverging patterns of fibres.

Figure: Estimated number of fibre orientations per voxel for a brain slice.

**Collaborators:** St George's, University of London: Dr Thomas Barrick,

Dr Nigel Lawes; Institute of Child Health: Dr Chris Clark.

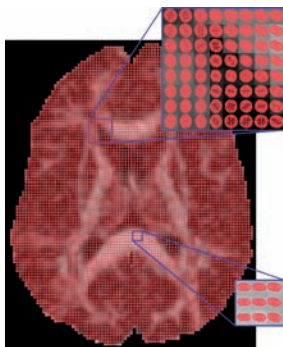
**Funding:** EPSRC.



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## Kiran Seunarine

Diffusion MRI is used to probe the microstructure of materials, such as the orientation of white matter fibres in the brain. The standard method for estimating the orientations of these microstructural fibres using diffusion MRI data is to fit the diffusion tensor and use the principal eigenvector. However, this method only provides one fibre-orientation estimate per voxel and fails at fibre crossings. This has spawned a new generation of reconstruction algorithms, such as Spherical



Deconvolution, Persistent Angular Structure MRI and Q-Ball imaging. These methods aim to resolve the directions of crossing fibres from a set of measurements acquired in a timescale that is comfortable for patients. The figure shows a Q-Ball reconstruction over a human-brain slice. The peaks of the functions provide estimates of the fibre orientations. However, these methods have yet to be compared using a single framework. The aim of my work is to perform a comprehensive evaluation and comparison of these methods and tune and optimize them ready for transfer to the clinical arena.



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## Tony Shepherd

### The use of Support Vector Machines in CT bone segmentation.

The segmentation of bone from computed tomography (CT) data is commonly achieved by intensity thresholding, due to the relatively high intensity values of bone voxels. However, intensity information alone is insufficient for segmenting the whole of some bones where the density is variable and internal structure is complex. I report on the use of a machine learning approach to bone segmentation. Support Vector Machines (SVMs) are used to discriminate data in a feature space chosen to exploit regional 3D texture properties of training data.

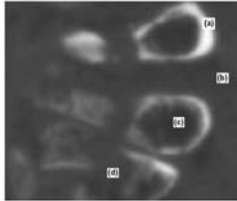


Figure: A transverse slice through a CT scan of the human foot. Individual bone units are discernible at the base of the metatarsals. (a) External bone, (b) surrounding tissue, (c) internal bone (d) regions badly defined by CT intensity.



**Collaborators:** Biotronics 3d; Haralambos Hatzakis

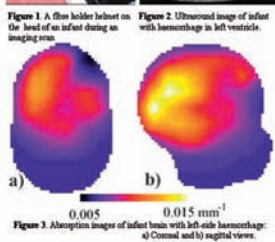
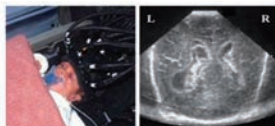
**Funding:** 'EPSRC CASE studentship' with joint funding from EPSRC and Biotronics 3D.

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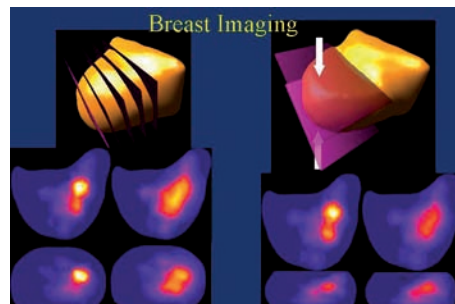
# Model Based Medical Imaging

## Simon Arridge – Principal Investigator

All medical imaging modalities that infer spatially distributed properties of tissues given measured values of propagated radiation make use of mathematical models of physical laws. In some cases such as line integrals of densities these models are only implicit. By contrast a number of questions in medical imaging require explicit models, controlled by input parameters, whence the imaging process can be cast as an inverse problem in the inference of the model parameters given the data. Several CMIC projects are in progress both for developing the computational aspects of the modelling problem using techniques such as Finite Elements and Boundary Elements, and for the inverse problem. This talk will give an overview of this work, and including aspects of Bayesian priors, multimodality and approximation error theory.



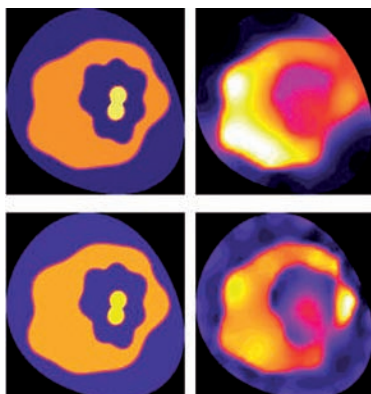
**Collaborators:** J.Kaipio, V.Kolehmainen, T.Tarvainen; Helsinki University of Technology : E.Somersalo, J.Heino, I.Nissila, J.Heiskala; Physikalisch-Technische Bundesanstalt: H.Rinneberg, H.Wabnitz, T.Dierkes; Universidad Carlos III de Madrid : O.Dorn; Inst of Electronic Structure and Laser - Forth : J. Ripoll Warsaw University of Technology : J.Sikora; Massachussets General Hospital : D.Boas, M.Francheschini, S.Diamond; University of Pennsylvania : A.Yodh, A. Corlu, R.Choe; University of Arizona : H.Barrett, A.Pineda  
**Funding:** EPSRC, Wellcome Foundation, European Union, MRC



## Abdel Douiri

### Anisotropic diffusion regularisation methods for diffuse optical tomography using edge prior information.

Diffusion Optical Tomography (DOT) is a non-invasive functional imaging modality that aims to image the optical properties of biological organs. In this work we will suggest a methodology for choosing an adequate prior function combined with a priori information on the edges that improves dramatically the quality of DOT reconstruction. In practice the edge prior can be provided from another medical modality such as magnetic resonance imaging (MRI) or computed tomography (CT). This methodology could be extended to other large scale nonlinear inverse problems.



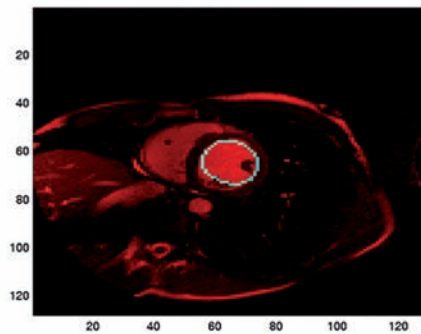
Reconstruction of the absorption and the scattering coefficient using the proposed method: target object on the left and reconstructed object on the right

**Funding:** EPSRC, GR/R86201/01

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## Jason Kastanis

Cardiac MR acquisitions are time consuming because of the need to sample all of k-space at many time points throughout the cardiac cycle in order to reconstruct a fully sampled image. The analysis of these images often involves delineating the left ventricle at each phase of the cardiac cycle, which requires substantial user interaction. In the two step approach, reconstruction and then segmentation, the quality of the segmentation is dependant on the quality of the reconstruction. If the image reconstruction is ill-posed, which is the case for undersampled MRI, the classification of pixels will be neither accurate nor robust. The proposed method



segments the endocardial boundary directly from highly undersampled k-space measurements, rather than first acquiring a fully sampled image, then reconstructing and finally segmenting.

A model is used to approximate the intensity variation and most important the shape of the left ventricle using basis functions. The model parameters are mapped  $G : P \rightarrow X$  from the space  $P$  of the parameters of the model to the pixel space  $X$ . This contains a natural classification of pixels. The data can be further considered to be a mapping  $F : X \rightarrow Y$  from the pixel space to the measurement space  $Y$ . The benefit of this is that the combined mapping  $y = Z(p) = F \circ G(p)$ ,  $p \in P, y \in Y$ , can be

treated as a forward model for the measurement of the object. The determination of the parameters of the model that produce the best fit of the forward model to the measured data is the inverse problem.

**Collaborators:** Kings College London: Professor Reza Razavi.

**Funding:** EPSRC, MIAS IRC



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## Christos Panagiotou

### **Incorporation of un-registered multi-modal prior information in optical tomography.**

Diffusion optical tomography is a novel, non-invasive, functional medical imaging modality. It works by probing a medium under consideration from its boundary with near-infrared light and measures the exitance at discrete boundary locations. The retrieved images reveal the spatial distribution of optical parameters - light scattering and absorption, inside the medium. The retrieval of optical parameters allows the inference of essential information about the probed anatomy, such as blood oxygenation levels, blood volume and blood flow. Through blood detection, optical tomography can detect abnormalities such as cancerous tumours or haemorrhages. In order to reconstruct these images from the measured data, we need to solve a non-linear, ill-posed and often under-determined inverse problem. In order to stabilize the solution we propose its regularization with unregistered prior information from a different modality.

**Funding:** EPSRC



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## Martin Schweiger

### Optical tomography - imaging the body with visible light.

Volume images of the body have become an indispensable tool in clinical diagnostics over the last decades. For applications like tumour detection doctors depend on the information provided by 3-D imaging modalities such as X-ray computed tomography and magnetic resonance imaging. While these mature techniques have developed into reliable systems delivering images of high quality, they require large and expensive instrumentation which is only of limited use when continuous monitoring of a patient at the bedside is required. Diffuse optical tomography is a novel functional imaging modality which has the potential to fill this gap. With this technique, images of physiologically relevant parameters such as blood and tissue oxygenation are obtained by illuminating a body organ with infrared light and measuring the distribution of light propagating through the tissue and re-emerging on the surface.



The use of infrared light provides however challenges to the problem of image formation that need to be overcome before optical tomography can become a mainstream tool in clinical diagnostics. The principal problem is the strong scattering of light in the infrared wavelength range by biological tissue. Unlike X-ray CT imaging, all the detected light has undergone multiple scattering, and the assumption of straight-line propagation cannot be applied.

This talk demonstrates the image reconstruction techniques that are required to turn surface measurements of light transmission into 3-D images. It will be shown that the nonlinear relationship between data and images requires an iterative optimisation approach that fits the parameters of a light transport model to the acquired data.

**Collaborators:** Dementia Research Group, Institute of Neurology UCL: N. Fox; Kuopio University: J. Kaipio, V. Kolehmainen; Physikalisches Technische Bundesanstalt: H. Rinneberg, H. Wabnitz.

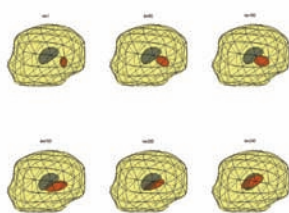
**Funding:** EPSRC MIAS IRC, MRC

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## Athanasios Zacharopoulos

### 3D Shape Based Reconstructions using parametric surfaces in model based medical imaging modalities.

We present a novel reconstruction scheme, which has the goal to finally yield fully 3D images from a set of Optical Tomography (OT) 3D data. For this purpose we use the assumption that the unknown objects can be characterized as shapes with a well-defined (but possibly only approximately known) parameter (light absorption



and diffusion) contrast to the known background distribution. These techniques start with an initial guess of the shape and define a shape evolution for solving the inverse problem. During the evolution, the shapes are constrained to stay in a certain class of shapes defined by geometric coefficients. We employ a parametrisation of closed surfaces using spherical harmonics based on constrained minimisation of the distortions occurring



by the mapping of the surfaces, acquired from voxel images (segmented Magnetic Resonance Images (MRI) or Computed Tomography (CT) scans), to a unit sphere. This method could be used to describe parametrically any closed surface, and overcomes the restriction to just star-shaped objects that is commonly found in literature. A surface meshing algorithm is proposed by applying the parametrisation to map regular surface meshes initially defined on the a unit sphere, by tessellation of an embedded icosahedron, upon the parametrically defined surfaces. This procedure creates regular sampled meshes, which is a prerequisite for a good discretisation of a surface, in an automatic procedure. Finally, a Boundary Element Method for OT is constructed, for the solution of the diffusion equation for the propagation of light on realistic geometrical models.

**Funding:** EPSRC

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# Advances in MR Imaging

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## David Atkinson – Principal Investigator

### Advances in MR Diffusion Imaging

Members of CMIC, in collaboration with colleagues from The Institute of Child Health, The Hammersmith Hospital and ENIT, Tunis have made wide-ranging advances in magnetic resonance diffusion weighted imaging. This talk will outline the background to diffusion weighted and diffusion tensor imaging, our advances in the understanding of how data should be acquired, how quantitative information might be extracted from images that are currently used largely for pretty visualisations and how we can achieve better quality diffusion imaging of the brain and spine

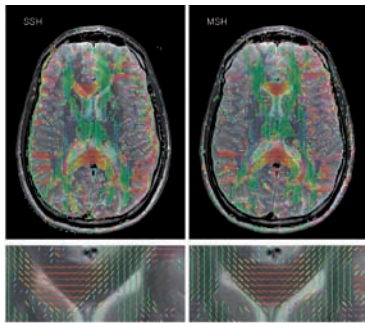


Figure: The colour coded fibre directions appear more anatomically correct using our method (MSH) compared to the standard clinical approach.



**Collaborators:** Imperial College London: Jo Hajnal; Serena Counsell, Dr David Larkman; Institute of Child Health: Alan Connelly, Fernando Calamante, Donald Tournier; Ecole Nationale d'Ingenieurs de Tunis: Dr Moakher.

**Funding:** EPSRC, Philips Medical Systems

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## Andrew Melbourne

### Remaining Motion in Breath-Hold MR Image Sequences of the Liver.

**Introduction:** The liver is a common site for the formation of secondary cancers. Treatment relies on acquiring images of the patient; however, motion during the image acquisition can generate artefacts and mis-alignment between successive images. Therefore it is necessary to limit this loss by restricting or training the patient. Here we look at the motion remaining when the patient lies supine with arms raised above the level of the head. Images are acquired at full-exhale breath-holds for use in a dynamic contrast-enhanced MRI study of the liver.

**Methods:** An in-house registration toolkit is used to register individual sequences to the first slice in the sequence, using a full 2D affine registration based on normalised mutual information. 29 Datasets (covering 7 patients returning at monthly between 2-5 visits) are examined; each with between 34-40 coronal slices taken at 13s intervals.

**Results:** We find evidence that 90% of motion in the cranial-caudal (rigid Y affine component) direction is restricted to  $\pm 3$ mm, although in one patient, motion has been shown to reach a range of 15mm.

**Conclusion:** Evidence has been found that suggests that patient motion can be restricted to a few millimetres of translation in the cranial-caudal direction. The reproducibility of this result by the patient-training method discussed in the introduction is of particular interest to radiotherapy groups, where patient movement remains a problem.

**Collaborators:** The Institute of Cancer Research: Martin Leach, David Collins

**Funding:** EPSRC, The Institute of Cancer Research



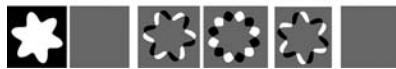
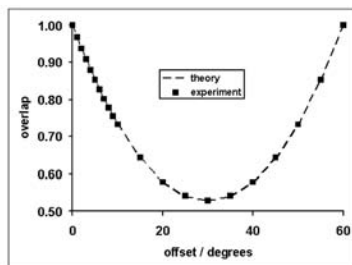
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# Generalised Overlap Measures in Medical Image Analysis

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**William R. Crum – Principal Investigator**

Measures of region overlap such as the Dice and Tanimoto (or Jaccard) coefficients have been widely used in evaluation of medical image analysis algorithms. Image segmentation and image registration are the two classes of algorithm most commonly evaluated in this way. Traditional overlap measures require binary labels (where each image voxel is defined as a member or non-member of a specific label) and cannot distinguish multiple different labels defined on the same image space, or labels that occupy fractions of a voxel. In my talk I will describe extensions of the traditional definitions of overlap measures that address these issues. Such generalised overlaps quantify the overall agreement of the partitioning of images by multiple fractional labels, and reflect the design of



modern evaluation studies. I will briefly describe the theory underlying the generalised overlaps and show their use in exemplar registration and segmentation applications. I will also define an estimate of the scale of error of non-overlap in terms of the overlaps and relate this to a classical measure of distance between sets, the Hausdorff distance.

The figure shows the results of an experiment using synthetic data where the overlap between two petal objects is controlled by rotating one with respect to the other. The graph shows the analytical result (dotted line) for the overlap, as a function of rotation angle, compared with that measured from the image pairs (black squares).

**Collaborators:** Imperial College London: Daniel Rueckert, Kanwal Bhatia; University of Oxford: Mark Jenkinson.

**Funding:** EPSRC, MIAS IRC

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# Imaging at Multiple Scales and Translation to Guided Interventions

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## David Hawkes – Principal Investigator

Within a few months of the discovery of X-rays by Wilhelm Röntgen, X-ray images were used to plan and guide a surgical intervention. In the 1950's real-time fluoroscopic imaging provided the means to place devices in cardiovascular interventions. In the 1970's the advent of 3D imaging, together with the stereotactic frame, allowed guidance of a needle at a 3D target in the brain. Improved methods for registration between images, plan and patient provided frameless surgical navigation. Parallel developments in image directed radiotherapy allowed planning and accurate delivery of radiation. Over the last two decades radio-frequency, high intensity focused ultrasound, photodynamic therapy and cryo-ablation have been developed for image directed tissue ablation. Image directed therapy has to-date primarily been restricted to applications that rely on a rigid body transformation between the patient's anatomy and the image derived plan. Where therapy is to be delivered to soft deforming or moving tissue methods



based on non-rigid registration, biomechanical models and models of tissue motion are required to maintain accurate spatial correspondence. Work is underway in applications in the lung, breast, liver and pelvis. Statistical shape models of anatomy will provide additional information otherwise not available. High-resolution cellular and molecular imaging based on optical, ultrasound or nuclear medicine technologies are now widely available in experimental biology and are becoming available for clinical use. Coupling molecular targeted therapy with image guidance technologies has the potential to provide the specificity required to translate these exciting new therapies to the clinic.

**Collaborators:** UCLH: Bill Lees, Steve Halligan, Margaret Hall-Craggs, Mark Emberton, Colin Hopper; IoN: Tarek Yousry, Rolf Jaeger, Marwan Hariz, Neil Kitchen, Mike Gleeson; Inst of Orthopaedics: David Marsh; Royal Free: Brian Davidson, Alex Seifalian; Guys and St. Thomas': David Landau, Prokar Dasgupta; Inst Cancer Research: Mike Brada, Martin Leach, Steve Webb

**Industrial Partners:** Depuy International, Philips, Kodak, Vision RT, Mauna Kea Technologies

**Funding:** EPSRC, DTI, MRC, CRUK, DoH.

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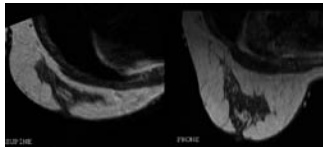
## Breast Cancer Diagnosis and Treatment

Tim Carter

### Registration of breast MRIs acquired in supine and prone positions.

Dynamic contrast enhanced magnetic resonance imaging can indicate the position and extents of breast cancer: information which, if it could be transferred to the operating theatre, might help to reduce the high re-excision rate associated with breast conserving surgery. However, the contrast enhanced images are acquired prone whilst surgery is performed with the patient lying supine. As can be seen from the figure, significant displacement of the structures of the breast occurs between these positions – therefore it is necessary to deform the prone image to the supine position in order to provide images which are surgically useful.

We have developed an approach to this registration problem based on applying displacement loads to a finite element model of the breast. The model is built from the prone image, and is assigned material properties for skin, fibroglandular and fatty tissue. The skin surface in the supine image is extracted. The finite element model of the prone breast is transformed to approximately align with supine surface by rigidly registering fiducial markers affixed to the skin surface. The prone model is then deformed to align with the supine image according to the following rules: (a) skin surface nodes in the model are constrained to lie on the supine surface, but are free to slide along it. (b) nodes corresponding to the fiducial marker locations are constrained to align with the corresponding locations on the prone surface (c) nodes along the chest wall are constrained to behave as a rigid body.



**Collaborators:** Guy's Hospital: N. Beechey-Newman.

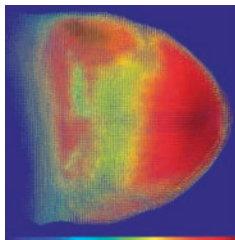
**Funding:** EPSRC, MIAS IRC

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## John Hipwell

### A New Validation Method for Establishing Correspondence Between Pairs of X-Ray Mammograms.

Establishing spatial correspondence between features visible in x-ray mammograms obtained at different times has great potential to aid assessment of change in the breast indicative of malignant changes and facilitate their quantification. The literature contains numerous non-rigid registration algorithms developed for this purpose, but quantitative estimation of registration accuracy is limited. We have developed a novel validation method which simulates plausible mammographic compressions of the breast using an MRI derived finite element model. By projecting the resulting known 3D displacements into 2D and simulating x-ray mammograms from these same compressed MR volumes, we can generate convincing images with known 2D displacements with which



to validate a registration algorithm. We illustrate this approach by computing the accuracy for a non-rigid registration algorithm applied to mammographic test images generated from three patient MR datasets. The algorithm registered these images to a mean accuracy of between 1.6 and 2.3mm, reducing the initial mean misregistrations which varied between 1.3 and 3.3mm. It is our intention to use this validation technique to develop new registration algorithms which will be able to distinguish 3D movement of tissue between two x-ray mammograms from changes in the mass of glandular tissue.



Figure: Projection of simulated 3D breast deformation.

**Collaborators:** University of Manchester: Chris Taylor; Oxford University: Mike Brady, Alison Noble, Nathan Cahill; Kodak Limited: Alan Payne, Graham Kiddle, Hani Muammar, Nathan Cahill.

**Funding:** EPSRC, MIAS IRC, DTI Technology Programme

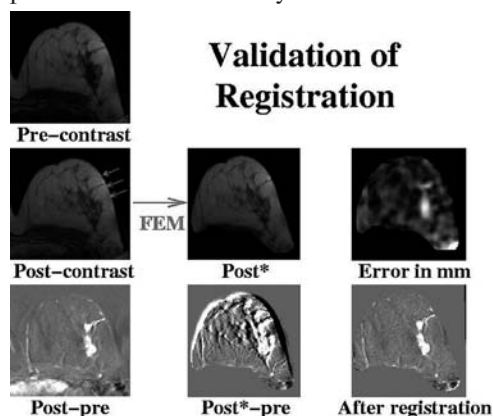
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## Christine Tanner

### Registration and Lesion Classification of Dynamic Contrast-Enhanced Magnetic Resonance Breast Images.

Dynamic contrast-enhanced (DCE) magnetic resonance mammography (MRM) provides information about tissue vascularity and permeability, which cannot be obtained by X-ray mammography. Initial DCE MRM screening studies of young, high-risk women have reported a greatly improved sensitivity at a slightly reduced specificity compared to X-ray mammography. A frequent, but often ignored error source is patient motion. We have developed a technique for the validation of registration algorithms for DCE MRM, which is based on simulating physically plausible deformations by biomechanical computer models using finite element



methods. Firstly, the influence of various parameters on the model's accuracy was assessed

using 2 volunteers. The model's accuracy was more sensitive to both the change in boundary condition and Poisson's ratio rather than the elastic properties. Suitable configurations improved the average accuracy from 6.6mm to 2.1mm. Secondly, plausible breast deformations were simulated for 10 patients and the performance of several registration configurations was then optimized for 5 of these patients. The better configurations reduced the mean registration error of the remaining 5 patients from 1.40mm to 0.45mm. We have created a computer aided diagnosis system for DCE MRM which includes registration. This system achieved an area under the receiver operator characteristics curve of 0.86 for



leave-one-out tests. The classification performance for rigidly registered images was statistically significantly better than for the original images.

**Collaborators:** Cancer Research UK: Martin Leach, Michael Khazen, Preminda Kessar; University of Sheffield: Rodney Hose; Guy's and St. Thomas' Hospital: Corrado D'Arrigo, Nicholas Beechey-Newman, Sarah McWilliams, Evelyn Sanderson, Annette Jones.

**Funding:** EPSRC, MIAS-IRC, EPSRC, MRC.

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## A system for motion compensation in image-guided radiotherapy for lung cancer

In radiotherapy treatment of lung cancer, maximal irradiation of the tumour as well as optimal sparing of the healthy surrounding tissue is a great concern. In conventional radiotherapy treatment, compensation for the breathing-induced motion of the structures of interest is achieved by setting safety margins, which ensure that the tumour, although moving, receives the clinically appropriate dose of radiation. The sparing of healthy surrounding tissue is consequently reduced. The lung radiotherapy project at CMIC, in collaboration with Guy's and St Thomas's Hospital, the Royal Marsden Hospital, and Vision RT (a company specialised in video-based patient tracking and positioning), aims at refining the radiotherapy treatment by adapting it to the breathing lung, ultimately enabling a reduction of the overall delivered dose by tailoring the radiation planning and delivery to the breathing motion. The project is three folded: (1) patient-specific motion models are being developed based on CT data captured from breathing lungs [Poster - Jamie McClelland]; (2) statistical analysis is performed on MR data captured from breathing lungs in order to identify breathing patterns and derive a generic motion model of the breathing lung [Poster - Jane Blackall]; (3) video-based tracking techniques are being integrated in order to non-invasively capture data from the breathing lungs and further deduce from this data information about the tumour motion.

**Collaborators:** Guy's and St. Thomas' Hospital: David Landau, Shahreen Ahmad, Simon Hughes, Charles Deehan; Institute of Cancer Research: Steve Webb, Michael Brada, Ruth Colgan, Dualta McQuaid; Royal Marsden Hospital: Margaret Bidmead, Catherine Coolens.

**Funding:** Cancer Research UK, EPSRC, Department of Health, VisionRT

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### Jamie McClelland

#### CT-based modelling of breathing motion.

Respiratory motion is a major factor contributing to errors and uncertainties when planning radiotherapy treatment of lung cancer patients. It would be very beneficial to incorporate knowledge of the motion of the tumour and surrounding healthy tissue into radiotherapy planning, and may even facilitate more effective treatment using gating or tracking techniques. In the past few years there has been much work on using 4DCT to address some of the problems caused by respiratory motion. We have developed a novel method of constructing subject specific computational motion models that expand and improve on current 4DCT techniques.

Our motion models are constructed using non-rigid registrations, and are able to predict the complex 4D motion and deformation that occurs over an average respiratory cycle. We have constructed motion models using data from 5 patients, and performed a number of validation experiments on them to assess their accuracy. The mean accuracy of the models was found to be 1.6mm over all patients, which was considered very good given the CT slice thickness of 1.5mm.

Further research is now underway into the possibility of modelling the variation between respiratory cycles (inter-cycle variation – this is currently averaged out), and using 3D surface measurements (acquired using the Vision RT system) to find the best respiration (model) parameters.

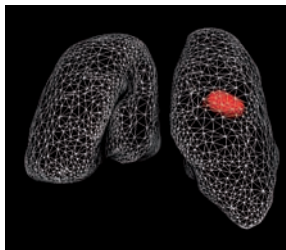


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## Jane Blackall

### **MRI-Based Measurements of Respiratory Motion Variability and Assessment of Imaging Strategies for Radiotherapy Planning.**

Respiratory organ motion has a significant impact on the planning and delivery of radiotherapy (RT) treatment for lung cancer. Currently widespread techniques, such as 4D computed tomography (4DCT), cannot be used to measure variability of this motion from one cycle to the next. We have used fast magnetic resonance imaging (MRI) techniques to investigate the intra- and inter-cycle reproducibility of respiratory motion and also to estimate the level of errors that may be introduced into treatment delivery by using various alternative imaging strategies for lung RT planning. A reference model of respiratory motion is formed to enable comparison of different breathing cycles at any arbitrary position in the respiratory cycle. This is constructed by using fast free breathing images from the inhale phase of a single breathing cycle, then co-registering the images, and



thereby tracking landmarks. This reference model is then compared to alternative models constructed from images acquired during the exhale phase of the same cycle and the inhale phase of a subsequent cycle, to assess intra- and inter-cycle variability (“hysteresis” and “reproducibility”) of organ motion. It is also compared to a series of simple models formed from breath-hold data. Evaluation of these models was carried out on data from 10 healthy volunteers and 5 lung cancer patients. Free-breathing models show reasonable levels of intra- and inter-cycle reproducibility, with RMS errors in the position of organ surface landmarks of 2-5mm for volunteers and 3-6mm for patients, with reproducibility being worse towards the inhale part of

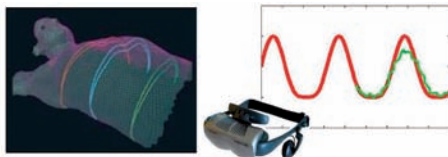
the cycle. Models based on breath-hold sequences have considerably larger associated errors. This approach to analysis of motion and variability has potential to inform decisions about treatment margins and optimise RT planning.

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## Ségolène Tarte

### **Video-based techniques for the acquisition of breathing parameters.**

In order to enhance the radiation planning and delivery, efforts are being directed towards non-invasive capture of breathing-related data. By linking the captured data with the motion models, the tumour motion at the time of treatment could be predicted. A stereo video-based system (Vision RT) enables to capture the motion of the chest and abdomen as surfaces. Capturing these surfaces at time of initial CT scanning allows establishing a spatial and temporal relationship between the CT data and the surface motion, while capturing this data at time of radiation exposure will enable to drive the motion model and consequently adapt the dose



delivery to the current breathing pattern. Ongoing research aims at establishing the relationship between surface motion and tumour

motion. Studies are thus being undertaken to extract meaningful breathing parameters from the captured surfaces. Examples of such parameters include but are not limited to physiological parameters such as tidal volume. Regularity of breathing remains an important issue; and coaching of patients is implemented to induce more reproducible and thus more predictable breathing motion. The demonstration setup presents the capture of breathing data concomitantly to a coupled video and audio feedback through which subjects can be coached to breathe more reproducibly.

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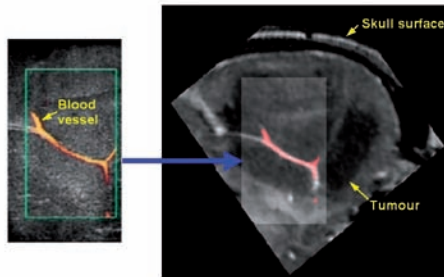
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## Image Guided Orthopaedic Surgery

### Dean Barratt

#### Ultrasound Guidance Medical Interventions.

The principal advantages of ultrasound imaging are that it is safe, non-invasive, relatively inexpensive, and widely available. Ultrasound scanners are extremely versatile, enabling realtime imaging of most of the organ systems of the body. The recent introduction of low-cost, portable scanners has increased access to this modality and has led to growing interest in its application to guiding interventions. Ultrasound images differ substantially from other types of medical images and are subject to numerous modality-specific artefacts. My current research focuses on addressing some of these challenges to develop practical solutions for a range of interventions including neurosurgery, orthopaedic surgery, and emerging minimally-invasive therapies for prostate cancer. In particular, I am interested in developing methods for registering 3D ultrasound images with images obtained using other modalities.



Registration of an intraoperative ultrasound image (left) of a brain tumour to a preoperative MR image (right)

For example, CT or MR images are now available prior to many interventions, potentially providing detailed anatomical (and sometimes functional) information during an intervention which augments that obtained with ultrasound.

**Collaborators:** Depuy International Ltd: Mike Slomczykowski; The National Hospital for Neurology and Neurosurgery: Neil Kitchen; Institute of Neurology UCL: David Thomas; Guy's and St. Thomas' Hospitals: Prokar Dasgupta; University College Hospital: Mark Emberton.

**Funding:** EPSRC, Department of Trade and Industry

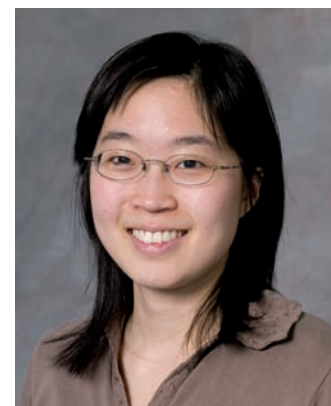
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### Carolyn Chan

#### Ultrasound-Instantiated Statistical Shape Models for Image-Guided Hip Replacement Surgery.

I have developed a method that uses tracked ultrasound as a non-invasive localiser to simultaneously instantiate and register 3D statistical shape models (SSMs) for image-guided hip replacement surgery. Bone surface points derived from a set of tracked B-mode ultrasound images acquired on humans are used to instantiate a patient-specific 3D model of the relevant anatomy.

Two methods were used to produce the SSMs. For both methods, a database of computed tomography (CT) scans were registered to a segmented template using an intensity-based non-rigid registration algorithm which generated deformation fields. The SSMs are generated directly from the deformation fields that are capable of providing a much more densely sampled bone volume for higher accuracy instantiations.



In a cadaver study, the femur and pelvis SSMs were built using 16 and 10 CT images respectively. The root mean square (RMS) distance between the model surface and ultrasound-derived bone surface points were iteratively minimised, the results ranged between 1.1 and 2.0mm for the femurs and 2.3 and 4.2mm for the pelvis. RMS distance between instantiated model and gold standard surface ranged from 1.8 to 3.7mm in the region of the femoral head when ultrasound images were sufficiently sampled, and 2.1 to 3.5mm in the region of the acetabulum.

**Collaborators:** Depuy International Ltd: Mike Slomczykowski; Imperial College London: Philip J. Edwards

**Funding:** EPSRC, DePuy International Ltd, Brainlab AG.

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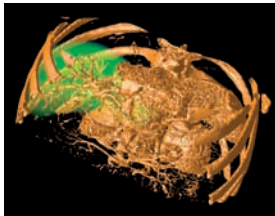
## Liver Disease and Treatment

### Damien Buie

#### Developing a dynamic inter-patient model of the liver.

The very function of the liver makes it exceptionally vulnerable to metastases. Typically the primary tumours arise from lung cancer, gastrointestinal cancers, breast cancer or melanoma and the prognosis from this liver disease are poor in patients where surgical resection is not an option. There are however methods to treat tumours, such as radio-frequency ablation and radiotherapy, that have varying degrees of success, success that is generally limited by the ability of skilled radiographers to isolate tumours.

The reasons that radiologist find it difficult to exactly identify the location of tumours is due to a number of reasons. Firstly, the liver is attached to the diaphragm that undergoes displacement during the breathing cycle of up to 5 cm, distorting the location and shape of the liver. Similarly, depending on the direction to which a patient is lying, the liver undergoes deformation by the other organs in the abdominal cavity potentially changing its shape from initial imaging. Coupled with this is the reality that there is a large degree of variability in the size and shape of the liver from patient to patient.



The core part of my research here at CMIC is to address this issue of the shape variability of the liver by building a statistical model that can parameterise the variation in the shape. The benefits of having an active shape model of a good cross-section of the population is that used in conjunction with non-rigid registration and finite element models, it may provide a real time solution to the dynamic structure of this organ.

**Collaborators:** University College Hospital: Bill Lees; Royal Free Hospital: Brian Davidson

**Funding:** EPSRC

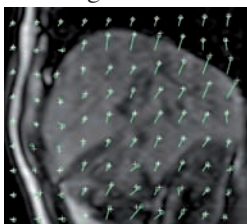
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### Mark White

#### Parameterized modelling of liver deformation during free breathing in MRI.

The liver moves with breathing, causing motion artefacts in some MR sequences. Here we suggest an approach to estimate deformation fields from patient-specific free breathing models. To build test models, we have obtained data from healthy volunteers on a 1.5T Philips Intera system; volume acquisitions of the liver were repeated about once per second, using a combination of SENSE, short echo-chain EPI and k-space undersampling. Continuous volumes were acquired over at least a minute of free breathing.

The aim is to use these data to build models of non-rigid deformation, using a small number of parameters (in this example, overall in-plane translation of the liver) measured during both model acquisition and subsequent MRI sequences targeted for correction. All images are non-rigidly-registered to a reference, then each degree of freedom of each control point is fitted (linear least squares) to the set of parameters across all acquired frames. This provides a model for deformation: given the two parameters of overall offset at some future time, a field of control point displacements can be estimated for the whole liver. An example is shown in the figure, comparing a model-estimated deformation field (based on a training dataset) with the true deformation at that time.



Estimated deformations could be used to reduce motion artefacts in several types of dynamic liver MRI or sequences taking longer than a single breath-hold to acquire. Parameters may be taken from the images themselves, as above, from separate navigator acquisitions, or from an external respiratory monitor.



**Collaborators:** Institute of Cancer Research: Martin Leach, Catherine Coolens

**Funding:** EPSRC

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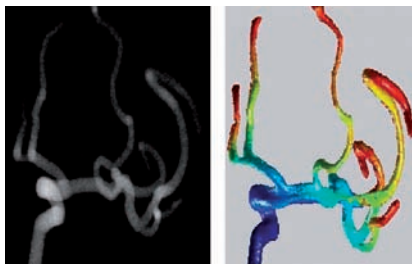
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## Neurovascular Disease

### Irina Waechter

**Purpose:** For the assessment of cerebral vessel diseases, it is very beneficial to obtain three dimensional morphologic and haemodynamic information about the vessel system. Our goal is to determine both concurrently using one rotational angiography sequence. To enable the extraction of flow information, the rotational angiography images should show inflow and outflow of contrast agent. Images with this property however, are not well suited to standard volume reconstruction algorithms. This work shows how flow information can support the vessel reconstruction to overcome this conflict.

**Method and Materials:** In our method flow information is used as follows to determine, for every voxel, the likelihood of being inside a vessel: First, the rotational time intensity curve (R-TIC) is determined from the image intensities at the projection points of the current voxel. Next, the arrival time of the contrast agent bolus at the voxel is estimated from the R-TIC. Finally, a measure of the intensity and duration of the contrast enhancement is determined. The likelihood is used to steer the Fast Marching algorithm, which determines the order in which voxels are analyzed. This enables the centreline of the vessels to be extracted by backtracking. The proposed method was tested on 80 computer simulated rotational angiography sequences with systematically varied blood flow and contrast agent injection parameters.



**Results:** The mean error in the 3D centreline and radius estimation was 0.62 mm and 0.28 mm respectively. Pulsatile blood flow was found to increase the error only slightly (0.05 mm).

**Conclusion:** Under pulsatile and non-pulsatile conditions flow information can be used to enable a 3D vessel reconstruction from rotational angiography with inflow and outflow of contrast agent. Future work will aim to extract more quantitative flow information.

**Collaborators:** Philips Research Aachen: Jörg Bredno, Jürgen Weese.

**Funding:** Philips Research Aachen



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# Cadaver Validation of Intensity Based Ultrasound to CT Registration

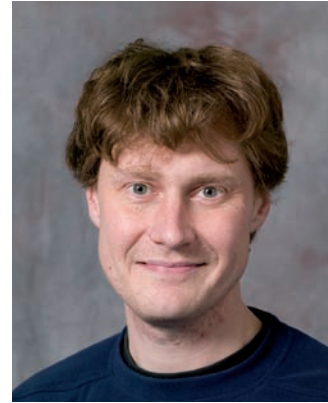
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## Graeme Penney – Principal Investigator

A method is presented for the rigid registration of tracked B-mode ultrasound images to a CT volume of a femur and pelvis. This registration can allow tracked surgical instruments to be aligned with the CT image or an associated preoperative plan. Our method is fully automatic and requires no manual segmentation of either the ultrasound images or the CT volume. The parameter which is directly related to the speed of sound through tissue has also been included in the registration optimisation process. Experiments have been carried out on six cadaveric femurs and three cadaveric pelvises. Registration results were compared with a “gold standard” registration acquired using bone implanted fiducial markers. Results show the registration method to be accurate, on average, to 1.6mm root-mean-square target registration error.

**Collaborators:** Depuy International

**Funding:** EPSRC Advanced Research Fellowship



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# Integrated Acquisition Analysis in Medical Imaging

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## Derek Hill – Principal Investigator

Medical image instrumentation and medical image analysis have traditionally been separate research fields, with physics departments frequently focusing on the former, and engineering and computer science departments on the latter. Reconstruction techniques for the mainstream modalities have typically been in the domain of the instrumentation research, and in MRI and CT have been restricted to FFTs and back projection. One of the major research themes in CMIC is at the interface of these traditional research areas: techniques that integrate the acquisition, reconstruction and analysis. These are all software problems, but involve software running both on the instruments as well as off-line. We show the benefit of these approaches in fast imaging of moving objects, especially the heart, and static objects for which motion is a problem, in particular neuroimaging. A key objective is not just better image quality, but to also improved quantification for diagnosis and clinical trials. The approaches we use include undersampled acquisition, adaptive motion correction using both image-derived and independently derived motion estimates, integrating image registration into reconstruction, and simultaneous reconstruction and segmentation.

**Collaborators:** Kings College London: Reza Razavi; Pontificia Universidad Catolica de Chile: Pablo Irarrazaval; GlaxoSmithKline: Nadeem Saeed, Brandon Witcher; Institute of Neurology: Nick Fox; Imperial College London: Daniel Rueckert, Jo Hajnal; Oxford University: Steve Smith; Guy’s and St Thomas’ Hospitals: Bruce Kirkham, Steve Oakley

**Funding:** EPSRC, MRC, GSK

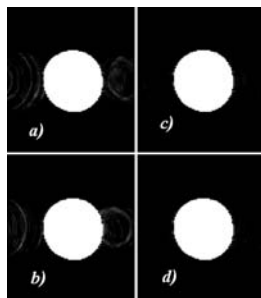


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## Sergio Uribe Arancibia

### Reducing Eddy Currents Artefacts for Self-Navigated Reconstruction in b-SSFP

Recently, there has been great interest in cardiac and respiratory self-navigated sequences for cardiac imaging. Common to these approaches is that the centre profile in  $k$ -space has to be traversed at a pre-defined frequency that properly samples the respiratory and cardiac motions. However, the repeated acquisition of the centre profile causes large jumps in  $k$ -space. These jumps, like the jumps in a regular segmented acquisition, can cause eddy-current artefacts in the images. In this work we present a new profile order scheme for 3D cine acquisition in order to avoid large jumps in  $k$ -space. To do that, the  $ky$ - $kz$ -space was divided into triangular areas. To order the profiles we defined two paths in each area, one



going from the centre to the periphery and one in the opposite direction. The path of the profiles starting at the centre was directed such that the following two expressions were minimized: a)  $\min(\text{disto} + \text{var}(\text{dout}))$  and b)  $\min(\text{disti} + \text{var}(\text{din}))$ , where  $\text{disto}$  and  $\text{disti}$  are the distances for the next jumps in the two paths and the  $\text{var}$  function indicates the variance of all previous jumps in the two paths,  $\text{dout}$  and  $\text{din}$ . The software has been entirely implemented on the scanner hardware (Philips intera 1.5T) using the proprietary pulse-programming environment.

The results of scanning a bottle of doped water using a b-SSFP sequence are shown in the figure:

Comparison of eddy-current artefacts a) standard segmented scan, b) segmented scan including the central profile, c) proposed method, d) proposed method including the central profile.

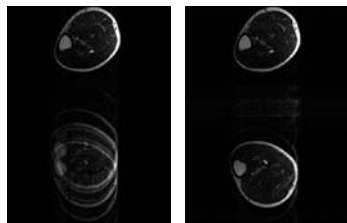
**Collaborators:** Kings College London: Reza Razavi, Vivek Muthurangu; Pontificia Universidad Catolica de Chile: Pablo Irarrazaval.

**Funding:** EPSRC, MIAS IRC

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## Philip Batchelor

Motion of an object degrades MR images, as the acquisition is time-dependent, and thus  $k$ -space is inconsistently sampled. This causes ghosts. Current motion correction methods make restrictive assumptions on the type of motions, for example, that it is a translation or rotation, and use special properties of  $k$ -space for these transformations. Such methods, however, cannot be generalized easily to nonrigid types of motions, and even rotations in multiple shots can be a problem. Here, a method is presented that can handle general nonrigid motion models. A general matrix equation gives the corrupted image from the ideal object. Thus, inversion of this system allows us to get the ideal image from the



corrupted one. This inversion is possible by efficient methods mixing Fourier transforms with the conjugate gradient method. A faster but empirical inversion is discussed as well as methods to determine the motion. Simulated three-dimensional affine data and two-dimensional pulsation data and in vivo nonrigid data are used for demonstration. All examples are multishot images where the object moves between shots. The results indicate that it is now

possible to correct for nonrigid types of motion that are representative of many types of patient motion, although computation times remain an issue.

**Collaborators:** ENIT-Lamsin: Maher Moakher; The Brain Research Institute: Fernando Calamante

**Funding:** EPSRC

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## Redha Bourbertakh

### Three Dimensional Catheter Tracking Using Real-Time Volumetric Imaging

Passive catheter visualisation in MR guided cardiac catheterisation is limited by ambiguity in catheter identification as well as the need for manual tracking. In this work, we present a technique for passive tracking of standard balloon angiographic catheters using real-time volumetric MR imaging.

A healthy male volunteer was imaged on a 32 channel scanner, 1.5T Philips Achieva, and using a custom built 32 channel coil. A flexible plastic tube, filled with manganese chloride solution, was attached to the volunteer's chest. Prior to catheter insertion, real-time 3D reference whole-heart volumes are acquired, sampling the cardio-respiratory space with a temporal resolution of over four volumes per second.

To simulate catheter manipulation, a balloon angiographic catheter was introduced in the tube and the balloon inflated. The catheter was manoeuvred along the tube whilst an interventional data set consisting of 50 free-breathing volumes was acquired. Subsequent image analysis was performed off-line.

After catheter insertion, the location of the tip of the catheter can be automatically identified in the real-time interventional volumes by: 1) calculating difference images by subtracting the current interventional volume from the reference data set, 2) finding the closest reference volume using a similarity measure metric, 3) localising the catheter in 3D from the selected difference image using simple image analysis operators. Figure 1 illustrates the three-dimensional nature of the technique: the tip of the catheter has been successfully localised and tracked.

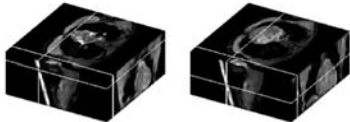


Figure 1: Volume localisation of the catheter tip in three orthogonal reformatted slices at two consecutive time frames.

**Collaborators:** King's College London: Reza S. Razavi, Vivek Muthurangu; University of Karlsruhe: Richard Winkelmann; Philips Research Laboratories Hamburg: Peter Bornert.

**Funding:** EPSRC



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## Matthew Browne

### PPA: Science, Maths and ICT in Medical Imaging

The aim of this project is to make a link between EPSRC-funded medical imaging research and the GCSE curriculum, and also to inspire pupils with a taste of more advanced topics that they might come across at university.

We have established a partnership with Walworth school in south London. Working with a group of high-achieving pupils in an after-school club we have developed teaching activities based on medical imaging. Eight of the pupils spent two weeks at UCL on a work experience placement to help produce teaching material.

By involving pupils and teachers alongside researchers in preparing the material we hope to maximise its relevance to the curriculum, and its interest to the target audience. To gauge the effectiveness of the project, we will be monitoring and assessing the pupils we worked with, in terms of their academic performance and interest in science/maths/ICT.

We provide presentations for interactive whiteboards, an accompanying worksheet, and an online version to facilitate independent study. The material is currently being tested in the classroom, and when complete will be disseminated nationally by means of press releases to education journals and reference as a recommended resource by Edexcel in their new GCSE specifications. All of the material will be made available via [www.howpetworks.com](http://www.howpetworks.com).

**Collaborators:** Edexcel, Walworth school

**Funding:** EPSRC

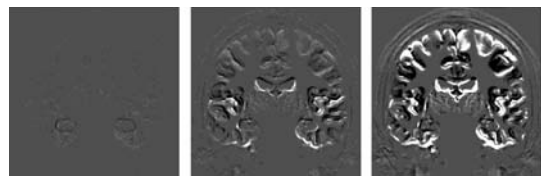


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## Oscar Camara-Rey

### Phenomenological model of diffuse global and regional atrophy using Finite-Element methods.

The main goal of this work is to devise a technique for generating cohorts of MR images with simulated atrophy that can provide a gold standard for the validation of structural MRI-based biomarkers. Several techniques have been used to measure atrophy in cross-sectional and longitudinal studies, but it is extremely difficult to compare their performance since they have been applied to different patient populations. We propose a method for atrophy simulation in structural MR images based on finite-element methods. The method produces cohorts of brain images with known change that is physically and clinically plausible, providing data for objective evaluation of atrophy measurement techniques. Atrophy is simulated in different tissue compartments or in different neuroanatomical



structures with a phenomenological model. This model is based on volumetric measurements from patients with known disease and guided by clinical knowledge of the relative pathological involvement of regions and tissues. The consequent biomechanical readjustment of structures is modeled using conventional physics-based techniques based on biomechanical tissue properties. A thermoelastic model of tissue deformation is employed, controlling the rate of progression of atrophy by means of a set of thermal coefficients, each one corresponding to a different type of tissue. Tissue characterization is performed by means of the meshing of a labeled brain atlas. A longitudinal set of simulated data is shown in the figure. We plan to generate a large cohort of brain images with different pattern of changes induced by dementia and make this database freely available to interested groups worldwide.

**Collaborators:** Institute of Neurology: Nick C. Fox, Rachael Scahill

**Funding:** EPSRC

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## David Cash

### Statistical Deformation Modelling with Intensity Information for Analyzing Changes in Small Brain Structures

Volumetric measurements of individual brain structures obtained from longitudinal MR scans have proven to be a reliable diagnostic marker for cerebral atrophy. For example, decreases in hippocampal volume are much greater in subjects with Alzheimer's related dementia than in ageing controls. These measurements are typically made by manually segmenting the structure of interest. Manual segmentation requires lengthy interaction by users familiar with the relevant neuroanatomy due to structure boundaries with weak edge information. Thus, an automatic segmentation method would be desirable, especially for clinical trials where there are a large number of data sets to process. For this purpose, an automatic segmentation technique was developed based on statistical deformation modelling (SDM). In SDM, non-rigid mappings are determined between each training volume and a single reference volume. Then, principal component analysis of the mapping parameters provides a model of anatomic variability across the training set population and intensity information is incorporated. Segmentation is then performed by fitting the model to unseen image data. The fitting process is based on normalized mutual information, where the intensity information provides more information to the joint histogram by including data from every training set.



**Collaborators:** Institute of Neurology: Nick Fox, Jo Barnes

**Funding:** EPSRC

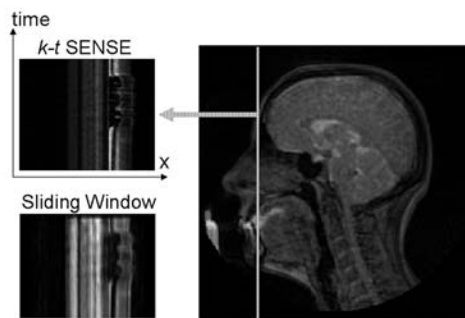
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## Michael Hansen

### Real-time imaging of speech using radial k-t SENSE

Introduction: k-t SENSE offers significant improvement in acquisition speed through the use of training data, which can be integrated into the acquisition using a radial k-space trajectory. A k-t BLAST reconstruction for such trajectories has previously been presented. Here we expand this to k-t SENSE and apply the new reconstruction to real-time imaging of speech.



Methods: Under-sampled 2D radial acquisition was used with a matrix size of 128x128 and 25 projections per frame. Eight receive coils were used. Spatial resolution: 2.0x2.0 mm<sup>2</sup>, temporal resolution: 80 ms. Iterative k-t SENSE reconstruction was compared to sliding window.

Results: Fig. 1 illustrates a volunteer saying “aba-adaaka”. The x-t plot demonstrates the improved temporal fidelity of the k-t SENSE reconstruction.

Discussion: Radial k-t SENSE improves temporal fidelity of speech imaging, but reconstruction is not yet real-time. Parallel computing or a simplified reconstruction could provide images during acquisition.

**Collaborators:** King’s College London: Reza S. Razavi, Vivek Muthurangu; Philips Research Hamburg: Holger Eggers

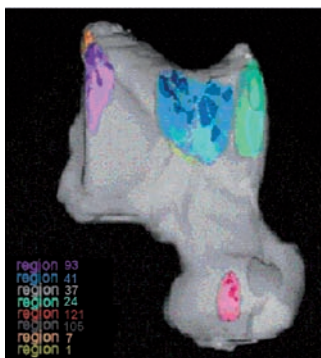
**Funding:** EPSRC, MIAS IRC

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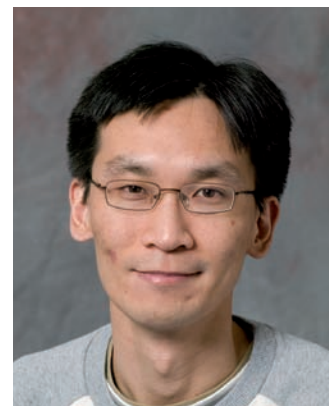
## Kelvin Leung

### Automatic quantification of changes in bone in serial MR images of joints.

Recent innovations in drug therapies have made it highly desirable to obtain sensitive biomarkers of disease progression that can be used to quantify the performance of candidate disease modifying drugs. In order to identify potential image-based biomarkers of disease progression in an experimental model of



rheumatoid arthritis (RA), we present two different methods to automatically quantify changes in a bone in in-vivo serial MR images from the model. Both methods are based on rigid and nonrigid image registration to perform the analysis. The first method uses segmentation propagation to delineate a bone from the serial MR images giving a global measure of temporal changes in bone volume. The second method uses rigid body registration to determine intensity change within a bone and then maps these into a common space using nonrigid registration. This gives a local measure of temporal changes in bone lesion volume. We compare our findings with histology of the subjects.



**Collaborators:** BioMedIA Lab: M. Holden; GlaxoSmithKline: N. Saeed, K. Brooks, J. Buckton, A. Williams, S. Campbell, K. Changani, D. Reid; Imperial College London: D. Rueckert, J. Hajnal

**Funding:** EPSRC, GlaxoSmithKline

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## Kate McLeish

### IXI

IXI is a 3 year e-science project aimed at using grid-enabled image analysis tools for scalable processing of data. For this project brain images are being acquired on 600 normal volunteers to create a database of images which can be used by interested groups with data available via the web. Each subject has T1, T2, Proton density, angio and diffusion tensor scans. Workflow tools are being produced for large scale image analysis, for example image registration and segmentation. Alongside the brain data we are also acquiring longitudinal images on the hands and wrist of patients with rheumatoid arthritis. Affected bones are segmented and automatically aligned to previous time points to establish if bone erosions have increased in volume over the course of a year. Neurogrid builds upon the work of IXI and at UCL we are part of the dementia exemplar. Longitudinal images will be acquired on 75 patients suffering from dementia at 4 sites in the UK. The aim is to increase the outcome of clinical trials by providing real-time quality assessment of the data. As with IXI, workflows are being developed to perform grid-enabled analysis.



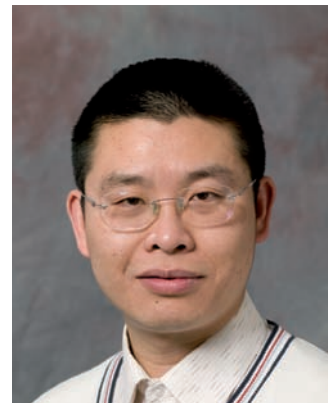
**Collaborators:** Imperial College London: Jo Hajnal, Daniel Rueckert; King's College London: Steve Williams; Oxford University: Steve Smith; Guy's and St Thomas' Hospitals: Steve Oakley, Dr Bruce Kirkham; Institute of Neurology: Nick Fox; Cambridge University: John Hodges; University of Newcastle: John O'Brien  
**Funding:** EPSRC, MRC, GlaxoSmithKline, Philips Medical Systems, Dunhill Charitable Trust

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## Jinsong Ren

### Agreement Measures between Fuzzy Labelling Images

To measure the general agreement between the fuzzy labelling images from brain tissue classification, we present the Partial Volume Overlap Similarity Index (PVOSI) that takes into account of partial volume overlap between voxels and therefore will not lose the advantage of the fuzzy labelling. PVOSI is defined as the ratio of partial overlap volume of two fuzzy labelling images  $C_1$  and  $C_2$  under the criteria  $E$  to the sum of the self partial overlap volume of them under  $E$ . The partial overlap volume of two fuzzy labelling images is calculated voxelwise with a weighting factor for each voxel pair. The value of PVOSI depends on the degree of both spatial overlapping of the labellings and the sum of the partial overlap volumes of two corresponding voxels in the labellings. When the weighting factor is set to a constant 1, the PVOSI is weighted towards the high spatial overlapping of high value voxels. The overlapping background voxels do not contribute at all. The contribution of the overlapping low value voxels is included in the measure but weighted down by their low values. Distinguishing between contributions of high and low value voxels is desired because we are more interested in the agreement of the major parts of the fuzzy labelling images and less interested in the agreement of low value voxels that are more prone to partial volume effect, noise and errors. PVOSI ranges from 0 to 1.



We also present the Binary Volume Overlap Similarity Index (BVOSI) that measures the spatial overlap between two fuzzy labelling images. BVOSI discards the weighting factor in PVOSI and measures only the spatial agreement of two fuzzy labelling images. It doesn't distinguish the voxels based on their values when all of their values satisfy the designated criterion. BVOSI can be used to analyze the spatial agreement distribution between two fuzzy labelling images by using varied criteria in the binary operator and facilitate further analysis or processing.

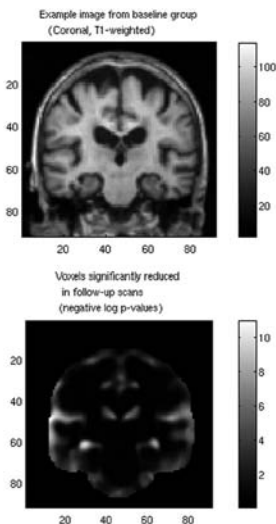
**Collaborators:** Imperial College London: Jo Hajnal, Daniel Rueckert  
**Funding:** EPSRC

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## Gerard Ridgway

Dementias such as Alzheimer's Disease cause chronological changes in the brain which can be detected with structural magnetic resonance imaging. My work is aimed at improving the analysis of longitudinal MRI studies of dementia, using computational techniques encompassing image processing, statistics, and pattern recognition.



The lower plot in the figure illustrates the results of a simple paired t-test applied on a voxelwise basis to a group of patients with two time-points. The image from each patient's second time-point has been affinely registered to that patient's first scan. In simple terms the plot is bright in regions of significant reduction (suggesting degeneration due to disease). The top plot is a single example from the group, provided for visual reference. [Data from the Dementia Research Centre, Institute of Neurology, UCL]



We hope to move beyond simple tests like these, using theory from the field of machine learning; and to capitalise fully on more sophisticated input data, for example maps of volume change produced using non-rigid registration between time-points. The goal is better diagnosis and progress-tracking of dementia.

**Collaborators:** Institute of Neurology UCL: Nick Fox  
**Funding:** EPSRC, GSK

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## Julia Schnabel

### Non-rigid registration using free-form deformations: concepts, applications and validation.

Free-form deformations have been found very useful in a number of medical image registration tasks, including patient motion correction in contrast-enhanced MR mammography, volume analysis in serial brain MR imaging, brain atlas generation, as well as motion correction and tracking in liver and cardiac imaging. We have developed a number of techniques to improve the registration performance, including the use of multi-level B-splines and non-uniform mesh generation. The accuracy of these techniques was established using a finite element simulator, which allowed us to simulate gold standard deformation fields for physically plausible registration scenarios. Learning from that, we have investigated the integration of biomechanical motion modelling into the registration framework. Furthermore, we have used FFDs to obtain statistical shape knowledge, allowing us to embed prior information about shape and location of structures into the registration process.



**Collaborators:** Philips Medical Systems: Frans A. Gerritsen, Marcel Quist; Royal Marsden Hospital: Martin O. Leach; Imperial College London: Daniel Rueckert; University of Manchester: Tim Cootes; Oxford University: Steve Smith, Mark Jenkinson; Institute of Neurology: Nick Fox

**Funding:** Philips Medical Systems, EPSRC

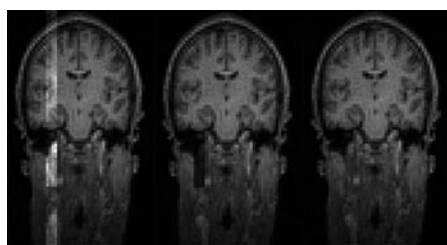
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## Bea Sneller

### Flow Artefacts in MR Imaging for Alzheimer's Detection and Progression.

Alzheimer's disease progresses with cerebral atrophy particularly in the medial temporal lobes. Serial 3D T1-weighted MRI can measure this progression with a sensitivity dependent on stable acquisition which may be undermined by image artefacts. We visually determined the frequency and cause of temporal lobe artefacts from 758 subjects' scans. 12.5% of subjects' scans suffered from temporal lobe artefacts, 65% due to pulsatile flow in the carotid artery. A technique was developed to reduce the total flow artefact intensity; factor 4 reduction in a 40 shot simulation. To simulate the artefact, we approximated the carotid artery by a cylinder in a volunteer's scan. We assumed flow was constant for each plane in 3D k-space, and generated one 3D image per shot, with the carotid intensity modulated according to a representative flow profile and acquisition sequence timing. Array coil data was modelled as multiple views generated using coil intensity profiles and Rician noise. We generated the artefact-corrupted image for each coil, by transforming into k-space the modulated image corresponding to each shot, assembling one plane from each modulated k-space to



Before (left), after (centre) artefact reduction.

Right: artefact-free scan.

**Collaborators:** Institute of Neurology: Nick Fox, Ellen Garde

**Funding:** EPSRC

form a new k-space, and transforming back into the image domain. To correct the artefact, information from the array coils was used to determine the un-known carotid intensities in the different shots. Artefact appears differently in each coil view, allowing determination of these unknown intensities by minimising the standard deviation of intensities between coil reconstructions, using a conjugate gradient algorithm. Work is ongoing to apply this technique to scans with physical artefact.

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# Polarised light imaging of white matter: useful or not?

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## Lewis Griffin – Principal Investigator

DT-MRI is a method of mapping the geometry of white matter that is possible as the water diffusivity tensors of the tissue are locally aligned with the fibre direction. The refractive index tensors of the tissue are similarly aligned, which forms the basis of polarized light imaging.

We will review the theory, methods and results of polarized light imaging with particular emphasis on the difficult aspects. These difficulties range from practical issues such as brain sectioning, to fundamental ambiguities such as recovery of fibre inclination. The strengths and weaknesses of polarised light imaging as compared to DT-MRI will be discussed. These differences relate to issues of resolution, field-of-view, 2D vs. 3D and fibre-crossing effects.

**Collaborators:** Friedrich-Schiller-University Jena: Hubertus Axer

**Funding:** EPSRC



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## Alex Nasrallah

### Dependencies between gradient directions at multiple locations are determined by the power spectra of the image

A well-known statistical regularity of natural image ensembles is that their average power spectrum exhibit a power-law dependency on the modulus of spatial frequency. The power spectrum describe the correlation which exist between pairs of pixel intensities, however, they do not describe the correlation between gradient directions. In this study, we have used information-theoretic measures to compute the amount of dependency which exists between two gradient directions at separate locales; we classify this result as 2-point statistics. This is then extended to measure the dependencies of gradient directions at three separate locales which we classify as 3-point statistics. To assess the influence of the power spectrum on the interactions of gradient directions, we collect statistics from four different image classes: A - natural images, B - phase-randomized natural images, C - whitened natural images and D - gaussian noise images. The image classes A and B have the same power spectra, as do C and D. The results show that for image classes A and B, as well as C and D, the 2-point and 3-point gradient direction interactions are indistinguishable. Further, we have studied other image classes with different forms of power-spectra, and these results do not invalidate the hypothesis that the dependencies between gradient directions at multiple locations are determined by the power spectra of images. This hypothesis is so precisely validated by our experiments that we suspect it is amenable to mathematical proof, though so far we have not found one.

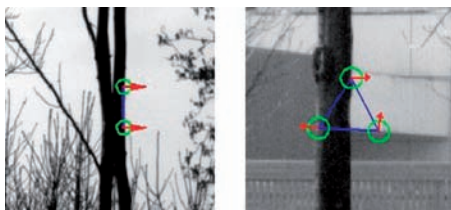


Figure: Examples of collecting gradient directions for 2-point (left) and 3-point statistics (right).

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## Tony Shen

### A framework that unifies segmentation, registration and shape models.

We propose a novel, semi-automated framework for medical image analysis unifying three processes – segmentation, registration and shape modelling. By tightly integrating these processes, the proposed framework aims to maximise the information extracted from an image while minimising user inputs.

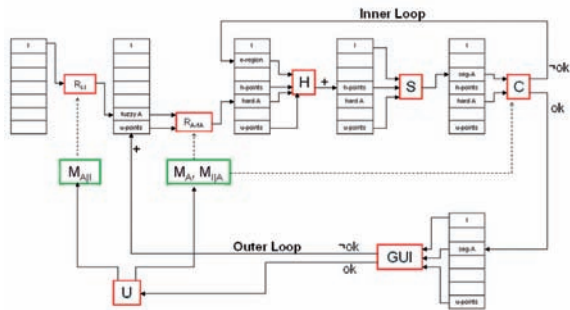
The core of the framework is the Segmentation Module. The segmentation process requires foreground and background points, which are acquired via user inputs and/or hypothesis made using Shape Models. According to changes in the list of the points, the Segmentation Module updates the segmentation. The framework consists of two loops of execution: the Inner and Outer Loops.

The Inner Loop is the automatic part of the framework. First, the image is registered with Shape Models to enable the Hypothesis Module to predict foreground and background points. Then, the points are processed by the Segmentation Module.

The output is compared with the Shape Models

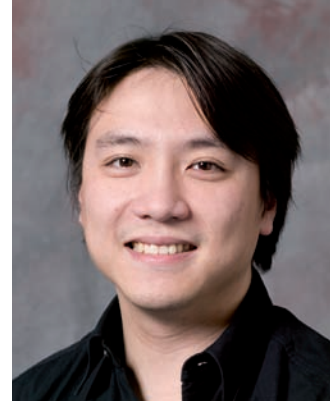
by the Consistency and Error Detection Module. Any inconsistency will cause the Hypothesis Module to update its predictions accordingly. The Inner Loop will continue until no more inconsistency has been found and the result will be passed on to the Outer Loop.

The Outer Loop displays the result in a GUI. Additional foreground/background points can be added via the GUI and fed back to the Inner Loop if the user is not satisfied with the result.



Initial evaluation has shown that integration of these processes improves speed and consistency of the results compared to using the Segmentation Module alone without using the Shape Models and Registration Module.

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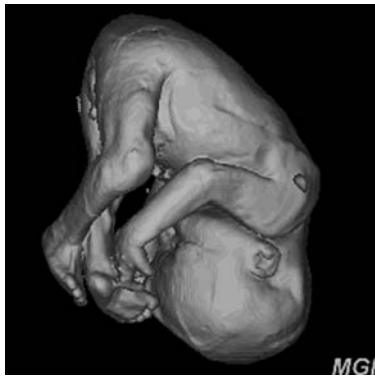
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# Segmentation, ASMs, and Reconstruction

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## Andrew Todd-Pokropek and Alf Linney – Principal Investigators

At UCL the group originally called the Medical Image Computing and Graphics combined with the Quantitative Medical Image group and is now established within CMIC. This group (6 PhDs, 3RAs plus associated NHS staff) was initially concerned with a number of projects in the segmentation area. Clinically these were applied to CT livers, aortic aneurisms, the colon, 3D foetal cardiac ultrasound images and MR brains. Methods that were been developed used: snakes (T-snakes and Gradient Vector Flow), Active Shape Models (ASM), watersheds, fuzzy connectivity, and level set methods in particular of multiple regions (for example chambers of the heart). This general topic has been associated with that of classification, of lesions, texture and shape changes, and includes other



target organs such as breast, lung and vocal folds. Wavelet based methods have been exploited and generalised and an innovation introduced has been that of ICA

based ASMs. Links between segmentation, feature detection and Non-rigid registration (NRR) have also been explored and include validation of NRR and the analysis for vector deformation fields. Additional topics have been those of partial volume correction, and the use of non-linear priors to improve the uniformity of resolution in tomographic reconstruction.

**Collaborators:** ULCH; W. Lees, A. Gillams, C. Rodeck; GOSH: C. Hall, A. Offiah; IOL R. Epstein

**Funding:** EPSRC, MIAS IRC, MRC



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## Irving Dindoyal

### Automated detection of foetal cardiac chambers with a deformable model.

Segmentation of the foetal heart can facilitate the 3D assessment of the cardiac function and structure. Segmentation of the cardiac chambers allows measurement of their absolute size for evaluation of the function of the heart, compromised either by cardiac malformations or by non-cardiac diseases such as immuno-haemolysis.

Manual tracing of the foetal cardiac chambers is tedious, time consuming and often difficult to achieve high confidence by manual means especially where there is missing structural information in echocardiographic images. We present a 2D/3D level set deformable model to automatically segment all four cardiac chambers simultaneously in the presence of drop out artefacts.

The mean intensity region was derived from a sphere placed manually inside each chamber. The sphere is grown to fill the chamber using a level set deformable model that utilises region based information and edge flow to direct the evolving surface towards myocardium boundaries. The segmented boundaries are automatically penalized from intersecting at walls with signal dropout by collision detection of the evolving surfaces.

Root mean square errors of the perpendicular distances between the algorithm's delineation and manual tracings are within 7 pixels (<2mm) in 2D (excluding outliers) and under 3 voxels (<4.5mm) in 3D. The obtained ejection fraction is consistent with manually measured values in the literature.

The automated algorithm provides comparable results to manual segmentation. The results are obtained quickly and are very repeatable. Future work will include further testing on additional datasets and validation on a phantom.

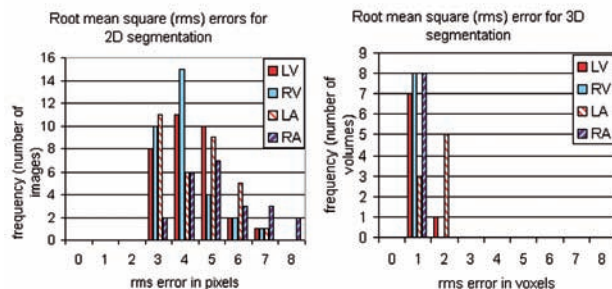


Figure. Root mean square errors for the segmentation of each chamber where LV and RV are the left and right ventricles respectively, LA and RA correspond to the left and right atria respectively.

**Collaborators:** University College Hospital: Jing Deng, Charles Rodeck

**Funding:** EPSRC, MIAS IRC, MRC

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## Alun Evans

### Automatic 3D Segmentation of Liver Tissue from CT Datasets.

Manual segmentation of liver tissue from computerised tomography (CT) datasets can provide useful information to clinicians, such as an estimation of the volume of the liver and the quantification of abnormalities. However, manual segmentation is a slow, laborious process, and an automatic segmentation method has potential to assist in both the diagnosis of disease and in treatment planning. This paper presents initial results from work that extends on previous 2D segmentation methods by implementing full 3D liver segmentation, using a self-reparameterising active contour model. 3D liver segmentation has the advantage over 2D techniques, as the whole liver dataset is analysed at once, rather than as a series of individual slices. Results are presented showing volumetric and overlap analysis of eight liver datasets. Further work on improving the segmentation technique, and methods to validate the results, are then discussed.

**Clinical Collaborators:** University College Hospital: Bill Lees

**Funding:** EPSRC, MIAS IRC

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## Tryphon Lambrou

### Wavelet-Based Analysis And Classification Of Liver CT.

Abstract: In this paper a feasibility study of liver CT dataset classification, using features from different scales of the wavelet transform analysis in conjunction with statistical pattern recognition methods is presented. In our study 720 extracted sub-images from 13 liver CT scans were used, in order to establish which features distinguish better between the normal/cancer classes. Statistical measurements were collected; from the sub-images as well as from their different scale wavelet transform coefficients. We found by using the Leave-One-Out method that the combination of the features from the 1st and 2nd Order statistics, achieved overall classification accuracy > 90.0%, both specificity and sensitivity > 90.0%. Features selected by the spatial domain performed better than the wavelet based techniques, under the classification rule of Quadratic Classifier (QC). In addition, features selected by the 3rd scale wavelet transform coefficients performed better than those collected from the other wavelet scales, under the classification rule of Bayesian Classifier (BC).

**Clinical Collaborators:** University College Hospital: Bill Lees

**Funding:** EPSRC, MIAS IRC

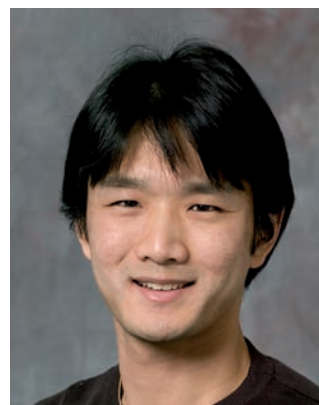


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## Richard Tsai

### Novel Vessel Tracking Algorithms for Extraction of Blood Vessel Trees within the Liver.

Blood vessel tracking is extremely important to diagnose abnormalities and diseases within the body. This type of research has important clinical applications. For example, 3d visualization models along with the separation of the hepatic and portal blood supplies can be used to optimise lesion ablation using RF or Focussed Ultrasound (FUS). Furthermore, the tracking of both these vascular trees and their placement within the surface outline of the liver is an important pre-requirement for accurate Non Rigid Registration (NRR) for tracking and measuring changes of lesions within the highly deformable liver. There are good indications that the location of lesions with respect to blood supply is more stable than location of lesion with the highly deformable liver itself. This research project, which has just started, involves using and comparing different segmentation methods in order to outline clearly and hence track both the major vessels and the smaller blood vessels along with identification of vessel bifurcations. Vessel can also be identified using appropriate filters and templates, and then vessel paths can be propagated through the 3D structures. Currently, multiscale vessel enhancement filters and level-set analysis for segmentation are in the process of being assessed. The methods being tested originated with those employed previously for vessel tracking in lungs and the blood supply to and within the brain, but they need to be modified and extended in particular with respect to NRR matching in the liver.

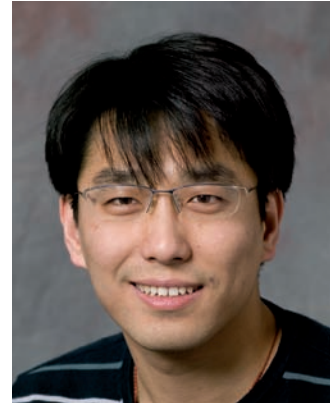


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## Zinhua Su

### **Markov Random Field Restoration of Independent Component Analysis Based Active Shape Model for Finding Correspondence.**

Statistical shape models use Principal Component Analysis (PCA) to describe the shape variations. However, PCA has the restriction that the input data must be drawn from a Gaussian distribution, and is only able to describe global decomposition. In recent years, Independent Component Analysis (ICA) has become a popular alternative for shape decomposition. Due to the local variations that ICA represents, the final optimal result usually turns out to be an invalid shape. In this paper, with the consideration of the influence from neighborhood points by using Markov Random Field (MRF), we overcome this drawback introduced by ICA. Our initial results show that our proposed method has advantages on both the convergence time and the rate of obtaining a valid shape. From this, we can conclude that the MRF based ICA model provides improved results to the Bayesian based ICA model currently used.



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