Theme 4
Biomedical Engineering and Imaging
2020/21
Contents

1.4 The earliest brain changes associated with Lewy body disease .......................................................... 4
2.4 Neuroadaptive functional MRI for characterisation of sensori-motor system development in the newborn infant .................................................................................................................. 5
3.4 Application of Deep Learning to Predict Optimal Ablation Therapy for Atrial Fibrillation from Magnetic Resonance Imaging Data ......................................................................................... 7
4.4 Clinically Feasible Whole-Brain Metabolite Mapping with Chemical Exchange Saturation Transfer (CEST) Magnetic Resonance Imaging (MRI) ......................................................................................... 8
5.4 Advancing intraoperative Optical Coherence Tomography (iOCT) capabilities for precise delivery of retinal therapeutics ........................................................................................................... 9
6.4 Cellular distribution of metals and radionuclides using novel elemental mapping techniques ........................................................................................................................................... 10
7.4 Optimising neuroimaging in the management of brain tumours using artificial intelligence 12
8.4 Non-invasive and quantitative imaging of fibrosis in deep vein thrombosis by MRI .............. 13
9.4 αvβ6-Targeted probes for pre- and intra-operative imaging of pancreatic cancer ................. 14
10.4 Fetal MR spectroscopy for non invasive assessment of liver, adipose tissue and placenta abnormalities in pregnancy complicated by maternal metabolic disease ..................................... 16
11.4 Unravelling the role of pericellular matrix mechanics in regulating stem cell fate in 3D .... 18
12.4 Artificial Intelligence (AI) based Multi-Organ segmentation of Healthy Tissue Metabolism in PET/CT imaging in Cancer. ............................................................................................................ 20
13.4 Sensing central blood pressure with advanced imaging and AI technologies ...................... 21
14.4 High Resolution Quantitative MRI for Neurology in Paediatric Subjects ............................... 22
15.4 Characterising Atrial Fibrosis Properties for Predicting Atrial Fibrillation Ablation Outcome ................................................................................................................................ 23
16.4 3D Cardiac Magnetic Resonance Fingerprinting with Deep Learning .................................. 24
17.4 Real time MR-guided radiofrequency ablation of cardiac arrhythmias .............................. 25
18.4 Multifunctional Molecular Probes for Integrin-αvβ6 Expressing Carcinoma PET Imaging and Fluorescence-guided Surgery ....................................................................................................... 27
19.4 Artificial Intelligence Enabled Evaluation of Congenital Heart Disease ............................. 29
Imaging and Biomedical Engineering

This theme focuses on the link between biomedical and physical sciences – particularly physics, engineering and computational approaches. Clinical functional and molecular imaging (MRI, PET, X-MR and PET-MR) is a major strength, along with computational modelling and biomaterials.

When choosing a project from this catalogue in the funding section of the online application form please enter: MRCDTP2020_Theme4

Deadline for application: Sunday 1st December 2019
Shortlisted candidates will be contacted in early January.

Interviews: 29th & 30th January 2020
The 2020/21 studentships will commence in September 2020.

For further Information or queries relating to the application process please contact mrc-dtp@kcl.ac.uk

Projects listed in this catalogue are subject to amendments, candidates invited to interview will have the opportunity to discuss projects in further detail.
The earliest brain changes associated with Lewy body disease

Co-Supervisor 1A: Prof Dag Aarsland
School/Division & CAG: IOPPN, Academic psychiatry, Dept of Old Age Psychiatry
KCL/KHP Email: dag.aarsland@kcl.ac.uk
KCL/KHP Website: https://www.kcl.ac.uk/ioppn/depts/oldage/index

Co-Supervisor 1B: Prof Gunter Schumann
School/Division & CAG: IOPPN, SGDP
KCL/KHP Email: gunter.schumann@kcl.ac.uk
KCL/KHP Website: https://www.kcl.ac.uk/ioppn/research/centres/pons/home

Project description:

We will carry out in-silico co-expression analyses of the most Lewy-body disease (LBD)-relevant mutated genes and derive mutation-based gene scores for genetic analyses, using the PROTECT platform, with > 25,000 people aged > 50 without dementia, with a wealth of health information, annual online cognitive assessments and genotyping of 10,000. Participants with mutations typical for LBD will be invited for deep phenotyping including structural and functional MRI. Scans from a large international multicentre KCL-lead cohort of LBD patients are available for comparing with established LBD. In addition, we will test if the gene groups related to disease-causing mutations affect brain and neurocognition across the life span. We will therefore analyse data of the longitudinal neuroimaging-genetics cohort IMAGEN with data of 2000 participants assessed at age 14, 16, 19 and 23 years.

Techniques and skills:

Imaging, Genetics, including working hands-on with genome-wide association study data and polygenic risk scores, big-data statistics including artificial intelligence, clinical phenotype of early neurodegeneration.

Skills training:

The student will gain experience from working with the Protect Steering group, and with experienced genetic scientists, imaging experts, and will be working with experienced bio-informaticians.

Over-arching Objectives: To characterize the brain changes in pre-clinical stage of LBD by state-of-the art brain imaging scanning in people with LBD-specific mutations.

Objectives:

Year 1: Understand the Protect database, including genetic dataset.
Year 2: Understand LBD; identify the relevant imaging clinical features indicating possible prodromal LBD. Perform first analyses.
Year 3: Perform main imaging analyses.
Year 4: Finalize statistical analyses. Write report.

One representative publication from each co-supervisor:


2.4 Neuroadaptive functional MRI for characterisation of sensori-motor system development in the newborn infant

Co-Supervisor 1A: Dr Tomoki Arichi  
School/Division & CAG: School of Biomedical Engineering and Imaging Sciences  
KCL/KHP E-mail: tomoki.arichi@kcl.ac.uk  
KCL/KHP Website: https://www.kcl.ac.uk/people/tomoki-arichi

Co-Supervisor 1B: Prof A David Edwards  
School/Division & CAG: School of Biomedical Engineering and Imaging Sciences  
KCL/KHP Email: ad.edwards@kcl.ac.uk  
KCL/KHP Website: https://www.kcl.ac.uk/people/david-edwards

Project description:

During early life, human motor behaviour rapidly evolves to enable independence and environmental interaction. This is accompanied in the brain by dramatic changes in the associated neural activity and establishment of sensori-motor network connectivity with increasing involvement of associative motor processing areas. Using state-of-the-art fMRI and MR-compatible robotics (Allievi et al. 2014, Front. Neurol.), this project will precisely characterise how sensori-motor activity and network integration evolves during this crucial stage of life.

In a traditional fMRI experiment, patterns of activity induced by pre-specified stimuli are identified. This approach typically only considers a few stimuli and constrains study populations to only those who can meet specific conditions. In contrast, we will use a new methodology: neuroadaptive Bayesian optimisation (Lorenz et al. 2017, Trends in Cognitive Sciences) combining real-time fMRI with machine learning to efficiently and automatically search through experimental conditions to identify those optimal for individual infants. This will allow us to adapt the task to individual infants and efficiently map brain responses across a large space of stimuli, allowing for greater understanding and generalisation across different infant populations and ages.

Objectives:

Year 1/3: Training in neuroimaging. Development of neuroadaptive Bayesian optimisation methodology in collaboration with Professor Leech (KCL) and robotic stimulation tools (Professor Burdet, Imperial College).  
Year 2/3: Data collection from newborn infants.  
Training:

fMRI methodology and analysis, machine learning, developmental neuroscience through the supervisory team; the School's educational program; external educational courses and conferences.

One representative publication from each co-supervisor:


3.4 Application of Deep Learning to Predict Optimal Ablation Therapy for Atrial Fibrillation from Magnetic Resonance Imaging Data

**Co-Supervisor 1A:** Dr Oleg Aslanidi, Reader in Biophysical Cardiac Modelling
School/Division & CAG: School of Biomedical Engineering and Imaging Sciences, Imaging and Biomedical Engineering Clinical Academic Group
KCL/KHP E-mail: oleg.aslanidi@kcl.ac.uk
KCL/KHP Website: https://kclpure.kcl.ac.uk/portal/oleg.aslanidi.html

**Co-Supervisor 1B:** Dr Andrew King, Reader in Medical Image Analysis
School/Division & CAG: School of Biomedical Engineering and Imaging Sciences, Imaging and Biomedical Engineering Clinical Academic Group
KCL/KHP Email: andrew.king@kcl.ac.uk
KCL/KHP Website: https://kclpure.kcl.ac.uk/portal/andrew.king.html

**Project description:**

**Background:**
Atrial fibrillation (AF) is a very common arrhythmia that affects millions of adults and is associated with high levels of morbidity and mortality. Catheter ablation (CA) has become one of the first line treatments for AF, but the success rate of empirical CA procedures remains poor.

**Aims and objectives:**
The project aims to develop a novel deep learning approach to predict patient-specific CA that can terminate AF efficiently. To achieve this, we will simulate multiple CA scenarios using computational models of 3D atrial electrophysiology based on patient MRI data, and use the outcomes to train a deep neural network. Thus, the predicted optimal CA strategy will be linked as a label to the underlying patient imaging data, and the network will be trained based on such model-informed MR images. The trained and validated network will be able to predict the optimal CA from the images only, providing a fast, clinically-compatible tool for improving CA therapy in a patient.

**Objectives:**
Year 1: Derive 160 image-based atrial geometries from MR images acquired from AF patients.
Year 2: Create MR image-based 3D atrial models for simulating patient-specific AF and CA scenarios.
Year 3: Train a deep neural network using the patient images labelled based on the model simulations.

**Skills:**
The student will learn about cardiac anatomy and function, pathophysiological changes of the heart underlying arrhythmias, computer models applied to study cardiac electrophysiology and arrhythmia mechanisms, as well as deep network architecture. They will also gain advanced skills in image-processing, computer programming, computational modelling and machine learning.

**One representative publication from each co-supervisor:**


**4.4 Clinically Feasible Whole-Brain Metabolite Mapping with Chemical Exchange Saturation Transfer (CEST) Magnetic Resonance Imaging (MRI)**

**Co-Supervisor 1A:** Prof Gareth J Barker  
School/Division & CAG: IoPPN, Division of Neuroscience, Department of Neuroimaging  
KCL/KHP Email: Gareth.Barker@kcl.ac.uk  
KCL/KHP Website: [https://kclpure.kcl.ac.uk/portal/en/persons/gareth-barker(d129c9dd-e4e8-490b-9eeb-3d1d13bea372)/biography.html](https://kclpure.kcl.ac.uk/portal/en/persons/gareth-barker(d129c9dd-e4e8-490b-9eeb-3d1d13bea372)/biography.html)

**Co-Supervisor 1B:** Dr Tobias C Wood  
School/Division & CAG: IoPPN, Division of Neuroscience, Department of Neuroimaging  
KCL/KHP Email: Tobias.Wood@kcl.ac.uk  
KCL/KHP Website: [https://kclpure.kcl.ac.uk/portal/en/persons/tobias-wood(f5fb2e5e-0d3b-4648-b9fa-c57c1a93bae).html](https://kclpure.kcl.ac.uk/portal/en/persons/tobias-wood(f5fb2e5e-0d3b-4648-b9fa-c57c1a93bae).html)

**Project description:**

**Background:**  
Chemical Exchange Saturation Transfer (CEST) is a Magnetisation Transfer (MT) preparation method which encodes quantitative information about certain proteins and neurotransmitters into Magnetic Resonance (MR) images. It has potential applications in pathologies including stroke and cancer. It is not yet in routine use, however, because the complex modelling involved requires the collection of multiple images and so, due to time constraints, the resulting maps are either low resolution or restricted to subsections of the brain. This project will investigate methods to speed up both data acquisition and analysis, by minimising the number of images to be collected, maximising their acquisition speed and optimising their CEST preparation. It will also investigate the feasibility of incorporating CEST into a unique, near silent, MR sequence, to enhance patient comfort.

**Techniques:**  
Reducing the required volume of data will entail building detailed numerical simulations of a CEST experiment and designing novel CEST preparation schemes. Optimising the acquisition time will require refining state-of-the-art MR sequences and image reconstruction methods to work with CEST. This will require developing expert knowledge of MR physics, plus scanner and general programming. Such expertise is highly transferable to industry, or other subject areas.

**Objectives:**  
Rotation project/Year 1 - Comparison of existing CEST strategies and selection of candidate methods.  
Year 1 – Development of CEST simulations/models and quantitative analysis methods. Learning MR scanner programming.  
Year 2 – Implementation and refinement of fast/silent CEST methods on MR scanner.  
Year 3 – Comprehensive testing and validation in healthy controls, and completion of PhD thesis.

**One representative publication from each co-supervisor:**


5.4 Advancing intraoperative Optical Coherence Tomography (iOCT) capabilities for precise delivery of retinal therapeutics

Co-Supervisor 1A: Dr Christos Bergeles
School/Division & CAG: School of Biomedical Engineering & Imaging Sciences
KCL/KHP Email: christos.bergeles@kcl.ac.uk
KCL/KHP Website: www.rvim.online

Co-Supervisor 1B: Prof Tom Vercauteren
School/Division & CAG: School of Biomedical Engineering & Imaging Sciences
KCL/KHP Email: tom.vercauteren@kcl.ac.uk
KCL/KHP Website: https://www.kcl.ac.uk/people/tom-vercauteren

Project description:

Ophthalmology has reached a point where gene vectors, small drug molecules, and stem cells are considered as hopeful treatments for degenerative diseases that cause blindness. These therapeutics need to be delivered to specific retinal layers for their promise to be fulfilled.

Precise delivery of novel therapies will be guided by Intraoperative Optical Coherence Tomography (iOCT) microscopes, a modality microscopically imaging not only the retinal fundus, but also the “hidden” subretinal layers where therapeutics should be delivered. Due to their requirement for real-time imaging, iOCT systems provide axial/slice images that sacrifice resolution for increased frame rates. Further, the images’ 2D/slice nature makes orientation/localisation of delivery sites within the 3D subretinal volume challenging for the surgeon.

Within the context of the proposed PhD Project, the student, of a computer science or computer engineering background, will develop deep learning algorithms that computationally enhance the image reconstruction process therefore improving the capabilities of iOCT devices.

Objectives:

Year 1 - Improve iOCT image resolution: Use high resolution pre-operative 3D OCT to improve the low axial and lateral resolution of 2D iOCT images and clearly delineate retinal layers.

Year 2 - Assist in target localisation: Visually direct scanning (assistive visual cues) to regions of the retina that have been pre-operatively selected as therapeutics-delivery sites.

Year 3 - Enable guided therapy delivery: Develop an iOCT-based navigation framework that detect and tracks therapy-delivery targets.

One representative publication from each co-supervisor:


6.4 Cellular distribution of metals and radionuclides using novel elemental mapping techniques

**Co-Supervisor 1A:** Prof Phil Blower  
**School/Division & CAG:** School of Biomedical Engineering and Imaging Sciences; Imaging Sciences CAG  
**KCL/KHP Email:** Philip.Blower@kcl.ac.uk  
**KCL/KHP Website:** https://kclpure.kcl.ac.uk/portal/philip.blower.html

**Co-Supervisor 1B:** Dr Samantha Terry  
**School/Division & CAG:** School of Biomedical Engineering and Imaging Sciences; Imaging Sciences CAG  
**KCL/KHP Email:** samantha.terry@kcl.ac.uk  
**KCL/KHP Website:** https://kclpure.kcl.ac.uk/portal/samantha.terry.html

**Project description:**

Molecular imaging and therapy with radionuclides relies on radiometals (Tc-99m, In-111, Zr-89, Ga-68, Cu-64 etc.) incorporated into molecular targeting vehicles. The cellular/subcellular location of these metals is key to optimal efficacy. For example, I-131 (for therapy of thyroid cancer) accumulates in thyroid colloid rather than in thyrocytes (see Figure below). We hypothesize that Tc-99m pertechnetate and Re-188 perrhenate accumulate within thyrocytes and thus may be more effective than I-131. The student will test this hypothesis by developing and using cutting edge analytical and imaging techniques: laser ablation-inductively couple plasma mass spectrometry (LA-ICPMS) and secondary ion mass spectrometry (SIMS). Similar studies with other beta, alpha and Auger emitters (e.g. Cu-64, Bi-213, Ga-67 respectively) for cancer treatment will follow. The student will become expert in targeted radionuclide therapy for cancer; molecular imaging; techniques for measuring and imaging the concentration of individual elements, especially metals, in cells and tissues: LA-ICPMS, SIMS, microautoradiography and electron microscope methods.

**Exemplar use of elemental mapping and microautoradiography.** Top left: schematic structure of thyroid follicle, Top right: SIMS image showing distribution of phosphorus (green) and iodine (red) in thyroid follicles. Iodine is confined to the colloid; Bottom left: fluorescence image of DAPI-stained thyroid tissue section and microautoradiograph, of thyroid tissue taken from a mouse injected with Tc-99m-pertechnetate; Bottom right: same section/autoradiograph showing silver grains enhanced (red) demonstrating radioactivity confined to the thyrocytes.

**Objectives:**

Year 1 rotation: in vitro tissue culture studies with I-131, Re188 and Tc-99m to determine relative radiotoxicity in relation to location of radionuclide (intracellular vs. extracellular).  
Year 2: method development and determination, using LA-ICPMS, of the cellular biodistribution of the above radionuclides in thyroid and other tissues, including tumours, of mice/rats  
Year 3: comparison of additional methods (SIMS, microautoradiography) to determine biodistribution  
Year 4: application of data thus obtained to estimate radiation doses to cells and tissues and hence the potential for improving radionuclide therapy by more appropriate selection of radionuclides; application to therapy of other cancers.
One representative publication from each co-supervisor:


Optimising neuroimaging in the management of brain tumours using artificial intelligence

Co-Supervisor 1A: Dr Thomas C Booth
School/Division & CAG: School of Biomedical Engineering and Imaging Sciences
KCL/KHP Email: thomas.booth@kcl.ac.uk
KCL/KHP Website: https://kclpure.kcl.ac.uk/portal/thomas.booth.html

Co-Supervisor 1B: Dr Marc Modat
School/Division & CAG: School of Biomedical Engineering and Imaging Sciences
KCL/KHP Email: marc.modat@kcl.ac.uk
KCL/KHP Website: https://kclpure.kcl.ac.uk/portal/marc.modat.html

Project description:

Glioblastoma is the most common primary malignant brain tumour in adults with ~2,500 cases diagnosed annually in England with one of the worst prognoses of any cancer. The current standard-of-care for newly diagnosed patients consists of surgery followed by radiotherapy and chemotherapy. MRIs plays an important role in treatment response assessment. It is unknown whether the MRI performed at each stage of the patient pathway after glioblastoma treatment changes outcomes (morbidity/mortality/health economics). The aim of this project is to model the co-variates for each imaging time-point using machine learning with Bayesian methodology. MRI co-variates of increasing granularity include (1) scan performed or not; (2) individual sequences, segmented volume, brain location and reported treatment response outcome; (3) radiomic features. Non-imaging co-variates include clinical (Karnofsky Performance Status), treatment type given, pathology (molecular markers) and demographics (sex, age).

The results, once disseminated, will inform standard practice in all UK neuro-oncology centres.

Objectives:

Year 1:
- Analyse curated data to understand the most informative variables of patient outcomes (e.g. survival metrics) using parametric approaches such as mixed effect and survival models.
- Develop a non-parametric tool, potentially relying on Gaussian Processes, to design a prognostic tool.

Year 2:
- Create a spatio-temporal atlas of tumour progression using retrospective clinical data. The aim of this atlas will be to later generate synthetic images of diseased patients at any stage of the pathologic process.
- Implement several approaches and contrast them. In particular, investigate dynamic programming, recurrent neuronal network (long-short-term-memory) and spatio-temporal variational auto-encoder. These models will be parametrised using the most informative parameters of patient outcome.

Year 3:
- Link the two aforementioned steps and design, based on simulated data, ideal clinical workflows that maximize the benefit to patient outcomes and generate prediction confidence.

One representative publication from each co-supervisor:


8.4 Non-invasive and quantitative imaging of fibrosis in deep vein thrombosis by MRI

Co-Supervisor 1A: Prof René M. Botnar
School/Division & CAG: Biomedical Engineering and Imaging Sciences and, KCL
KCL/KHP E-mail: rene.botnar@kcl.ac.uk
KCL/KHP Website: https://kclpure.kcl.ac.uk/portal/rene.botnar.html

Co-Supervisor 1B: Dr Alkystis Phinikaridou (Lecturer)
School/Division & CAG: Biomedical Engineering and Imaging Sciences and, KCL
KCL/KHP E-mail: alkystis.1.phinikaridou@kcl.ac.uk
KCL/KHP Website: https://kclpure.kcl.ac.uk/portal/alkystis.1.phinikaridou.html

Project description:

Deep vein thrombosis (DVT) affects 1 in 1000 people. Although collagen concentration determines the response to thrombolytic treatment there are no established methods to quantify thrombus fibrosis. We aim to develop non-contrast T1rho and magnetisation transfer (MT) MRI and collagen-specific imaging probes to quantify thrombus fibrosis to characterise the composition of venous thrombus and provide ‘virtual histology’ in an experimental animal model and in man that would help guide treatment.

Objectives:

Year 1: To optimise non-contrast enhanced imaging protocols (T1rho & MT) in phantoms and implement these sequences to quantify collagen remodelling in a murine model of DVT in vivo
Year 2: To test the merits of a commercially available collagen I-specific probe and develop a collagen III-specific probe to quantify the changes and biological role of these collagens in thrombus resolution and treatment-response in a murine model of DVT (year 2 & small part of year 3). All MRI findings for Aims 1&2 will be validated ex vivo.
Year 3: To test the translational value of the non-contrast enhanced sequences in quantifying thrombus fibrosis in DVT patients scheduled for endovascular treatment.

Techniques:

- Animal husbandry, handling and surgical techniques.
- Co-ordination of lanthanides and radioisotopes to Dota-peptides.
- In vitro binding and biodistribution studies.
- In vivo thrombus MRI imaging protocols.
- Ex vivo tissue analysis: histology, immunohistochemistry, proteomics, western blotting, ELISA, ICP-MS, radio-immunoassay and proteomics.
- Matlab simulations of MRI signal and pulse sequence development.
- Image processing and statistical software.

One representative publication from each co-supervisor:


9.4 αvβ6-Targeted probes for pre- and intra-operative imaging of pancreatic cancer

Co-Supervisor 1A: Dr Agostino Cilibrizzi
School/Division & CAG: School of Cancer and Pharmaceutical Sciences
KCL/KHP E-mail: cilibrizzi.agostino@kcl.ac.uk
KCL/KHP Website: https://kclpure.kcl.ac.uk/portal/agostino.cilibrizzi.html

Co-Supervisor 1B: Dr Daniele Castagnolo
School/Division & CAG: School of Cancer and Pharmaceutical Sciences
KCL/KHP Email: daniele.castagnolo@kcl.ac.uk
KCL/KHP Website: https://kclpure.kcl.ac.uk/portal/daniele.castagnolo.html

Project description:

Pancreatic cancer (PaCa) is a leading cause of cancer-related death in Western countries. Although partial/total pancreatectomy can be performed, morbidity, mortality and recurrence rate associated with such procedures are high. Integrin receptors are ubiquitously expressed in various cell types. αvβ6 is an isoform the levels of which are generally low, while overexpression is recorded in epithelial cells of many cancers, including PaCa. The RGD-based cyclic peptide FRGDLAf(NMe)K (AC27) possesses outstanding αvβ6-affinity/selectivity and high metabolic stability.

This project will identify AC27-based imaging agents to innovate diagnosis and surgical precision, primarily in PaCa, through efficient multimodality visualisation, for simultaneous and complementary pre-operative (via PET/SPECT) and intra-operative (via NIR imaging) future applications.

We have been working towards multimodality tracers for PaCa. This work has led to:

1) an improved synthetic route for AC27 (automated on peptide synthesizer);
2) measurement of affinity of previously prepared AC27-conjugates for αvβ6 in cellulo, confirming that excellent binding (low nM) is maintained (i.e. not altered by introduction of metal complexes).

Objectives:
For this project, we have identified 3 research objectives (RO), in order to prepare for subsequent clinical translation:

RO1) Synthesis/radiolabelling, to generate new probes for PET, SPECT and NIR (Fig. 1).
RO2) αvβ6 affinity and preclinical validation, to evaluate binding of the probes in αvβ6-expressing cells through in-house competitive assays.
RO3) evaluation of αvβ6 as PaCa biomarker, to study αvβ6 signalling in real-time in live cells through lifetime and super-resolution experiments (to be performed at the KCL-Nikon Centre).

This project is multidisciplinary, combining synthetic chemistry, radiochemistry, and microscopy.

One representative publication from each co-supervisor:


10.4 Fetal MR spectroscopy for non invasive assessment of liver, adipose tissue and placenta abnormalities in pregnancy complicated by maternal metabolic disease.

**Co-Supervisor 1A:** Dr Enrico De Vita  
School/Division & CAG: School of Imaging Sciences and Biomedical Engineering  
KCL/KHP Email: enrico.devita@kcl.ac.uk  
KCL/KHP Website: https://kclpure.kcl.ac.uk/portal/enrico.devita.html

**Co-Supervisor 1B:** Prof Catherine Williamson  
School/Division & CAG: School of Life Course Sciences  
KCL/KHP Email: catherine.williamson@kcl.ac.uk  
KCL/KHP Website: https://kclpure.kcl.ac.uk/portal/catherine.williamson.html

**Project description:**

Prenatal screening with ultrasound and MRI can diagnose many structural and vascular abnormalities in the fetus and the placenta affecting pregnancy outcomes.

Magnetic Resonance spectroscopy (MRS) provides a complementary dimension by revealing metabolic problems, assessing the chemical balance in the fetal brain and the placenta and allowing lipid quantification in fetal liver. This information is likely to influence and improve pregnancy management. MRS is widely employed in adults but rarely used prenatally due to long acquisition times (5-10 min) and corresponding sensitivity to fetal motion, compromising data-quality.

Maternal metabolic diseases, e.g. gestational diabetes mellitus (GDM), are associated with increased fetal and neonatal adiposity.

**Objectives:**

Year 1:  
Identify existing motion-tracking/motion-correction methods suitable for fetal/placental MRS, including machine learning for tissue/organ segmentation and registration with real-time feedback.  
Adapt/develop and implement appropriate methods on software/hardware used for pre-natal MRI at KCL/GSTT/Evelina.

Years 1-2:  
Evaluate selected methods’ efficiency on adults, healthy neonates and subsequently fetuses from GDM and uncomplicated pregnancies. Further, optimise as appropriate. Investigate state-of-the-art MRS data quantification methods such as Deep Learning.

Year 3:  
Deploy optimised MRS method (acquisition + processing) on cohorts of healthy fetuses and fetuses from GDM pregnancies.

**Skills Training:**

Training in MRI/MRS pulse sequences and data acquisition/analysis (including metabolic profiling) directly through supervisory team; MR-scanner software/hardware training by scanner manufacturers. The student will be supported by the School’s research/educational programme.
One representative publication from each co-supervisor:


11.4 Unravelling the role of pericellular matrix mechanics in regulating stem cell fate in 3D

Co-Supervisor 1A: Dr Cecile Dreiss  
School/Division & CAG: Cancer & Pharmaceutical Sciences  
KCL/KHP E-mail: cecile.dreiss@kcl.ac.uk  
KCL/KHP Website: [https://www.kcl.ac.uk/lsm/research/divisions/ips/about/people/dreiss/index.aspx](https://www.kcl.ac.uk/lsm/research/divisions/ips/about/people/dreiss/index.aspx)

Co-Supervisor 1B: Dr Eileen Gentleman  
School/Division & CAG: FoDOCS/Centre for Craniofacial and Regenerative Biology  
KCL/KHP Email: eileen.gentleman@kcl.ac.uk  
KCL/KHP Website: [https://kclpure.kcl.ac.uk/portal/eileen.gentleman.html](https://kclpure.kcl.ac.uk/portal/eileen.gentleman.html)

Project description:

Many tissue engineering (TE) strategies aim to replace damaged tissues by directing human mesenchymal stem cell (hMSC) differentiation with soluble chemicals/growth factors; however, physical factors such as stiffness also influence differentiation. By encapsulating hMSC in modifiable 3D biomaterials called hydrogels, we recently discovered that in addition to detecting hydrogel stiffness, hMSC also assemble secreted proteins around themselves (Ferreira, Nature Communications). They then mechano-sense the stiffness of their secreted pericellular matrix (PCM) to direct their own fate.

This PhD project will build on these findings to untangle how hMSC-mediated local mechanical modifications impact fate. Using multiple particle tracking microrheology (MPT, Figure), we will measure pericellular stiffening/softening in situ as differentiation proceeds. We will then determine mechanistically if PCM mechanics direct differentiation, and if specific secreted proteins mediate this process. To accomplish this, we will incorporate non-cell-mediated controlled softening/stiffening into hydrogels, tether specific proteins to the hydrogel (identified by proteomics), and treat cells with targeted RNAi or protein secretion inhibitors. Uncovering how local mechanical changes influence hMSC fate will yield design criteria for TE scaffolds that incorporate dynamic mechanical properties and tethered secreted proteins to create tissues.

This interdisciplinary project requires a motivated student with a background in either the biological or physical sciences who is willing to cross the boundaries of stem cell biology, mechanics and biomaterials synthesis.

**Figure**: Multiple particle tracking microrheology (MPT) on hMSC in hydrogels using embedded fluorescent beads. As hMSC alter their local environment through ECM secretion or degradation, changes in local mechanical properties can be quantified as *in situ* stiffness maps.
Skills training:

hMSC culture, live cell imaging, microrheology, hydrogel synthesis, peptide design/synthesis, molecular biology techniques.

Objectives:

Year 1: MPT on hMSC in hydrogels.
Year 2: Design/synthesise softening/stiffening/protein-tethered hydrogels.
Year 3: Mechanistic understanding of PCM-driven fate.

One representative publication from each co-supervisor:


https://doi.org/10.1016/j.jcis.2019.08.057
12.4 Artificial Intelligence (AI) based Multi-Organ segmentation of Healthy Tissue Metabolism in PET/CT imaging in Cancer.

Co-Supervisor 1A: Dr Malene Fischer, Senior Clinical Lecturer
School/Division & CAG: School of Biomedical Engineering and Imaging Sciences, Cancer Imaging
KCL/KHP E-mail: malene.fischer@kcl.ac.uk
KCL/KHP Website: https://www.kcl.ac.uk/people/malene-fischer

Co-Supervisor 1B: Prof Paul Marsden
School/Division & CAG: School of Biomedical Engineering and Imaging Sciences, Biomedical Engineering
KCL/KHP Email: paul.marsden@kcl.ac.uk
KCL/KHP Website: https://www.kcl.ac.uk/people/paul-marsden

Project description:

This project aims to establish a new paradigm that will enable prediction of patient response, side-effects and survival following specific anti-cancer treatments from PET-CT imaging data. State-of-the-art AI methods such as deep learning will be used to perform a comprehensive analysis of whole body PET/CT images, in order to extract information not currently available or utilized in large scale data-analysis or in clinical routine. A key aspect of this project is the availability of a series of standardized datasets of PET-CT scans from patients taking part in phase II/III clinical trials curated by the UK PET Core Lab at St Thomas Hospital.

The PhD-candidate will be trained to develop, validate and apply new tools based on artificial intelligence (AI) for automated multi-organ segmentation of PET/CT using deep learning approaches based on convolutional neural networks. This project will also involve close collaboration with Professor Julia Schnabel, and with the newly established London Medical Imaging and AI Centre for Value-Based Healthcare based at St Thomas’. You will also acquire in depth training in all aspects of PET/CT scanning especially image reconstruction and data analysis, but also clinical application.

Objectives:

Year 1 - 2: Identification and optimisation of CNN tools for single-organ segmentation, including validation in clinical data sets. This will include addressing specific challenges related to combining information from both the CT and the PET part of the study.
Year 3: Combining above into one multi-organ segmentation tool.
Year 4: Test and validate in own and external data sets. Writing of thesis.

One representative publication from each co-supervisor:


13.4 Sensing central blood pressure with advanced imaging and AI technologies

Co-Supervisor 1A: Dr Pablo Lamata
School/Division & CAG: School of Biomedical Engineering and Imaging Sciences / Dept of Biomedical Engineering
KCL/KHP E-mail: pablo.lamata@kcl.ac.uk
KCL/KHP Website: http://cmib.website

Co-Supervisor 1B: Dr Ronak Rajani
School/Division & CAG: GSTT
KCL/KHP Email: Ronak.Rajani@gstt.nhs.uk

Project description:

Some cardiac conditions cause an obstruction to the blood flow, and thus an extra burden to our heart that needs to be measured. A second problem is the limited ability of cardiologists to assess central blood pressure, inside the heart, key to risk stratify several conditions such as heart failure. In these two scenarios cardiologists need to use either accurate but risky sensors, or non-invasive but less accurate measurements or surrogates.

The aim is to equip the cardiologist with the non-invasive and accurate measurement of central blood pressure and the extra burden caused by a flow obstruction. This will be possible combining sophisticated imaging, the properties of contrast agents and computational technologies. The idea is to exploit two complementary approaches, the possibility to derive pressure differences based on the observation of blood velocity [1], and the ability to estimate absolute pressure with changes in the sub-harmonic response of microbubbles [2].

By building on existing unique expertise and equipment [1,2], the candidate will thus learn about advanced ultrasound acquisitions, the Navier Stokes equations, the wave-matter interaction, and the design and validation of novel remote sensing technology towards clinical impact.

Objectives:

The first year will be devoted to the construction of phantom models and testing of ideas for the estimation of pressure. The second year will then focus on the optimization of the imaging and analysis protocol, aiming to reach a real time performance, in order to be able to focus on the clinical translation and evaluation on the third year

One representative publication from each co-supervisor:


High Resolution Quantitative MRI for Neurology in Paediatric Subjects

Co-Supervisor 1A: Dr Shaihan Malik
School/Division & CAG: BMEIS
KCL/KHP E-mail: Shaihan.malik@kcl.ac.uk
KCL/KHP Website: https://kclpure.kcl.ac.uk/portal/shaihan.malik.html

Co-Supervisor 1B: Dr Jonathan O'Muircheartaigh
School/Division & CAG: IoPPN, Imaging & Biomed Engineering CAG
KCL/KHP Email: JonathanOM@kcl.ac.uk
KCL/KHP Website: https://kclpure.kcl.ac.uk/portal/jonathanom.html

Project description:

Neuroimaging in childhood is technically and clinically challenging. In children with neurological disorders, abnormalities sought using Magnetic Resonance Imaging (MRI) can be visually subtle, needing better image contrast than currently available on conventional scanners. In addition surgical targets for treatment (e.g. subthalamic nucleus) can be physically very small, needing higher resolution than is available on conventional scanners.

Ultrahigh-field (7T) MRI may be able to address both problems, providing higher signal to noise and better image resolution. The overarching goal of this PhD project is to use a cutting edge new 7T MRI scanner based at St. Thomas' hospital to develop high resolution and robust quantitative neuroimaging for use in paediatric subjects with neurological conditions (movement disorders and epilepsy).

There are a number of technical challenges for 7T-MRI stemming from the much higher resonant frequency required, which can lead to non-uniform image properties and higher energy deposition in patients. Furthermore children in general, and those with movement disorders in particular, cannot easily remain still, causing blurring that fundamentally limits the resolution that can be achieved. This project (suitable for a student with an engineering/physical science background) will develop methods for high precision quantitative MRI (measuring relaxation parameters $T_1$, $T_2^*$ and tissue susceptibility) and make these inherently motion tolerant, tailored for use in children (years 1&2). They will apply them to small cohort studies of children with movement disorders and focal cortical dysplasias (year 3). The student will be trained in MR physics, operating and programming MRI scanners and neuroimaging analysis.

One representative publication from each co-supervisor:


15.4 Characterising Atrial Fibrosis Properties for Predicting Atrial Fibrillation Ablation Outcome

Co-Supervisor 1A: Prof Steven Niederer  
School/Division & CAG: Biomedical Engineering & Imaging Sciences  
KCL/KHP E-mail: steven.niederer@kcl.ac.uk  
KCL/KHP Website: https://kclpure.kcl.ac.uk/portal/steven.niederer.html

Co-Supervisor 1B: Dr Martin Bishop  
School/Division & CAG: Biomedical Engineering & Imaging Sciences  
KCL/KHP Email: martin.bishop@kcl.ac.uk  
KCL/KHP Website: https://kclpure.kcl.ac.uk/portal/martin.bishop.html

Project description:

Atrial fibrillation (AF) is the most common arrhythmia. AF is often treated by catheter ablation to isolate aberrant atrial tissue. However, response is suboptimal and patient-specific. Atrial fibrosis is a common change in the atrial substrate in AF patients that has repeatedly been identified as a predictor of patient response to catheter ablation. Some patterns of fibrosis are benign while others are critical to sustaining AF. Cardiac magnetic resonance (CMR) late gadolinium enhancement (LGE) imaging currently provides the only non-invasive measure of atrial fibrosis. Typically, most of the information from these images is discarded and fibrosis is characterised by the percentage of the atria surface that it covers, with no consideration for the pattern or distribution of fibrosis and how this may relate to electrophysiology activation patterns that lead to or sustain AF. This PhD project will develop a combined modelling and imaging approach to apply machine learning image analysis techniques to identify critical structures in the LGE-CMR fibrosis distribution that support atrial fibrillation to guide ablation therapy.

This project provides training in signal and image processing techniques (Dr Bishop), computational modelling and machine learning algorithms (Prof Niederer), in close collaboration with the clinical teams at GSTT.

Objectives:

Year 1: To use and develop registration techniques for fusing electro-anatomical mapping data and LGE-CMR data.
Year 2: To determine local electrical properties from LGE-CMR data using Gaussian Markov Random Fields and Convolutional Neural Networks approaches.
Year 3: To investigate arrhythmia sustaining features by combining biophysical simulations and machine learning techniques.

One representative publication from each co-supervisor:


16.4 3D Cardiac Magnetic Resonance Fingerprinting with Deep Learning

Co-Supervisor 1A: Dr Claudia Prieto
School/Division & CAG: School of Biomedical Engineering and Imaging Sciences
KCL/KHP E-mail: Claudia.prieto@kcl.ac.uk
KCL/KHP Website: https://kclpure.kcl.ac.uk/portal/claudia.prieto.html

Co-Supervisor 1B: Prof Julia Schnabel
School/Division & CAG: School of Biomedical Engineering and Imaging Sciences
KCL/KHP Email: julia.schnabel@kcl.ac.uk
KCL/KHP Website: https://kclpure.kcl.ac.uk/portal/julia.schnabel.html

Project description:

Magnetic Resonance Imaging (MRI) is an important non-invasive tool for risk assessment and treatment monitoring of cardiovascular disease. Conventional MR images are qualitative measurements that depend on different parameters such as the longitudinal T1 and the transverse T2 relaxation times. Recently, T1 and T2 mapping techniques are emerging to provide quantitative tissue characterization and objective assessment of myocardial tissue properties [1]. However, clinically used cardiac mapping methods still present several limitations in terms of accuracy, precision, robustness, reproducibility, coverage (usually limited to 2D images), spatial-resolution and long scan times. Magnetic Resonance Fingerprinting (MRF) is a novel technique that promises to alleviate most of these problems [2-3], however several challenges need to be tackled to allow the application of MRF in 3D cardiac imaging. This project aims to develop, implement and test the clinical feasibility of a novel 3D MRF approach for free breathing multiparametric whole-heart cardiac MRI, providing quantitative information of multiple tissue parameters for an efficient and comprehensive assessment of cardiovascular disease.

Objectives:

Year 1: Develop a 3D respiratory motion compensated cardiac MRF acquisition
Year 2-3: Develop machine-learning and deep-learning based reconstruction methods for 3D cardiac MRF
Year 3: Develop spatiotemporal convolutional neural networks for highly efficient parametric maps estimation
Year 3-4:
  • Validate the proposed approach in healthy subjects and patients with cardiovascular disease
  • Compare the performance of the proposed method against current state-of-the-art methods for MR parameter mapping

This project joins expertise from MR physics, MR image reconstruction, MR motion compensation, Machine Learning and Deep Learning with clinical translation.

One representative publication from each co-supervisor:


Catheter-based radiofrequency ablation (RFA) is a medical procedure for the treatment of cardiac arrhythmias. This procedure aims at creating permanent destruction of critical tissue/pathway causing arrhythmias. However, current guidance systems are unable to predict the extent of permanent lesions, which is likely related to the high recurrence rate of arrhythmias following ablation (up to 50%). Magnetic resonance (MR) thermometry is a non-invasive MRI technique, which enables real time assessment of tissue temperature and prediction of permanent ablation lesions. Although this technique has a high potential to improve RFA procedure outcome and patient care, many technical challenges remain to be addressed before its potential use in patients.

The aim of this project is to develop new cardiac MR-thermometry techniques, which will include new cardiac MR sequences, new image reconstruction/processing algorithms, and efficient implementation for real time applications. This project also has a strong translational component since these developments will be validated in phantom and in-vivo in animal and ultimately in patients using the XMR platform recently installed in St Thomas’s Hospital. The successful candidate should have a strong interest in inter-disciplinary research, excellent programming skills, and a background related to one of the following areas: engineering, physics, and computer science.

Skills training:
Specific training will be provided in MRI physics, MR-thermometry, and pulse sequence programming.

Objectives:
Year 1: To develop a platform for real time MR-thermometry. Several state of art MR-thermometry techniques will be implemented and compared. Each technique could be implemented/tested during a 3 month rotation if this project follows the 1+3 MRes+PhD scheme.
Year 2: To develop a new high spatial resolution MR-thermometry sequence using advanced acquisition and reconstruction schemes.
Year 3: To develop a fast MR-thermometry sequence to enable 3D MR-thermometry.
Year 4: To develop novel approaches for 3D motion corrected temperature maps to compensate for respiratory, cardiac and spontaneous motion.
One representative publication from each co-supervisor:


18.4 Multifunctional Molecular Probes for Integrin-αvβ6 Expressing Carcinoma PET Imaging and Fluorescence-guided Surgery

Co-Supervisor 1A: Dr. Ran Yan
School/Division & CAG: School of Biomedical engineering and imaging sciences/department of Imaging chemistry and biology
KCL/KHP E-mail: ran.yan@kcl.ac.uk
KCL/KHP Website: https://kclpure.kcl.ac.uk/portal/en/persons/ran-yan(3cd6dac8-12a6-4179-b213-1db6041af9d5).html

Co-Supervisor 1B: Prof. Gary Cook
School/Division & CAG: School of biomedical engineering and imaging sciences/ Cancer Imaging
KCL/KHP E-mail: gary.cook@kcl.ac.uk
KCL/KHP Website: https://kclpure.kcl.ac.uk/portal/gary.cook.html

Project description:

Integrin αvβ6 over-expressing carcinomas such as ovarian, breast, and non-small cell lung cancer are highly invasive and metastatic resulting in a poor prognostic phenotype. There is an unmet clinical need for the early diagnosis, better characterisation, and treatment of these types of cancer. This interdisciplinary project aims to develop multifunctional theranostic tools for positron emission tomography (PET) imaging and fluorescence-guided surgery of integrin-αvβ6 over-expressing carcinomas. We envisage that these theranostic molecular probes could be developed by labelling the integrin-αvβ6 targeting antibodies with the near infrared indocyanine green (ICG) based dual PET and fluorescent labelling reagent, 124I-ICG. [124I]PET/CT imaging would enable more sensitive cancer staging and allow accurate pre-operative surgical planning. During surgery, the tumour deposits could be rapidly localized with a handheld β-radiation detector and simultaneously fluorescence imaging would ‘light up’ these tumours for real-time assessment and more accurate resection.

![Figure 1. A) PET/CT and ex vivo fluorescence imaging of the 124I-Green labelled CEA targeting antibody in a CEA-expressing human cancer xenograft model;[1] B) proposed dual PET and fluorescent labelling reagent, 124I-ICG.](image)

Skills training:

1. Radiation protection and safely handling radioactive material.
2. Analytical methods: HPLC, LC-MS etc.
3. Organic synthesis, radiolabelling, and bioconjugation techniques.
5. Animal handling to obtain personal animal licence, tumour-xenograft development, and tumor surgery in mice.
7. MicroPET/CT, ex vivo fluorescence imaging and data analysis, autoradiography.
Objectives:

Year 1: 124I-ICG preparation, antibody bioconjugation, and characterisation
Year 2: 124I-ICG antibody conjugates in vitro biological evaluation on the αvβ6-positive ovarian carcinoma OVSAYO cells and the αvβ6-negative TOV21G control carcinoma cells
Year 3: 124I-ICG antibody conjugates in vivo PET imaging and ex vivo fluorescence imaging in the paired OVSAYO and TOV21G tumour xenograft-bearing SCID mice.

One representative publication from each co-supervisor:


19.4 Artificial Intelligence Enabled Evaluation of Congenital Heart Disease

Co-Supervisor 1A: Prof Alistair Young
School/Division & CAG: Imaging Sciences and Biomedical Engineering
KCL/KHP E-mail: Alistair.young@kcl.ac.uk
KCL/KHP Website: https://www.kcl.ac.uk/people/alistair-young

Co-Supervisor 1B: Dr Kuberan Pushparajah
School/Division & CAG: Cardiology
KCL/KHP Email: Kuberan.Pushparajah@kcl.ac.uk
KCL/KHP Website: https://kclpure.kcl.ac.uk/portal/kuberan.1.pushparajah.html

Project description:

Medical imaging examinations like MRI or CT provide a wealth of shape and motion information which is largely ignored. This project will develop new deep learning methods for analysing patient data and predicting disease progression. These methods will be translated to the clinical workflow for evaluating children with congenital heart disease with the aim to determine the best time for surgical intervention. The project will teach the student strong programming and data analysis skills, how to work in an inter-disciplinary environment with world-leading cardiologists and engineers, and how to develop cutting-edge machine learning algorithms with explainable generative deep models.

Objectives:

Year 1: Learn state of the art machine learning and AI algorithms in order to apply them to patient data. Perform a literature review of on Tetralogy of Fallot, current clinical issues with timing of pulmonary valve replacement, and deep learning methods such as generative/adversarial networks. Write software for the automatic generation of biventricular finite element models from patient data.

Year 2: Develop data mining methods to take advantage of a large amount of imaging data derived from a multinational consortium investigating Tetralogy of Fallot. Characterize cardiac shape and function in the development of heart failure and the effects of surgical intervention.

Year 3: Apply the methods in a cohort of patients imaged before and after percutaneous replacement of the pulmonary valve. AI predictions will be compared against real outcomes. Software will be disseminated on institutional website as well as the Cardiac Atlas Project website, in addition to thesis write-up, conference and journal publications.

One representative publication from each co-supervisor:
