University of Nottingham
UK | CHINA | MALAYSIA

Precision Imaging – Business Engagement Webinar 18 June 2020

Dorothee Auer, Professor of Neuroimaging, MD, PhD

Director, Precision Imaging Beacon of Excellence, Imaging theme lead, NIHR Nottingham BRC

About us

Vision

- Become the international centre for precision imaging to pioneer personalized healthcare for reduction of global burden of disability.

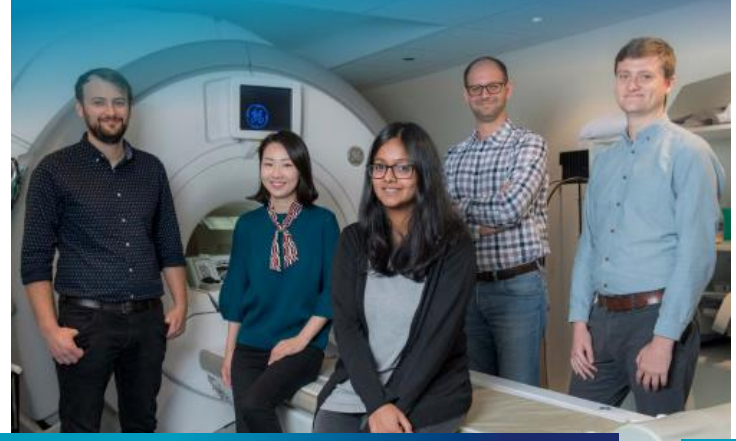
Mission

- Innovate and apply imaging tools for a step change in understanding, diagnosis and prediction of outcomes in mental health and chronic diseases.

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."

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



Mathematical models of large-scale brain activity

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.

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."

Fighting Fatty Liver – imaging world health

Added Value for Business

Solutions from internationally leading experts

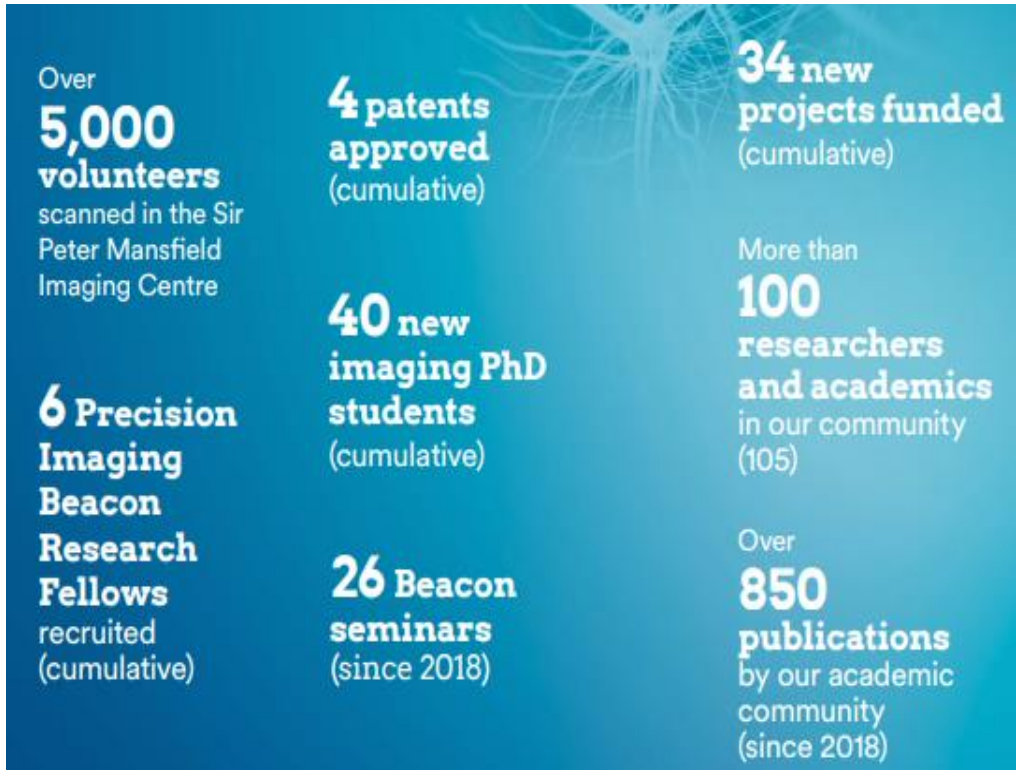
Expertise in next generation biomedical Imaging

Expertise in mathematical modelling and computational imaging

Expertise in neurosciences

Expertise in biomedical sciences & experimental medicine

Expertise in clinical medicine, biomarkers and clinical trials



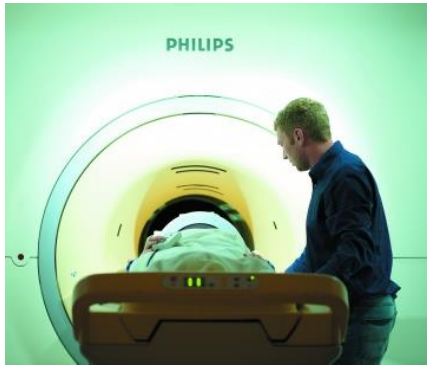
Added Value for Business

Access to world class imaging facilities

Upright MRI

1.5T/3T/3T

7 T



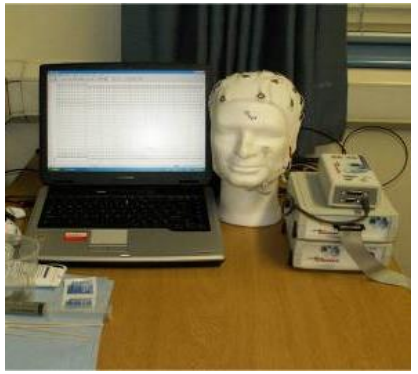
Pre-clinical facilities

MRI and MRS (NMR spectroscopy)
Electrophysiology in brain and body
Ancillary equipment

DNP

MEG

EEG and NIRS



Patient friendly

Precision Imaging at Nottingham – working with companies

Prof Luca Marciani

Precision Imaging Beacon

Industrial Strategy and Business Engagement Lead

Zsofia Toth & Claire Bicknell

How to boost your business attractiveness

Live webinar
21 April 2020

Mail Online

Heston Blumenthal:
BBC2
In Search of Perfection

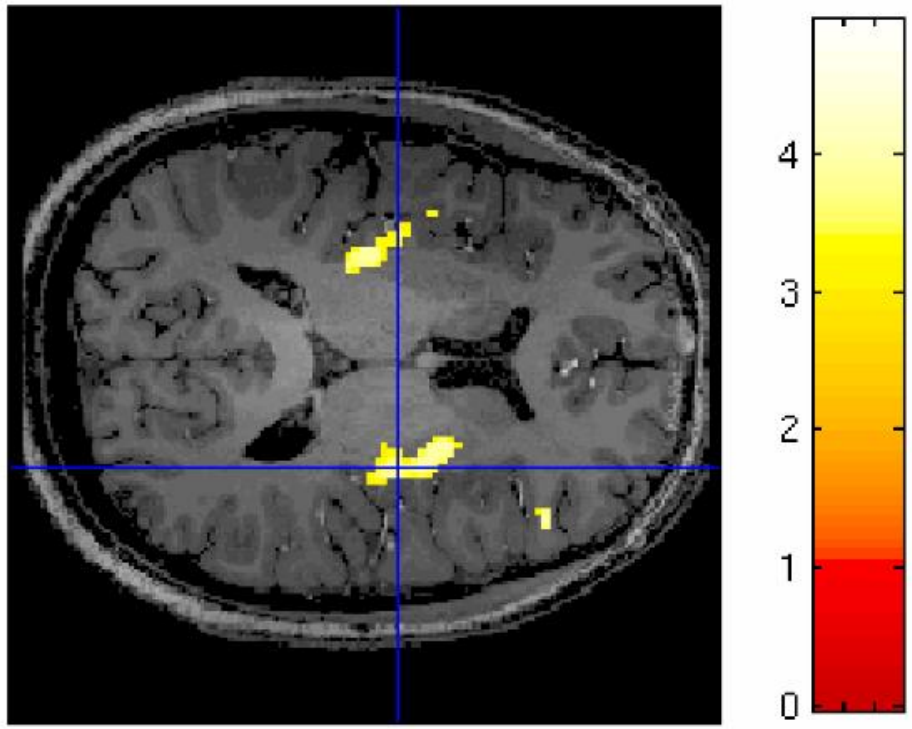
He recently injected his head chef with a dangerously high dose of chilli oil, intravenously, and then slid him into a £5 million MRI scanner to see how the spices reacted with his brain. "I used the brain scanner at Nottingham University," he says.

“I wanted to see what parts of his brain my spices would affect so I could create the perfect chilli”

“You could see all his brain cells light up on the screen and it helped me understand how chilli works”

Mail Online

Heston Blumenthal:
BBC2
In Search of Perfection



He recently injected his head chef with a dangerously high dose of chilli oil, intravenously, and then slid him into a £5 million MRI scanner to see how the spices reacted with his brain. "I used the brain scanner at Nottingham University," he says.

“I wanted to see what parts of his brain my spices would affect so I could create the perfect chilli”

“You could see all his brain cells light up on the screen and it helped me understand how chilli works”

Outline

- All you need to know about MRI imaging (in 3 slides !)
- “What about my business ?”

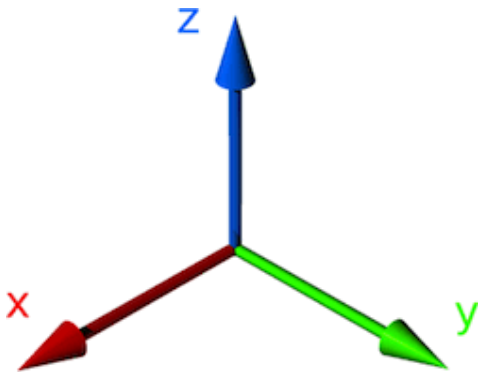
All you need to know about MRI imaging

All you need to know about MRI imaging

All you need to know about MRI imaging

Put a sample in the magnetic field and transmit radio frequency

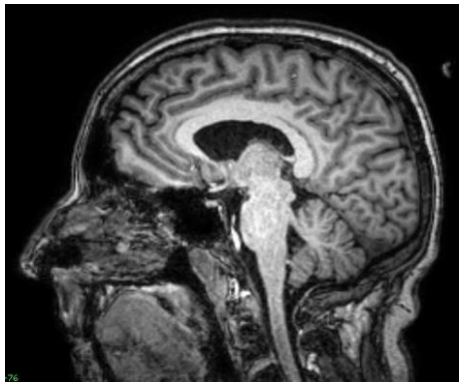
Add spatial information using magnetic fields



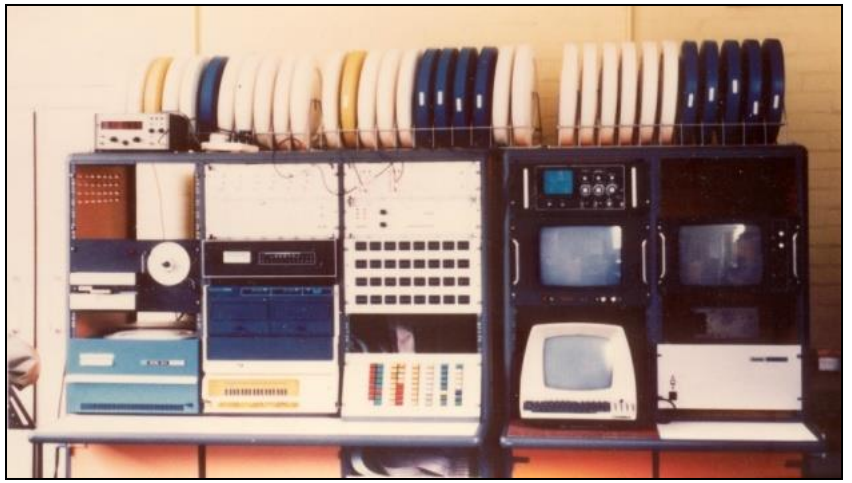
Receive the resulting signal with an aerial

Reconstruct the signal's spatial information (simple maths)

MRI image !



All you need to know about MRI imaging



“What about my business ?”

Foods / ingredients / nutraceuticals

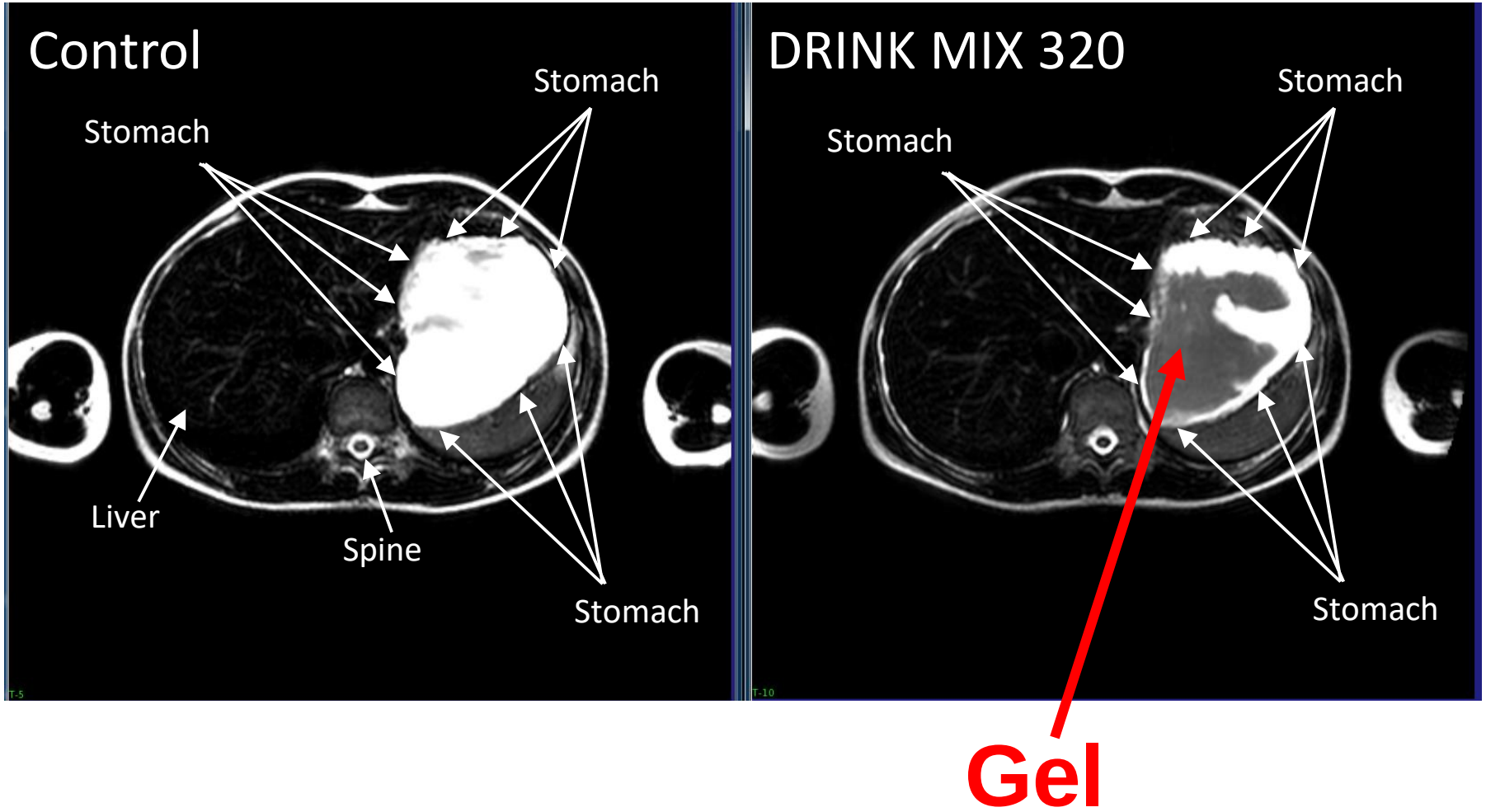
MAURTEN

Swedish company Maurten developed a new hydrogel technology whereby a liquid sports drink can convert to a hydrogel in the stomach environment, modulating the transportation of the nutrients and increasing tolerability.

- Tested the hypothesis that DRINK MIX 320 gels in the stomach
- Demonstrated intragastric gelling

Foods / ingredients / nutraceuticals

MAURTEN



Foods / ingredients / nutraceuticals

MAURTEN

Food & Function

ROYAL SOCIETY OF CHEMISTRY

PAPER

View Article Online
View Journal

Alginate and HM-pectin in sports-drink give rise to intra-gastric gelation *in vivo*

Luca Marciani, [a,b] Patricia Lopez-Sanchez,†[c] Stefan Pettersson, [d] Caroline Hoad, [a,b] Nichola Abrehart, [a,b] Martin Ahnoff [c] and Anna Ström *[e,f]

Check for updates

Cite this: DOI: 10.1039/c9fo01617a

The addition of gelling polysaccharides to sport-drinks may provide improved tolerability of drinks with high concentration of digestible carbohydrates (CHO), otherwise known to increase the risk of gastro-intestinal complaints among athletes under prolonged exercise. The physico-chemical properties of a drink containing 14 wt% of digestible CHO (0.7 : 1 fructose and maltodextrin-ratio), 0.2 wt% of HM-pectin/alginate and 0.06 wt%. sodium chloride were examined under *in vitro* gastric conditions using rheology and large deformation testing. The *in vivo* gelling behaviour of the drink was studied using magnetic resonance imaging of subjects at rest together with blood glucose measurements. The *in vivo* results confirm gelation of the test drink, with no gel remaining in the stomach at 60 min and blood glucose values were similar to control. The physico-chemical characterisation of the acidified test drink confirms the formation of a weak gel through which low M_w CHO can diffuse.

Received 22nd July 2019,
Accepted 19th November 2019

DOI: 10.1039/c9fo01617a

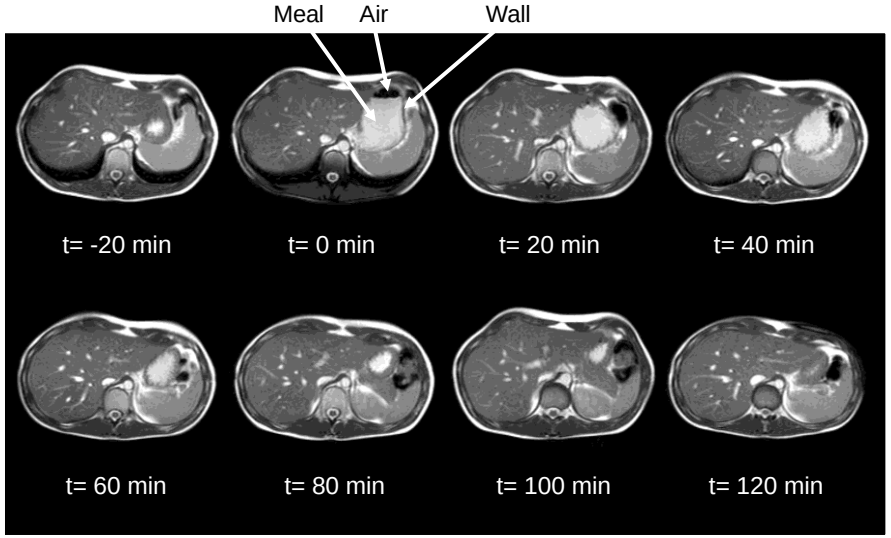
rsc.li/food-function

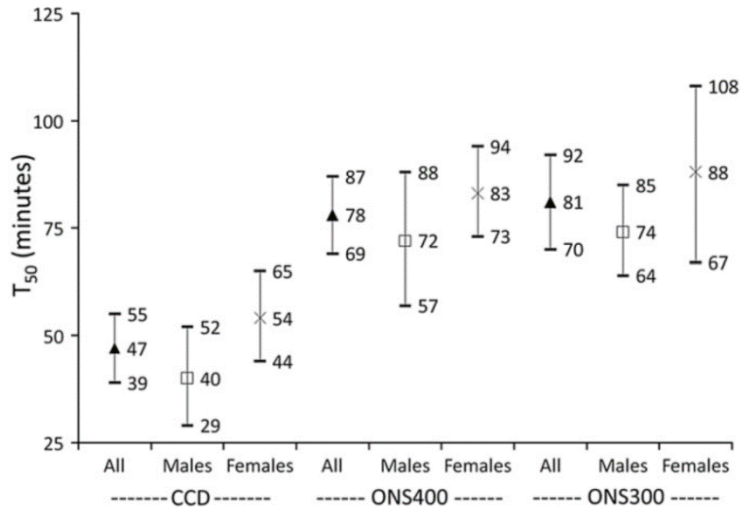
Foods / ingredients / nutraceuticals

FRESENIUS KABI
caring for life

Global healthcare/nutrition company Fresenius Kabi developed new preoperative energy drinks to help recovery after surgery. These must clear the stomach before anaesthesia but gastric emptying time unknown.

- Compared gastric emptying of market product with 2 new formulations in clinical trial
- Determined gastric emptying time

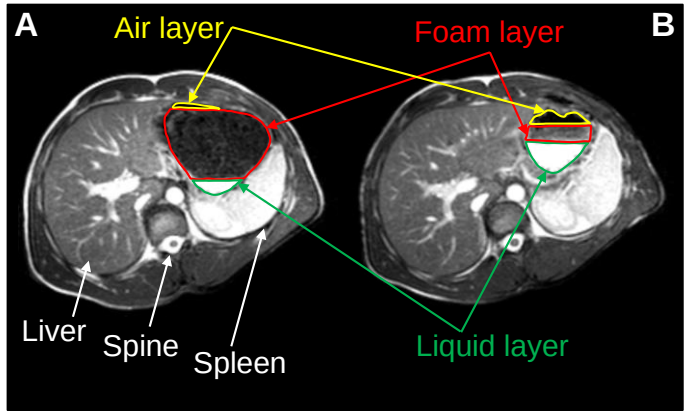




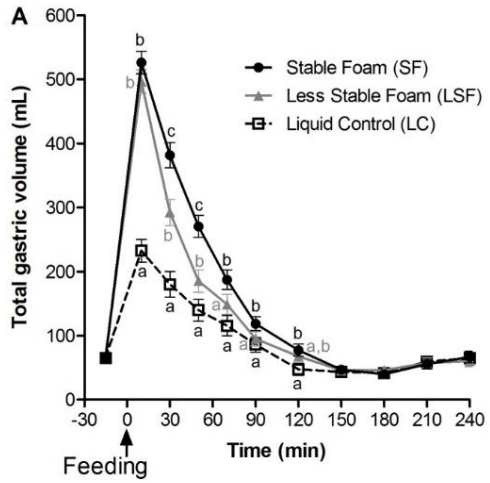
DN Lobo et al. Clin Nutr 28: 636-641, 2009

Foods / ingredients / nutraceuticals

Global food/personal care company Unilever developed new aerated drinks (foams) to increase gastric distension and reduce appetite.
In vivo performance unknown.



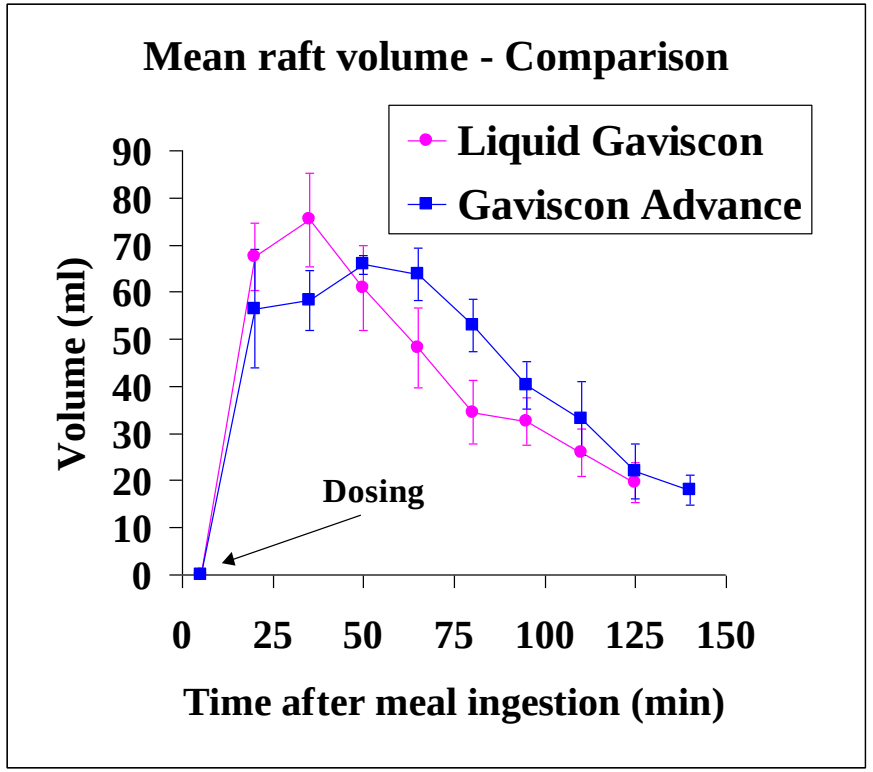
- Tested two aerated formulations against an isocaloric control drink
- Demonstrated increased gastric distension and reduced appetite for the aerated drinks



K Murray *et al*. *Am J Clin Nutr* 101: 270-278, 2015

Foods / ingredients / nutraceuticals

Health, hygiene and nutrition company Reckitt Benckiser developed a new formulation of heartburn relief product Gaviscon and wanted to investigate performance *in vivo*.



- Tested old and new formulation
- Demonstrated intragastric raft formation for both and demonstrated performance
- Our images featured in the marketing brochure

L Marciani et al. J Pharm Pharmacol 54: 1351-1356, 2002

Multimodal Biomarkers of Brain Health

Brain structure
- Development
- Resilience
- Prodromal disease

Brain metabolites
- Neurotransmitter
- Metabolism
- Anti-oxidative markers

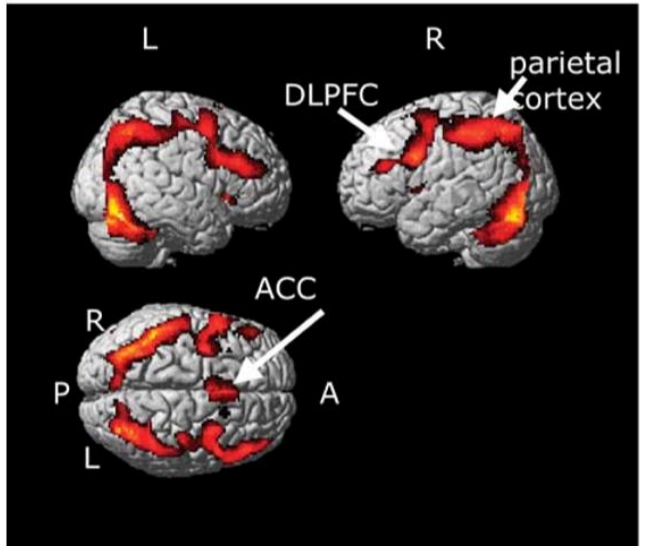
Brain function
- Cognitive Health
- Emotional Health
- Pharmacodynamic and mechanistic effects

Brain blood flow
- Neurovascular health
- Disease pattern
- Response pattern

Precision Imaging provides added value for
- Experimental medicine studies
- Phase 2a pharmaceutical / nutraceutical trials

Brain Health

Flavonoids have beneficial physiologic and antioxidant effects. Food products company Mars Incorporated interested in understanding potential effects on the human brain, particularly blood flow.



- Tested effect of high and low flavanol content cocoa drink
- Showed high flavanol can increase cerebral blood flow – potential to aid treatment of vascular impairment

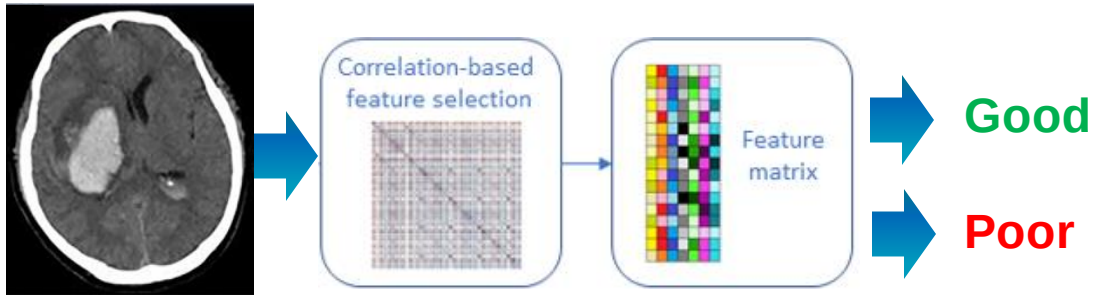
ST Francis et al. J Cardiovasc Pharmacol 47, S215-S220, 2006

Next generation imaging-guided therapy

Stratification
- Response prediction
- Radiomics/AI

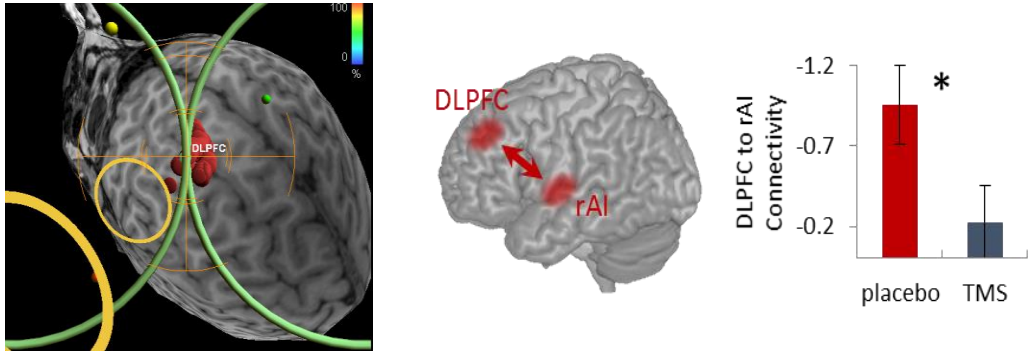
Target selection
- Brain stimulation
- Surgical/Radiotherapy planning

From CT of brain haemorrhage to outcome prediction



Pszczolkowski et al, under review,
Courtesy Prof Dineen

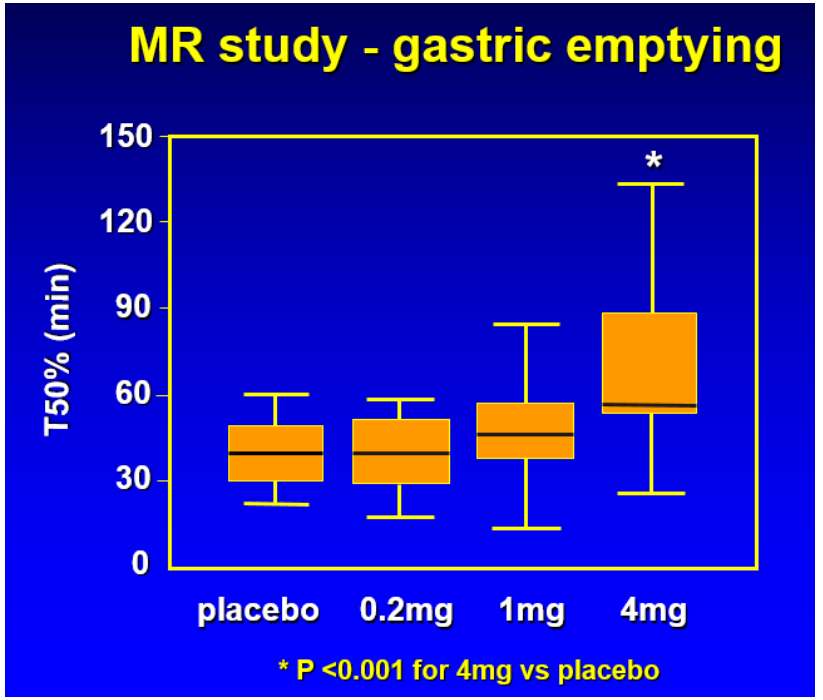
MRI for neuronavigated depression therapy



Iwabuchi et al., 2017,2019

Pharmacodynamics / drug delivery

Japanese pharma company Mitsubishi developed a new serotonin receptor agonist (gastrointestinal motility) drug. Effect in humans unknown.



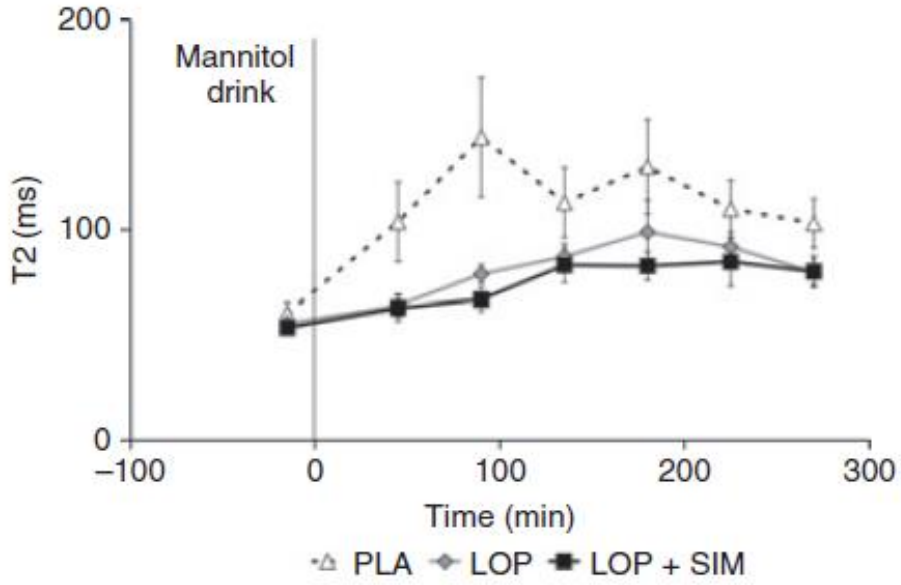
- Run first-in-man MRI clinical trial of 3 escalating doses versus placebo
- Demonstrated delay in liquid gastric emptying in association with relaxation of the proximal stomach

NS Coleman et al. Aliment Pharmacol Ther 18: 1039-1048, 2003

Pharmacodynamics / drug delivery

Healthcare company McNeil interested in understanding mode of action of two anti-diarrhoea formulations of loperamide on intestinal water distribution.

- Tested both formulations versus placebo in clinical trial
- Demonstrated that both formulations reduced small bowel water content and delayed arrival of fluid in the colon

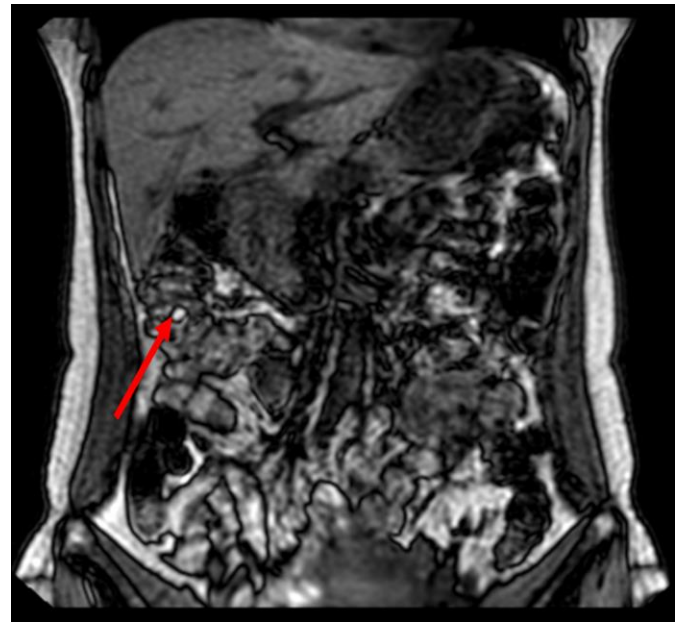


E Placidi et al. Aliment Pharmacol Ther 36: 64-73, 2012

Pharmacodynamics / drug delivery

Some of the science behind drug dissolution modelling and bench apparatuses is 40 years old.

- Work to improve *in vitro-in vivo* relevance of drug dissolution science using MRI data of the fluid, motility and transit in the undisturbed bowel
- Studied novel dosage forms and looking at colon targeted delivery



DM Mudie et al. Molecular Pharmaceutics 11, 3039-3047, 2014

Medical devices

JEB Technologies Limited

Partnership with medical device manufacturer JEB Technologies to develop a new MRI visible mini-capsule to measure gastrointestinal transit in children with constipation.

- Two NIHR i4i research grants (£1.8M)
- Made the device, run first-in-child trial
- Setting up multi-site clinical trial to demonstrate effectiveness and going towards CE marking

Medica expo Düsseldorf 2019

Supporting regulatory claims

Our collaborative imaging work has helped to support regulatory claims by providing data that demonstrated mode of action and feasibility.

- One EFSA claim for health benefits of food produce
- One patent on a novel digestion bench machine
- One patent on a novel thermal gelling material

Conclusions

University of Nottingham
UK | CHINA | MALAYSIA

Thank you !

Discover how we can help you achieve your vision

Our expertise in precision imaging is underpinned by world leading experts in medicine, physics, mathematics, psychology, life sciences and computer science. The Sir Peter Mansfield Imaging Centre and the NIHR Nottingham Biomedical Research Centre offer a great diversity of skills to identify and implement solutions to your problems and needs.

Innovations in the application of our imaging tools are shaping a step-change in understanding, diagnosis and prediction of outcomes focusing on mental health and chronic diseases.

Pharmaceuticals

We work with the pharmaceutical industry to demonstrate **mode of action**, assess **product performance** *in vivo* and generate **evidence** of **efficacy** to aid development, marketing and regulatory submissions. We also develop new surrogate imaging biomarkers to assess drug efficacy from early to late clinical trials.

Collaborations with the pharmaceuticals industry

- Imaged the heart's response to dialysis treatments, and studied cardiac and renal response to fluid therapy
- Assessed changes using multiparametric liver MRI following therapy with direct-acting antivirals in chronic hepatitis C virus patients
- Studied the mode of action and efficacy of different dosing regimes of a novel 5HT4 agonist active, anti-diarrhoeal drugs and macrogol formulations
- Imaged deployment and performance of different alginate formulations for heartburn and laxative products

Food and beverage

We work with the food and beverage industry to **image** new pre-competitive materials and finished products *in vivo* in the gastrointestinal tract. This helps commercial partners to understand and demonstrate **mode of action**, assess **product performance** and generate **evidence** for marketing and regulatory submissions.

Collaborations with the food and beverage industry

- Demonstrated self assembly of gelling hydrocolloid materials in the stomach
- Demonstrated the mode of action of products for digestive comfort
- Provided proof of survival of aerated drinks for weight management
- Highlighted the mode of action of performance sport drinks
- Used functional MRI brain imaging to study food eating and sensory perception, and taster phenotype

Medical devices

We continue Nottingham's tradition of **innovation** by working with small and medium-sized enterprises to develop new medical devices. We help companies to guide the development, assess **performance**, demonstrate deployment and investigate mode of action of novel devices and formulations.

Collaborations with the medical device industry

- Producing new MRI marker capsules to measure gastrointestinal transit in children with constipation
- Used our imaging techniques to demonstrate deployment of gastroretentive devices inside the human stomach

Biomarkers for health

We develop imaging biomarkers available for **precision medicine** ranging from population health and **diagnostic** to **predictive** outcome markers, for example:

- Fibrosis markers in liver and kidney disease
- Markers to track Parkinson's Disease
- Preclinical markers of neurodegenerative diseases

Other body and brain imaging work

- We carry out leading work including lung, kidney, liver and MSK diseases
- We are developing imaging methods for the prediction of chronic kidney disease
- We develop unique experimental neuroimaging for clinical neuroimaging and mental health leading the first imaging connectivity-guided and neuromodulation trial in treatment resistant depression

Collaborate with us

We can help you to:

- achieve your research ambitions
- find facilities and expertise to help with product development
- place a student or graduate into your business to work on a project

PI-Beacon@nottingham.ac.uk
@UoNPIBeacon
Precision Imaging Beacon

nottingham.ac.uk/precision-imaging