

**NIHR GREAT ORMOND STREET HOSPITAL / UCL INSTITUTE OF CHILD HEALTH
BIOMEDICAL RESEARCH CENTRE**

**Translational Clinical Research in Diagnostics and Imaging in Childhood Diseases
PhD Project Portfolio**

1. Understanding and predicting neurological disability in cerebral palsy (CP) using advanced neuroimaging

Project Aim

This project aims to investigate how damage to specific white matter tracts in CP is related to loss of motor function by using new imaging techniques we have recently developed for measuring the size of the portions of the thalamus that connect to the motor and sensory parts of the cortex of the brain in individual children.

Clinical Relevance

This project seeks to establish a new imaging measure (biomarker) of motor disability in CP that can predict the future clinical status of the patient. Critically, it will be readily available in the clinical setting. At the conclusion of the study the methodology proposed in this project will be followed as part of routine radiological assessment of patients with CP and will then be used by clinicians in the Department of Neurodisability at Great Ormond Street Hospital to inform patients and their families and to make decisions concerning rehabilitative strategies and early intervention, which in turn, is envisaged to lead to improved outcomes.

For information please contact Dr Chris Clark, christopher.clark@ucl.ac.uk

2. Using prospective motion correction for advanced neuro-MRI in children

Project Aim

This program of research is aimed towards reliable non-invasive structural and functional MRI based biomarkers of disease in children. The specific project is aimed at patients undergoing investigation for epilepsy surgery to reliably map epileptogenic areas in relation to white matter structures and grey matter areas that are responsible for eloquent brain function non-invasively.

Plan of investigation

- A scan protocol can be implemented consisting of DTI, fMRI, T1 and FLAIR images with prospective motion correction that is robust to head motion.
- Motion tracking improves fMRI sensitivity and is able to obtain useful data where subjects scan-scan movement is <10mm that is not recoverable via conventional analysis.
- Motion tracking improves EEG-fMRI sensitivity by suppression of variance due to motion.
- Motion insensitive high resolution DTI can improve resolution of tissue microstructure including variable axonal diameters and can improve the fidelity of tractography for neurosurgical planning.

Clinical Relevance

This program of research is aimed towards reliable non-invasive structural and functional MRI based biomarkers of disease in children. The specific project is aimed at patients undergoing investigation for epilepsy surgery to reliably map epileptogenic areas in relation to white matter structures and grey matter areas that are responsible for eloquent brain function non-invasively. This aims to improve the diagnostic and prognostic information provided to the surgical team. Further, if seizure free as a result of surgery, the cost related to antiepileptic medication is reduced as well as the overall burden to health care services in the long term. The developments described in this proposal are applicable to other patient groups who could similarly benefit such as patients undergoing assessment for tumour resection. More practically by reducing the motion sensitivity of MRI fewer patients might require sedation also with a large impact on cost. More will be able to achieve acceptable scan quality and so be able to have a greater range of image types obtained successfully within a session.

For information please contact Dr Chris Clark, c.clark@ucl.ac.uk

3. Towards patient specific modelling in congenital heart disease (CHD)

Project Aim

The aim of this study is to create a seamless clinical solution that will start to realise the potential of personalized medicine in CHD. This will incorporate novel, comprehensive, magnetic resonance imaging (MRI), improved image processing/model production and validation of model predictions in patients with a simple paradigm of CHD. The project will be split into 3 work packages, each of which will address one of the previously discussed impediments to personalized medicine in CHD. The end product should be a clinically useable, imaging-based framework for personalized decision-making that can easily be modified for different types of CHD. Such a framework could significantly improve patient outcome and would serve as a model for others areas of cardiovascular personalized medicine.

Plan of investigation

- Development and validation of a high resolution 4D-flow sequence, which can be acquired and reconstructed within 5 minutes. This data will form the foundation of the patient-specific models
- Development and validation of a seamless tool for patient-specific model production that is built into a clinically useful, image processing environment

Clinical Relevance

The main improvement in children's health is that we should be better able to tailor treatment in congenital heart disease to each patient. This should ensure increased success rates and better safety profile. The first stage is to create the models, which is highly imaging based project. Once this is done, these models can then be expanded on by our engineering team to model different interventions. This has the potential to revolutionize how we manage congenital heart disease.

For information please contact Dr Vivek Muthurangu, v.muthurangu@ucl.ac.uk

4. Optimising minimally-invasive treatments for valve dysfunction: predictive medicine based on computational modelling

Project Aim

The research proposed in this project combines engineering, imaging and clinical tools in a cardiovascular application for minimally invasive treatment of valve disease in children and adults with congenital and acquired heart disease. A reliable, comprehensive modelling tool will be developed that could potentially provide a great advance towards 'tailored' treatments, allowing the interventional cardiologist to virtually test a range of treatment options and select the most successful one for each individual patient.

Plan of investigation

- Analysis of patient specific image data along with clinical information to develop realistic in-silico and in-vivo models
- Computer simulation of different surgical/minimally invasive treatments for each specific patient
- Validation of computer models and results using in-vitro models

Clinical Relevance

The project will affect those patients requiring treatment for right ventricular outflow tract dysfunction but considered borderline or not suitable for the currently available percutaneous pulmonary devices. An image-based, computational assessment of these patients, along with conventional clinical tests, will help optimise treatment outcomes, by testing different options and device behaviour in a time-efficient and reliable manner. The modelling methodologies developed during this project will also be applicable to the study of other devices in children and adults, not only in the cardiovascular field but also in other pathologies.

For information, please contact Dr Silvia Schievano, s.schievano@ucl.ac.uk