



University of  
**Nottingham**  
Precision Imaging

# Personalising healthcare with pioneering imaging

**Precision Imaging**  
Beacon of Excellence

[nottingham.ac.uk/precision-imaging](https://nottingham.ac.uk/precision-imaging)

2019–2020

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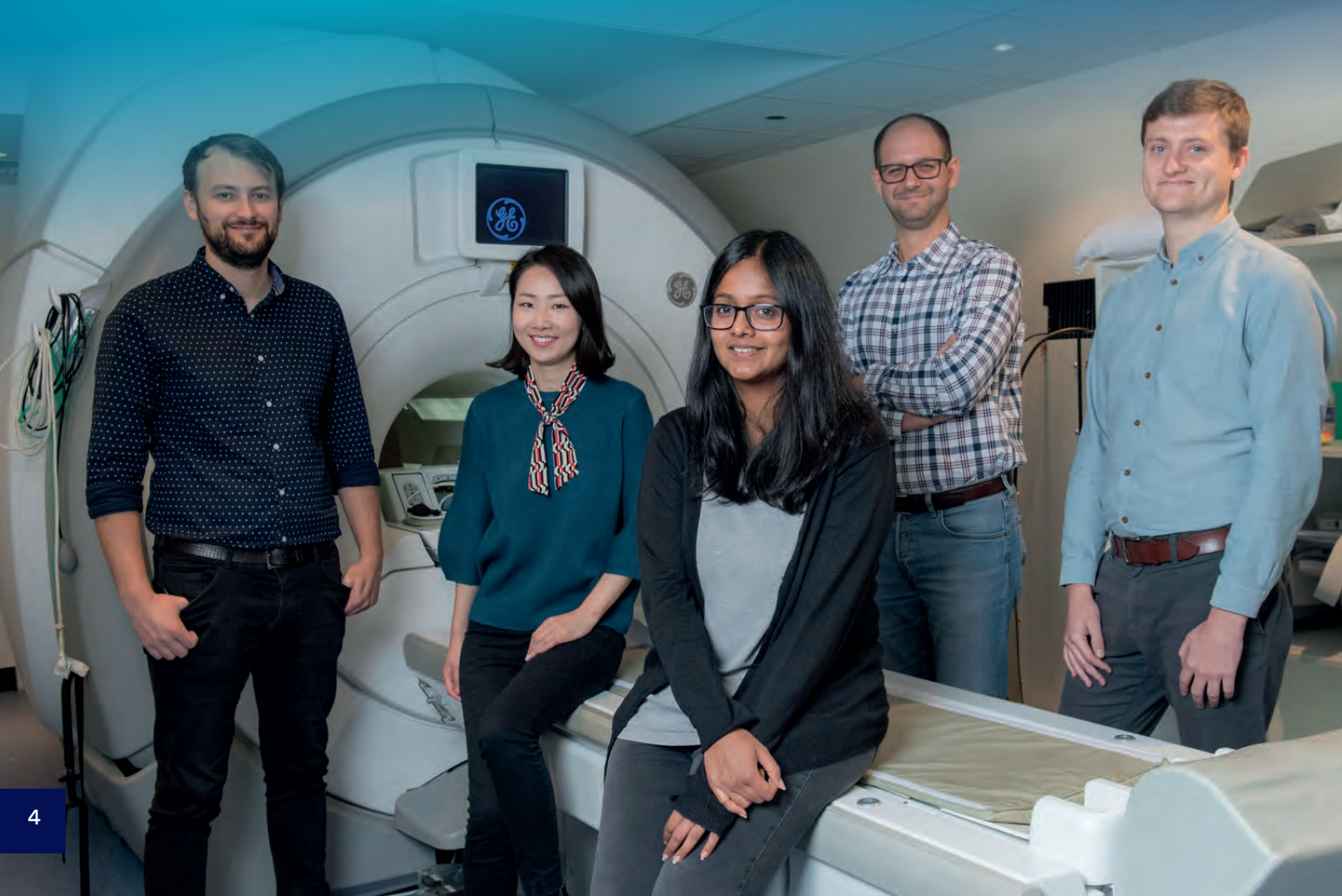
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Beacon  
Leadership team,  
experts and  
research fellows

20–23



# Mental and chronic physical health conditions cost the UK up to £150bn annually



## Overview

### Our vision for resolving some of the biggest challenges to society and the economy

Mental and chronic physical health conditions cost the UK up to £150 billion annually and pose some of the biggest challenges to our society and economy. In most cases, these conditions are responsible for the majority of years lived with disability, and account for more than half of GP visits.

They also incur a huge economic burden – £100 billion for mental health conditions alone. But what if personalised therapies, tailored to individual needs, could stop such chronic conditions from arising in the first place?

To achieve this, a fundamentally new approach lies at the core of the Precision Imaging Beacon's mission: pre-emptive and personalised interventions – known as precision medicine – enabled by transformation of diagnostic tests and pathways – precision radiology.

#### Our goals

1. Discover new imaging contrasts and biomarkers that enhance our understanding of disease mechanisms
2. Develop imaging tools, analytics and biophysical models to diagnose disease earlier
3. Develop personalised treatment – stratify patients, assess treatment response and define treatment targets

#### Our vision

We want to achieve a new medical era where every individual will receive the right test at the right time. Tailored imaging tests will detect subtle abnormalities before they cause problems and provide the relevant anatomical and physiological information to forecast the treatment that is best for that individual.

Nottingham has led the world in developing the technology for this vision – MRI. We will now lead a further step change based on advances in imaging technology, big data analysis and biophysical modelling. This programme will provide the tools to secure personalised precision healthcare for major causes of disability. We will focus on depression, dementia, and chronic diseases of the lungs, liver, gut and musculo-skeletal system.

Pictured: Precision Imaging Beacon Early career researchers



# Snapshot of achievements

## Grants

**£15.2m**  
grants won since  
2017

**£4.2m**  
awarded by UK  
research Councils

**£1.5m**  
awarded from  
Charities

**£4.1m**  
industry funding

Over  
**30** new  
studies and  
projects  
funded

**£5.4m**  
awarded from  
NIHR

Over  
**5,000**  
**volunteers**  
scanned in the  
Sir Peter Mansfield  
Imaging Centre

**4** **patents**  
**approved**  
since 2017

**26** **Beacon**  
**seminars**  
since 2018

More than  
**120**  
**researchers**  
**and academics**  
in our community

Over  
**1,100**  
**publications**  
by our academic  
community  
since 2018

Around half of  
all our research  
involves  
**international**  
**collaborators**

**54% of our**  
**research**  
is published in the  
top 10% of journals  
(around a third of  
our publications are  
in the top 10% most  
cited publications  
worldwide)

**14,000**  
**visitors**  
attended the  
Quantum Sensing  
the Brain at the  
2018 Royal Society  
Summer Exhibition

Professor  
**Matt Brookes**  
nominated for the  
**Times Higher**  
**Education**  
**Awards**  
for Research  
Project of the Year

**Professor Penny**  
**Gowland** appointed  
as secretary of the  
International Society for  
Magnetic Resonance in  
Medicine (ISMRM)

**Six activities at**  
**Wonder 2019**  
with over  
**5,000**  
**visitors**



# A revolution in brain scanning

“The new system has been used to make MEG measurements while subjects make natural movements, including head nodding, stretching, drinking and playing a ball game.”



## Moving magnetoencephalography towards real-world applications with a wearable system

Imaging human brain function with techniques such as magnetoencephalography (MEG) typically requires a subject to perform tasks while their head remains still within a restrictive scanner. This artificial environment makes the technique inaccessible to many people and limits the experimental questions that can be addressed.

Through a Wellcome-funded collaboration between the University of Nottingham and University College London (UCL), we have developed a MEG system that can be worn like a helmet, allowing free and natural movement during scanning. This is made possible by the integration of quantum sensors, which do not rely on superconducting technology, with a system for nulling background magnetic fields. The new system, which uses optically pumped magnetometers (OPMs), has been used to take MEG measurements while subjects make natural movements, including learning to play a musical instrument.

Our work has been extended this year with the first study of children using OPM MEG. This was reported in *Nature Communications* in November 2019, attracting considerable media interest. The OPM MEG work has recently moved into a new magnetically shielded room which was installed in the Sir Peter Mansfield Imaging Centre, with support from the ATEP scheme of the EPSRC-funded Quantum Technology Hub in Sensors and Metrology and the Precision Imaging Beacon. The new room

provides a better magnetic environment and more open space for OPM MEG work, opening up the prospect of experiments involving subjects who are walking or socially interacting. Working with the manufacturer of the shielded room, Magnetic Shields Ltd, we have now commercialised the coil technology that underpins the OPM MEG systems.

The OPM MEG work was selected by Physics World as one of the 10 *Breakthroughs of the Year* and was also *highly commended* in the *Research Project of the Year: STEM* category at the *Times Higher Education Awards*.

We have now built a 50-channel OPM MEG system using a novel, generic 3D printed helmet and this is being used to pursue a wide range of additional applications of the wearable MEG system.



We are now pursuing a wide range of additional applications of the wearable MEG system

Pictured: MEG system patient playing mandolin

Pictured above: The MEG team

# A 'magic' new medical device for MRI assessment of gut transit in children with constipation



“Constipation is common in young people. We invented a new medical device to assess gut transit time using MRI.”

## The problem

**The problem: 14% of young people suffer from constipation during their childhood. Constipation becomes chronic in 30% of young people, affecting both themselves and their parents or carers.**

Based on symptom reports, overall this complicates their care. An objective measure of the time that food takes to travel through the gut - the 'gut transit time' - could help doctors make a more informed, early selection of therapy. This could speed up treatment success, improve children and parents' satisfaction and potentially save NHS money.

An existing method to measure gut transit time involves ingesting plastic pellets and taking X-ray images to see how much time it takes for the pellets to travel through the gut. However, X-ray images are unable to reveal the colon anatomy well and provide a harmful radiation dose, so the method is not very effective.

## Our 'magic' new medical device

Dr Luca Marciani and his team of scientists, doctors, young people, parents and medical technology companies have designed a new medical device aimed at measuring gut transit time using magnetic resonance imaging (MRI). MRI has better image quality than X-rays and uses no harmful radiation.

We created new, small plastic capsules filled with liquid that can be seen by MRI. The capsules are only a few millimetres long and are easy for young people to swallow. They do not dissolve in the body but travel

along the gut, where they can be imaged using a quick MRI scan. We have carried out a first-in-child feasibility clinical study of the mini-capsules in 35 young persons with and without constipation. We called the study 'MAGIC' for MAGnetic resonance Imaging in paediatric Constipation. The study confirmed that the mini capsules can be swallowed easily by young people and successfully imaged in the gut using MRI, thereby proving a measure of whole gut transit time.

Our young people were directly involved in designing and producing the mini capsules, test kit packaging and all the recruitment materials. The next phase of this work aims to:

- develop new methods of manufacturing the mini-capsules so that it is faster and more cost-effective, so that the mini-capsules can be made on an industrial scale and distributed worldwide
- carry out a multi-centre clinical trial in constipated young patients, recruited from eight UK hospitals to show that using the mini capsules can improve treatment success
- inform early choice of therapy
- develop computer software that can detect the mini-capsules semi-automatically and produce reports of the gut transit time test

This work is funded by two NIHR Invention for Innovation (i4i) awards and has already generated two patents.

Pictured: A mock MRI scanner designed to help children become comfortable with the process



# Easing the impacts of depression

## Economic costs of major depression

- £1.7bn to the NHS
- £5.7bn in England alone

Source: Balestri M et al. Socio-demographic and clinical predictors of treatment resistant depression: A prospective European multicenter study. *J Affect Disord.* 2016;189:224-32. Morriss R et al. Clinical and cost effectiveness of a specialist depression service versus usual specialist mental health care for managing persistent depression (CLAHRC): a RCT. *Lancet Psychiatry.* 2016;3:821-31.

## BRIGHtMIND – a randomised controlled trial of image-guided Transcranial Magnetic Stimulation (TMS) for depression

As well as crippling personal turmoil, major depression currently costs the NHS £1.7 billion and the British economy £7.5 billion every year. Unfortunately, a high proportion of cases respond inadequately to treatment. TMS is approved for treatment of depression in the NHS, yet only a minority of cases have substantial therapeutic benefit, and of these, the effect is typically short-lived, lasting only a few months. Identifying cases likely to respond well and for longer is a high priority.

Recent research confirms that depression is associated with abnormal communication between neurons in distributed brain circuits, linking deep brain ‘limbic’ regions involved in emotional expression with more superficial areas that are accessible to TMS. Our research, directed by Professor Richard Morriss, has demonstrated that a particular limbic region, the insula in the right hemisphere, is a key node within the relevant brain circuits, and is likely to mediate therapeutic effects.

In a study of healthy participants, we have shown that a particular type of TMS – ‘theta burst’ – produces changes in the strength of connection between a superficial brain region in the frontal cortex and the insula, together with biochemical changes expected to be of therapeutic relevance. The brain site in the frontal cortex most strongly connected to the insula differs between people, suggesting that the site at which TMS is delivered is likely to influence the therapeutic effect. Using functional Magnetic Resonance Imaging (fMRI) we can identify the optimum site in each individual.

In a small pilot study led by Dr Sarina Iwabuchi and Dr Lena Palaniyappan using fMRI to guide TMS therapy in cases of treatment resistant depression, we observed substantially greater therapeutic effects than typically reported in previous studies. We allocated patients to receive either theta burst TMS or standard repetitive TMS. We found a trend toward greater therapeutic effect with theta burst TMS as opposed to repetitive TMS, but due to the small sample size we did not have the power to determine if the magnitude of this therapeutic advantage was significant.

On the basis of our previous studies, we have been awarded £1.8 million by the National Institute for Health Research and Medical Research Council, for a large multi-site study directed by Professor Richard Morriss designed to produce a definitive answer to the question – is image-guided theta burst TMS more effective than conventional TMS? If we confirm that this is the case, the findings are likely to guide future clinical practice, with the potential to reduce the burden of depression on lives and on society.



Pictured: Community Psychiatric Nurse setting up the TMS equipment with a participant



# Mathematical models of large-scale brain activity

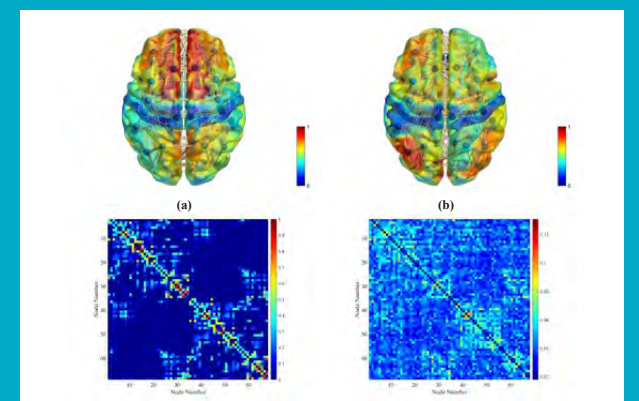
The use mathematics has many historical successes, especially in the fields of physics and engineering, where mathematical concepts have been put to good use to address challenges far beyond the context in which they were originally developed. Physicists in particular are well aware of the “The Unreasonable Effectiveness of Mathematics in the Natural Sciences”. Indeed, modern society either knowingly or unknowingly makes everyday use of deep mathematical ideas when it uses technologies like those of mobile phone networks, secure banking, and genetic data analysis. Mathematics is equally at home in a Healthcare setting, and has a number of applications in Precision Imaging, ranging from the use of statistics to find patterns in complex medical datasets, through to mechanistic modelling of tumour growth.

## A mathematical breakthrough

A collaboration between Mathematics, Medicine, and the Sir Peter Mansfield Imaging Centre, under the umbrella of the Beacon of Excellence in Precision Imaging, developed a model for large scale brain activity. This mathematical model traces its roots back to models of spiking neurons arranged in a network with interactions that describe the chemical process of neurotransmission. Given the billions of neurons in even a small region of brain tissue a mathematical challenge has been to reduce the model complexity so that it can be efficiently simulated on our High Performance Computing cluster. Borrowing ideas from statistical physics, whereby a gas filled room is adequately described by a handful of macroscopic variables for pressure, volume, and temperature, we have managed a similar reduction that describes a vast array of neurons in terms of their population firing rate and their degree of network synchrony. Synchrony is a very important descriptor of neural tissue dynamics, as a more coherent firing pattern generates a larger electromagnetic field, and this change in power is

the one readily detected in electro- and magneto-encephalography (EEG/MEG) imaging. A first major success of the model has been in explaining the phenomenon of beta-rebound, with the model matching data from the MEG group led by Dr Matt Brookes. Here a sharp decrease in neural oscillatory power in the 15 Hz beta band is observed during movement followed by an increase above baseline on movement cessation. Subsequent work with Professor Peter Liddle from the Institute of Mental Health has also shown that the model is capable of explaining the abnormal beta-rebound seen in patients with schizophrenia.

By merging this new dynamical model of neural tissue with connectome data describing the anatomical structure of individual brains, we gain a perspective on whole brain dynamics that naturally complements many of the neuroimaging studies ongoing within the Beacon. A current use of the model is for *in-silico* experiments to help improve the design of transcranial magnetic stimulation protocols for the treatment of mental health conditions. Future mathematical extensions will tap into powerful ideas from data-assimilation and uncertainty quantification that are commonly used in meteorology, and will ultimately allow for large scale brain state forecasting.



Pictured: Visual representation of (a) structural network and (b) simulated functional network. The surface of the brain visualisations are coloured depending on how connected a brain region is.



# Fighting Fatty Liver – imaging world health



India has the highest number of diabetics in the world with over 30 million sufferers, and a rising problem of non-alcoholic fatty liver disease and related metabolic disorders. This has a significant impact on day-to-day living for many people.

The University set up the Global Challenges Research Fund (GCRF) to support cutting-edge research that addresses challenges faced by developing countries. Through it we have received funding for an imaging project – ‘Fighting Fatty Liver’.

Working alongside the Population Health and Research Institute (PHRI) and Holistic Health and Research Institute (HHRI) in Trivandrum, India, we have helped to set up a dietary and lifestyle intervention study with the aim to equip local social workers, scientists and radiographers to perform similar studies in the future. Magnetic Resonance Imaging (MRI) and Spectroscopy (MRS) provide key non-invasive measures to monitor the progress of health outcomes in these studies, and with our expertise at Nottingham we have been able to introduce novel and important imaging markers to aid future research.

Pictured: Dr KT Shenoy and Dr Leena Mohan from PHRI together with their team of social workers who conducted the study

The main project was a four-month intervention study, which replaced white rice with red rice in order to lower the glycaemic index of meals throughout this period. The hypothesis was that lowering the glycaemic index over this period would reduce liver fat content.

Patients were scanned in a 3 Tesla (3T) system at a local scanning facility, before and after the study. Breath-held Dixon scanning was used to determine abdominal fat and liver volumes, and localised MRS was used to calculate liver fat fraction. Our team also worked closely with local radiographers to provide them with equipment and training, preparing them with the skills needed to run future studies.

This project is an excellent example of our Beacon's global impact, showcasing how our interdisciplinary team can help to improve health concerns in developing countries.

**The overall goal is to improve the metabolic health and well being of individuals and reduce the burden of non-alcoholic fatty liver disease and concurrent metabolic syndrome in Kerala.**



## Our global network

The map shows research collaborations from the Beacon's academic community in Nottingham with researchers around the world 2018–present



# Snapshot of investment

## Infrastructure

### Precision Imaging Beacon high performance computing cluster

- Allows use of larger datasets and more advanced/accurate processing and modelling
- Currently hosts more than 35 users from 7 schools and 15 projects/groups

### New Beacon hub offices opened

Space for over **40** researchers, academics, technical and administrative staff

### £100k Magnetically shielded room (MSR)

Initial measurements show that the remnant Earth's field in the new room is about 20 times smaller than current MSR

### £480k of internal funding awarded

through our Catalyst and Accelerator schemes  
Projects funded include:

- AI to diagnose hand fractures
- eye-tracking for training radiologists
- wearable MEG for children

### Upgraded 3T scanner

- completion due in summer 2020
- Human Brain Connectome trial ready

### Other equipment

- **Imaging phantom** – a specially designed object that is scanned or imaged in the field of medical imaging to evaluate, analyse, and tune the performance of various imaging devices
- **Ergometer** – uses the most advanced technology to simulate stress in an MRI bore, to mirror routine daily situations or training conditions
- **OCT device** – captures high-resolution, and high-density optical coherence tomography (OCT) images to aid in the diagnosis of physiological and pathologic conditions of the eye

## Recruitment and development

Over **£400k** on our PhD studentships scheme

Over **40** new imaging PhD students

### 8 Research Fellows

- **Two Nottingham Research Fellows:**  
Dr Matteo Bastiani and Dr Pete Harvey
- **Two Anne McLaren Research Fellows:**  
Dr JeYoung Jung and Dr Paula Croal
- **Four Precision Imaging Beacon Early Career Research Fellows:**  
Dr Jyothika Kumar, Dr Adam Berrington, Dr Flora Kennedy McConnell and Dr Sieun Lee

**Senior Chair appointed** in Biomedical Imaging:  
Professor Michael Chappell



# Beacon Leadership team



**Dorothee Auer**  
Precision Imaging Director and  
Professor of Neuroimaging



**Richard Bowtell**, Head of  
Sir Peter Mansfield Imaging  
Centre and Professor of Physics



**Stephen Coombes**  
Professor of Applied  
Mathematics



**Penny Gowland**  
Professor of Physics



**Cheryl Ruse**  
Head of Operations for  
Precision Imaging Beacon



**Mike Chappell**  
Professor of Biomedical  
Imaging

# Some of our experts

**Guruprasad Aithal**  
Head of the Nottingham Digestive  
Diseases Centre and Professor of  
Hepatology

**Matthew Brookes**  
Professor of Physics

**Victoria Chapman**  
Professor of Neuropharmacology

**Xin Chen**  
Assistant Professor of Computer  
Science

**Jane Daniels**  
Professor of Clinical Trials

**Robert Dineen**  
Professor of Neuroradiology

**Susan Francis**  
Professor of Physics

**Jon Garibaldi**  
Professor and Head of the  
School of Computer Science

**Paul Greenhaff**  
Professor of Muscle Metabolism

**Ian Hall**  
Professor of Molecular Medicine

**Chris Hollis**  
Professor of Child and Adolescent  
Psychiatry

**Stephen Jackson**  
Professor of Cognitive  
Neuroscience

**Padraig Kitterick**  
Associate Professor of  
Translational Hearing Research

**Katrin Krumbholz**  
Scientific Programme Leader

**Peter Liddle**  
Professor of Psychiatry

**Luca Marciani**  
Associate Professor in  
Gastrointestinal MRI

**Thomas Meersmann**  
Professor of Translational Imaging

**Richard Morriss**  
Professor of Psychiatry and  
Community Mental Health

**Alan Montgomery**  
Director of the Nottingham  
Clinical Trials Unit and Professor  
of Medical Statistics and Clinical  
Trials

**Philip Quinlan**  
Senior Analyst

**Andrew Reid**  
Assistant Professor of Psychology

**Stam Sotiropoulos**  
Associate Professor of  
Computational Neuroimaging

**Michel Valstar**  
Associate Professor of Computer  
Science

**David Walsh**  
Director, Pain Centre Versus  
Arthritis

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Beacon Core Team

**Elizabeth Hufton**  
Research Development Manager

**Alison Mellor**  
Beacon Administrator

**Rebecca Stevenson**  
Information Specialist

**Chris Tench**  
Senior Medical Statistician



# Our research fellows



**Dr Pete Harvey** is a Nottingham Research Fellow within the Precision Imaging Beacon. He will be developing new platforms for molecular imaging of central nervous system disorders, with a focus towards neurodegeneration. His approach will utilise a combination of strategies including new imaging methodologies, contrast agent design for targeting and reporting on disease markers, and improving brain delivery of agents.



**Dr Adam Berrington** is a Precision Imaging Beacon Early Career Research Fellow. His research largely focuses on the development of methodology for MR spectroscopy (MRS) with the aim to improve its clinical value. At 7 T, MRS is emerging as a promising tool for neurochemical measurement in diseases such as psychiatric illness. Adam's current research interests are therefore to develop parallel transmit methods for MRS to overcome challenges associated with ultra-high field. This will result in improved robustness and coverage of MRS across the brain for elucidation of sensitive neurochemical changes in disease.



**Dr Jyothika Kumar** is a Precision Imaging Beacon Early Career Research Fellow. Broadly, Jyothika is interested in using multimodal neuroimaging techniques to investigate translational mental health research questions. She is also interested in understanding how pharmacological and cognitive interventions affect the brain. Along with Dr Mohammad Zia Ul Haq Katshu, Jyothika was awarded this year's Margaret Temple grant by the BMA Foundation for Medical Research for a study titled 'Towards precision treatment in schizophrenia: investigating the role of glutamate and glutathione in persisting deficits'.



**Dr JeYoung Jung** is an Anne McLaren Research Fellow within the Precision Imaging Beacon. JeYoung's primary research aims to reveal the neurochemical mechanisms of human semantic cognition and its neuroplasticity in healthy and impaired system by establishing combinations of neuroscientific methods including MR Spectroscopy, fMRI, DTI, and brain stimulations (TMS/tDCS). She is also interested in the ways in which semantic cognition interacts with other domain-general higher cognitive functions (for example, default mode network and executive control system) by utilising advanced neuroimaging approach.



**Dr Matteo Bastiani** is a Nottingham Research Fellow within the Precision Imaging Beacon. His central research interest is the development and application of magnetic resonance methods for neuroimaging to study the structural architecture of the brain. Matteo has been working on the analysis of data acquired using diffusion-weighted imaging to study the anatomical connectivity of the brain both non-invasively and *in vivo*. Such a combination of methodological aspects with neuroanatomy helps to improve and advance our understanding of the architectural organization of the human brain in health and disease alike.





**University of  
Nottingham**  
Precision Imaging

# Discover more about our world-class research

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