Telemetric Home Blood Pressure Monitoring in Stroke Prevention

Home BP monitoring can improve accuracy and help provide more appropriate treatment. We are evaluating the effectiveness and acceptability of Bluetooth-based remote home blood pressure (BP) monitoring in transient Ischaemic attack (TIA) and stroke patients.

High blood pressure (hypertension) is one of the most prevalent diseases worldwide and a major modifiable risk factor for recurrent stroke and vascular disease. However, in practice, rates of control are low, often partly due to reliance on single BP readings taken in clinic.

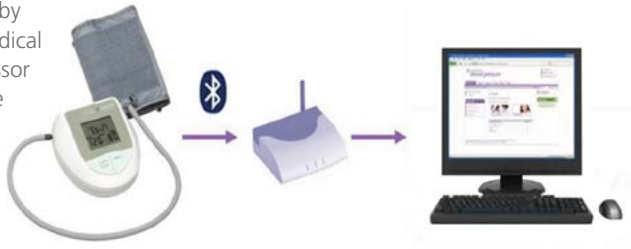
Home BP monitoring is becoming increasingly important in the diagnosis and management of hypertension, and it has been recommended in international guidelines.

It negates the effect of 'white coat hypertension' and allows for multiple BP readings to be collected, thus giving better prognostic accuracy than clinic measurements alone and helping detect BP variability. This allows for more informed titration of treatment.

Patients are also able to see the direct effect of antihypertensive medication on their BP, which may aid long-term compliance.

A team led by Professor Peter Rothwell at the University of Oxford have been working on a project to introduce Bluetooth-enabled home BP monitoring to patients following a TIA or stroke. The benefit of this system is that the BP readings are transmitted automatically at the time the measurement is taken, so clinicians can see up-to-date readings and adjust treatment if necessary.

The main aims of the project are to evaluate whether home Bluetooth BP monitoring will help us identify post-TIA/stroke patients with variable blood pressure, thus enabling us to refine our understanding of the causes and consequences of BP variability. This will hopefully lead to more effective future treatment of hypertension with existing medication.



The project, supported by the NIHR Oxford Biomedical Research Centre, Professor Lionel Tarassenko at the University of Oxford and OBS Medical Ltd, now has data from over 1000 patients. Results so far have shown that regardless of age, telemetric home BP monitoring is feasible and acceptable in patients with TIA and non-disabling stroke. Monitoring-informed titration of medication in the majority of patients is also associated with good BP control.

Professor Peter M Rothwell
Professor of Clinical Neurology
University of Oxford
peter.rothwell@ndcn.ox.ac.uk

Cardiolyse - Prevention Rather than Emergency

Cardiolyse is an ECG processing platform that provides preventive and easy-to-understand ECG analytics for everyone, via an application programming interface (API). Cardiolyse provide easily understood information about current heart state, personal recommendations and months-ahead forecast about dangerous heart disease. It enables users to see the connections between their lifestyle (such as exercise or treatment) and the state of their heart.

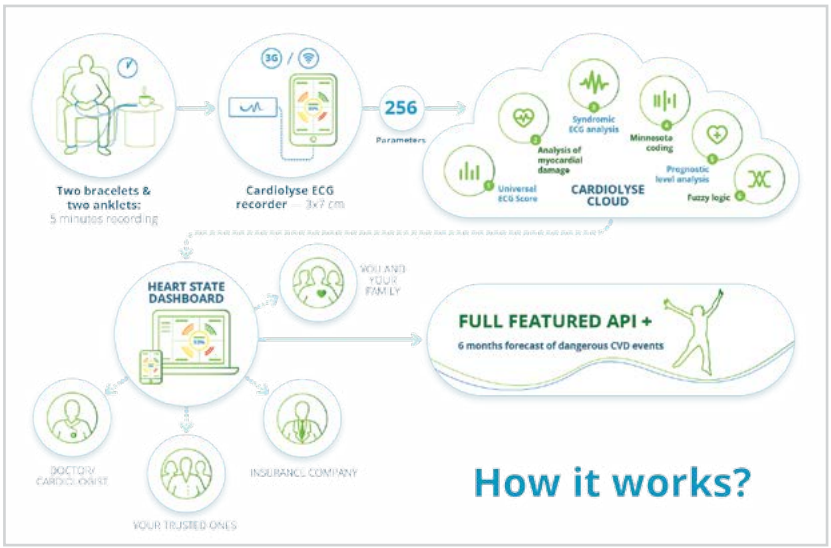
Any fixed or wearable ECG device can transfer data to Cardiolyse Cloud, where our powerful algorithm defines over 250 different parameters essential for understanding heart health. The analysis is based on the Universal Score System (USS), and the algorithm analyzes all ECG curves in less than two seconds, faster than any human doctor.

We have developed a cloud-based ECG processing platform that gives everyone access to our powerful algorithms via a full-featured API. ECG USS is an advanced proprietary technology, designed to analyze more than 250 ECG parameters (all known electrocardiography codes) and then visualize the results in colour logic, along with a quantitative assessment.

ECG USS technology uses an individual's unique electrocardiogram (or ECG) for authentication. Individual norms based on the ECG USS allow for enhanced accuracy, and for individualized recommendations.

The system also provides a mid-term forecast of serious cardiovascular events.

The classification system used is based on an assessment of 256 ECG variables, the highest possible number. Each ECG parameter is given a certain number of scores, depending on how well this value corresponds to the recognized standard.



The USS in turn consists of four blocks, which are:

- Heart muscle state: based on parameters of electrocardiographic curves, including multiple existing ECG scoring systems
- Stamina: based on parameters of heart rate variability and autonomic nervous system measures
- an analysis of heart rhythm disturbances
- a psycho-emotional status, based on an evaluation of specific aspects of heart rate variability.

Dr Wenming Ji, MD
Oxford Cardiomox Ltd
wenming.ji@cardiomox.com

Oxford Cardiomox - a New Generation of Magnetocardiography (NG-MCG)

New generation magnetocardiography uses a fully non-invasive medical device which can detect local current signals emitted by heart muscle cells. The 3-D current density vectors images generated by this method can indicate the electrophysiological condition of the heart, and support the diagnosis of early-stage heart diseases.

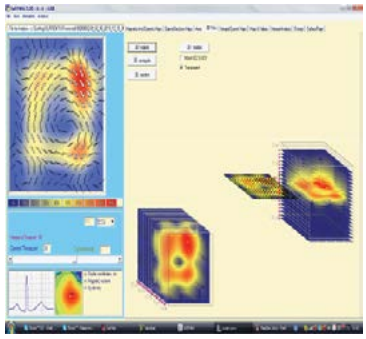
NG-MCG focuses on non-invasive mapping of weak biomagnetic signals around the thorax of the heart, and it works in an unshielded environment. It can investigate the factors determining whether there is sufficient signal-to-noise ratio and spatio-temporal signal resolution for practical clinical applications.

We have been exploring, developing and implementing innovative physical and mathematical formulations and algorithms for analysis of clinical magnetocardiogram data.

With the high sensitivity and specificity of MCG, the result will be analyzed based on patient data recorded both at rest and under conditions of controlled cardiac stress. Validation will be by comparison with a technique such as coronary angiography, the current gold standard for cardiac pathology.

The advantages of using MCG advanced imaging and quantitative analysis techniques to detect abnormal electrophysiological cardiac phenomena include:

- non-invasive and risk-free surface mapping of the magnetic fields generated by the electrical activity of the heart
- the MCG system's Superconducting Quantum Interference Device (SQUID)-based magnetometer can be used in hospital environments without expensive shielded rooms, increasing potential usage in health care settings.



MCG is superior to ECG because:

- its ultra-sensitive SQUID detector has increased sensitivity to local myocardial currents
- it is sensitive to vortex currents undetectable by ECG
- Unlike ECG, the MCG signal is not perturbed by electrical signals from tissues near the heart.

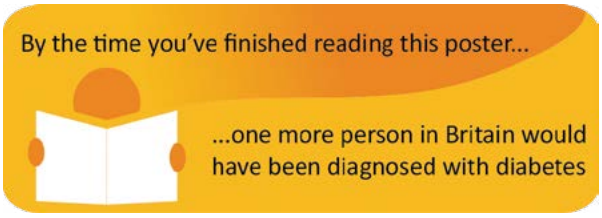
In comparison to expensive and invasive clinical practice techniques such as Single Photon Emission Computed Tomography (SPECT), coronary angiography, magnetic resonance imaging (MRI), etc., MCG allows for:

- the detection of ischemic changes in viable myocardium
- an evaluation of patients with cardiac conduction disease
- assessment of the risk for developing arrhythmias, and localizing the arrhythmigenic substrate;
- evaluating pro-arrhythmigenic drug properties.

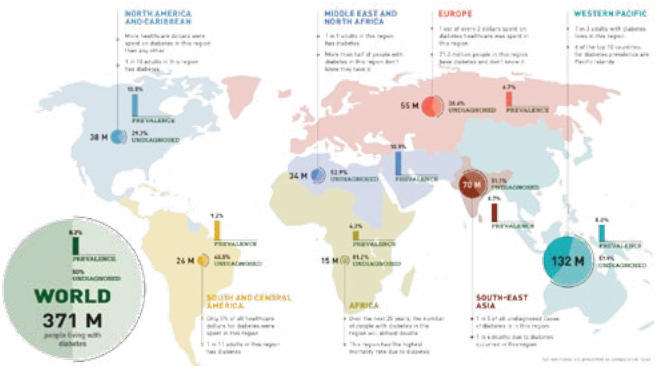
Dr Wenming Ji, MD
Oxford Cardiomox Ltd
wenming.ji@cardiomox.com

Assessing Outcomes in Diabetes Studies from the Patient's Perspective: The Diabetes Health Profile

The Diabetes Health Profile (DHP) is a multidimensional, diabetes-specific, patient self-report outcome measure of the psychological and behavioural impact of living with diabetes. The DHP was designed to measure the impact of diabetes in a variety of settings, from clinical practice, population surveys to clinical trials. It is simple to complete and score.



The ability to measure the benefit of interventions in diabetes is becoming of greater importance, and healthcare providers and medical product companies are increasingly interested in measuring the patient's perspective of healthcare pathways or specific interventions.



Reference: IDF Diabetes Atlas |5th edition/ http://www.diabetesatlas.org/

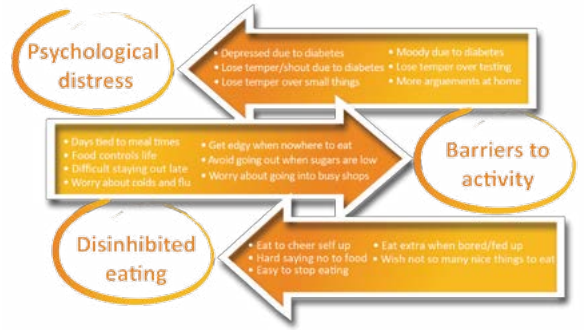
Diabetes health Profile conceptual framework

The DHP-18 has proven measurement properties and measures three distinct aspects of living with diabetes:

- Psychological distress
- Barriers to activity
- Disinhibited eating

It includes a measurement of dysfunctional eating behaviour, which despite its importance in the management of diabetes is absent in other scales.

The DHP-18 is suitable for use with people with Type 1 as well as Type 2 diabetes. This makes it a valid instrument for routinely measuring patient reported outcomes in diabetes studies.



Some key attributes of the DHP which make it suitable for use in clinical trials include:-

- Content reported by patients as highly relevant to living with diabetes
- The exclusion of skip and hypothetical questions
- The use of straight-forward language and simple phrasing
- Simple scoring algorithm
- Easy to complete / Low respondent burden (approx. 6 minutes to complete)
- Norm-referenced database
- Supported by a comprehensive user manual
- Available in over 30 different translations
- Support and advice in the use and analysis of the DHP available from the developer

The DHP-18 has therefore been used in numerous clinical trials with pharmaceutical companies, and it has been adapted to various modes of administration to best suit the conditions of the trial.

Dr Keith Meadows, Director DHP
Research and Consultancy Ltd, and DHP author
info@dhpresearch.com

Dr David Churchman
Business Lead for Oxford University Innovation Clinical Outcomes
Oxford University Innovation
david.churchman@innovation.ox.ac.uk

Evaluating a Self-Administered Glucose Tolerance Test for Diabetes

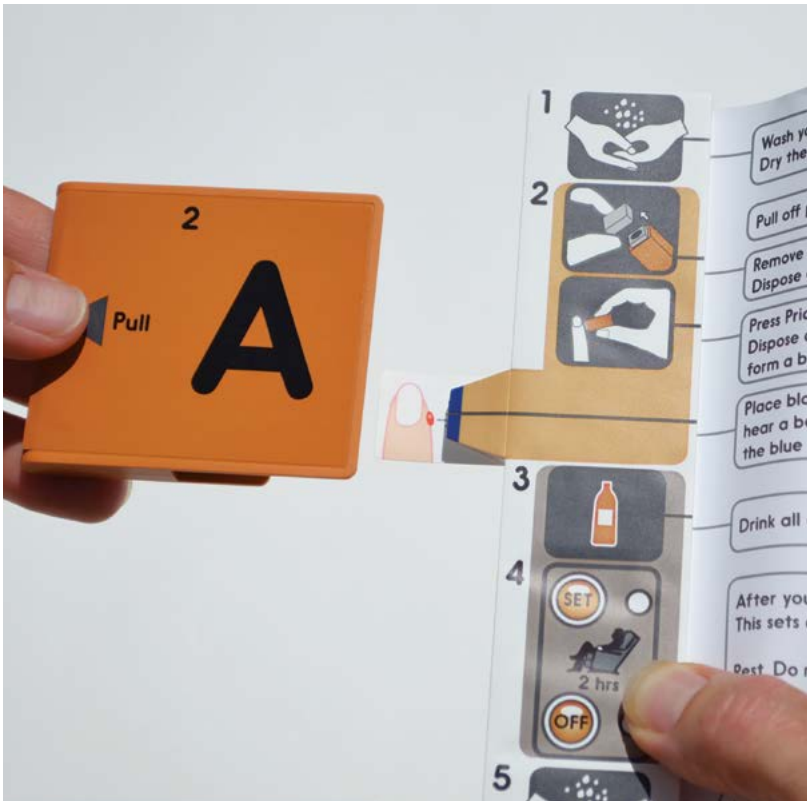
Oxford University researchers have evaluated an at-home alternative to the current clinic-based oral glucose tolerance test. This has allowed SmartSensor telemed Ltd to further development activities.

SmartSensor telemed Ltd has developed a unique disposable device that enables people to self-administer the gold-standard oral glucose tolerance test (OGTT) conveniently at home. An evaluation of a prototype system, conducted at the University of Oxford, found that the device might enable people to test themselves for diabetes in the comfort of their own home.

The study, performed by the NIHR supported Diabetes Trials Unit's Translational Research Group (TRG), found that the device was popular, easy to use, and did not require any special training. The TRG observed that the prototypes tested lacked the necessary accuracy, but concluded that once this was corrected, home diabetes screening could become a real possibility.

SmartSensor found the TRG study invaluable in guiding subsequent development of the Home OGTT system. The study's findings about the ease of using the device without any training and the high level of patient approval suggested that the user-centred device design and its novel user guidance features were very successful, and required little further attention. This allowed the company to focus on improving the test accuracy, by working to refine the sensors and electronics used in the device.

Further trials in 2015 and 2016 have confirmed the high levels of usability and patient acceptance found in the Oxford study. SmartSensor also reports that the accuracy of the Home OGTT system has now improved and that the system is performing well analytically: further studies are now planned, to verify performance ahead of product launch.



OGTT is the most sensitive and specific test for all forms of diabetes, but is difficult to provide at scale and inconvenient for patients. Home OGTT could make significant contributions to the prevention of diabetes and its complications.

James Jackson
SmartSensor telemed CEO
jj@smartsensortelemed.com

Dr Angelyn Bethel,
Diabetes Trial Unit Deputy Director
University of Oxford
angelyn.bethel@dtu.ox.ac.uk

Smartphone Based Management of Gestational Diabetes

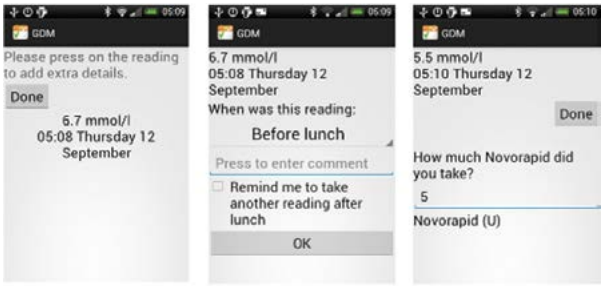
We have developed a digital, remote monitoring system to allow women with gestational diabetes to better track their blood glucose levels and communicate with their healthcare team. Results suggest improved glucose control and a reduction in the number of clinic visits for these women.

Gestational diabetes mellitus (GDM) is the new onset or recognition of glucose intolerance in pregnancy. Blood glucose levels must be tightly regulated during pregnancy to prevent adverse maternal and fetal outcomes. While finger-prick blood glucose (BG) testing with frequent clinic review is the most common method of managing diabetes in pregnancy, rising global GDM rates mean that services are increasingly pressured. New methods of managing patients are therefore required.

We have developed an intuitive, reliable, and accurate management system to record BG measurements and deliver management of GDM remotely. The system is composed of two parts:

1. Smartphone and blood glucose kit: Women monitor their BG using a glucose meter that connects to a smartphone via wireless technology (Bluetooth and NFC). A custom-designed application on the smartphone receives the BG information, uploads data to a secure NHS server, and allows for review of previous readings.
2. Website for data review: The GDM website allows the women's clinical care team to review patient data remotely, add patient notes, and prioritise patients who require more urgent review.

Our system allows two-way communication between women and healthcare professionals. BG data are uploaded in real-time, reducing errors from manual transcription and alerting to periods of missed readings. Nurses can respond quickly to patient data, potentially improving glycaemic control without the need for frequent time-intensive clinic visits. Women can add comments to each reading, and request a call back from a member of the clinical team.



The GDM management system was initially co-designed with patients and healthcare professionals to ensure it fulfilled the requirements of all users. After beta-testing and service development, a successful 200 patient randomized control trial was completed at the Oxford University Hospital NHS Trust in mid-2015. The GDM system is now being incorporated into standard gestational diabetes care for patients in several Thames Valley hospitals.

Dr Lucy Mackillop and the GDM team
Contact: lucy.mackillop@obs-gyn.ox.ac.uk

ELFIN: Globalization of an Electronic Patient Management system for Fracture Liaison Services

We have developed a secure web-based system to meet the complex needs of patients with fractures, saving clinicians' time and increasing their effectiveness.

Ensuring patients who break a bone are tested and treated for osteoporosis is important: it improves patient outcomes and reduces avoidable hospital admissions, resulting in significant cost savings.

Electronic patient management systems are needed to ensure consistent and efficient patient flow for this complex and high volume care pathway.

We worked with Seven Informatics to develop the ELectronic Fracture LiasoN system (ELFIN), a secure web-based application that meets the needs of this patient group and care pathway. The application uses a highly configurable open source platform based on ontology models of the data dictionary and care pathway, which can be specified by clinicians for clinicians.

ELFIN can report to different outputs – GP letters, patient information prescriptions and national audits, all using one-time data entry. It reduces the time specialist nurses spend on routine administration, and it improves clinical effectiveness by reducing variation in care and improving patient safety through the use of templates. It also permits real-time updates on service performance indicators, enabling integral service reporting as well as service benchmarking through exports into national audits.

ELFIN has now been implemented in three UK hospital Trusts, and it is in the process of implementation in one other Trust and in New Zealand. We have been awarded a UCSF award to refine the ELFIN clinical pathways, enabling improvements such as local configuration, an auto-installer function and a web-portal to market and provide critical support documentation for ELFIN.

The aim is to develop ELFIN as a global model for this patient group and apply its functionality to other long-term conditions/care pathways in healthcare.

Dr John Chelsom
CEO Seven Informatics Ltd
john.chelsom@gmail.com

Professor Kassim Javaid
Lecturer in Metabolic Bone Disease
University of Oxford
kassim.javaid@ndorms.ox.ac.uk

Isis Innovation (Hong Kong)

Isis Innovation (Hong Kong) is a bridge between Europe and China, enabling innovation transfer. It is focussed on the demands of the Chinese economy, and it works through a network of local Chinese joint ventures.

The ISIS Innovation Hong Kong Team

The Chinese healthcare market is currently undergoing a major transformation, with an unprecedented growth in obesity and diabetes: it currently has 200 million patients with metabolic syndrome.

3.5 million people die of cardiovascular diseases every year, accounting for 41% of all deaths.

At 212 million in 2014, China also has the world's largest elderly population, and 6 million patients with dementia.

Lifestyle programmes and new drugs are therefore in high demand. Isis Innovation (Hong Kong) therefore provides consultancy support for the expansion of established countries into China, through distribution, licensing, joint ventures and securing investment.

The ISIS Innovation Changzhou facility

It also helps clients leverage funds from government. Supported schemes include:

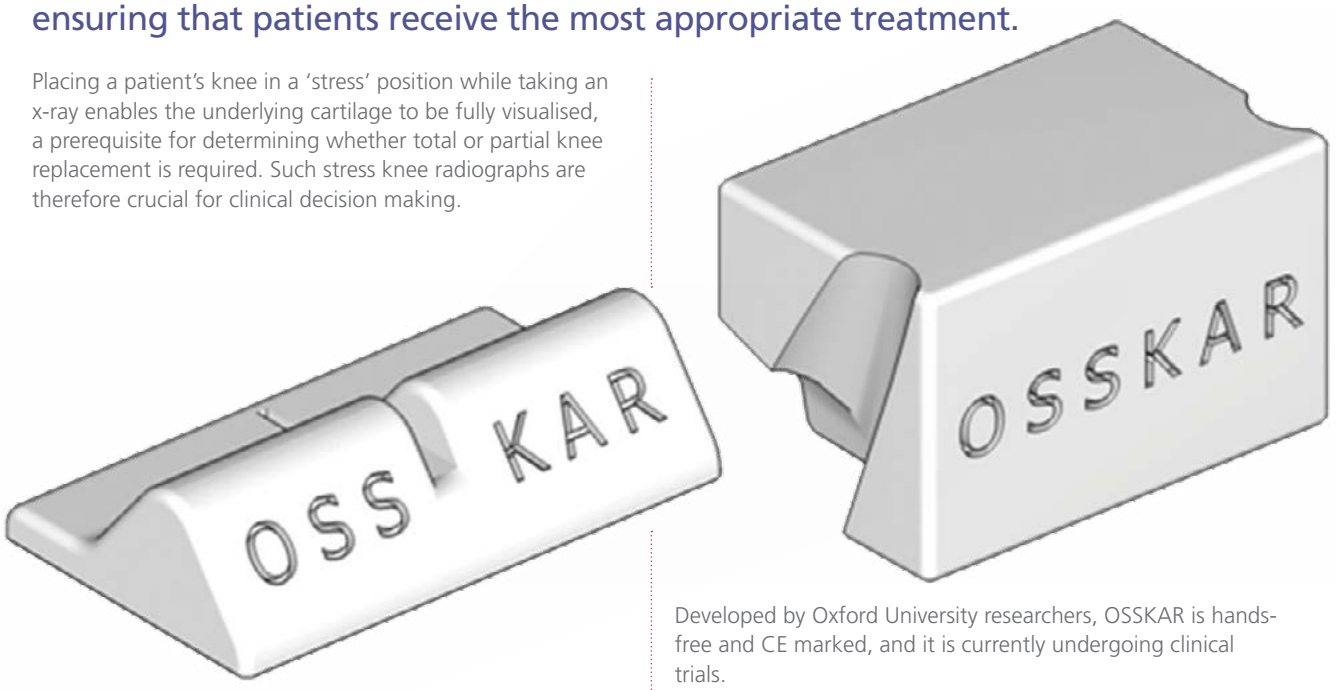
- National programmes, with support in excess of 1 million
- Provincial schemes: support of £100k per project
- Local schemes; office/lab space, up to £100k start-up funds, up to £650k in follow-on investment

For further information, please contact:
Dr David Baghurst
david.baghurst@innovation.ox.ac.uk
Tel: +44 (0)7920 460123

OSSKAR – a Positioning Device for Hands-Free Stress Imaging of the Knee

Many patients with knee problems don't receive the appropriate treatment because stress-positioning radiography (which provides crucial clinical information) is expensive and uncomfortable for the patient. OSSKAR is a simple hands-free device that facilitates knee stress radiography, ensuring that patients receive the most appropriate treatment.

Placing a patient's knee in a 'stress' position while taking an x-ray enables the underlying cartilage to be fully visualised, a prerequisite for determining whether total or partial knee replacement is required. Such stress knee radiographs are therefore crucial for clinical decision making.



Stress positioning is currently carried out using complex medical devices that are heavy, expensive and unpleasant for the patient. Alternatively, the lower limbs can be manually held in place: this is not only expensive, it also exposes the clinician to x-ray radiation.

Due to these problems, stress-positioning radiography is often not carried out and patients are inappropriately referred for total knee replacement.

Researchers from the University of Oxford have developed OSSKAR, a simple hands-free device that could greatly facilitate knee stress radiography and consequently ensure all patients receive the most appropriate and cost-effective knee replacement surgery.

OSSKAR (the Oxford Stress System for Knee Arthroplasty Radiographs) provides a simple and light-weight medical device for comfortably placing patients in standardised stress positions for x-ray radiography, while removing the need for a clinician.

Developed by Oxford University researchers, OSSKAR is hands-free and CE marked, and it is currently undergoing clinical trials.

Key benefits

Simple, lightweight and inexpensive to manufacture

CE-marked

Allows both legs to undergo stress simultaneously

Causes minimal patient discomfort

Removes need for costly and invasive MRI or arthroscopy

Removes need for manual positioning and therefore clinician radiation exposure

Potential for horizontal beam lateral x-ray and ligament insufficiency assessment

Dr Thomas Hamilton
NIHR Doctoral Research Fellow, University of Oxford.
thomas.hamilton@ndorms.ox.ac.uk

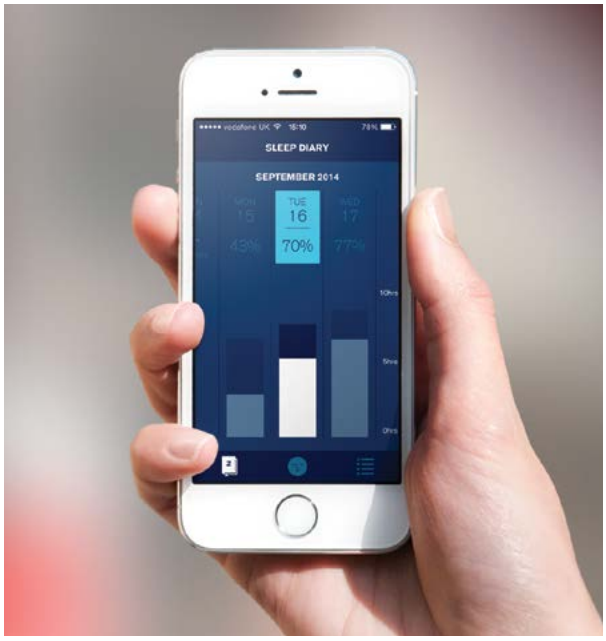
Sleepio - a Digital Sleep Improvement Programme

Sleepio is clinically proven to help overcome even long-term poor sleep without pills or potions, using Cognitive Behavioural Therapy (CBT) techniques personalised to you.

It's hard to think of an area of life that sleep doesn't affect - from how you feel on a daily basis to your long-term health. A good night's sleep is the most important health behaviour in our lives.

Unfortunately, sleep problems affect 1 in 3 people in the UK at any one time, and about 10% of the population is affected on a chronic basis. That can mean problems falling asleep, staying asleep or with the quality of sleep. In addition, poor sleep can be linked to other mental and physical health problems such as anxiety and depression.

That's where Sleepio comes in.



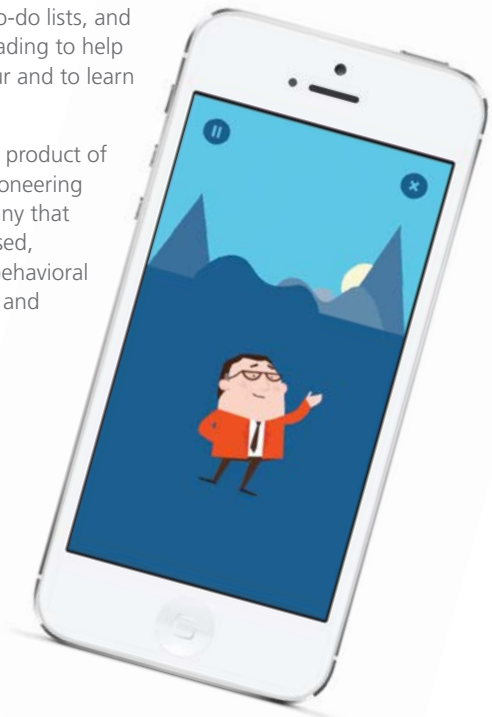
Sleepio was created by ex-insomnia sufferer Peter Hames and world sleep expert, Professor Colin Espie at the University of Oxford. Unable to access anything other than sleeping pills from his GP, Peter, an experimental psychologist, was forced to resort to a self-help book written by Professor Espie. In six weeks, he had made the necessary cognitive and behavioural changes to overcome his own sleep problem.

Frustrated by his own experience, Peter, along with Colin, began developing a technological solution to address insomnia: Sleepio.

Sleepio offers a highly personalised experience based on the patient's goals, needs, and sleep history and is accessible through online and mobile platforms. The lessons are taught by 'The Prof', a virtual sleep expert, whose use of humor and light-heartedness offers an entertaining way of learning critical sleep knowledge. The sessions are underpinned by a motivational system and community support.

Sleepio also provides tools such as a sleep diary, to-do lists, and recommended reading to help manage behaviour and to learn about sleep.

Sleepio is the first product of Big Health, the pioneering healthcare company that delivers personalised, clinically-proven behavioral medicine via web and mobile.



Professor Colin Espie
Sleep Medicine, NDCN
University of Oxford
colin.espie@ndcn.ox.ac.uk

Development and Initial Evaluation of the Nutrition and Dietetic Patient Outcomes Questionnaire (NDPOQ)

The Nutrition and Dietetic Patient Outcomes Questionnaires (NDPOQ) are self-reporting questionnaires developed for use with adults and parents of children who are receiving nutrition and dietetic care. Both the adult and parent versions of the questionnaire help inform the quality of the Nutrition & Dietetic services.

Nutrition and dietetic advice is important not only for general health care, but also for people living with chronic conditions and diseases such as diabetes.

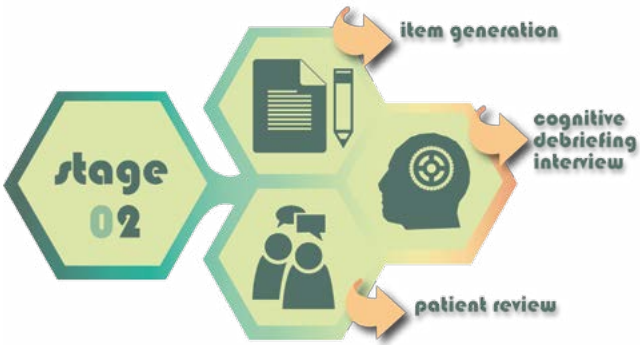
However, it has so far not been possible for a dietetic service to accurately quantify the benefits of their advice and support in helping the patient manage their condition.

This drove the development and evaluation of a patient self-report questionnaire – The Nutrition and Dietetic Patient Outcome Questionnaire (NDPOQ), designed to inform members of Dietetic Teams about the outcomes of their services and support patients' and parents' management of the condition/disease.

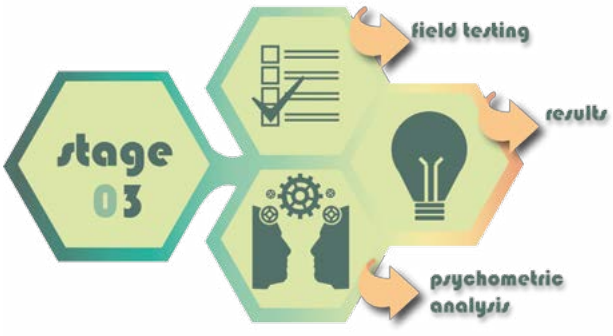
The design of the NDPOQ involved a multi-stage study:

Stage one – CONCEPT ELICITATION

Stage two – ITEM DEVELOPMENT



Stage three – PSYCHOMETRIC EVALUATION



The NDPOQ, both Adult and Parent versions (A and P versions respectively), are newly developed health outcome measures which can be routinely used to inform dietetic service providers managing the patient's condition of the outcome of their services and support for patients (and parents of patients).

The NDPOQ-A and NDOPQ-P have demonstrated psychometric properties supporting their validity and reliability. Additional research is recommended to further validate the measures.

As far as can be ascertained, there is no existing measure assessing the impact of dietetic and nutritional care on patients' and parents' daily living and consequently the NDPOQ-A and NDPOQ-P are an important addition to the portfolio of measures of the patient's experience.

Dr Keith Meadows, Director DHP
Research and Consultancy Ltd., and DHP author.
info@dhpresearch.com

Dr David Churchman
Business Lead for Oxford University Innovation Clinical Outcomes
Oxford University Innovation
david.churchman@innovation.ox.ac.uk

Development and Validation of a Short Pro Measure of Health Status for Individuals with Acute Myocardial Infarction: The Myocardial Infarction Dimensional Assessment Scale (MIDAS)

The Myocardial Infarction Dimensional Assessment Scale (MIDAS) is a PRO measure developed and validated to specifically measure the health status of individuals who have suffered a myocardial infarction (MI).

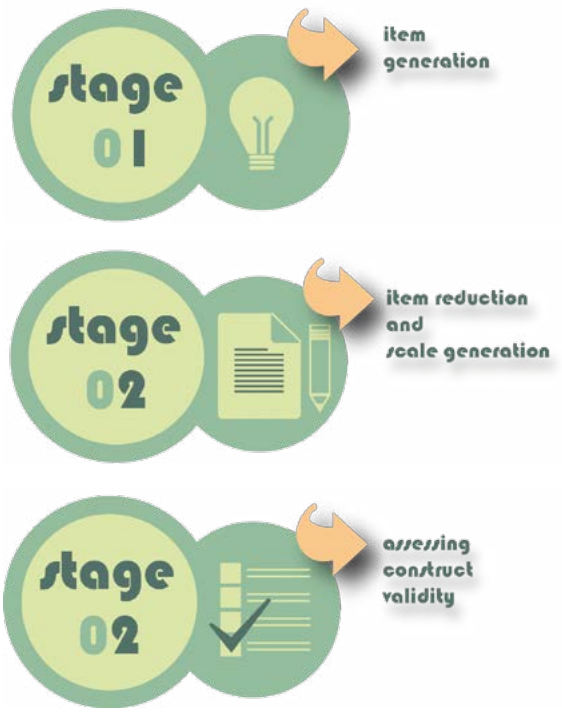
Myocardial infarction (MI) is a major cause of mortality and morbidity in the Western world: in the UK alone, roughly 2.6 people out of every 1000 have a MI incident each year.

Educational, behavioural, pharmacological and surgical interventions can reduce the risk of an MI and death from MI, but while these interventions have an impact on longevity, their impact on quality of life remains unknown. The development of an MI-specific measure is therefore of particular importance.

MIDAS-35

The 35-item Myocardial Infarction Dimensional Assessment Scale (MIDAS) was designed by a collaboration between PRO experts at the University of Oxford (Professor Crispin Jenkinson) and the University of York (Professor David Thompson, now at ACU Melbourne, and Mr Alun Roebuck). It was developed to measure dimensions of specific importance to MI patients, and to be sensitive to change in health status.

MIDAS development followed three main stages:-



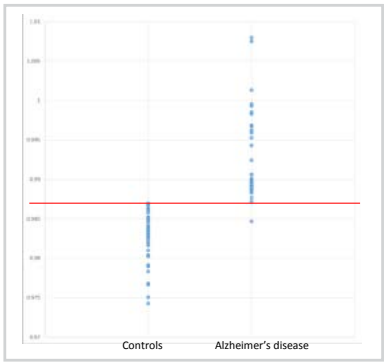
MIDAS is:

- Validated

  For use in patients in the early recovery period following MI and in the long term.

- Sensitive to change in health status

  The MIDAS can readily be used to measure the outcome of any therapeutic intervention.



99% classification accuracy (80/81 subjects) using just one of the new measures (Two different study datasets using conventional MRI scanners in UK and Italy have been combined)

- Reliable

  Results show that the MIDAS is highly reliable, both in terms of internal reliability at the patient group level and, given the magnitude of the reliability results, potentially at the individual level.

  The MIDAS contains seven dimensions (physical activity; insecurity; emotional reaction; dependency; diet; concerns over medication; side effects) and so addresses a combination of concerns distinctively associated with MI patients.

Easy to use

Short and simple in format, MIDAS can be used in a wide range of healthcare applications, and the ease of use promotes high response rates. Although predominantly used as patient self-complete questionnaire, the MIDAS can be interviewer administered as well.

Condition specific

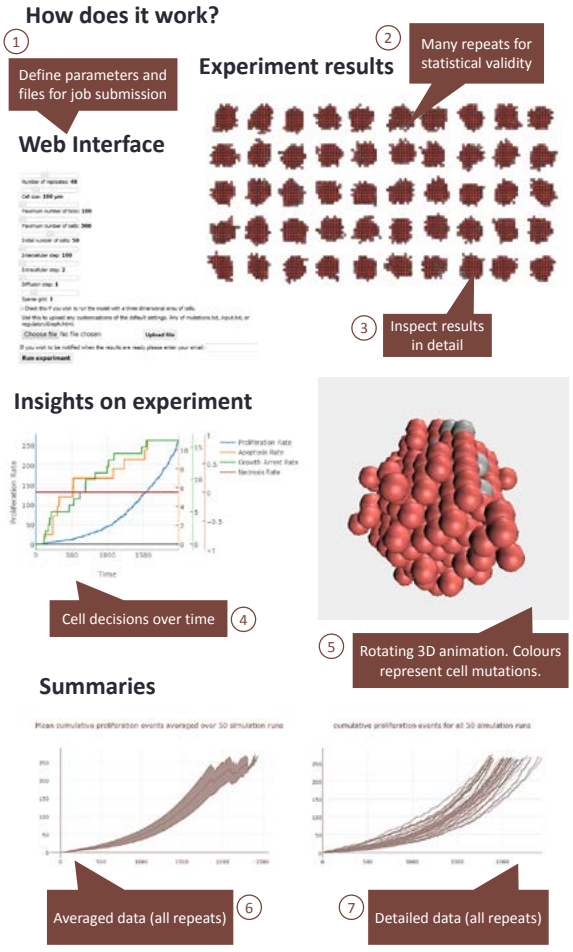
MIDAS addresses aspects of MI not covered by generic PROs.

Dr David Churchman
Business Lead for Oxford University Innovation
Clinical Outcomes
Oxford University Innovation
david.churchman@innovation.ox.ac.uk

MicroC: a Simulation Environment to Study Evolution and Growth of Heterogenous Cell Populations

MicroC is a novel computational framework for conducting in-silico biological experiments and generate or test new hypotheses. MicroC may be used to study the effects of mutations and cell-cell or cell-microenvironment interactions on the dynamics of cell growth. Almost all features of MicroC (networks, cell-microenvironment, cell-cell interaction, mutations) can be customized by the user.

MicroC is accessed via a web portal and uses the supercomputing cluster of Oxford University (ARC), to simulate biological experiments. It offers an interactive environment for visualizing the results.

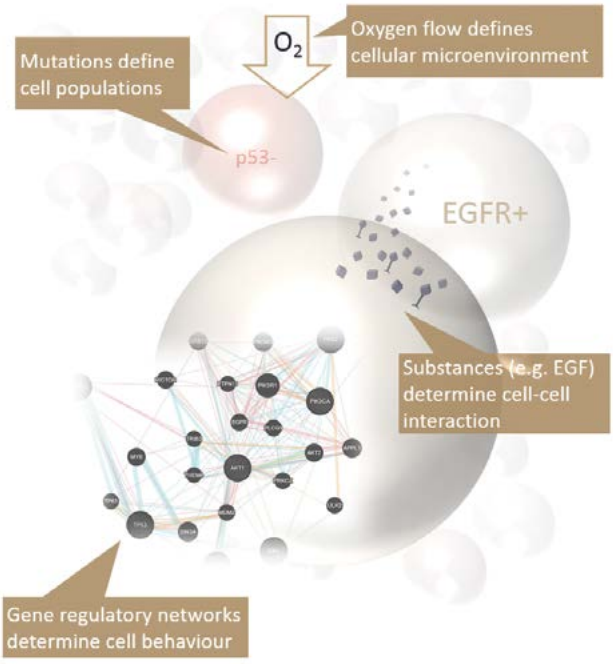


Case Studies:

I. Cell Heterogeneity

MicroC may be used to study population heterogeneity, because each cell is modeled individually. In this experiment (10 repeats), we simulate 8 different cell populations, using the same gene network, but different mutation profiles. Differences on gene status activation may be traced down to single cells.

II. Cellular (micro)environment. We test cells under hypoxia and under normal oxygen conditions, to evaluate the effect of oxygen on the cell population. We observe that under the hypoxic condition, growth is slower. This is because under hypoxia part of the simulated spheroid becomes necrotic, and affects overall proliferation rate.



III. Cell signalling. We test the hypoxic and well-oxygenated condition, for signalling cells, by introducing EGF in our experiment.

We observe that there is more growth when the population of cells doesn't have an EGFR activating mutation. This is because EGF has autocrine and paracrine functions, triggering proliferation of cells producing EGF but also nearby cells.

Professor Francesca Buffa
Computational Biology and Integrative Genomics Group
University of Oxford
francesca.buffa@oncology.ox.ac.uk

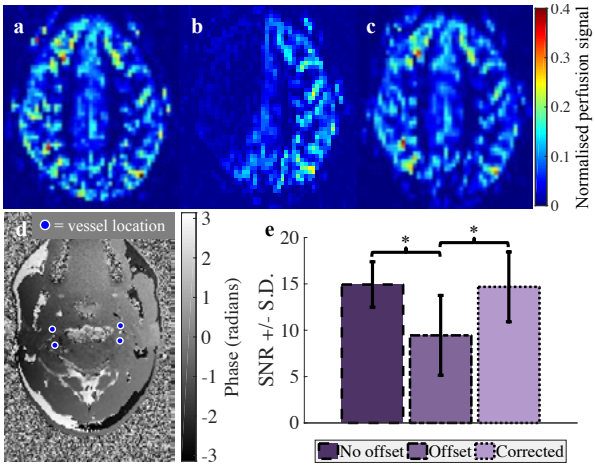
Off-resonance Correction Method for Magnetic Resonance Perfusion Imaging and Angiography

We present here a novel method to correct the effects of magnetic field inhomogeneity on a popular, non-invasive magnetic resonance technique used for both perfusion imaging and angiography. This correction greatly improves the robustness of the technique, both in terms of its image quality and quantitative accuracy.

Imaging of blood flow, both through the arteries (angiography) and into the tissue (perfusion), are of great importance in the assessment of vascular diseases, such as stroke and arteriovenous malformation. They provide information on the function and health of tissue and blood vessels in the brain. This knowledge aids clinicians with diagnosis, prognosis and treatment planning.

Common perfusion imaging and angiography methods require injection of contrast agents and/or use of ionising radiation. Arterial Spin Labelling (ASL) is a non-invasive imaging technique based on Magnetic Resonance Imaging (MRI) that can be used to acquire perfusion images and angiograms in the brain without the use of contrast agents. The most popular ASL technique is Pseudo-Continuous ASL (PCASL). A related method, vessel-encoded PCASL (VEPCASL), is also able to provide vessel-selective information about which arteries feed different parts of the brain. However, magnetic field inhomogeneity (off-resonance) leads to a reduction in labelling efficiency, resulting in poor image quality, underestimation of blood flow and inaccurate vessel-selective information. Current methods for off-resonance correction are limited, with many requiring additional lengthy scans or manual intervention.

The method presented here corrects for off-resonance effects present during (VE)PCASL by incorporating knowledge of magnetic field inhomogeneities into the labelling process using an Optimised Encoding Scheme (OES). It is simple, fast, automated and allows off-resonance to be corrected without increasing the PCASL scan time: only a rapidly acquired field map is required. Unlike other correction methods, it is applicable to VEPCASL and PCASL, and can account for any pattern of off-resonance and any number of vessels. We have shown both theoretically and experimentally that this method greatly improves the robustness of these techniques in the presence of magnetic field inhomogeneity, which could significantly boost their clinical utility in a range of patient groups.



Images of the PCASL perfusion signal in the brain of a representative subject and the mean SNR of this perfusion signal across a group of subjects. The perfusion signal is shown for a: no offsets in the labelling plane, b: offsets, un-corrected in the encoding, leading to loss of perfusion signal in part of the brain, and c: an offset corrected encoding, which recovers the lost perfusion signal. d: Field map of the labeling plane showing the field offsets. e: Mean signal-to-noise ratio (SNR) ± standard deviation of the perfusion signal across all subjects, showing quantitatively the signal loss due to field inhomogeneity which is recovered using the proposed correction method.

Dr Thomas Okell
FMRIB Physics Group, Oxford University
tokell@fmrib.ox.ac.uk

Up-Stream Treatment Strategies for Patients with Atrial Fibrillation

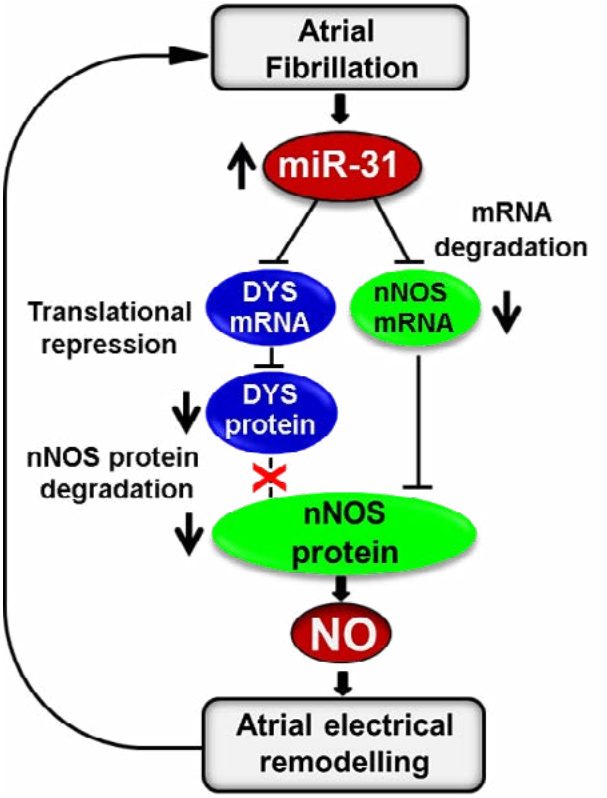
Atrial fibrillation (AF) is the most common heart rhythm disorder worldwide and a major public health burden due to its impact on the risk of stroke and heart failure. To date, therapeutic strategies to restore sinus rhythm in patients with AF have been marred by poor efficacy, lack of benefit on patient outcomes, and safety concerns.

AF leads to electrical remodelling of the atria, which in turn promotes AF maintenance and resistance to treatment. Although remodelling has long been a therapeutic target in AF, its causes remain poorly understood.

We show that atrial-specific up-regulation of microRNA-31 (miR-31) in goat and human AF depletes neuronal nitric oxide synthase (nNOS) by accelerating mRNA decay and alters nNOS subcellular localization by repressing dystrophin translation. By shortening action potential duration and abolishing rate-dependent adaptation of the action potential duration, miR-31 overexpression and/or disruption of nNOS signalling recapitulates features of AF-induced remodelling and significantly increases AF induction in vivo.

By contrast, silencing miR-31 in atrial myocytes from patients with AF restores dystrophin and nNOS and normalizes action potential duration and its rate dependency. These findings identify atrial-specific up-regulation of miR-31 in human AF as a key mechanism causing atrial dystrophin and nNOS depletion, which in turn contributes to the atrial phenotype begetting this arrhythmia.

These data have uncovered similarities between AF-induced molecular and electrical remodelling of the atrial myocardium and the cardiomyopathy of Duchenne Muscular Dystrophy, and identified miR-31 as a potential therapeutic target for both conditions.



Professor Barbara Casadei
Professor of Cardiovascular Medicine, Oxford University
barbara.casadei@cardiov.ox.ac.uk

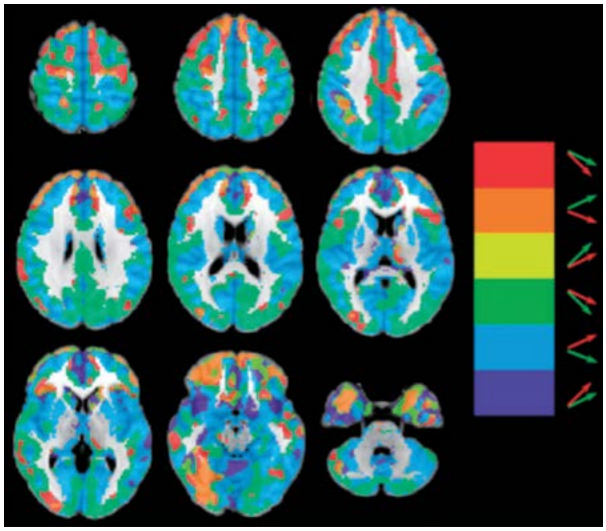
The FMRIB Software Library

Oxford Centre for the Functional Magnetic Resonance Imaging of the Brain Software Library

The FMRIB Software Library (FSL) is a comprehensive library of analysis tools used worldwide to quickly and effectively analyse complex brain imaging data.

The Oxford Centre for Functional Magnetic Resonance Imaging of the Brain (FMRIB) is a multi-disciplinary neuroimaging research facility, which focuses on the use of Magnetic Resonance Imaging (MRI) for neuroscience research, along with related technologies such as Transcranial Magnetic Stimulation, Transcranial Direct Current Stimulation and EEG. FMRIB is composed of research groups studying all aspects of brain imaging, including physics, analysis, basic science and clinical neuroscience.

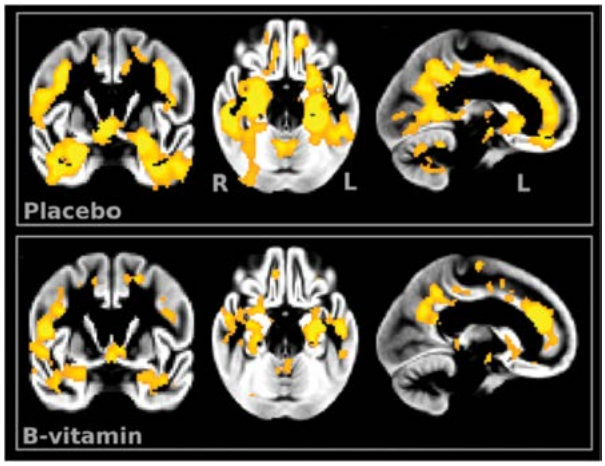
To assist researchers in the often complex and labour intensive analysis of MRI data, an innovative team, led by Professor Steve Smith, began developing the FMRIB Software Library (FSL) in 1998. Their algorithms worked robustly on a wide variety of real data, and they also generated leading-edge mathematical theory feeding into what was rapidly becoming a powerful standalone analysis pipeline.



Binarised representation of all the combinations of grey matter development over 2.5 years between healthy adolescents (green arrows) and the schizophrenic patients (red arrows). [Dauaud et al, 2009]

FSL was released in 2000 and has received over 2,500 citations. The latest version has been downloaded over 10,000 times and is used in nearly 1,000 hospitals and university labs.

This success has been hard earned. For over ten years the core team has continually developed, refined and extended FSL, as well as creating extensive documentation and training courses with over 1,000 attendees since 2002, and maintains an active user community through its email support list.



Regional loss of Grey Matter (GM) volume in placebo and B-vitamin groups. Placebo-and B-vitamin–treated groups showed significant reduction of GM volume over the 2-year period in similar regions. The extent and significance of volume loss appeared markedly greater in the placebo group compared with the B-vitamin group and is confirmed by direct statistical comparison. [Dauaud et al, 2013]

With the addition of a user-friendly graphical interface, and a high degree of automation, this robust, powerful and flexible analysis pipeline is now the recognised standard in academia for multi-modal MRI analysis. FSL is also commercially licensed to 7 of the top 10 global pharmaceutical companies and many others, whose activities range from drug discovery and clinical trials to neuromarketing, and even iPhone app development.

Professor Stephen Smith
Associate Director FMRIB
steve@fmrib.ox.ac.uk

Dr Fred Kemp
Deputy Head of Technology Transfer,
E-Health & Bioinformatics,
Oxford University Innovation
fred.kemp@innovation.ox.ac.uk

Microdetect
– Diagnosis of Dementia, Autism and Other Conditions

A new level of precision in brain measurements identifies patterns in the microstructure of the human brain which can be used to classify a range of cognitive and neurological diseases.

In England alone there are more than 670,000 people with dementia. 350,000 remain undiagnosed and without access to support. Over the next 30 years, the cost of dementia in England is set to rise by £19 billion. In order to minimise cost and improve care for an ageing population, improvements in diagnosis need to be made.

Autism is a developmental condition with brain effects that are too subtle to detect with conventional brain imaging methods. 1% of the human population have autism but many are undiagnosed. The cost of autism in the UK is estimated at £32 billion per year and improved diagnosis is crucial to enable intervention and support in early life.

Diagnosing Dementia

Diagnosis of Alzheimer's disease and other dementias can only be confirmed by post-mortem examination. 'Probable diagnosis' in life depends on clinicians' judgement and current brain imaging tests rely on imaging agents which are expensive and radioactive.

Diagnosing Autism

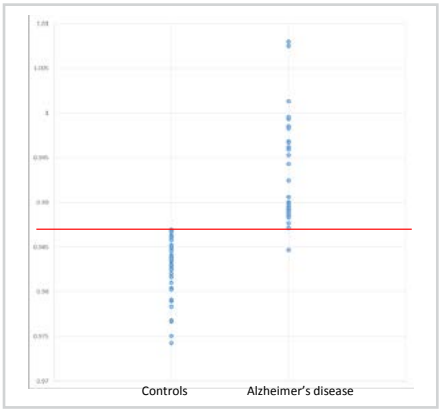
Current methods depend on clinicians' judgement and family interviews. No brain imaging or other biological test currently exists.

Oxford Invention

Unique new diffusion MRI measurements which are low cost, non-invasive and do not rely on ionising radiation have been developed by scientists at the University of Oxford. The technology establishes signature patterns in the microstructure of the human brain which can provide differential diagnosis between dementias such as Alzheimer's disease (AD) and cerebrovascular dementia (CVD) in late life, or detection of developmental conditions such as autism in early life. It is expected this technology could have positive implications for the clinical management of patients with cognitive diseases.

The Oxford invention has been developed through studies of post-mortem histology of the brain and with diffusion tensor imaging (DTI) MRI scans.

A patent application protecting a broad range of microstructural signature patterns of disease in the human brain has been filed. Further development work is ongoing.



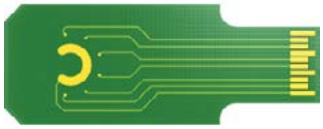
99% classification accuracy (80/81 subjects) using just one of the new measures (Two different study datasets using conventional MRI scanners in UK and Italy have been combined)

Professor Steven Chance
Associate Professor in Clinical Neurosciences
steven.chance@ndcn.ox.ac.uk

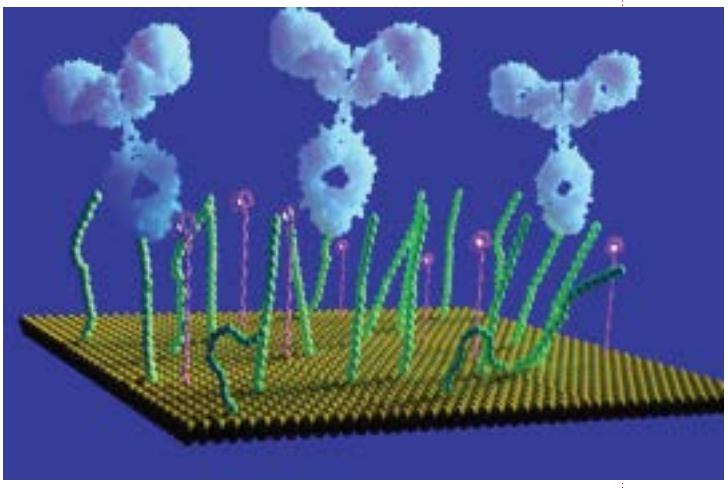


Oxford Impedance Diagnostics – Changing Medical Diagnostics

New impedance technologies produced by a collaboration between the Universities of Oxford and São Paulo in Brazil will allow cheaper, faster and more sensitive medical diagnostics for diseases ranging from breast cancer to dengue fever and Parkinson's Disease.



Over the last five years, researchers at the University of Oxford have developed new impedance technologies which have the potential to change diagnostic pathways for many diseases, reducing healthcare costs while improving patient outcomes.



Oxford Impedance Diagnostics is the company marketing these news tests, which will change the way medicine is delivered over the next ten years.

The core technology is based upon micro electrical impedance and it enables the development of assays with a unique combination of sensitivity, low cost, speed, convenience and multiplexing.

Professor Jason Davis at the University of Oxford is one of the co-inventors of the technology, and the expertise of his research group allows the development of tests for new biomarkers within six to eight weeks.

This will enable the company to quickly develop collaborations with academic groups and pharmaceutical companies seeking new companion diagnostics or improved assay performance for existing biomarkers.

In parallel, the company will also develop three of its own assays for Parkinson's disease, breast cancer and dengue fever. These tests will validate the platform capability, and once launched, offer significant revenue streams.

The proprietary platform technology at the heart of Oxford Impedance Diagnostics is based upon high-quality, peer-reviewed research by Professor Jason Davis and his group at the University of Oxford and Professor Paulo Bueno at the University of Sao Paulo in Brazil.

The technology is protected by five strong patents owned by Oxford University and licensed exclusively to the company.

Professors Davis and Bueno are the co-inventors of the technology, and along with the University of Oxford, they will also be the co-owners of the company.

External investment has already been secured, and it will help transfer the research platform into a commercially viable, high volume and robust assay system for use in clinical laboratories or at the point of care.

The combination of rapid assay development, multiplex capability, exceptional sensitivity and very low cost has the potential to disrupt the current diagnostic patient pathways for many diseases, reduce healthcare costs and improve patient outcomes.

Mr Andy Anderson
Chief Executive Officer
Oxford Impedance Diagnostics
andyanderson@oxfordimpedance.com

Professor Paulo Bueno
Research Director,
Sao Paulo State University
prbueno@iq.unesp.br

Professor Jason Davis
Reader in Chemistry,
University of Oxford
jason.davis@chem.ox.ac.uk

Virtual Reality Can Help Treat Severe Paranoia

By combining evidence-based psychological treatment techniques with state-of-the-art virtual reality simulations, we were able to bring about a significant reduction in paranoid symptoms in patients, after a short 30 minute session.

About 1-2% of the population has severe paranoia, typically as a central feature of mental health disorders such as schizophrenia. Patients show extreme mistrust of other people, believing that others are deliberately trying to harm them. The condition can be so debilitating that sufferers may be unable to leave the house.

Coping mechanisms such as avoiding social situations, reducing eye contact or making any social interaction as short as possible worsen the situation, since they reinforce paranoid fears: patients come to believe that they avoided harm because they used these 'defence behaviours'.

By getting patients to drop these defence behaviours in a virtual reality simulation, Professor Daniel Freeman's team at Oxford University's Department of Psychiatry was able to get patients to 're-learn' that situations they feared were safe.

After the virtual reality therapy sessions, over 50% of these patients no longer had severe paranoia at the end of the testing day. The benefits also carried over into real-world situations, such as going to the local shop.

We are currently testing how long-lasting these benefits are, and how well they transfer to real-world situations.

These results demonstrate that our custom-build virtual reality system is an effective way of treating patients with otherwise difficult-to-treat conditions, such as paranoia.

Dr James Groves
Technology Transfer Manager
Oxford University Innovation
james.groves@innovation.ox.ac.uk

Professor Daniel Freeman
NIHR Research Professor in Clinical Psychology
Consultant Clinical Psychologist
University of Oxford
daniel.freeman@psych.ox.ac.uk

The Out of Hospital Emergency Multidisciplinary Unit

Meeting the healthcare demands of our population both now and in the future will need a new approach to crisis presentation. The Future Hospital Commission report, the NHS Five Year Forward View and the Primary Care Workforce Commission, all call for greater integration between primary and secondary care and an 'ambulatory by default' approach in acute medicine.

The Emergency Multidisciplinary unit in Oxfordshire delivers comprehensive assessment and treatment of acute medical illness in a community setting for older patients living with frailty (cognitive, social and physical). It provides acute ambulatory care where appropriate to patients who would otherwise be referred to an acute hospital site and therefore delivers care in a setting closer to their home or care home.

Patients can be referred from their general practitioner/family physician or from paramedics from the ambulance service for an escalation of care.

Rapid assessment from multiple healthcare disciplines (nursing, medicine, physiotherapy, occupational therapy, social care) provides comprehensive care delivery to address the multiple dimensions of need in this complex patient group. Clinical decision making is underpinned in this 'out of hospital' setting with point of care (POC) diagnostic testing. A range of biochemical tests with results available within minutes can detect acute kidney injury, electrolyte disturbance, acid-base disorders, coagulopathy, myocardial damage, infection and anaemia.

The central hospital laboratory service provides quality assurance and stock control to ensure seamless delivery of POC testing and additional connectivity transmits all POC results back to the laboratory database. As a result there is a continuous electronic record of all blood results for patients in the population wherever they seek healthcare, which allows for comparison of results at any subsequent healthcare attendance to determine stability, deterioration or recovery.

A full range of parenteral medical treatments can be given, guided by POC tests and where necessary cross-sectional imaging arranged at the local acute trust. Over 60% of patients (with a median age of 80) are managed on a purely ambulatory path without needing a hospital bed at any point during the month after initial assessment on EMU. The EMU won the inaugural Guardian Healthcare Innovation Award for Service Delivery in 2013.

Professor Daniel Lasserson
Clinical Lead for Diagnostics & Pathways,
Wealth Creation Programme, Oxford AHSN
Nuffield Department of Medicine
Oxford University
daniel.lasserson@phc.ox.ac.uk

Wireless Assessment of Surgical Performance

Through an exciting collaboration between the Nuffield Department of Orthopaedics, Rheumatology & Musculoskeletal Science, and McLaren Applied Technologies, we have developed a novel wireless method for assessing surgical performance in both operating theatres and surgical skills training centres.

The burden of orthopaedic and musculoskeletal disease is a major problem worldwide. In the UK alone orthopaedic operations are the most frequent in any hospital. Besides joint replacements, arthroscopic (keyhole) surgery has also expanded significantly in the last decade. Skilled and competent surgeons are needed and the acquisition of technical skills remains a fundamental goal of surgical training. However, training has been restructured and there are now restrictions on trainees' working hours, particularly in Europe and North America, that have resulted in a huge reduction in the average number of operative cases per trainee. This reduction is an alarming 80% in the United Kingdom.

While surgical competence consists of a complex combination of technical dexterity, knowledge, decision-making, and communication skills, technical dexterity remains particularly important and underperformance in this domain leads to poorer results. Greater peer and public scrutiny means that improving surgical learning and demonstrating competency is evermore important.

We have previously validated methods of assessing surgical dexterity, studied the learning curves of some procedures, and demonstrated the value of surgical skills simulators. Through our exciting collaboration with McLaren Applied Technologies we have now developed a novel 'wireless' objective surgical dexterity assessment tool that not only assesses surgical dexterity in a simulated setting, but for the first time in the real operating theatre. This wireless elbow-worn motion sensors system now allows for feasible objective assessment of surgical performance. In turn, this is facilitating a programme of surgical simulation and patient outcome research in Oxford that will ultimately improve the delivery of surgical treatments and improve patient outcomes in orthopaedics.

UNIVERSITY OF OXFORD

McLaren APPLIED TECHNOLOGIES

Professor Jonathan Rees
Orthopaedic Surgery and Musculoskeletal Science
University of Oxford
Collaborating with Dr Caroline Hargrove
and Dr Georgina Kirby at McLaren.

Pro-Mapp
Software for Managing Orthopaedic Care Pathway

Pro-Mapp is a software enabled system for orthopaedic care pathway management, implant safety monitoring, and patient reported outcome delivery.

Pro-Mapp is a new spinout venture originating from research collaboration between Oxford University researchers and expert health care software collaborators, Fr3dom Limited. It is currently seeking first round investment of $900,000 to be followed with $2-4m in 9 to 12 months' time, and a third round likely at 3 years.

Pro-Mapp is a software enabled system for orthopaedic care pathway management, implant safety monitoring, and patient reported outcome delivery. The orthopaedic implant industry is worth over $6bn per year and the founding board members include world leading clinicians and academics.

There are three initial revenue and business channels:

- Joint Access is a clinical pathway system that uses patient reported outcome measures (PROMS) intelligently to support clinical pathway management of hip, knee and shoulder procedures.

- SSAFE is a long term surveillance system that allows large scale post-operative surveillance at a cost previously inaccessible to implant manufacturers.
- Fr3PROMS is a tool that can be used to distribute, monetise if necessary, and present PROM tools and shared decision making tools (SDMs) digitally. It does not own or create content, but is a delivery system. Fr3proms already carries content for all mandated procedures in England as well as a large number of tools for other organisations including the Kettering Cancer Centre, New York and iOutcomes for the Oxford Scores.

Revenue will be generated through sales of SSAFE and Joint Access to manufacturers and large hospitals, clinics and high volume surgeons. Fr3proms is distributed and bought online, giving immediate market accessibility. Users of Fr3proms may upgrade to Joint Access on the unified software platform. This is further enhanced by the links with SSAFE allowing primary, secondary and follow up care to access the same information when a patient is consented.

The platform is now fully developed and ready for field testing and scale up in different environments and countries. Customers already include Zimmer, Biomet (SSAFE), Oxford University Hospitals (Joint Access) NHS Scotland and SITU the surgical trials unit at Oxford.

Professor David Beard
Musculoskeletal Sciences, NDORMS
University of Oxford
david.beard@ndorms.ox.ac.uk

Mr Toby Knightley-Day
Managing Director, Fr3dom Ltd
toby@fr3dom.net

Working Towards a Personalised Surgical Pathway

In collaboration with McLaren Applied Technologies, University of Oxford researchers are working to improve patient preparation and flow through the surgical pathway, improving both surgery outcomes and patient experience. Researchers are developing a system of remote monitoring and personalised patient feedback that can be integrated into the care of surgical patients, improving the care provided.

On average, a person will have four operations in their lifetime. The pathway from initial contact through to the postoperative recovery period is complex and can be confusing.

Many factors along the pathway will affect patient experience and outcomes, but most current research has only focused on improving the 'hands on' care provided by doctors to patients in hospitals.

Our research will investigate ways of using innovative technology to involve patients in their entire surgical pathway, in order to provide better care.

We have used commercially available wearable remote activity monitoring technology to assess patient' fitness levels before and after an operation, adding value to the care of surgical patients in the NHS.

Our findings will help keep doctors better informed of a patient's health status, and help patients to optimise their health before an operation.

The project aims to use a new patient pathway, supported by innovative patient monitoring methods and software design to achieve:

- Patient Centred Care
  - Empowering patients with timely and relevant information about their operation so they feel fully prepared
  - Enable patients to control and update their own medical information and alert their doctors of any problems
  - Improve communication between the patient, GP and the hospital before an operation to avoid delays and errors in patient care
- Personalised Care
  - Individual monitoring of patients at home before their operation using wearable technology to give detailed patient profiles
  - Ability to build an accurate patient profile and therefore target areas needing intervention well in advance of the operation
  - Providing personalised feedback on the patient's health status and advice on how to optimise their health before their operation
  - An app that helps patients to understand their test results and medication changes before their operation.

Dr Helen Cui
Oxford-McLaren Clinical Researcher
Urology Registrar, NHS England
Helen.Cui@ouh.nhs.uk

Dr Ben Turney
Clinical Lecturer in Urology,
Oxford University
ben.turney@nds.ox.ac.uk

UKPDS OM version 2:
a Type 2 Diabetes Outcomes Model

The UK Prospective Diabetes Study (UKPDS) outcome model uses 89,760 patient-years of data to estimate life expectancy and cumulative costs of complications in people with Type 2 Diabetes.

Type 2 diabetes is estimated to affect 9% of adults, and it costs $465 billion each year. With these figures predicted to rise by 50% over the next 20 years, providing Type 2 Diabetes care represents a major economic challenge for the healthcare industry.

Because of the extended timeframe over which the multiple outcomes associated with Type 2 Diabetes unfold, stakeholders frequently make use of health economic models to support evidence-based decision making related to funding allocation.

The Oxford UKPDS Outcomes Model is a computerised simulation tool designed to estimate life expectancy, quality adjusted life expectancy and the cumulative costs of complications in people with Type 2 Diabetes.

The newly released version 2 makes use of data from all 5,102 UKPDS patients who entered the trial, as well as the 4,031 survivors who entered the 10 year post-trial monitoring period. This equates to 89,760 patient-years of data, which is double the number of events in version 1.

Key new features in version 2 include:

- Additional risk factors: Albuminuria, Heart rate, WBC, Haemoglobin and eGFR
- Additional clinical events: Diabetic ulcer and CVD death
- New equations predict second events for MI, Stroke and amputation
- Supports up to 3 groups of patients in a single run and provides a summary for each group as well as group differences
- Cost / utility values can now be varied by age and sex
- Addition of therapy costs and pre and post complication costs
- Calculation of Monte Carlo Error allows simulation fine-tuning
- Can queue workbooks to run multiple unattended simulations, while parallel processing can take full advantage of up to 10 computer cores

The UKPDS Outcomes Model has already been adopted by a range of companies, government bodies and Universities, including the UK's National Institute of Health and Care Excellence (NICE) and four out of five largest diabetes drug manufacturers.

Professor Alastair Gray
Professor of Health Economics and Director
HERC, University of Oxford
alastair.gray@dph.ox.ac.uk

Professor Rury Holman
Diabetes Trial Unit Director
Professor of Diabetic Medicine
University of Oxford
rury.holman@dtu.ox.ac.uk

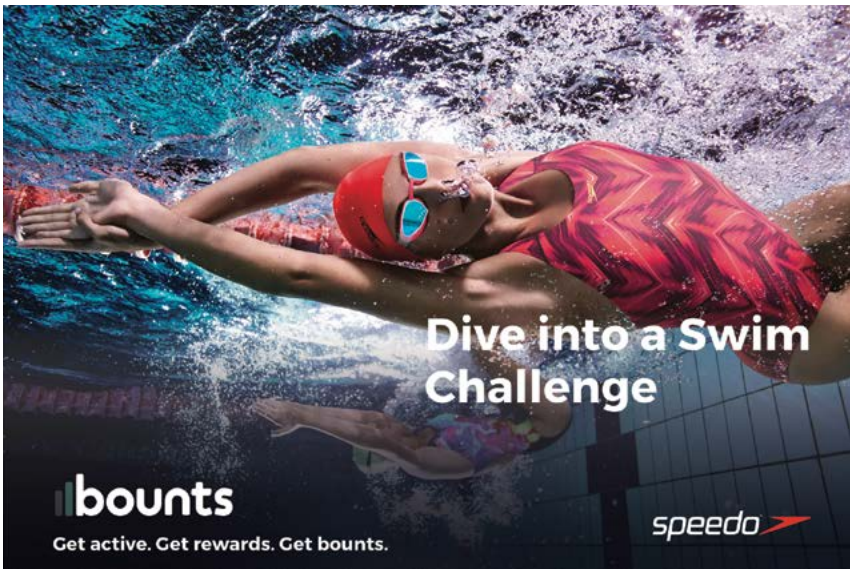
bounts
Incentives to Get Active

bounts is a profitable, fast growing, lifestyle rewards company turning healthy activity into habit. Over 3 million members and growing rapidly in the UK (#1 Health & Fitness App in Jan 2016).

bounts is a profitable, fast growing, lifestyle rewards company which turns healthy activity into habit.

Founded in 2011 with backing from Oxford University Innovation's Startup Incubator, bounts was ranked #1 Health & Fitness App in Jan 2016.

With over 3 million members, bounts is growing rapidly in the UK and has a reward shop that covers the UK, USA, Canada, India, and UAE. The free and innovative bounts app (iOS and Android) rewards members for being active. Once signed-up, members connect it to a fitness tracker and exercise to earn points; the points can then be redeemed for high street vouchers. The more active they are, the more points they earn.



Providing rewards and incentives is an effective strategy to increase physical activity and improve health behaviours in a variety of settings. The evidence suggests that incentives on their own or in combination with other strategies can significantly increase physical activity, lead to improvement in health and weight management.

The bounts Team

Participation levels are found to be 30 per cent higher in people using a fitness reward system, and a recent study revealed that bounts members are twice as likely as non-members to keep using their gym membership for a period of 12 months or longer.

Oxford University Index of Multiple Deprivation (IMD) tool provided highly insightful data about bounts members:

- 34% are from the 2 most deprived quintiles (Q4 and Q5)
- 31% who paid for themselves to upgrade to Premium+ (£14.99) were from Q4 and Q5
- 29% of our top 500 members (based upon current points balance) are from the 2 most deprived quintiles

bounts members are reward driven, focussed on the collection of points (through various forms of exercise) in order to achieve a reward. They range in age from 8-87 with the key age groups being 25-34, 35-44, and 15–25, with over 60% being female.

bounts is a natural fit for sports operators, gyms, national governing bodies, and organisations seeking insight into usage data and to improve retention rates.

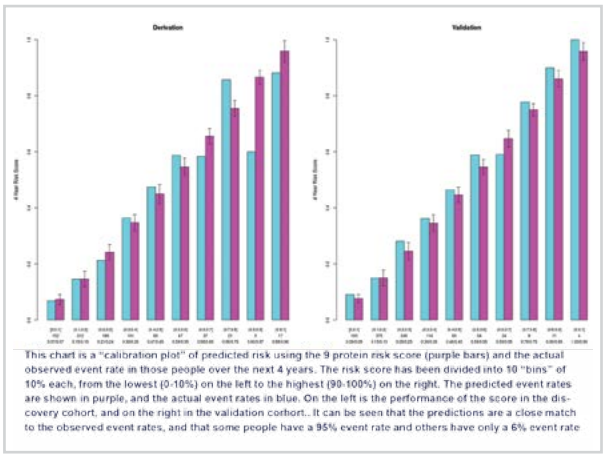
Mr John Stuart
CEO, Bounts Ltd
john.stuart@bounts.it



Precision Risk Profiling in Heart Disease and Stroke for Tailored Care and Health Behaviour Advice

Cardiovascular disease is the UK's biggest killer but existing risk scores are imprecise and inaccurate; perhaps because of this, most people don't reliably take their medicines or change their lifestyles effectively. This project is to develop and implement within the NHS a protein-based risk profile that enables care teams to individualise interventions and motivates patients to improve lifestyles.

People with known coronary heart disease are all told they are at high risk but not everyone is the same. We describe how measuring thousands of proteins using modified DNA-based reagents has led to the ability to discover signatures for risk which can discriminate between people who otherwise look similar, but some have a 9 in 10 chance of death or hospitalisation within 4 years, and others with only a 1 in 20 chance.

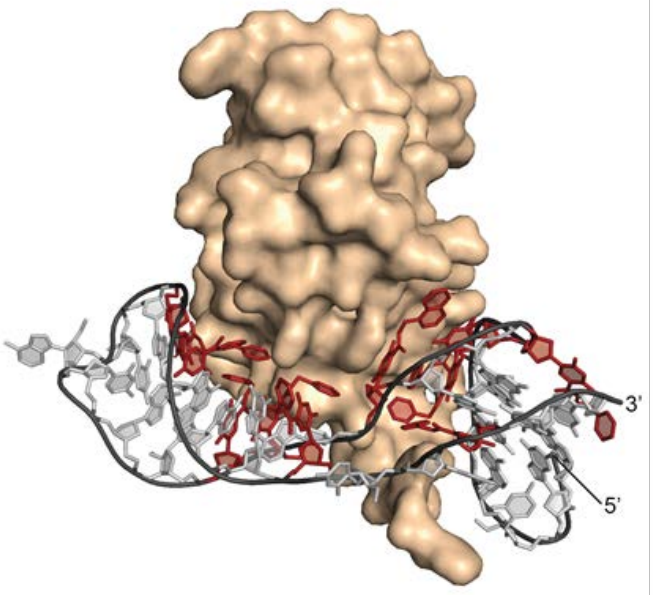


This chart is a "calibration plot" of predicted risk using the 9 protein risk score (purple bars) and the actual observed event rate in those people over the next 4 years. The risk score has been divided into 10 "bins" of 10% each, from the lowest (0-10%) on the left to the highest (90-100%) on the right. The predicted event rates are shown in purple, and the actual event rates in blue. On the left is the performance of the score in the discovery cohort, and on the right in the validation corhort.. It can be seen that the predictions are a close match to the observed event rates, and that some people have a 95% event rate and others have only a 6% event rate

We made 2.7 million individual measurements in plasma from ~1800 people with apparently stable heart disease to discover the optimal combination of proteins to predict poor outcomes such as death, heart attack, heart failure and stroke over the 1-5 years after their blood sample. We used mathematical machine learning techniques to finalise an algorithm that used 9 proteins, and then applied it to an independent validation set. When the population is ranked for risk using this score, the actual observed event rate in the top 20% is >10 fold higher than that in the bottom 20%. This is better than any combination of traditional markers, demographics or known risk factors.

Now the project has evolved into planning, with the Oxford AHSN, the early implementation of this product within the NHS in this region. The development of an individualised and accurate prediction is only the first step towards improved outcomes and reduced costs. Can the score be used to direct more medical resources towards the most needy?

Can and will patients improve their lifestyles and nutrition with a less deniable and frighteningly accurate prediction? Will the monitoring of within-person changes in risk help? Can the medical care teams tailor interventions based on individualised risk? Those are the key questions that the prospective early implementation program will seek to address.



The picture above is a DNA-based reagent (a SOMAmer or Show, Off-rate Modified Aptamer) binding to a protein commonly found in the blood. Thousands of these reagents are used together to measure thousands of proteins in the blood simultaneously.

Dr Stephen A Williams MD
Chief Medical Officer, SomaLogic Inc
swilliams@somalogic.com

Islet Cell Transplantation for Type 1 Diabetes – Current Status and Future Opportunities

Islet cell transplantation has achieved considerable clinical success in adults over the past two decades. However, the ultimate aim of using it to treat children soon after diagnosis is yet to be realised.

Pancreatic Islet cell transplantation is a state-of-the-art, minimally invasive treatment that has the potential to reverse type 1 diabetes mellitus. Over the past two decades, the clinical outcomes of this procedure have improved dramatically, with up to 80% of selected adult patients now achieving insulin independence for at least one year post transplantation in clinical trial

Oxford DRWF Human Islet Isolation Facility

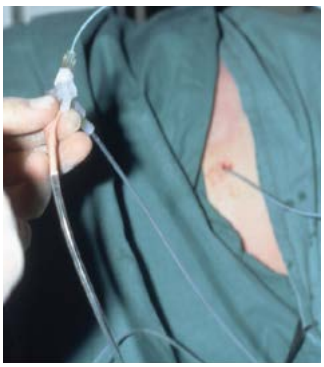
That said, the ultimate goal for this treatment is to be able to transplant children soon after diagnosis. For this to be achieved, a number of challenges still need to be overcome, the main one being to develop strategies that prevent the need for long-term immunosuppression with its associated risks.

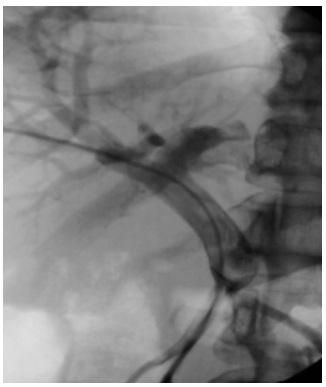
Purified Islets

One of the approaches is to develop implantable macro-encapsulation devices that isolate the islets from the immune system, but that still allow the islets to secrete the pancreatic hormones including insulin and for them to accurately detect subtle fluctuations in blood glucose.

Oxford has been at the forefront of the field of islet transplantation for many years. We have one of only three commissioned clinical isolation facilities in the UK and are one of a few commissioned supra-regional islet transplant centres.

Dovetailed with this clinical programme is our collaborative, multi-disciplinary research programme, which includes paediatric transplant surgeons, islet biologists, transplant immunologists, tissue engineers, and industrial partners.





Islet Transplant

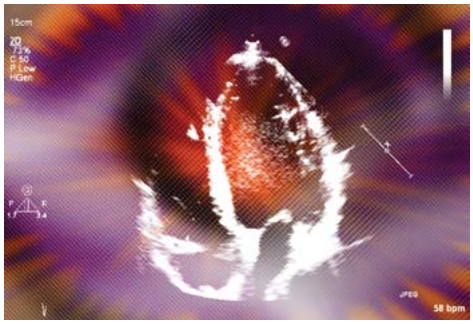
Immunoisolation and islet macro-encapsulation are major foci of the translational research programme and Oxford has been chosen as one of two European centres to conduct 'first in man' trials of a novel macroencapsulation device. This talk will outline the current status of islet transplantation and address some of the ongoing challenges. It will then focus on immunoisolation and pancreaticomimetic bioscaffolds.

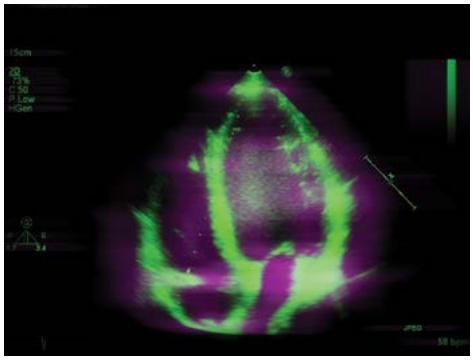
DIABETES RESEARCH WELLNESS FOUNDATION™

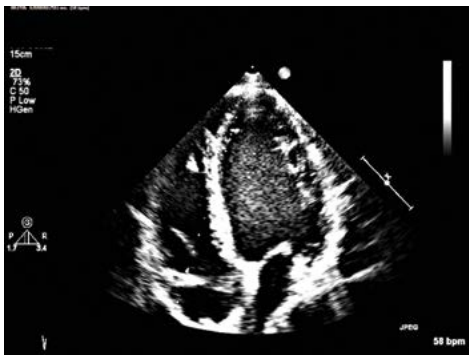
Professor Paul Johnson
Professor of Paediatric Surgery University of Oxford
& Director of the Oxford Islet Transplant Programme
paul.johnson@nds.ox.ac.uk

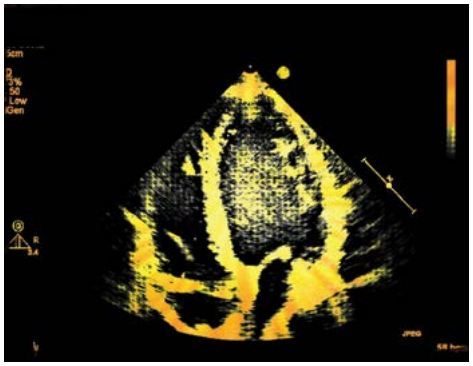
ULTROMICS
- Advanced Ultrasound Analysis Made Simple

By simplifying the way echocardiographers and doctors are able to extract complex information from echocardiograms, we can increase their confidence in image interpretation.









If a doctor wants to look at the structure or function of your heart, the first test they request is an echocardiogram. Thousands are performed, in every hospital, every year.

Ultrasound images are rich in detail but, because of the time taken to extract quantitative data from the images, most of this detail is ignored: diagnosis is instead based on visual assessment, supported by a minimal set of measurements.

Simple ways to extract the complex information contained in ultrasound images are therefore needed.

We have developed such techniques and compared the information we extract against reference datasets of large numbers of people with known diseases.

The measures appear to have the potential to identify a range of heart problems. Placing the techniques into clinical practice should therefore help technicians and doctors reach clinical decisions faster and with greater confidence.

The first, proven application of the system is in stress echocardiography. This is a test, performed widely within the NHS, to decide the significance of chest pain symptoms in different patients. It notoriously requires a Consultant Cardiologist to supervise the test, having developed specific skills in visual interpretation of a series of images collected at rest and after stress.

We have shown that, with a simple data extraction from stored images, the tool works as well as the Consultant Cardiologist: it can even identify some tests that were incorrectly classified by the doctor.

We have also been able to adapt the methods to work on large, stored, echocardiogram archives. As the process is relatively simple, we can now quickly re-evaluate datasets from pharmaceutical clinical trials, academic research groups or clinical departments. Retrospective, re-examination of studies using the complex image analysis metrics captured by the technique, has the potential to provide a 'second look' at a drug or clinical research finding.

Professor Paul Leeson
Head of Cardiovascular Medicine,
University of Oxford
paul.leeson@cardiov.ox.ac.uk

Dr Ross Upton
Research Fellow, Cardiovascular Medicine,
University of Oxford
ross.upton@cardiov.ox.ac.uk

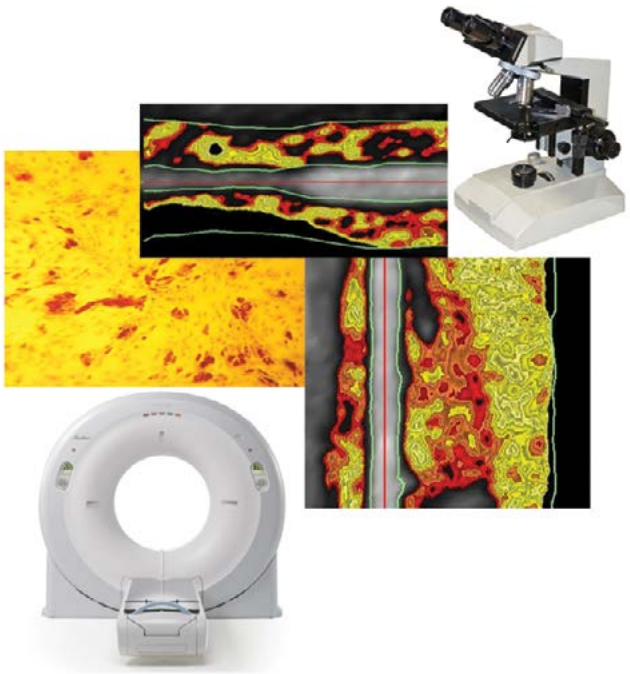
Inflammation Quantification for Cardiovascular Disease Risk Characterisation

An unconventional method uses common computerised tomography to detect vascular inflammation by tracking changes in the perivascular fat.

Coronary artery disease (CAD) is the most frequent cause of death in industrialised nations and it is responsible for billions of pounds of healthcare spending annually: in the EU alone, £169 billion is spent every year dealing with CAD.

The first sign of the disease in roughly 50% of men and 64% of women is a heart attack or death. There is therefore significant value in identifying apparently healthy individuals with 'at-risk' pathology.

Following our landmark discovery that inflammation in the coronary artery (the major driver of CAD development and subsequent heart attacks) drives changes in the surrounding fat, we have developed a non-invasive method for quantifying inflammation in the coronary artery.



The method uses coronary computerised tomography (CT) to estimate the changes in the size of fat cells around the arterial wall.

These changes are expressed as a single index, (the 'Fat Attenuation Index, (FAI), which provides an estimate of site-specific coronary inflammation. Non-invasive detection of vascular inflammation is the 'holy grail' of cardiovascular medicine, as it will significantly affect clinical practice by allowing early cardiovascular risk stratification of the population and deployment of therapeutic strategies to prevent CAD and heart attacks.

Currently protected by a patent application, our method offers major advantages over existing approaches for the diagnosis of vascular inflammation.

Following very positive commercial feedback, a multidisciplinary team funded by the UCSF scheme and led by Professor Antoniades, Professor Channon (both at the Division of Cardiovascular Medicine, Radcliffe Department of Medicine) and Professor Noble (Oxford Institute of Biomedical Engineering) is currently working on developing a stand-alone, automated and user-friendly software.

This will increase the commercial value and attractiveness of the method and allow further validation in large-scale clinical studies. Overall, we believe that the current method has the potential to deliver both health and wealth and revolutionise the ever-expanding market of non-invasive cardiovascular imaging.

Professor Charalambos Antoniades
Associate Professor of Cardiovascular Medicine, RDM
University of Oxford
charalambos.antoniades@cardiov.ox.ac.uk

Dr Evangelos Oikonomou
University of Oxford
evangelos.oikonomou@cardiov.ox.ac.uk

System for Electronic Notification and Documentation (SEND)

Using in-house IT resources alongside human factors, engineering, and clinical expertise from the University of Oxford, the Oxford University Hospitals Foundation Trust (OUH) has developed bespoke 'early warning' software that integrates with the electronic patient record.

Recognising the limitations of a paper-based approach to routine vital signs recording, OUH determined that an electronic solution could further improve patient safety. The team, which includes members from both the OUH Trust and the University of Oxford, has designed an electronic early warning system to help clinical staff make the best decisions for their patients.

Patient notes could previously only be reviewed in one location. SEND now allows multi-disciplinary teams to access the information they need from different places within the Trust.

This avoids medics noting readings on a piece of paper to transcribe to charts later, thus avoiding transcription errors. Any errors on the electronic record can be corrected immediately.

SEND also automatically calculates the 'trigger' score for each patient, and offers clinical decision support through links to hospital escalation protocols, and real-time audits that facilitate clinical governance processes.

The easy-to-use interface uses human factors expertise that fits the task to the human, so that systems flow intuitively. The tablet expects inputs in the same order that staff work, saving around three minutes per observations set. Staff are able to use this extra time to complete other patient care tasks.

The team is now looking to take the principles of SEND further. HAVEN, a new research project funded by the Department of Health and Wellcome Trust Health Innovation Challenge Fund, will test the process of issuing alerts using algorithms that monitor not just vital signs but blood tests results, demographic information and medication.

Dr Peter Watkinson
Intensive Care Consultant, NDCN,
University of Oxford
peter.watkinson@ndcn.ox.ac.uk

SEND team, including project leader Dr Peter Watkinson at centre, back row.

Novel Small Molecules to Treat Familial High Cholesterol Levels

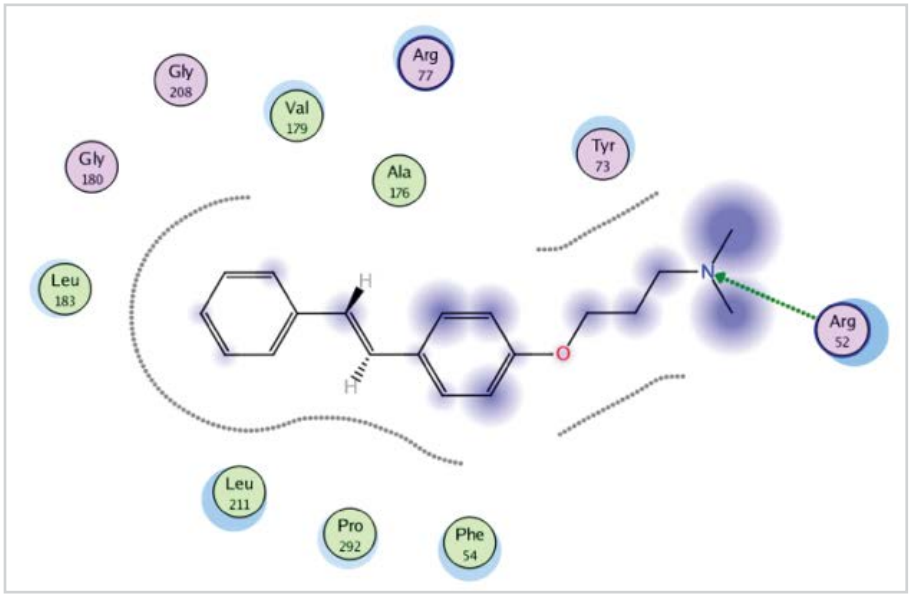
Novel small molecules that inhibit the formation of cholesterol might help lower 'bad' cholesterol in patients who otherwise have difficulty in reducing their cholesterol levels sufficiently.

High cholesterol blood levels (hypercholesterolaemia) are one of the leading factors for the development of cardiovascular disease.

While using a statin to lower low density lipoprotein (LDL)-cholesterol can reduce the risk of a cardiovascular event by ~30%, some patient populations are unable to sufficiently lower their LDL-cholesterol.

This is especially true for patients with familial hypercholesterolaemia, whose high levels of LDL-cholesterol are the result of a genetic disorder.

Lowering LDL-cholesterol in these patients may require the production of more Low-Density Lipoprotein Receptors (LDLRs), on top of what maximal dose statins are capable of. LDLRs are cell-surface receptors which recognise and help in the removal of LDL-cholesterol.



In silico modelling of Compound 15a binding in the active site of the enzyme Squalene Synthase

We have used a compound screen to identify a novel series of small molecules which can upregulate LDLRs in mouse and human liver cell lines, even at nano-molar potencies (EC50: 39nM). Structure-activity relationship studies carried out on the lead compound (Compound 15a) lead to the identification of Compound 40, which has improved potency (EC50: 28nM) and pharmacokinetic profile.

Compound 40 and 15a were found to inhibit squalene synthase, the first committed step in the formation of cholesterol in the body. When combined with statins in a test-tube, these squalene synthase inhibitors increase LDLR expression more than either class of drug alone can achieve.

These small molecules could therefore be useful in treating patients that require further lipid lowering to reach a desired cholesterol goal.

Professor Richard Wade Martins
Head of Molecular Neurodegeneration Lab & OPDC Lead
University of Oxford
richard.wade-martins@dpag.ox.ac.uk

Alastair Kerr
DPhil Student
Molecular Neurodegeneration Lab,
University of Oxford
alastair.kerr@stx.ox.ac.uk