FAST HEALTHCARE NETWORKS PLUS

Final Report

MARCH 2021

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ANNUAL REPORT MARCH 2021

Executive Summary

The effective development and deployment of new technology for optimising treatment in healthcare requires a systems-based engineering approach. This EPSRC NetworksPlus has brought together engineers and physical scientists with clinicians to develop accessible roadmaps that identify where collaborative research could lead to transformative outcomes and seed new specific interdisciplinary collaborations to initiate these.

Technology is becoming an ever more important part of effective prevention and treatment in healthcare, whether that is through the development of new diagnostic techniques, better use of data for risk stratification or new devices for treatment and monitoring. When this Network was set up in 2016, it was against a backdrop of a predicted significant rise in the number of people with long-term health conditions in the UK, challenges around integrating diagnosis, treatment and support across hospital and community-based healthcare, and a rapidly rising cost of delivery. The experience of the COVID-19 pandemic has only reinforced this; we need to diagnose early and deliver effective and timely treatment either at home or in hospital. This requires rapid deployment of new technology with a joined-up approach across the healthcare system.

Systems-based engineering takes as its premise that effective development of new technology requires an understanding of the complete system in which it is to be deployed. In this NetworksPlus, we have taken this approach to investigate where clinically focussed engineering and physical sciences

(EPS) research could make a significant impact in improving the effectiveness of medical interventions whilst also reducing cost and enhancing patient experience.

> *"We want to make you aware of how you could continue to benefit from the work that has been carried out.*

We have produced detailed reports in three contrasting clinical areas: cardiovascular disease, digital health for remote monitoring and self-management and early detection of cancer. For each, we have identified specific opportunities for clinically driven EPS research. What has been notable is the emergence of some cross-cutting themes, such as the need for obtaining better longitudinal data on wellbeing and analysing this in an effective way which leads to timely interventions. We have built a connected community of over 250 people across the UK with an interest in our approach to conducting healthcare technology research and have seed funded new collaborations between EPS researchers and clinicians.

As our NetworksPlus draws to a close, we want to make you aware of how you could continue to benefit from the work that has been carried out by

1. discovering new areas for collaborative research in healthcare technology which align with your interests
2. identifying researchers who you might be able to collaborate with
3. seeing where opportunities exist for policy-makers with an interest in healthcare

You can find out about the amazing research that has been carried out in this Network of researchers over the last five years and I hope that this will inspire new research in the years to come.

Professor Andrew Flewitt
University of Cambridge

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Introduction

Find out about the motivation behind this NetworksPlus, the people involved and the philosophy underpinning the approach that we have taken.

INTRODUCTION

Motivation for the Network

A survey of healthcare professionals in Europe has shown that patients are demanding higher standards of care, more information about their treatment, more involvement in treatment decisions and access to the latest treatments. Set alongside this is the inexorable rise in the cost of healthcare. In the EU, public expenditure on healthcare is predicted to rise between 2000 and 2030 from 8% of GDP to over 14%. There is therefore an inherent tension between meeting rising patient expectations without raising expenditure.

This tension was clearly articulated in the publication by **NHS England** entitled **'The NHS Belongs to the People: A Call to Action'**, which was also signed by the heads of other major public health bodies (including the **Care Quality Commission, the Local Government Association, the National Institute for Health and Care Excellence** and **Public Health England**) in the 65th anniversary year of the NHS. It articulated the aspiration to deliver the very highest standards of patient care against the reality that the projected total cost of running **NHS England** would rise from £95Bn in 2013 to £137Bn in 2020, whilst the resource would only rise to £108Bn in the same period. Change was and continues to be essential. The **FAST Healthcare NetworksPlus** in the field of optimising treatment was a practical response to this **Call to Action**.

There are a number of factors that lead to rising costs, and the Call to Action highlighted three:

1. an ageing population
2. out-dated management of long-term conditions
3. poorly joined-up care between adult social care, community services and hospitals

It is this final factor that we aimed to address in **FAST Healthcare**.

The NHS delivers healthcare to patients across a number of different levels depending on need, from Primary Care dispensed by non-specialist medics at surgeries and community health centres through to specialised treatment at local or regional hospitals at the Tertiary or Quaternary Care levels. However, as a patient moves 'upwards' through the care levels, the length of time for treatment tends to increase, as does cost.

Therefore, it is important that patients are treated at the lowest care level that is effective for as much of the time as possible, as this will reduce the cost.

There is a benefit to patient experience too. Moving treatment back to a community-delivered level increases patient involvement. This means that they are better informed as they have to take greater responsibility for themselves, which was one of the key demands. Therefore, reducing the cost of healthcare does not mean a poorer service. Quite the reverse can be true and the potential to both improve the experience of patients and reduce the cost could be made possible by developing a new methodology for the clinical diagnostics and treatment process.

This can be realised by taking a systems-based engineering approach to designing such a new methodology which is then enabled by appropriate technological and medical advances and permits a holistic approach to care delivered in a joined-up fashion across the care levels. In this Report, we set out how interdisciplinary research bringing together engineers and physical scientists with clinicians can make specific differences in diverse clinical areas and give examples through projects that the NetworksPlus has funded of how this can be achieved.

INTRODUCTION

Meet the Lead Investigator Team

Professor Ann Blandford

Ann Blandford is Professor of Human–Computer Interaction at University College London and formerly Deputy Director (Digital) of the UCL **Institute of Healthcare Engineering**. She is an expert on human factors for health technologies. Her first degree is in Mathematics and her PhD is in Artificial Intelligence. She was a post-doctoral researcher at the Applied Psychology Unit in Cambridge then a Lecturer, rising to Professor, at Middlesex University (Computer Science). She moved to UCL as Senior Lecturer in 2002, and was (re-)promoted to Professor in 2005. She was Director of UCL Interaction Centre 2004-2011, and of the UCL Institute of Digital Health 2015-2019. She is the Human Factors lead on multiple research projects on health technology design and deployment. The question that motivates her research is: how can we design and deploy health technologies that really work for people, rather than technologies that force us into undesirable modes of working, cause stress, or are rejected as not being fit for purpose? She has published widely on the design and use of interactive health technologies, and on how technology can be designed to better support people's needs and values.

Professor Lisa Hall

Lisa Hall is a Professor of Analytical Biotechnology and Deputy Head of **Department of Chemical Engineering and Biotechnology** at Cambridge University. Her research links transduction technologies (electrochemistry, optics, ultrasound) with synthetic biology and nanomaterials in the context of sensors and diagnostic systems. She has extensive leadership experience in fundamental research and the translation of research.

Professor Andrew Flewitt

Andrew Flewitt is Professor of Electronic Engineering at the **Engineering Department**, Cambridge University, and is currently Head of the **Electrical Engineering Division**. His research spans both large area electronics and microelectromechanical systems with a particular interest in how electronics is deployed in the real world. It is in this regard that he has gained an interest in the application of electronics in healthcare. His research has included the development of small acoustic resonator-based sensors which can be used to detect specific biomarkers in blood, such as prostate-specific antigens. His latest work is looking at using these sensors for rapid and highly specific detection of COVID antibodies in small blood samples.

Professor David Clifton

David Clifton is an Associate Professor in the **Department of Engineering Science** of the University of Oxford, and a Governing Body fellow of **Balliol College**, Oxford. He is a Research Fellow of the Royal Academy of Engineering.

A graduate of Oxford's Department of Engineering Science, David trained in information engineering and was supervised by Professor Lionel Tarassenko. He spent four years as a post-doctoral researcher in biomedical engineering at Oxford before his appointment to the faculty, at which point he started the CHI Lab.

His research focuses on the development of "big data" machine learning for tracking the health of complex systems. His **previous research** resulted in patented systems for jet-engine health monitoring, used with the engines of the Airbus A380, the Boeing 787 "Dreamliner", and the Eurofighter Typhoon. Since 2008, he has translated his work into the biomedical context for healthcare applications. He has worked on Visensia, the world's first FDA-approved multivariate patient monitoring system, and the SEND system, which is now used to monitor 20,000 patients each month in the NHS. His research has been commercialised via university spin-out companies OBS Medical, Oxehealth, and Medyc, in addition to collaboration with multinational industrial bodies.

Professor Clifton teaches the undergraduate mathematics syllabus and biomedical syllabus in Engineering Science, runs the graduate course in machine learning at the Oxford **Centre for Doctoral Training in Healthcare Innovation**, and teaches engineering policy at the **Blavatnik School of Government**, Oxford. He is a founding Associate Editor of the IEEE Journal of Biomedical & Healthcare Informatics (JBHI), and is the Associate Director of the Oxford Centre for Affordable Healthcare (OxCAHT).

In 2016, Professor Clifton was awarded a Grand Challenge award from the EPSRC, which is a personal award that provides long-term strategic support for nine "future leaders in healthcare".

Professor Lionel Tarassenko

Professor Lionel Tarassenko CBE FREng FMedSci is a world-leading expert in the application of signal processing and machine learning to healthcare, with a strong track record in translation to clinical medicine. His work has had a major impact on the identification of deterioration in acute care and on the management of chronic disease.

Professor Tarassenko received the BA in Engineering Science in 1978 and the DPhil in medical electronics in 1985, both from the University of Oxford. After a period in industry, he was appointed University Lecturer and Tutorial Fellow in Oxford (St Hugh's College) in 1988. He was elected to the Chair of Electrical Engineering and to a Professorial Fellowship at St John's College, also at the **University of Oxford** in 1997. He was the driving force behind the creation of the **Institute of Biomedical Engineering (IBME)** which he directed from its opening in April 2008 to October 2012. Under his leadership, the IBME grew from 110 to 220 academic researchers, and it was awarded a Queen's Anniversary Prize for Higher Education in 2015 for "new collaborations between engineering and medicine delivering benefit to patients".

Professor Tarassenko was elected to a Fellowship of the Royal Academy of Engineering in 2000, and to a Fellowship of the Academy of Medical Sciences in 2013. He is the author of 250 journal papers, 220 conference papers, 3 books and 32 granted patents. He was the Head of the Department of Engineering Science (Dean of Engineering) from 2014 to 2019, and is now the Founding President of Reuben College, the University of Oxford's newest college. He has founded four University spin-out companies and is the R&D Director of Sensyne Health, an AIM-listed company. He was made a CBE for services to engineering in the 2012 New Year's Honours List.

INTRODUCTION

Advisory Board: Membership

(September 2017)

Chair

Prof. Duncan Young
Nuffield Department of Clinical Neurosciences, Oxford University

Academics

Dr Niels Peek
MRC Health eResearch Centre, Manchester University

Prof. Stephen Morgan
University of Nottingham

Prof. John King
Nottingham University

Prof. Mary Dixon-Woods
Department of Public Health and Primary Care, University of Cambridge

NHS Clinicians

Dr David Kwo
UCL Hospital

Prof. Hugh Montgomery
Institute for Human Health and Performance, UCL

Dr Shankar Sridharan
Great Ormond Street Hospital

EPSRC

Kate Reading
EPSRC

Katherine Freeman

NHS Management

Lawrence Ashelford
Formerly Addenbrookes NHS Trust

Industry

Dr Luis Garcia-Gancedo
GSK

Prof. Ian Gilmore
National Physical Laboratory

Shaun O'Hanlon
EMIS Group

Charity

Prof. Richard Gilbertson
Cancer Research UK Cambridge Centre

Users

Debby Lennard

Kevin Decoteau

INTRODUCTION

Approach

The approach that we have taken in the FAST Healthcare NetworksPlus is to apply systems-based engineering to understanding the appropriate engineering and physical sciences (EPS) research that could enable the technological and medical advances which permit a holistic approach to healthcare delivered in a joined-up fashion across the care levels.

Systems-based engineering applied to healthcare is built on four pillars:

1.
Systems thinking which considers the entire healthcare process from clinician to patient

2.
Design thinking which identifies real needs as opposed to perceived problems

3.
Risk thinking which identifies critical risk points and mitigation strategies

4.
People thinking which ensures that a system is designed around the people who will use it and where they will use it

You can read more about systems-based engineering applied to healthcare in **Engineering better care: a systems approach to health and care design and continuous improvement**, (Royal Academy of Engineering, London, 2017)[1].

To achieve this, we have run a number of Workshops in different clinical areas. In each case, the Workshop was broadly divided into three sections: the first considered the clinical scenario, the second the relation of EPS research to the clinical scenario and the third the barriers and opportunities that existed between the two. The output was a three-plane diagram which attempted to show in the graphical form how fundamental EPS research links to specific real clinical needs and the intended outcomes from such a research programme. You can find a summary of each of these Workshops in this Final Report as well as a link to a more detailed Workshop Report.

The Workshop Reports were then used as a basis for calls for Discipline Bridging Initiator Projects. These were aimed to pump prime research which addressed the outcome of the Workshops. A key feature of these was that they had to enable a new collaboration and have a clear route to future development if the project was successful as anticipated. You can also read about these projects in this Final Report and find out how to contact the research teams involved if you would like to engage with them in future development.

[1] https://www.raeng.org.uk/publications/reports/engineering-better-care

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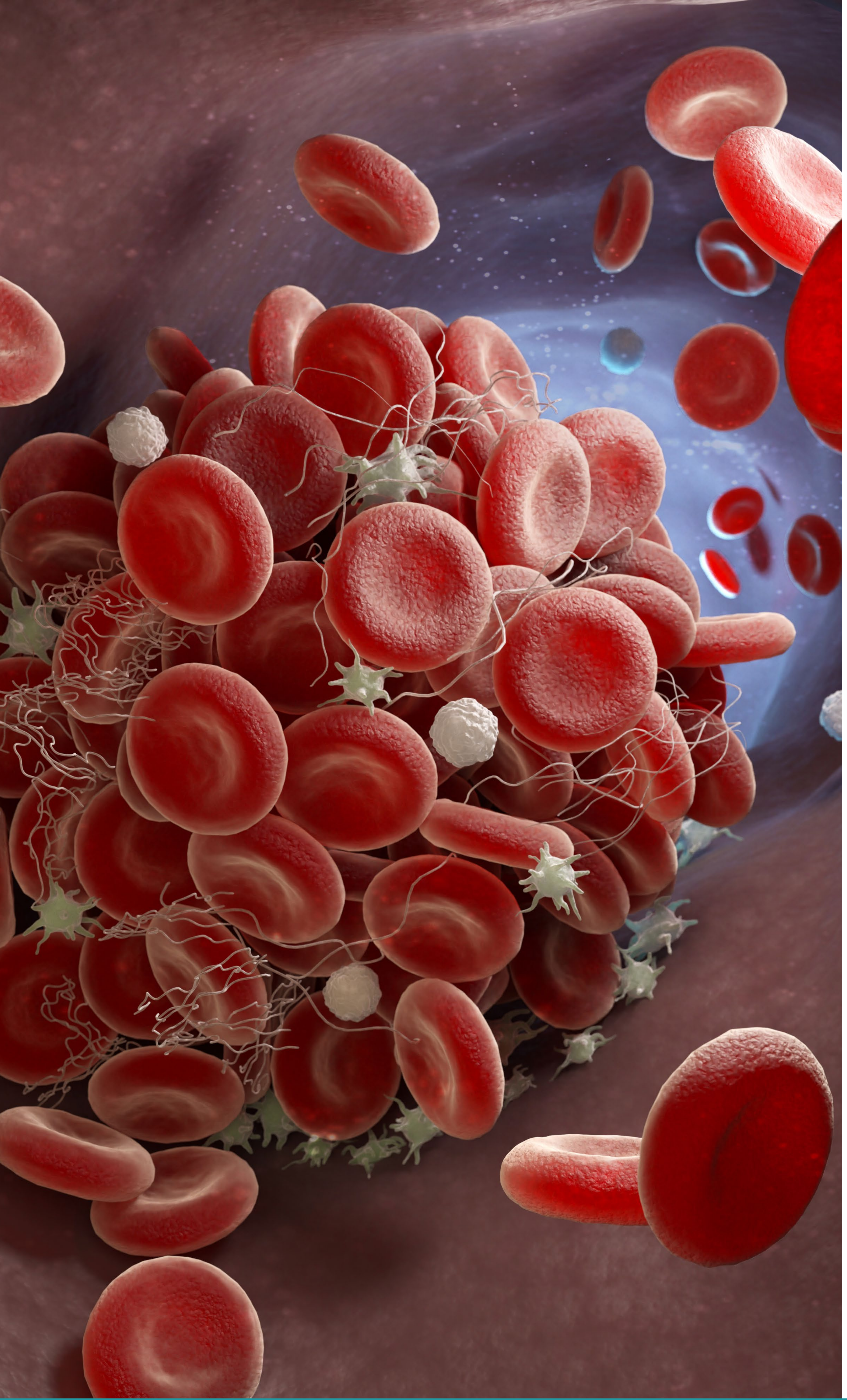
Workshops

We have run five main Workshops which have each looked at a different clinical scenario. You can find out about the top-level outputs from each of these as well as the overarching themes that have emerged from this research.



SUMMARY OF THE WORKSHOPS

Fast Assessment and Treatment of Cardiovascular Disease

Cardiovascular disease is the most common cause of death globally and places particular demands on the National Health Service due to the diverse range of treatment pathways and the chronic nature of the condition. There is a clinical need to provide safe, accurate, rapid and seamless care across the healthcare system in a way that is efficient and cost-effective through the optimised use of staff.

A clinically focussed engineering and physical sciences research agenda could address this through fewer referrals between care providers and a reduced number of hospital re-admissions following discharge, better long-term treatment which is more personalised, and fast triage of individuals with cardiovascular disease into one of the seven treatment pathways.

WORKSHOP: FAST ASSESSMENT AND TREATMENT OF CARDIOVASCULAR DISEASE

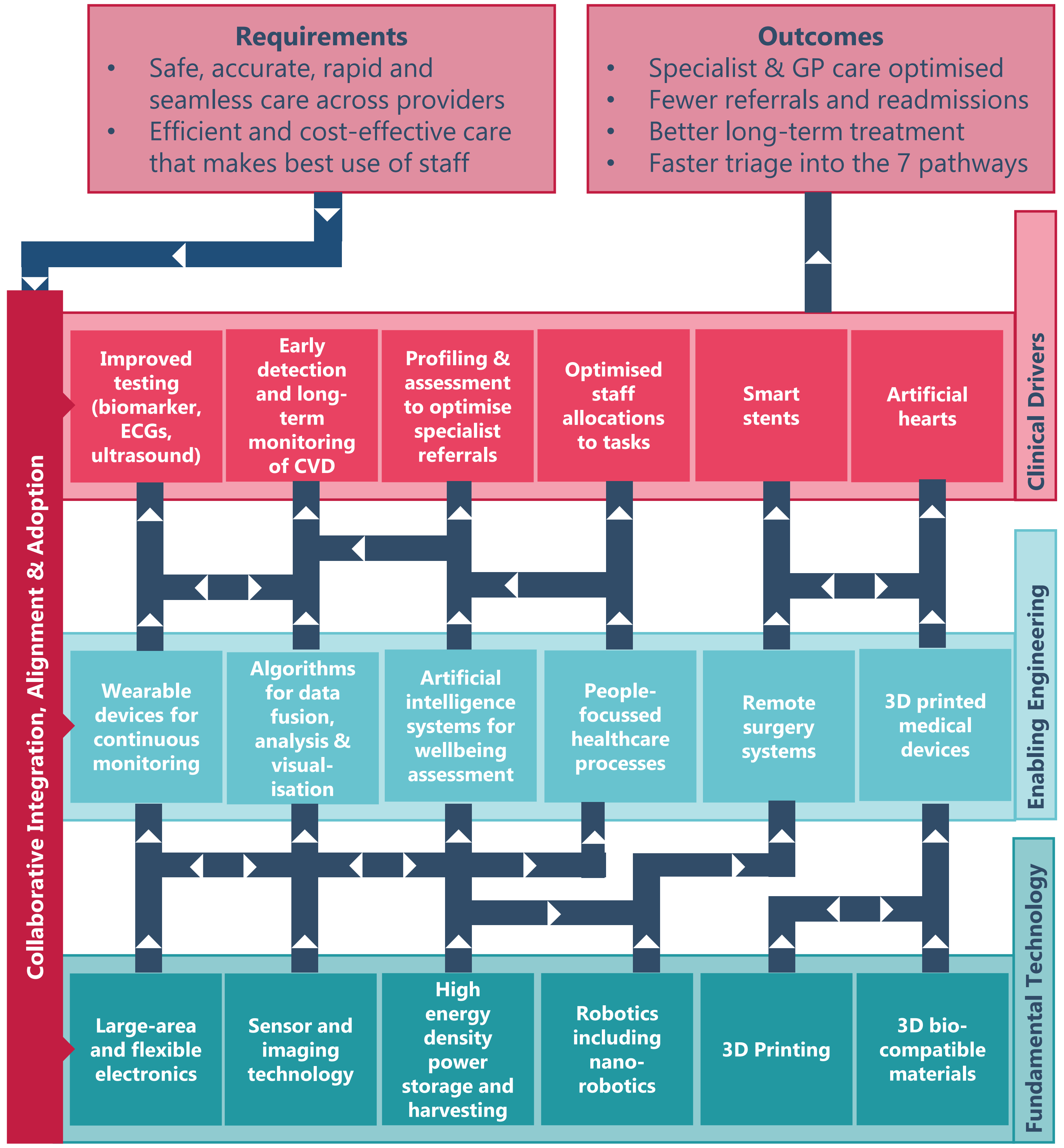
A key pressure on the National Health Service (NHS) is how long-term conditions, like diabetes and cardiovascular disease, are treated. Around one third of the difference in life expectancy between the most affluent and deprived areas in the UK is believed to be attributable to CVD.

If we are looking to make a significant impact on the assessment and treatment of CVD through engineering and physical sciences (EPS) research, then a good starting point is to bear in mind that around 85% of all CVD cases fall into four groups:

1. **Coronary heart disease** (including heart attacks and angina)
2. **Heart failure** (which can be because of a heart attack, but may have other origins resulting from inefficiencies in the circulatory system)
3. **Rhythm disorders**
4. **Valve disorders** (including narrow, leaking or infected valves in the heart)

Acute symptoms which commonly cause people to present in the health system for the first time include chest pain as a result of a heart attack, shortness of breath due to heart failure (often associated with the left ventricle), and rhythm disorders leading to fainting, palpitations or cardiac arrest. Chronic symptoms are often very similar to acute symptoms but can develop incrementally with time, and it often requires a sudden step-change in how a person feels to prompt them to seek medical advice. In practice, therefore, it can be very challenging to make an initial assessment as to whether a particular combination of symptoms is due to a cardiac condition, or something else which has a similar set of symptoms. There may also be some other underlying disease which has led to an individual's cardiac condition. Severe symptoms may also mean that assessment has to be made very rapidly. EPS research should aim to assist with the safe, accurate, rapid and seamless assessment and treatment of CVD across the primary, secondary and tertiary heath sectors, and efficient and cost-effective care of people with CVD which makes the best use of staff, recognising that they are the single most expensive asset in the health system.

This leads to two broad research fields. One is in the area of flexible and large-area electronics with specific sensor and imaging technologies and power systems. This enables wearable devices for continuous monitoring, which can be combined with algorithms for data fusion and interpretation, including AI to address the clinical drivers of needing improved testing, early detection and long-term monitoring and better decision making as to when care is delivered by generalists in the primary sector or specialists through the secondary and tertiary sectors. When coupled with people-focussed systems-based engineering of healthcare processes, this can allow optimisation of the use of staff for specific tasks. The second area sees two strands of technology and engineering linking together to enable smart stents and artificial hearts. One is in robotics and high energy density power storage systems enabling remote surgery. The other is in 3D printing techniques and the development of 3D bio-compatible materials to enable 3D-printed medical devices.



WORKSHOP: FAST ASSESSMENT AND TREATMENT OF CARDIOVASCULAR DISEASE

Such a research agenda would lead to:

- optimised use of specialist and generalist-led CVD assessment and treatment;
- fewer referrals between care providers and a reduced number of hospital re-admissions following discharge;
- better long-term treatment which is more personalised; and
- fast triage of individuals with CVD into one of the seven treatment pathways.

It is based on developing six fundamental technology areas:

- **Large-area and flexible electronics** for the development of devices that can be incorporated into clothing or other products, such as patches that can be applied directly to the skin.
- **Sensors** for biomarkers associated with CVD (such as troponin), sensors for detecting ECG signals and potentially even ultrasound imagers that could be used more widely by non-specialists.
- **High density power storage devices coupled with harvesting** to increase the time between charging events or to reduce the size of the battery packs for continuous monitoring systems and for applications where devices are embedded inside the body meaning that charging may be impractical. An extreme example of this is an artificial heart, which would need a significant, highly reliable and long-term power source.
- **Robotics** for remote surgery which would allow a person to be treated by a specialist without having to be physically close to them and, in the longer term, nanorobotics to allow procedures to be carried out by a small robot implanted inside the body which could, again, be controlled remotely.
- **3D printing** for fabricating complex structures out of biocompatible and even biological materials that are tailored to an individual, such as a replacement heart value which is designed to fit an individual.
- **3D biocompatible materials** which could be used as the basis for a smart stent, or in the longer term even an artificial heart. There is existing work on a diversity of 3D scaffold materials, but these need to be manufacturable in the structures required clinically.

Read the full Report of the Workshop on Cardiovascular Disease[2] to find out more about how research between engineers, physical scientists and clinicians could lead to a real advancement in cardiovascular disease treatment.

[2] http://www.fast-healthcare.org.uk/cardiovascular-disease-workshop/

SUMMARY OF THE WORKSHOPS

Digital Health

Increasingly, healthcare is being shifted from hospital to home. This has benefits, including more comfortable care environments for patients as well as reduced costs for care providers. This brings with it many opportunities to re-design care systems to exploit innovative technologies and reconfigure care practices to optimise care at home. This will demand better systems for remote monitoring and intervention, and also technologies that are usable by patients and lay carers as well as professionals. Addressing these demands was the challenge discussed in the FAST Workshop on Digital Health for Remote Monitoring and Self-Management. The outcome from the workshop was written up collaboratively between FAST and **PHG Foundation**.

WORKSHOP: DIGITAL HEALTH

Healthcare delivery is changing rapidly. This is partly in response to the increased age of the population and rises in the number of people with long-term chronic conditions such as diabetes or heart disease and partly also in response to increased demands and recognised benefits for patients in terms of autonomy and their ability to self-manage their care. The monitoring and careful long-term management of chronic diseases is essential for extended life expectancy and quality of life. Age related decline is associated with increased frailty, increased risk of developing chronic illnesses, and increased likelihood of rehabilitation needs following surgery or a stroke. All these factors complicate the way individuals can be treated and monitored. Conversely, technologies that are designed for use by individuals and families in their own homes need to be safe, reliable and easy to use.

This is a multidisciplinary challenge, requiring collaboration between specialists with a diversity of backgrounds for success. This workshop addressed three focus areas.

1.

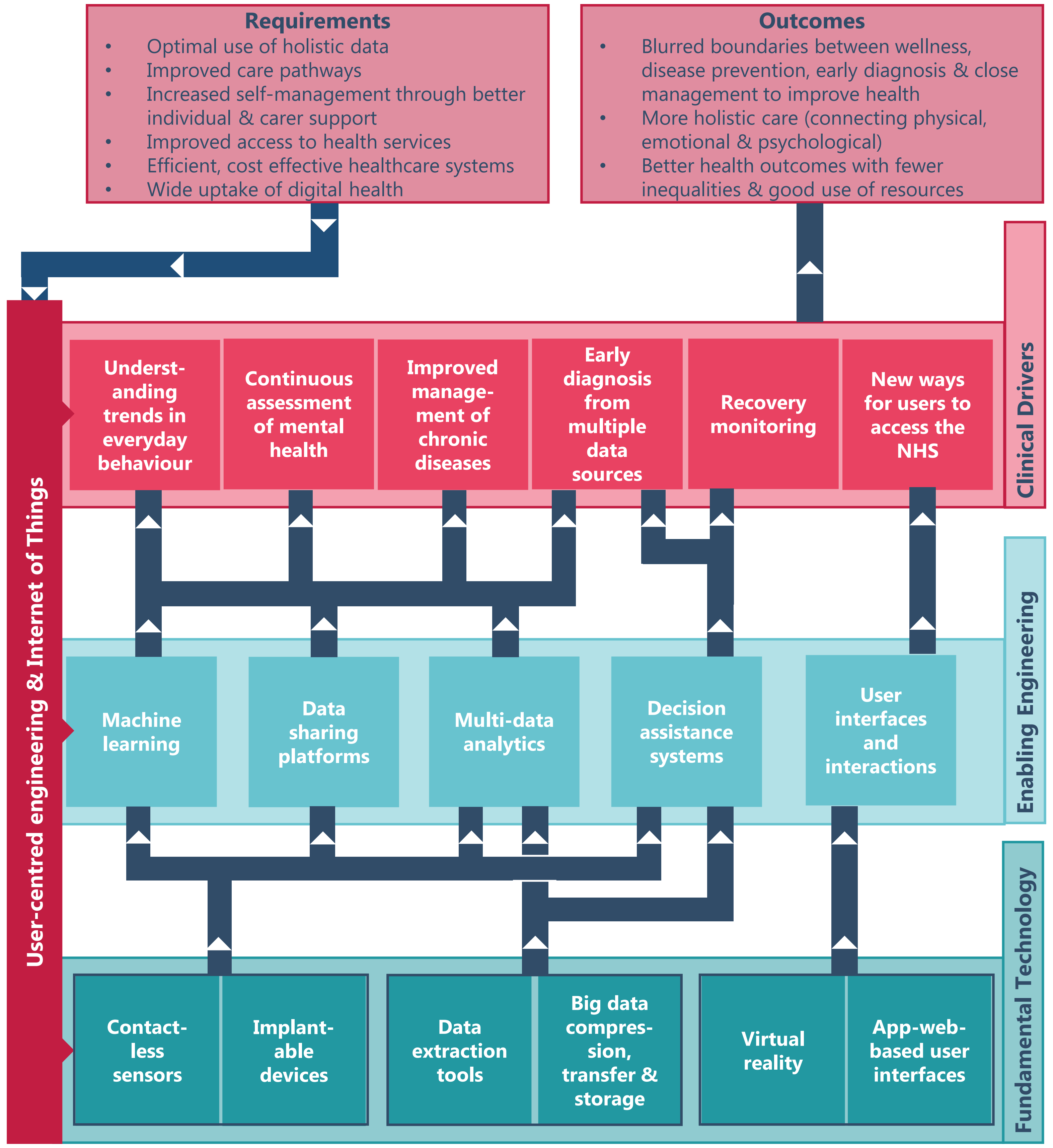
Experiences of developing and deploying digital health management solutions for remote monitoring and self-management.

Various scenarios were considered, including the management of long-term conditions such as diabetes and care of the elderly, who may have multiple co-morbidities, and also the management of acute medicine episodes such as a sexually transmitted infection. For diabetes, there is an established practice of self-monitoring of blood glucose levels (since the 1970s), but digital tools are making new practices possible. These include sharing data with care providers, to enable more timely and proportionate care, and also addressing cognitive and emotional aspects of self-care alongside physiological aspects. Similar trends can be found in the management of many other long-term conditions. For some sexually transmitted infections, if diagnosis and treatment are uncomplicated, self-testing kits have been available for some time and it is, at least in principle, possible to prescribe and deliver antibiotics without the individual needing to attend a clinic in person. As long as safety measures are in place to ensure that those who need clinical consultations receive them, remote management can reduce the barriers to and costs of care for many individuals.

2.

Challenges to uptake.

Challenges to uptake that were identified include themes around patient acceptance, data management, the ill-defined structure of the development process, and barriers to deployment. Within the theme of patient acceptance, it was recognised that there is a digital divide, with the people with the greatest need for self-management often being those with more limited access to digital tools and lower health literacy. Digital tools (whether worn



3 http://www.fast-healthcare.org.uk/digital-health-workshop/

WORKSHOP: DIGITAL HEALTH

or home-based) are often regarded as intrusive, and many people value direct contact with health professionals. Data management presents challenges relating to data privacy, security and integration across multiple data sources and types. Data also needs to be converted into actionable information to be useful. In terms of tool development, there are typically challenges around funding developments that may take many years to deliver any return on investment as the financial models for care delivery for self-management and remote care are currently immature. There are also requirements to comply with national and international medical device regulations, with their requirements for risk assessment, rigorous testing and documentation of processes.

3.

Future opportunities.

Various benefits of remote monitoring and self-management were identified. Benefits to the patient (or lay carer) include patient empowerment; convenience; reduced anxiety; better outcomes and quality of live; and preventive benefits. Benefits to healthcare providers include the ability to make more informed clinical decisions; improved clinical outcomes; a reduction in unnecessary appointments; greater efficiency; and preventive benefits.
Two technologies were identified as being foundational to deliver these benefits: sensor technologies (for seamless data gathering) and tools for data management and analytics. But it was emphasised that for technologies to deliver on the anticipated benefits they need to be usable, effective, safe and cost-effective.

Read the full **Report on the Workshop on Digital Health**[3] to find out more about how research between engineers, physical scientists and clinicians could lead to real advances in digital health technologies for remote monitoring and self-management.

SUMMARY OF THE WORKSHOPS

Fast Assessment and Treatment of Asthma

5.4 million people have asthma in the UK, which means asthma affects one in every 11 people and one in 5 households. Every 10 seconds someone is having a potentially life-threatening asthma attack.

Imagine being paralysed by fear as you struggle to breathe, unable to speak, unable to ask for help. That's what an asthma attack feels like. 3 people a day die from an asthma attack. Tragically, two-thirds of those asthma deaths could be prevented with better care but two-thirds of people with asthma are still not receiving this. The cost burden to the UK is also significant. Asthma costs £1.1bn in the UK alone and it has a significant impact on productivity, with ~6.9 million school and working days lost each year due to asthma.

It is becoming increasingly clear that asthma is not a single condition, but a collection of symptoms caused by different mechanisms, but little is understood about the different subtypes of asthma.

WORKSHOP: FAST ASSESSMENT AND TREATMENT OF ASTHMA

This workshop was born out of an EPSRC-organised Healthcare Technologies Hive Meeting held in November 2017. Run in collaboration with AsthmaUK, it focussed on four key asthma innovation challenge areas and the development of collaborative research proposals to address these areas of unmet need and improve the quality of life of people living with asthma. The scale, complexity and episodic nature of the asthma means that it is highly suited to a systems-engineered approach.

The four challenge areas were:

1.

Danger in the home.

Some aspects of the home are known to trigger asthma including dust, dust mites, damp and mould. For children, poor quality housing is a key driver of the development of asthma, along with socioeconomic status. How can we protect children from these environmental dangers in the home?

2.

Getting kids active.

How can we encourage children with asthma to be more active safely?

3.

Teaching inhaler technique.

With low cost digital technology how can we tell whether people with asthma have taken their inhaler correctly and offer tailored advice?

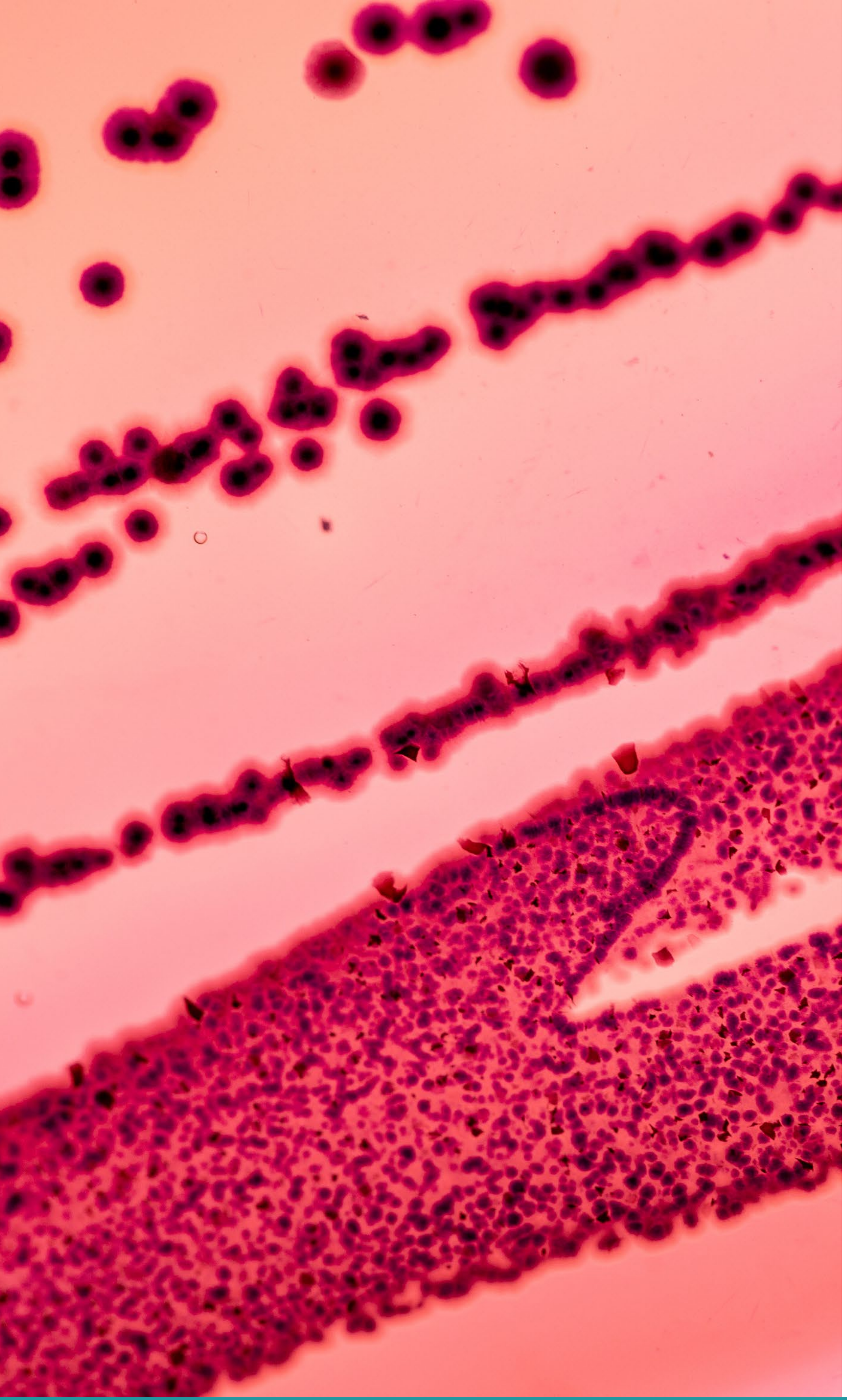
4.

Scaling personalised asthma health advice.

How can we automate Asthma UK's personalised and empathic nurse advice channels to deliver 24/7 personalised asthma health advice?

Read about the **Workshop**[4] to find out more about how research between engineers, physical scientists and clinicians could address these challenges.

[4] http://www.fast-healthcare.org.uk/ercasthma/



SUMMARY OF THE WORKSHOPS

Raman Spectroscopy as a Tool for Clinical Applications

Raman spectroscopy is an optical technique that measures the chemical composition and molecular structure of a sample. Utilisation of the 'molecular fingerprint' of Raman spectra has proven an effective analytical approach in geology, semiconductors, materials and polymer science fields. The application of Raman spectroscopy and microscopy within biology is rapidly increasing and clinical applications include the detection of various cancers, antimicrobial resistance (AMR), neurodegenerative disease, renal disorders and the diagnosis of primary immunodeficiency amongst other areas. This Workshop considered how to advance the clinical application of Raman spectroscopy with a particular emphasis on AMR.

WORKSHOP: RAMAN SPECTROSCOPY AS A TOOL FOR CLINICAL APPLICATIONS

Raman spectroscopy uses a laser to excite the bonds in a sample and the scattered light therefore contains information about the sample. It is an extremely powerful technique as minimal sample preparation is required for a response to be measured in a well-designed system. No 'labelling' of the sample under test is required, and no previous knowledge about the sample is assumed. Therefore, the technique is well-suited to measurements where there is a 'poorly posed problem' being assessed. For example, if there is a concern that a surface is contaminated with some biological molecule, then Raman spectroscopy can test the surface without needing to make any decisions about what type of molecules are being looked for, as would be needed for a specific test. The ability to choose the wavelength of the laser used allows different responses to be measured, which provides significant practical flexibility. It is also known that different biological molecules give very characteristic responses as a function of wavelength and therefore high specificity can be achieved. Furthermore, the technique is non-invasive, fast and a surface can be mapped. Consumables for running a test are also very cheap.

Like many optical systems, the capital cost of a Raman spectrometer is high, although by engineering a system for a specific clinical application, there is room to ensure that this is kept as low as reasonably possible. The sample volume under test is also very small, as it is only a surface that is being probed by the laser beam and the spot size is usually small. This places an upper limit of sensitivity when low concentrations of a biological molecule are being measured. Although biological molecules have a distinctive spectrum, there are few publicly available databases of spectra that can be accessed for interpretation of Raman spectra from a sample. Finally, the high laser power that is required can cause unintentional sample heating, which can be particularly problematic for biological samples.

A consequence of the lack of current databases of spectra is that there is a real opportunity for a good library of clinically relevant Raman spectra to be created. This could be linked with cloud-based artificial intelligence for analysis of data, with the result that the technique could be used for the identification of very many target biomolecules. There are technical opportunities, including the development of surface-enhanced Raman spectroscopy and correlation of Raman data with other analysis techniques and tools such as genomics.

The main challenge is around the time to clinical adoption of Raman spectroscopy. This is a result of the complexity of clinical samples and the need for good calibration and use standards to ensure the quality of data and the ability to effectively use databases of Raman spectra for analysis. In addition, there are significantly cheaper specific tests available for certain targets.

With this in mind, it is possible to consider the short, medium and long term clinical opportunities that Raman spectroscopy might address.

Raman spectroscopy could be quickly applied to a variety of fairly basic, but important, clinical scenarios. One is the detection of antimicrobial-resistant pathogens alongside drug resistance in patient treatment. There is an urgent clinical need for a robust technique for the identification of sepsis, and in particular the ability to differentiate between bacterial and viral forms of sepsis which Raman spectroscopy could address as well as opportunities in more broad disease classification.

To achieve this, there is a need to develop reference materials and calibration techniques for Raman spectroscopy to allow confidence in the quantitative output from instrumentation. There are also no standards currently for how clinical samples should be prepared for analysis, and these are also urgently required if there is to be clinical confidence in the results obtained. Other barriers to adoption include the development of standards for how tests using Raman spectroscopy are actually performed, and the agreement in the community of what quantitative measurement parameters should be used for the different specific biomolecular targets that each clinical scenario is focussed on detecting. There is also the issue of reimbursement. The development of clinical Raman tools ultimately requires industry investment, potentially both in capital cost of equipment and in the running of tests as a service. It is not clear how this could be reimbursed by the NHS.

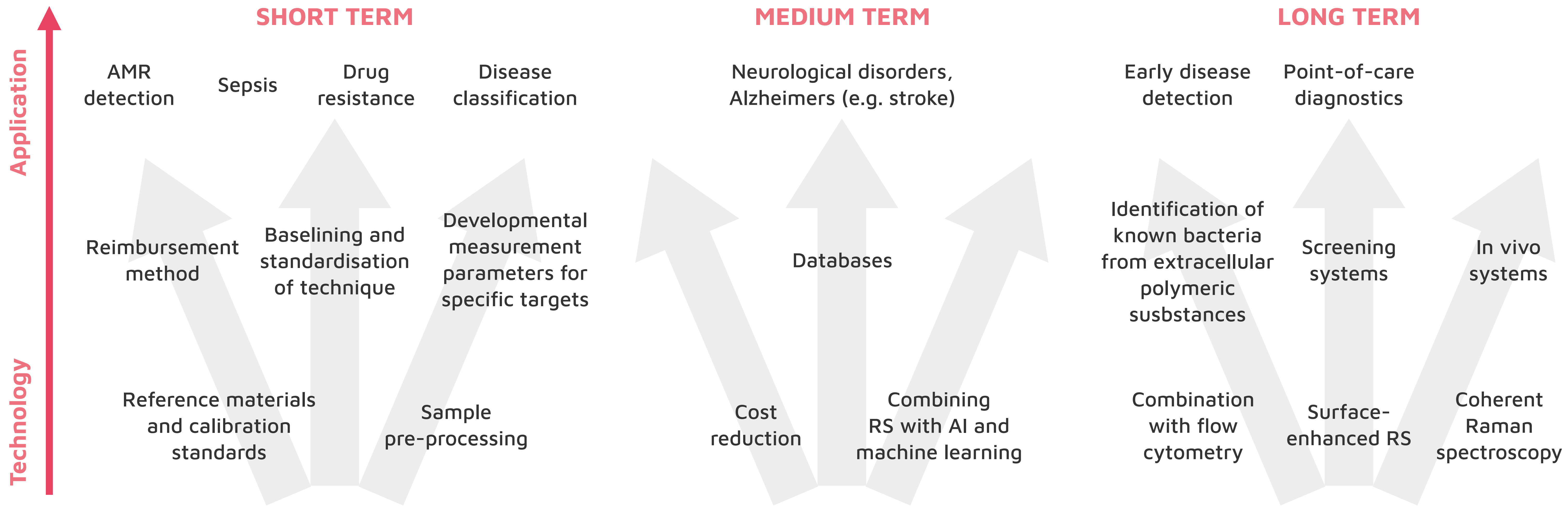
A medium term timescale should allow the development of a tool for detecting neurological disorders, such as Alzheimer's disease (where there are benefits of early detection) and strokes (where diagnosis can be difficult). Key technological developments in this period should focus on reducing the cost of Raman spectroscopy as a clinical tool. This is essential to open up new application areas in the long-term too. The spectra obtained from Raman spectroscopy of biomolecules are complex, and would benefit

WORKSHOP: RAMAN SPECTROSCOPY AS A TOOL FOR CLINICAL APPLICATIONS

from the application of artificial intelligence (AI) and machine learning (ML) to interpretation to allow more complex problems to be addressed. Associated with this is the need for comprehensive databases of Raman spectra of a diversity of biomolecules which could be used either by humans looking to match spectra or by AI and ML systems. It is not clear where ownership of such a database would lie (equipment manufacturers, NHS) or the cost model for accessing such a database.

In the long term, Raman spectroscopy could be applied to the rapidly growing area of point-of-care test (POCT), if the cost structure could be developed to allow this. There are also opportunities in early disease detection, including conditions such as cancer. Early detection is seen as a national priority for the future of the NHS to reduce cost of treatment and improve quality of life in an ageing population. In this time scale, it should be possible to make some significant technological improvements to Raman spectroscopy. This includes combination with flow cytometry (which is an emerging technique in its own right) and the development of both Surface-Enhanced Raman Spectroscopy (SERS) and Coherent Raman Spectroscopy for clinical applications. Early detection of certain diseases could be made more likely if it becomes possible to identify bacteria from extracellular polymeric substances. By this time, Raman spectroscopy could be developed into a tool for screening of certain diseases and In-vivo systems might also be feasible.

Read the full **Report on the Development of Raman Spectroscopy as a Tool for Clinical Applications**[5] to find out more about how research between engineers, physical scientists and clinicians could lead to more rapid and wider clinical deployment of this powerful technique.



[5] http://www.fast-healthcare.org.uk/wp-content/uploads/2019/01/Raman-workshop-report.pdf

SUMMARY OF THE WORKSHOPS

Early Detection of Cancer

Improved early detection and diagnosis could lead to a step change improvement in cancer survival rates as well as less invasive treatment. Technology could play a key role in enabling this, but only if the outcome is both actionable and applicable to the individual patient. Otherwise the result is clinically meaningless or can potentially lead to overdiagnosis or overtreatment. This is the challenge discussed in the FAST Workshop on Early Detection held in collaboration with Cancer Research UK. The outcome from the workshop was written up collaboratively between FAST, Cancer Research UK and PHG Foundation.

CANCER RESEARCH UK

Contact: Dr Alexis Webb
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WORKSHOP: EARLY DETECTION OF CANCER

Cancers that are detected at an early stage of development are easier to treat and the treatment tends to be more successful in terms of long-term survival rates. Indeed, the survival rate for cancers that are treated at Stage 1 (the earliest stage of progression) is 90% after ten years. However, only 25% of cancers are actually detected at this stage. Detection at Stage 2 results in the survival rate dropping to 70% after 10 years, with further significant decreases for Stage 3 and Stage 4 detection. Therefore, there is a need to be able to better detect cancer at the earliest stages of development.

This is a multidisciplinary challenge, requiring collaboration between specialists with a diversity of backgrounds for success. Cancer Research UK (CRUK) have produced an **Early Detection and Diagnosis (ED&D) of Cancer Roadmap**[6] in consultation with over 100 stakeholders from across the entire ED&D ecosystem. One of the key outputs from this Roadmap is a set of around 15 prioritised research interventions with each addressing a well-defined early detection challenge, but this Workshop focussed on just three of these that would be of most relevance to the engineering and physical sciences community.

1. Analysis of Electronic Health Records

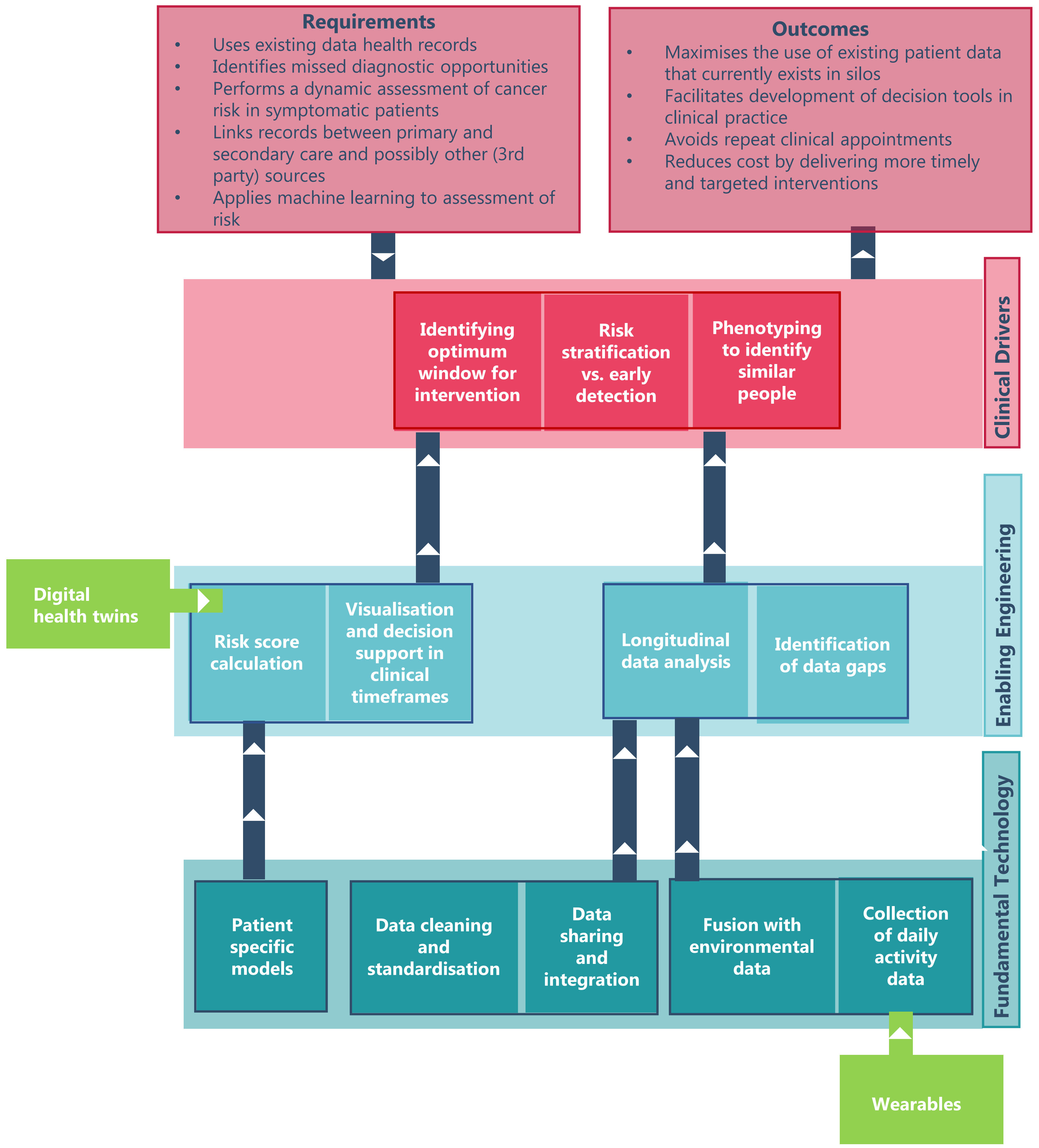
2. Wearables and Point of Care Devices

3. Digital Health Twins

1.

Analysis of Electronic Health Records.

A patient's electronic health record (EHR) refers to the digital format of the information collected during their encounters with the health service, which was traditionally stored on paper. Unlike paper-based system, an EHR can combine information from the primary, secondary and tertiary care settings along with other data, potentially from third party sources (e.g. wellbeing monitors). By drawing together information from multiple sources over time, it becomes possible to build up a more complete picture of an individual. This is important, as early detection is built upon carrying out some diagnostic intervention, and this needs to be done at the right time. Screening programmes are good example of this, but they generally rely on a simple age-based assessment of risk. Analysis of EHRs could allow phenotyping to identify groups of similar people that an individual is similar to clinically and personalised risk stratification. Given that all diagnostic techniques have a non-zero false positive and false negative detection rate, such risk stratification allows effective deployments of techniques which would otherwise generate too many false results if deployed on a large population with a low risk. There are many opportunities for clinically-focussed EPS research in this space. There is one potential research stream around construction of patient-specific models leading to risk score calculations and systems for timely visualisation of data and decision support. A second research stream is around the collection of daily activity data, its fusion with environmental data and subsequent combination with clinical data in EHRs to allow an individual longitudinal analysis of an individual's wellbeing.



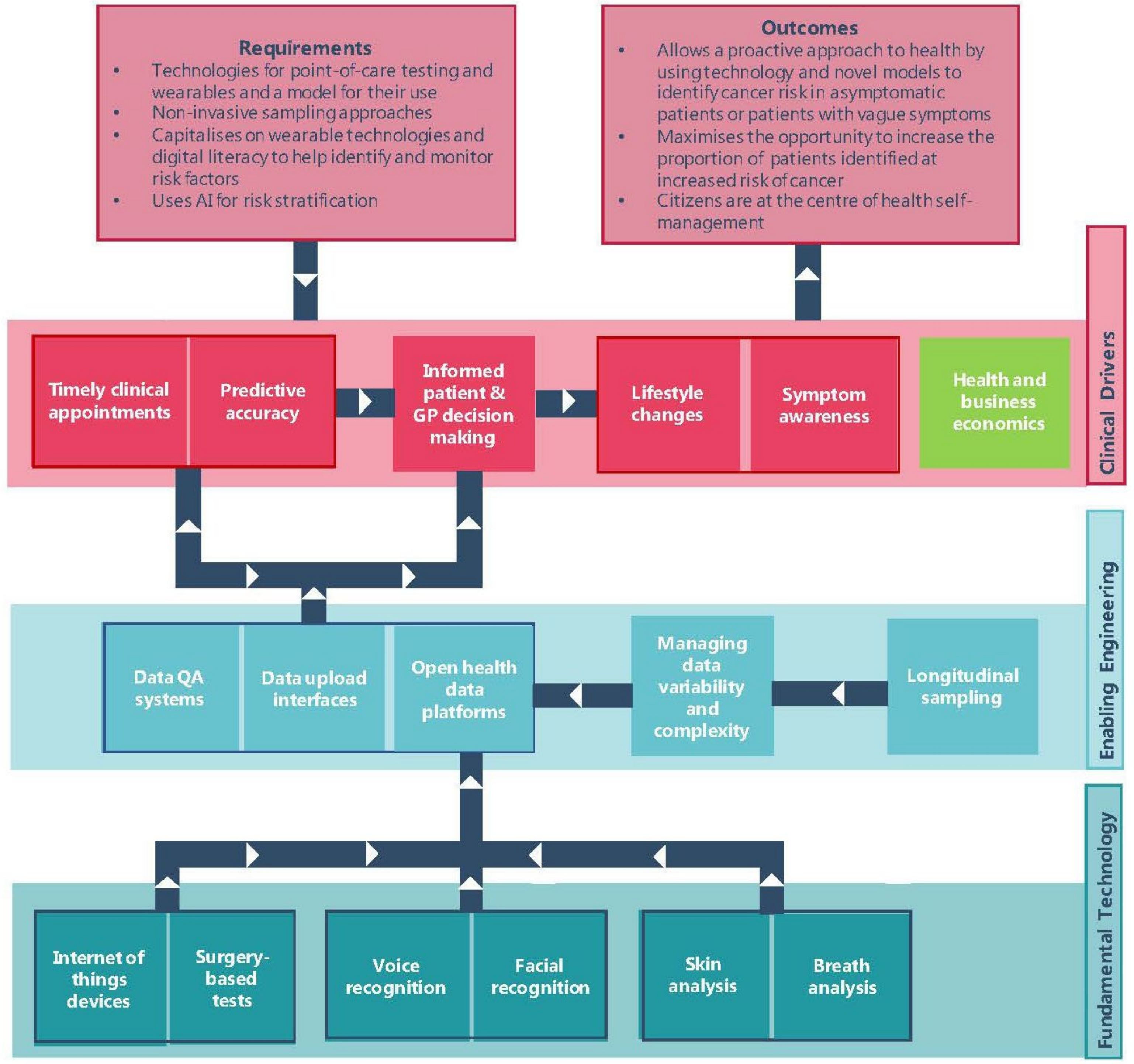
[6] https://www.cancerresearchuk.org/sites/default/files/early_detection_diagnosis_of_cancer_roadmap.pdf

WORKSHOP: EARLY DETECTION OF CANCER

2.

Wearables and Point of Care Devices.

Point of care testing (POCT) refers to the use of tests that are carried out at the time and place of initial contact/care to deliver rapid results. POCTs can lead to a better patient experience, lower costs and reduced time pressure on clinicians. It can also improve the likelihood of detecting cancer early though increasing the uptake and use of diagnostic testing, as there may be a much lower barrier to carrying out the test if it is faster and can provide clear results to enable decision making. This also means that testing can be carried out more readily to provide longitudinal data, which can be useful in identifying long term trends that would indicate a developing medical condition. It should be noted that not every cancer diagnosis will require a point of care test and that even if used, it would only form one step in a medical diagnostic pathway; the presence of cancer is confirmed via biopsy and histology. In contrast, wearable devices are technologies that are work on the body to constantly measure parameters from activity level and heart rate to blood glucose levels allowing useful and actionable results. There are strong links here to the analysis of EHRs and the power of combining data. The starting point is the aim to improve the awareness of both patients and GPs to early symptoms of cancer. There is also the possibility of encouraging lifestyle changes which may reduce cancer risk. For this to happen, we need to provide better information to both patients and GPs to enable them to make decisions, which means having timely clinical appointments and good predictive accuracy based on POCT and wearable data. Data must be managed well with a need for open health data platforms, secure upload interfaces and a quality assurance (QA) system for validating data. Longitudinal data from wearables and POCTs is inherently complex and highly variable, and so means of managing this is required. Underpinning all of this are the basic wearable and POCT devices which collect data in the first place. The 'Internet of Things' provides an opportunity to embed healthcare sensors which interact with patients in their everyday lives, collecting data with minimal invasiveness. There are also opportunities for GP surgery-based tests which might make use of the time a patient is waiting to be seen by a clinician. In addition, there are emerging opportunities for skin and breath analysis, and for voice and facial recognition; these could all be used over an extended period of time to identify changes in an individual's general wellbeing.



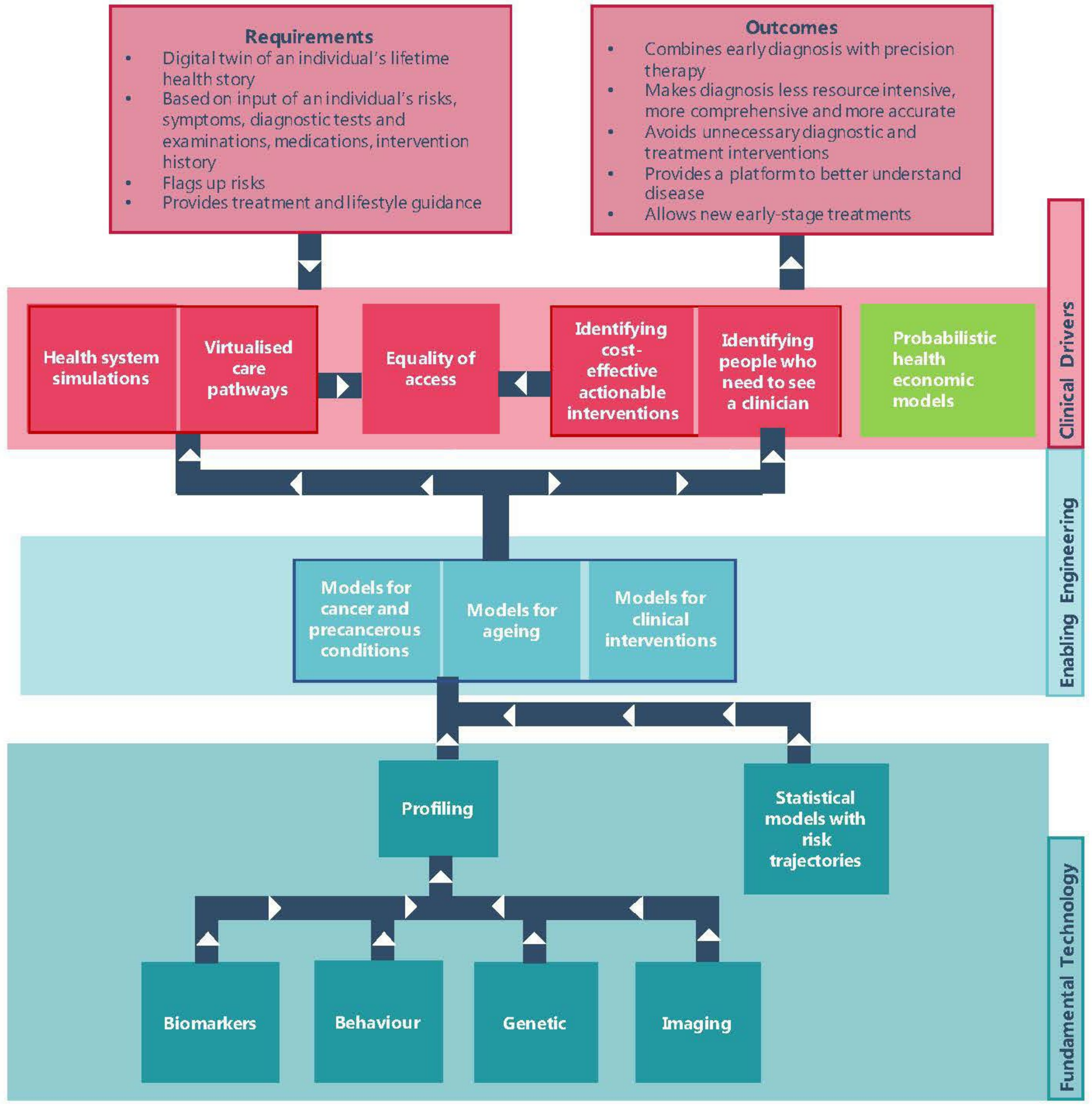
WORKSHOP: EARLY DETECTION OF CANCER

3.

Digital Health Twins.

A digital health twin can be thought of as a virtual physiological copy of a human patient, created by collecting and storing their entire health history. For example, this could include inputting their disease risks, symptoms, diagnostic test and examination results, medications, intervention history, and other data into a digital storage system. Such a model could be used to simulate the effect of lifestyle changes or care pathways on an individual to allow for more informed decision-making. It can also be used to flag up risks and alert healthcare systems in advance. This will need the development of high-quality models for ageing in general (so that deviation from an expected wellbeing trajectory can be identified), models for cancer and precancerous conditions and models for clinical interventions to understand the effectiveness of specific interventions in the context of broader care pathways. Finally, these models must be underpinned by accurate profiling of individuals based on biomarkers, behaviour, genetic information and imaging data, coupled with statistical models for risk trajectories.

Several themes stand out in early detection and diagnosis of cancer. One is around the need for access to high quality, real world, longitudinal data as algorithms are only as good as the data input, but which also respects the privacy of individuals. A second area is around regulation, both in that of the clinical validation of new technologies, and of wearable devices themselves so that data can be trusted for the purpose of informing healthcare.



Read the full Report of the Workshop on the Early Detection of Cancer[7] to find out more about how research between engineers, physical scientists and clinicians could lead to a real advancement in early detection.

7 http://www.fast-healthcare.org.uk/roadmap-detection-diagnosis-of-cancer/

WORKSHOPS

Key Themes

The FAST Healthcare NetworksPlus was set up to address the challenge facing the NHS of improving care whilst also reducing cost through a more joined-up approach to healthcare enabled by systems-based engineering. Although the specific Workshops that we have run and summarised in this Report have covered a very diverse range of clinical scenarios, there are some clinical drivers which have repeatedly emerged throughout.

Clinical Drivers

The first of these is the need for better **disease prevention and early detection**. This plays into the long-term trend in healthcare to move from the historical position of medicine being a response to illness to one where medicine proactively keeps people well for longer. By its very nature, this has to be something which is very community-focussed. It needs an understanding of the health risks that an individual has, a means of monitoring key indicators of wellbeing and a mechanism for engaging with an individual to make active lifestyle choices to maintain wellbeing or obtain further medical investigation in the case of early detection.

The second is the ability to **make clinical decisions in a timely fashion**. One aspect of this aligns with the prevention and early detection driver. In the absence of a critical change in an individual's health, at what point should an intervention be made to encourage someone to change their lifestyle or to obtain further investigations? It would be easy to convert everyone into a patient just by testing them until you find something to treat. A significant body of data is required to be able to make these decisions in the best interest of the individual. In other scenarios, such as in the event of a suspected heart attack, time is of the essence, and it is necessary to make very rapid decisions based on limited data or by assimilating a variety of complex data to select the most appropriate course of action.

The third is the need to **effectively manage long term chronic conditions** or long term rehabilitation following significant medical interventions. This often requires close partnership between different parts of the healthcare system, including both community-based and hospital-based care. It also requires positive engagement with the patient and patient acceptance. The digital divide can be a major problem in this regard, with those who would benefit most from digitally-assisted self-management of conditions being the very group who have the least access to, and poorest understand of, digital platforms.

WORKSHOP: KEY THEMES

Systems-Based Engineering Response

Systems-based engineering is all about taking a holistic view of a complete system when engineering how that system should operate. For technology, this means not only developing new tools but building into that development how they will be used. The report by the Royal Academy of Engineering in 2017 on **Engineering better care: a systems approach to health and care design and continuous improvement** looked at the application of systems-based engineering to healthcare specifically, and provided a framework for thinking based on four perspectives: systems thinking (considering the entire process), design thinking (tackling the real need), risk thinking (identifying risk points and mitigation) and people thinking (designing for users).

With both the clinical drivers and the systems-based engineering approach in mind, perhaps the single most pervasive common theme which has been present through all of the workshops has been around the opportunities offered by longitudinal monitoring.

Longitudinal Monitoring

Gathering data on in individual's wellbeing over a long period of time can serve several purposes. It can help with disease prevention and early detection as it allows an estimation of the 'wellbeing envelope' that an individual lives within normally. For disease prevention, this can assist with understanding an individual's risk profile for different diseases and the likely impact of making changes. For early detection, it can help to identify when an individual deviates from their 'wellbeing envelope' in an unexpected way that may indicate further investigation would be beneficial. Even in the case of making rapid decisions in the face of a sudden and life-threatening situation, access to longitudinal data can be coupled with immediate data to better understand an individual's risk profile in terms of both diagnosis and treatment.

We can attempt to break down the engineering and physical sciences research identified in the different roadmaps that relates to longitudinal monitoring in terms of the four perspectives for engineering better care.

In terms of the system and thinking about the entire process, a recurring theme is around how we transfer and store longitudinal data between the home, GP surgery and hospital when the data itself is coming from a huge diversity of sources, whether that is electronic health records written by a healthcare professional or data, such as pulse, from a wearable monitor. At some point in the complete system, specific data needs to be validated against some quality assurance standards, gaps in data required to enable some action identified and some algorithms (AI-based or otherwise) applied leading to timely decision support.

Design thinking to tackle the real need, means avoiding the temptation to try and measure 'everything'. Instead, it is important to identify what could actually make a real difference and the specific context in which it could be used. Opportunities were identified for voice and face recognition, skin and breath analysis and data from both wearable and potentially implantable devices. However, good models for ageing which pick out the key parameters to measure are important, bearing in mind that what should be measured will vary from person to person depending on their specific risk profile.

In people thinking, the design needs to work for both the general public and healthcare professionals, and user interfaces for both groups are critical. This plays back into the issue of the digital divide – technology needs to be accessible for all. Apps need to be user focussed in design, and opportunities to help with this are emerging in virtual reality. Devices also need be engineered so that people feel empowered to adopt them. The importance of engagement with users at the earliest possible stage of development cannot be overstated.

A major consideration in risk thinking is around missing timely interventions, either because significant data is not collected, lost or misinterpreted, or because no one acts on the output from a decision support system. This should partly be mitigated by good system design, but points of human intervention probably need to be identified and carefully considered. Another key risk is around the inappropriate use of data, because it is not held securely or it is used in an inappropriate way which compromises an individual's privacy.

WORKSHOP: KEY THEMES

Outcomes

There are a few common outcomes for healthcare which should flow from the development of the longitudinal monitoring research that is embedded in all of the roadmaps.

Perhaps the most fundamental is the blurring of the boundary between wellness, disease prevention and early diagnosis. This is founded on a more proactive approach to health than moves us away from the current, largely reactive, approach to medicine. This requires thinking about people in a holistic way considering physical, emotional and psychological wellbeing together and puts people at the centre of their own health management.

There is a real promise of less costly and more effective medical intervention from such a programme of research, not least by making the best possible use of the people delivering healthcare. People are the single greatest asset that the healthcare system has and the single greatest cost. A well-engineered system should ensure that healthcare professionals are empowered to work at the level appropriate with their training and expertise for as much of the time as possible, and in doing so this makes the best use of this precious resource.

WORKSHOPS

Conclusions

The purpose of the series of Workshops that the FAST Healthcare NetworksPlus organised was to bring people together from very different backgrounds and to find a framework for them to contribute effectively together to a research vision.

The structure of the Workshops that we adopted, starting with setting out the clinical need, discussing an engineering and physical sciences response and then considering known barriers where research would be most valuable, proved to be a good formula for achieving this.

However, it is also noticeable that people also sit at the heart of both the research agenda that has emerged and in the envisaged outcomes. Perhaps this is not surprising, given that ultimately health is about people, but it is easily forgotten in the enthusiasm for driving forward engineering and physical sciences research in this space.

Only by placing people at the centre of how we engineer healthcare systems and conduct the research which underpins this can we hope to deliver better health outcomes with fewer inequalities and which makes the optimum use of resources – in particular people's time and skills.

FAST HEALTHCARE NETWORKS PLUS

ANNUAL REPORT MARCH 2021

Projects

Using our EPSRC 'Plus Funding', we have been able to support a portfolio of seven projects which each address different aspects of our Roadmaps. In addition, we have funded work to enhance translation of technology to clinical practice.

MAIN PROJECT INVESTIGATORS

Professor Ruth Cameron
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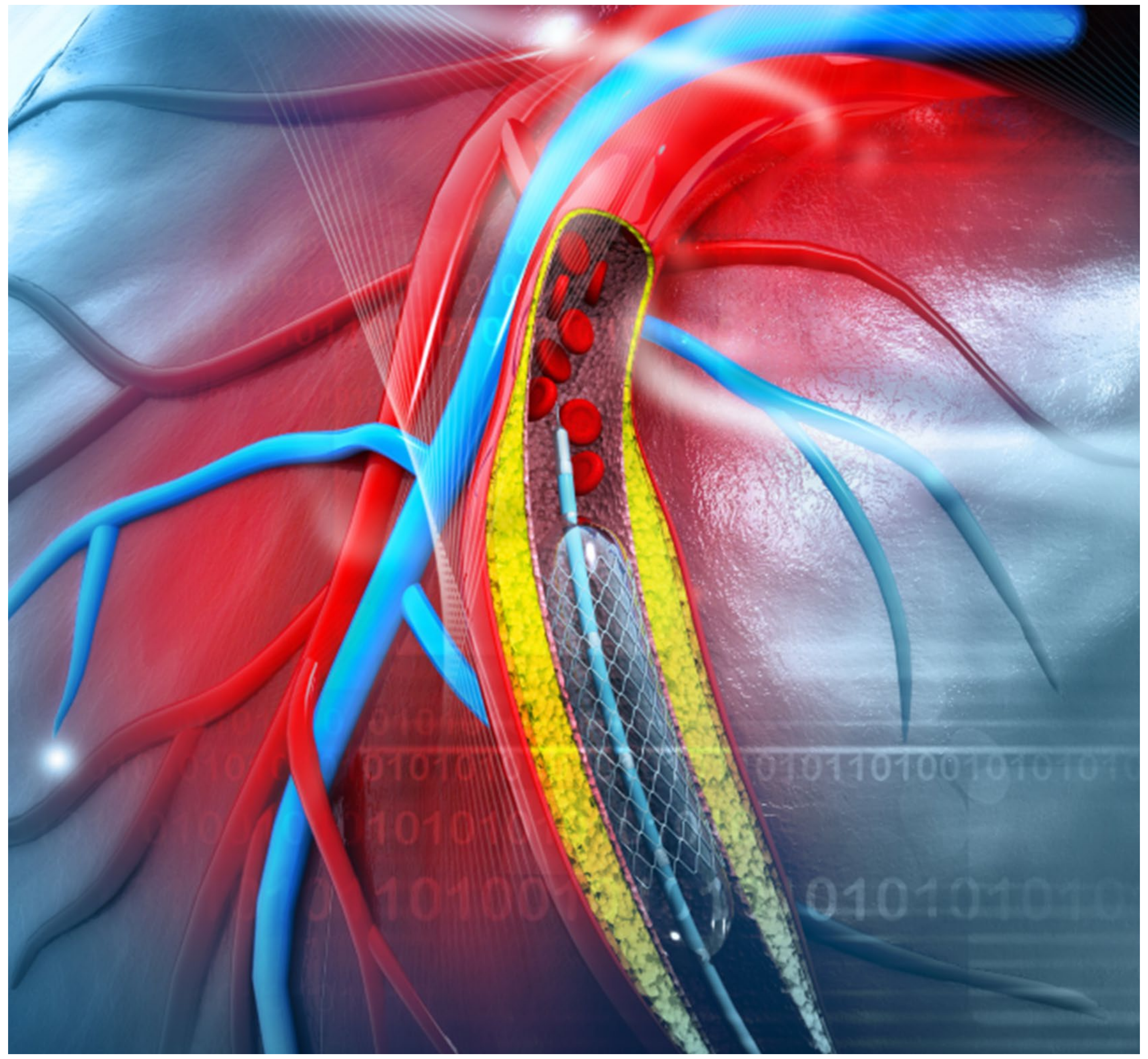
PROJECT

3D printing of a smart coronary stent prototype using novel bioresorbable polymer blends

1ST OCTOBER 2017 – 30 SEPTEMBER 2019



Why is this Important?

According to British Heart Foundation statistics, there are an estimated 7 million people living with cardiovascular disease in the UK. Amongst these, 2.3 million people are living with coronary heart disease. This disease is the leading cause of death worldwide and, in the UK alone, is responsible for an average of 180 deaths each day[8]. It occurs when coronary arteries become narrowed as a result of deposition of atheromatous plaques within the arterial walls, causing partial or complete restriction of blood supply to the heart[9]. Minimally invasive surgical management, a procedure called percutaneous coronary intervention, involves the placement of a coronary stent in the narrowed artery to widen its lumen, and restore blood flow to the affected myocardium. The number of these procedures performed per year increased ten-fold between 1991 and 2015, and will increase still further with an aging population.

Current drug-eluting stents are predominantly metallic and remain in the patient's body indefinitely. This can cause complications such as inflammation, vessel straightening, late stent thrombosis and in-stent restenosis. In addition, permanent placement prevents the

[8] "BHF CVD statistics Factsheet - UK" at https://www.bhf.org.uk/statistics accessed on 05/03/2018

[9] Neamtu, I., Chiriac, A.P. and Diaconu, A. *et al.* "Current concepts on cardiovascular stent devices" (2014) Mini Rev Med Chem. 14(6):505-536

PROJECT: 3D PRINTING OF A SMART CORONARY STENT PROTOTYPE USING NOVEL BIORESORBABLE POLYMER BLENDS

stented vessel from being restored to a normal physiological state and may block operative access for a future surgery. Bioresorbable polymeric stents can overcome these problems by degrading and being absorbed within the body over a period of time, after mechanical support is no longer required. However, they can exhibit stent elastic recoil, strut fracture upon over-expansion and can be bulkier than metallic stents. Poor clinical performance of bioresorbable stents to date has resulted in many manufacturers reconsidering development, or to product recalls being necessitated to manage a reported increased rate of major adverse cardiac events. Hence there is a need for innovation in the development of bioresorbable stents.

What was Achieved?

To address these limitations, this project aimed to develop next-generation bioresorbable stents by using novel bioresorbable polymers and exploiting 3D printing techniques. These techniques would enable production of personalised and patient-specific stents using information from 3D segmentation of the patient's medical imaging, printable on demand within 20 minutes in the clinic. In this way, a patient with atypical artery anatomy could be better treated, with the 3D-printed stent much more effectively matching the patient's unique blood vessel contours.

> *A leap forward in bioresorbable stenting*

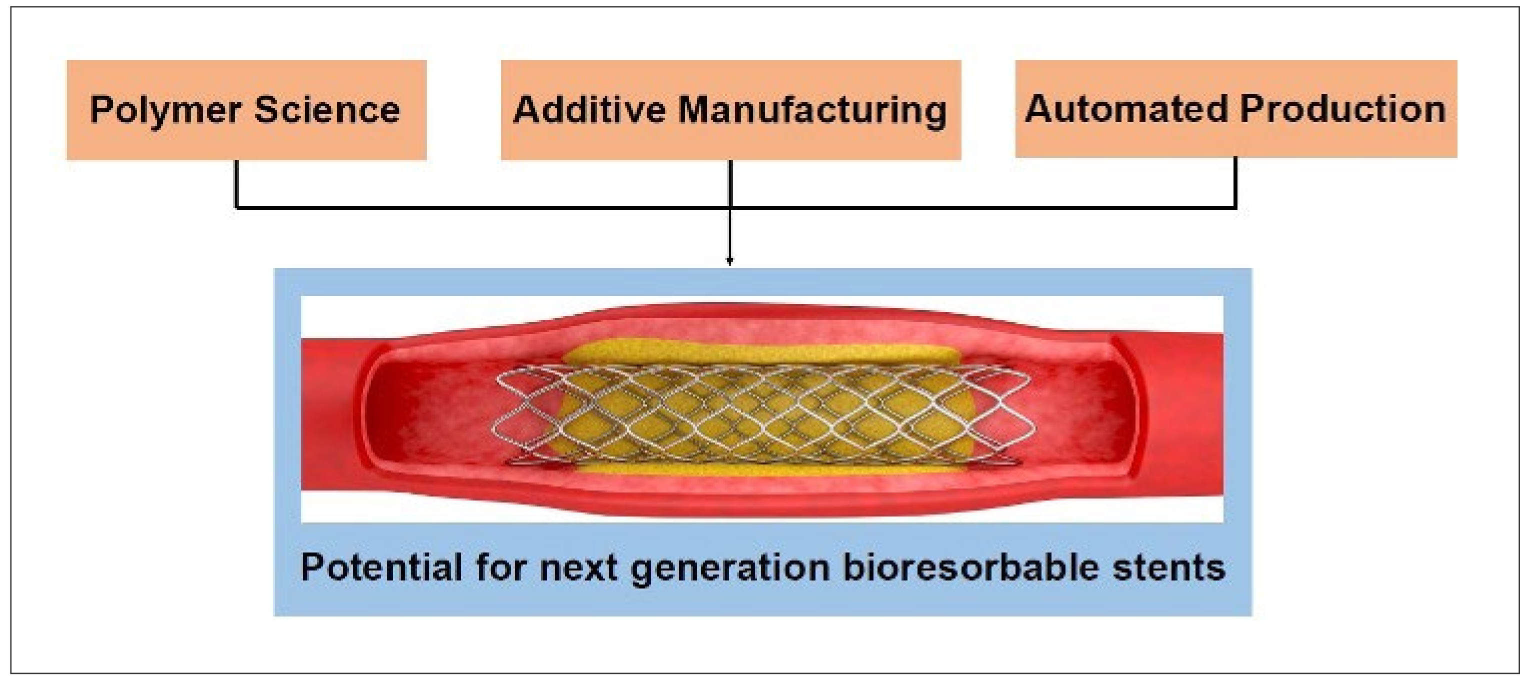
This initiator project not only gave the group the opportunity to test their hypotheses but also allowed them to form a new multi-disciplinary research team involving early career researchers, experts and clinicians in the field. A new collaboration between universities and hospitals was established through this Network with the aim of working together to fabricate a proof of concept 3D printed coronary resorbable stent prototype.

Within the remit of this FAST Healthcare project, new 3D printing techniques were developed that have the potential to revolutionise the manufacture of BioResorbable Stents for use in coronary stenting.

This technology is inspired by polymer science and harnesses additive manufacturing and automated production control principles leading to a potential for thinner stents that are less susceptible to strut fracture by counterbalancing the varying strains and stresses experienced during a stenting procedure such as crimping, balloon-expansion and implantation. Degradation modes are controlled for safe resorption in use. Units can be made to specific size but as units can be rapidly 3D printed, these techniques not only offer the potential for improved stenting, but can also allow stents to be personalised to patient's anatomy.

Key Benefits of the new bioresorbable stents:

- Fully resorbable
- Reduced stent thickness to improve laminar flow, reducing thrombogenicity and restenosis
- Low stent recoil to reduce risk of restenosis
- Tailored stent ductility enhancing range of dilation rate and extent, giving ease of deployment and greater procedural success rate
- Optimised stent degradation times to avoid premature or delayed resorption
- Controlled stent degradation modes to reduce risk of catastrophic failure after implantation
- Can be produced in a range of sizes or be highly personalised to match patient's vessel anatomy.



What's Next?

A priority patent application in the UK has been filed and the Principal Investigators, Professors Ruth Cameron and Serena Best, are now keen to collaborate with partners to pursue further implementation of this technology into the stenting market.

MAIN PROJECT INVESTIGATORS

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PROJECT

Wearable Device Intervention for Promoting Physical Activity in Children with Asthma

1ST JUNE 2019 – 30TH APRIL 2021

Why is this Important?

Asthma is the most common chronic disease in children globally[10]. In the UK, the prevalence of childhood asthma is among the highest, with 1 in 11 children affected. Childhood asthma can cause a great burden to the healthcare system and the home setting. According to Asthma UK, the National Health Service (NHS) spends £1 billion a year treating and caring for people – around 25% are children – with asthma, highlighting the extent of care given to both adults and children with asthma.

One of the goals of asthma treatment, under the self-care umbrella, is to maintain normal physical activity levels including everyday activities such as walking. Epidemiological evidence to date suggests that regular physical activity is beneficial for people with asthma because it can strengthen the respiratory muscles and reduce instances of pulmonary inflammation. However, children with asthma are usually less active than their healthy peers, getting 30 minutes less physical activity per day than healthy children. The negative health perceptions from caregivers such as parents and school teachers are likely a major contributor to the reduced levels of physical activity in children with asthma. Restrictions can be imposed

[10] WHO 2018

PROJECT: WEARABLE DEVICE INTERVENTION FOR PROMOTING PHYSICAL ACTIVITY IN CHILDREN WITH ASTHMA

because physical activity is often perceived as a dangerous 'trigger' rather than something beneficial[11]. If managed appropriately by considering asthma severity and personalised 'triggers', there is no reason why children with asthma should not be as active as children without asthma. Studies have used active video game and physical training to promote activity in children with asthma[12]. However, these interventions are limited to a specific setting which is not appropriate for pervasive applications. It is therefore important to provide a ubiquitous and evidence-based way to encourage more physical activity in children with asthma.

Given the potential of wearable trackers to increase physical activity via real-time feedback of physical activity through personalised goals and presentation of rewards, this study aims to use a wearable tracker to encourage children with asthma to be more active. With the simultaneous monitoring of heart rate, the tracker is able to provide a visible evaluation of activity of the children with asthma for the caregiver. Ultimately, increases in daily physical activity and improvements in asthma control would enhance the quality of life for the family as a whole. This approach has future potential to reduce healthcare resource burden and subsequently NHS costs.

What was Achieved?

FAST Healthcare made it possible for us to conduct a cohort feasibility study to primarily explore the use of a wearable tracker to monitor the levels of physical activity participation in children with asthma. We recruited 22 children who were aged from 6 to 14 years and who had a clinical diagnosis of asthma, using asthma medications, as well as having self-reported asthmatic symptoms in the last month prior to the time when they participated in the study.

Data were collected via a wearable tracker and daily/monthly follow-up questionnaires for 3 months; we started the data collection from the first subject on 10 January 2020 and completed the data collection from the last subject on 19 June 2020. The data were used to evaluate: 1) the effect of wearing an activity tracker on the level of physical activity in children with asthma, and 2) the effect of physical activity on the outcome of asthma control. Due to the COVID-19 outbreak and its resulting lockdown (the first lockdown which started on 22 March 2020), it became challenging to verify the first assumption as we were unable to collect the follow-up physical activity questionnaire to the quality expected. We found something new instead.

We have three main findings.

- **First,** daily physical activity levels of the children with asthma significantly reduced after the lockdown, with the average steps and very active minutes decreasing from pre-lockdown levels, by 3300 steps and 11 minutes, respectively.
- **Second,** physical activity has a mostly positive effect on asthma control and asthma quality of life, as indicated by the inverse relationship between the activity level and asthma control score and the positive relationship between the activity level and asthma quality of life score. That is, the more active the subject was, the better their asthma condition, and the better their asthma quality of life.
- **Third,** physical activity level had a more significant effect on asthma control during the lockdown than before the lockdown. These findings suggest that physical activity can positively impact on asthma condition of children with asthma. Further, physical activity may play a more definitive role on asthma control in settled circumstances (e.g. at home) than being exposed to an environment with uncertain factors.

What's Next?

Given what we have achieved via the proposed pilot work, we need further adjustments to the intervention and future study designs. We will collect data about the acceptability and feasibility of the interventions, as well as data on potential larger study outcomes. These will be used to inform design of future pilot and feasibility work, including a large-scale trial. More samples will also make it more feasible to predict exacerbations of asthma to provide timely (earlier) intervention.

> *"Wearable trackers can potentially improve physical activity and thereby asthma symptoms in children.*

[11] Williams et al., BMC Family Practice 2008
[12] Gomes et al., PloS One 2015

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PROJECT

Automated Decision Support Tools for Diagnosing Heart Attack and its Occurrence-time using Electrocardiogram

1ST APRIL 2018 — 30TH SEPTEMBER 2019

Why is this Important?

Chronic diseases are the leading cause of death for both developed and developing countries, representing 70% of all deaths, and cardiovascular disease (CVD) accounts for most of these (17.9 million annually). It is estimated that 85% of CVD deaths are due to heart attacks (i.e., myocardial infarctions) and strokes. Traditional diagnosis of myocardial infarction (MI) mainly employs interpretation of electrocardiogram (ECG) recordings and blood tests, which requires precise acquisition devices and clinical expertise. While blood tests are invasive and can take up to 60 mins turnaround time, the inter-observer variability in ECG interpretation can lead to disagreement, making MI diagnosis difficult and tedious. Particularly in the case of an ambulatory setting, where only ECGs are available, pre-diagnosis of MI would better prepare clinicians to make a treatment decision.

In order to address these challenges, research on automated algorithms for heart disease classification serving as data-driven decision support tools is increasingly popular with growing amounts of available ECG data being collected in wearable devices. However,

PROJECT: AUTOMATED DECISION SUPPORT TOOLS FOR DIAGNOSING HEART ATTACK AND ITS OCCURRENCE-TIME USING ELECTROCARDIOGRAM

most automated ECG analysis has relied on feature engineering, where hand-crafted features are proposed for the purpose of heart disease classification. These methods require application-specific knowledge, a large amount of effort to preprocess ECG data and beat-extraction, which produces variant results depending on the algorithm used for analysis.

Deep neural networks (DNNs) have become increasingly popular in the domain of ECG analysis. However, most DNN experiments in the literature focus on single-lead ECG analysis for the detection of arrhythmia, heartbeat classification, or serve as a general-purpose abnormal ECG detector. This motivates research involving DNNs with 12-lead raw ECG waveforms, in order to assess their performance accurately for diagnosing MI in a clinical environment, which has not previously been performed.

Additionally, there are currently no studies that have investigated the prediction of occurrence-time in MI (i.e., the age of a MI), information that is crucial for preoperative risk assessment: patients with acute (i.e., within seven days) and recent (i.e., less than 30 days but longer than seven days) MIs are considered to be at higher risk of a perioperative cardiac event, while those with old MIs (i.e., more than 30 days) are at higher risk of perioperative cardiac morbidity. Therefore estimating the occurrence-time of a MI using only ECGs when a patient history is not readily available, would provide useful insights for triaging treatment.

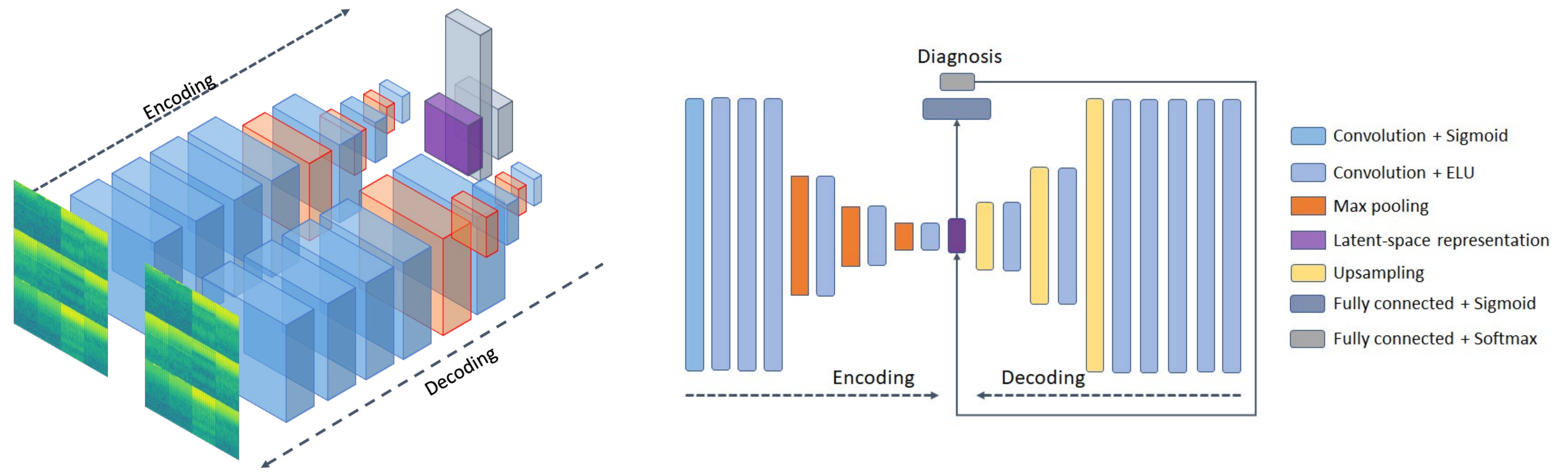


Figure 1: (left) 3D illustration of Tool 1; (right) Detailed DNN architecture of Tool 1: It consists of two components: (i) feature extraction via convolutional autoencoder and (ii) classification via fully connected and softmax layers. The latent-space representation is constructed from these two components and is optimised simultaneously to formulate dimension-reduced features that provide the optimal accuracy in classification.

What was Achieved?

In this project, we proposed two automated decision support tools, diagnoses of MI and its occurrence-time, respectively, using only ECG data. In order to create robust tools leveraging DNNs, a large anonymised ECG dataset collected previously in Guangdong Provincial People's Hospital (GPPH), China, was considered. Ethics committee approval and informed patient consent were previously obtained by GOPH. This GPPH dataset contains 12-lead ECG waveforms from 17,381 patients (11,853 MI and 5,528 normal cases) sampled at 500 Hz. Each patient had one ECG recording that contained the standard 12 leads, and each ECG diagnosis was confirmed based on hospital records for coronary angiography and ICD-10 codes at discharge. The MI cases included ST-segment elevated MI, non-ST-segment elevated MI, and unspecified MI. Each MI case was then labelled based on hospital records for its occurrence-time, resulting in 1,489 Acute, 5,377 Recent, and 4,613 Old MI cases.

Tool 1: A novel end-to-end deep framework for screening heart attack utilising 12-lead ECGs.

The contributions of the proposed work are as follows (see Figure): (1) introduction of a spectral-based pre-processing step that transforms raw ECG time-series waveforms to spectrogram representations, reducing the variability in sampling rates and device specifications across different ECG machine manufactures; (2) proposal of a novel stacking order, by fusing the 12 leads of ECG waveforms to form a generic image-like representation for

PROJECT: AUTOMATED DECISION SUPPORT TOOLS FOR DIAGNOSING HEART ATTACK AND ITS OCCURRENCE-TIME USING ELECTROCARDIOGRAM

deep learning analysis; (3) deployment of an end-to-end DNN leveraging the characteristics of convolutional neural networks and autoencoders, which (i) exploits abstract features describing the intrinsic relationships among 12 ECG leads via convolutional layers; (ii) applies unsupervised encoding of such features via AE with dimension reduction; and (iii) targets the dimension-reduced features that provide the optimal classification accuracy.

Tool 2: An novel end-to-end deep framework for diagnosing the occurrence time of MI using 12-lead ECGs.

The contributions of the proposed approach are as follows (see Figure 2): (1) application of cross-domain transfer learning between natural images classification and ECG waveform detection, to extract spectral features to reduce the dimension of the spectrograms and minimise redundant information; (2) utilising joint spectral-temporal modelling to encode the spatial and temporal information from multi-channel ECG waveforms; and (3) proposing the use of a variety of fusion approaches to combine information at different levels of data representation (i.e., data, feature and decision level fusions) aiming to utilise distinctive characteristics offered by each ECG lead.

What's Next?

We have filed an international patent application for tool 1 and are currently waiting for its outcome. We are in the process of applying for funding to support the software development and clinical trial of our tools in order to translate the proposed work to be used in hospitalised and/or ambulatory settings.

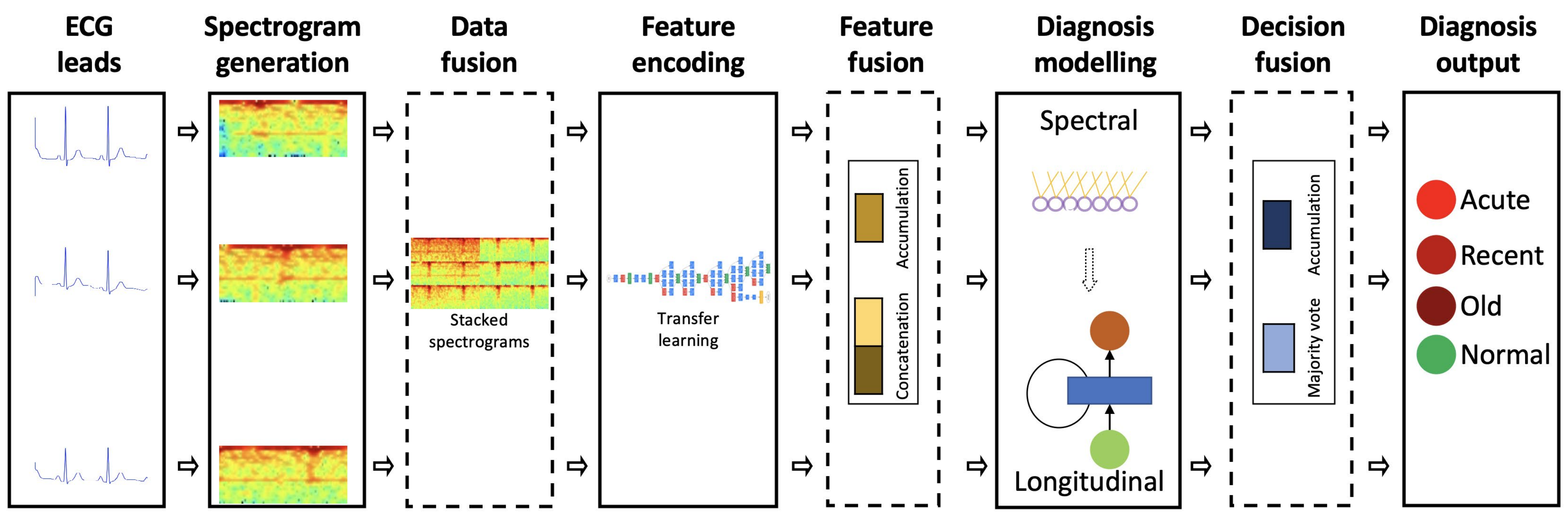
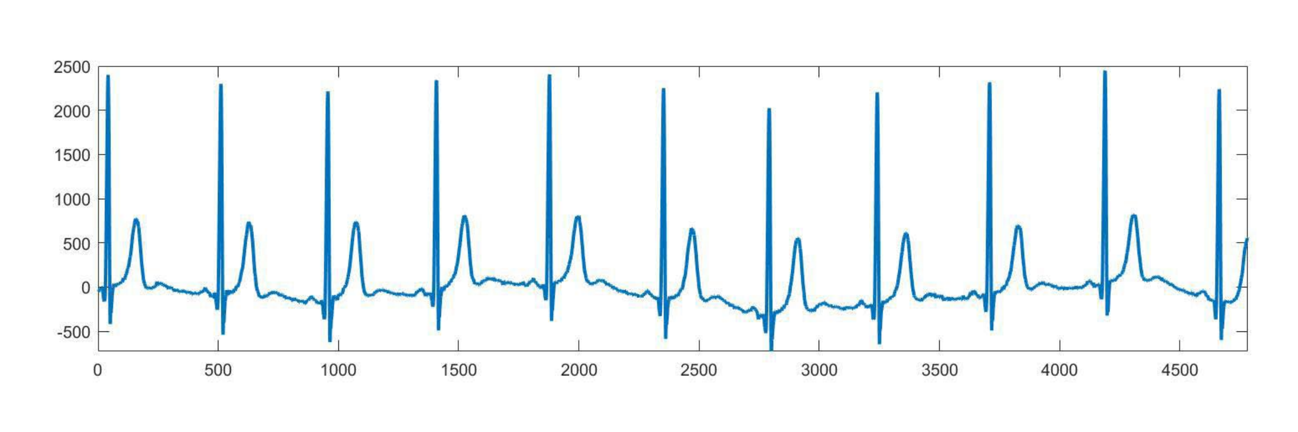


Figure 2: Overview of Tool 2: multi-lead ECG waveforms are provided as input, and spectrogram generation is used to encode the frequency-time characteristics. Transfer learning is applied to encode deep features using existing computer vision networks. Spectral and temporal models were employed for diagnosis modelling.

We proposed automated decision support tools for diagnoses of MI and its occurrence-time using only ECG data.



PROJECT

Non-invasive spectroscopic methods to diagnose Colorectal Neoplasia

1ST NOVEMBER 2020 — 30TH APRIL 2021 (6 MONTHS)

MAIN PROJECT INVESTIGATORS

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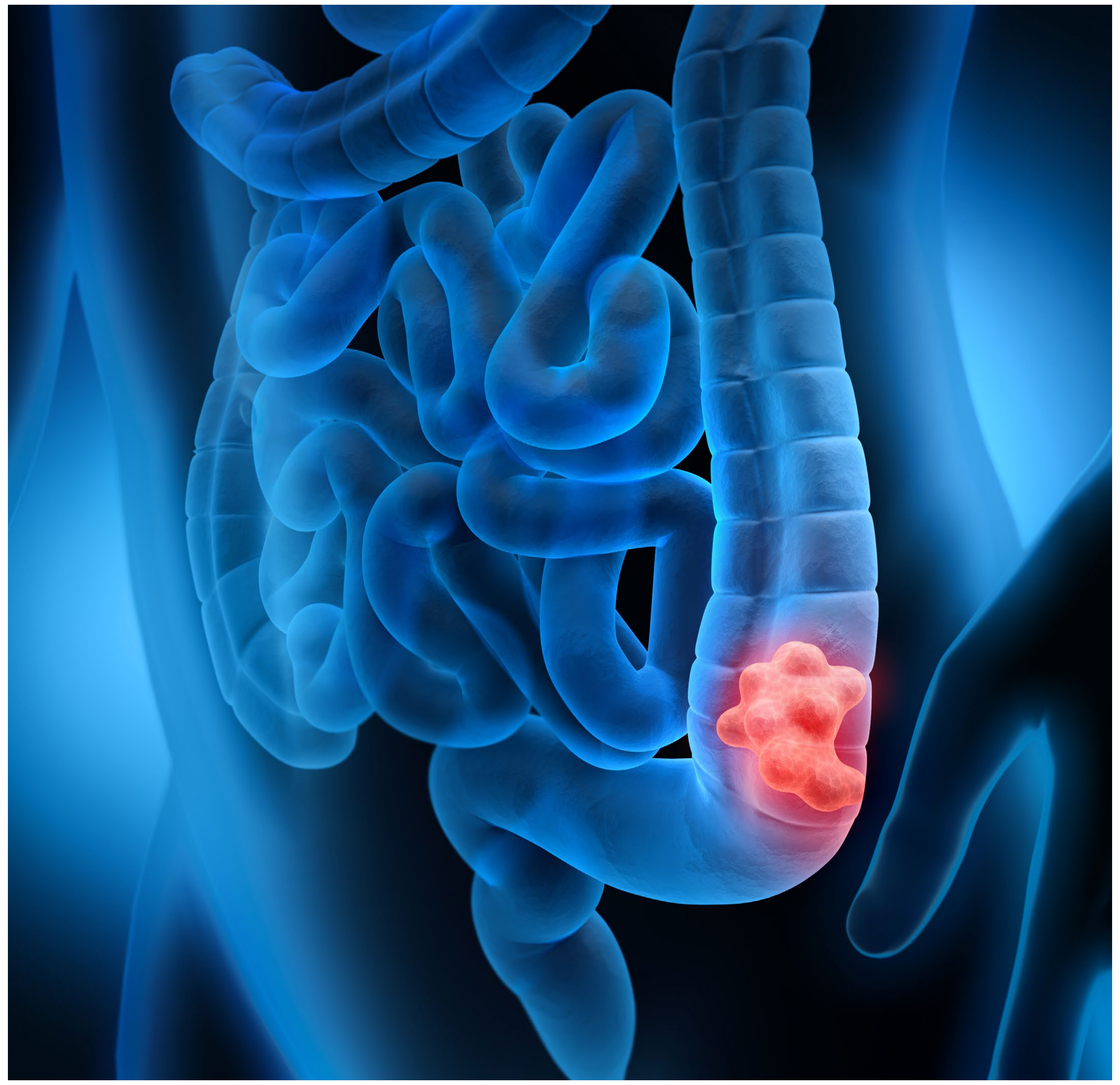


Why is this Important?

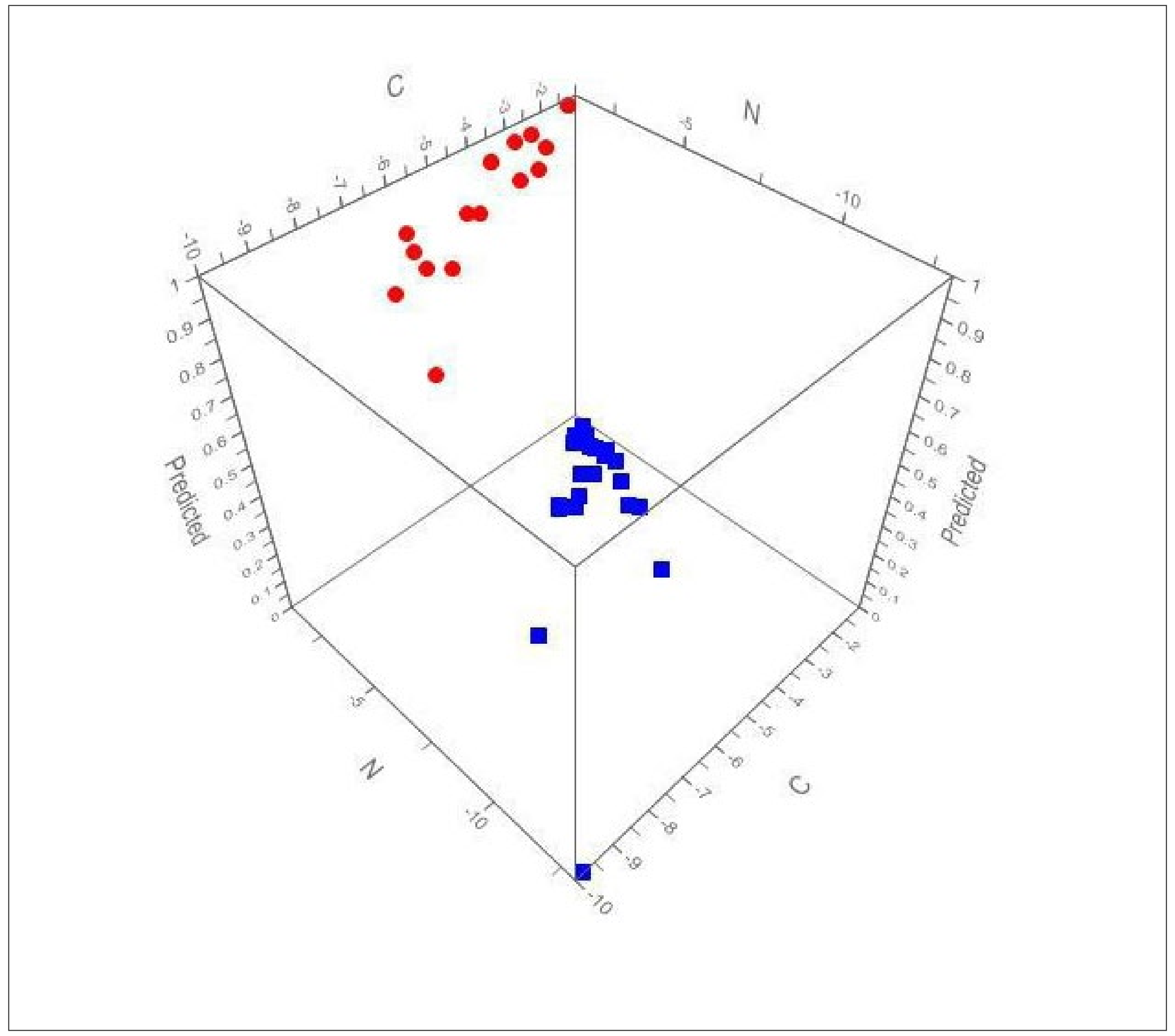
This project is to demonstrate that spectroscopy of biofluids can serve as an early detection technique in colorectal cancer, significantly improving prognostic outcomes and non-invasive follow-up of patients. Therefore, patients will be the ultimate beneficiaries of such a method, which offers an important step forward for patients, clinicians and the research community. The aim of the project is to develop non-invasive point of care methods for the diagnosis of colorectal neoplasia (polyps and carcinomas) that are highly sensitive and specific.

Existing methods such as Faecal Immunohistochemistry Test (FIT) have shortcomings (sensitivity for cancer is >70% and for advanced polyps <20%). Analysis of body fluids via Raman and Infrared spectroscopy could augment or potentially replace FIT because of superior sensitivity and specificity plus improved patient acceptability, in this pilot study.

Experimental work is exploring the use of Raman micro-spectroscopy – combined with chemometric analysis – to understand the dynamics of colorectal neoplasia by analysing

PROJECT: NON-INVASIVE SPECTROSCOPIC METHODS TO DIAGNOSE COLORECTAL NEOPLASIA

biofluids from patients undergoing colonoscopy. The aim of this is to identify changes in the chemical structure of normal vs. cancerous samples, which will be used to detect and monitor cancer non-invasively. A major outcome of the project is to establish a new detection method and develop a new research partnership of interdisciplinary and translational nature.



What was Achieved?

1. This work resulted in a new collaboration with colorectal surgeons. A total of 42 serum samples have been analysed – 23 patients with CRC vs. 19 with a non-cancer diagnosis, such as adenoma or diverticulosis. There was a difference in median age [range] of CRC patients compared to controls (74 years [61-86] versus 55 [range 32-78], $p = 0.0004$), but not in gender. PCA and LDA were able to identify variations in the FTIR spectra and distinguish between normal and CRC samples with 85% sensitivity and 78% specificity.
2. Spectral data collected, interpreted and validated.
3. Chemometrics analysis performed to identify differences and similarities between the cancer and normal cohort using Principal Component Analysis (PCA), Linear Discriminate Analysis (LDA) and Cluster Analysis (CA).
4. Abstract submitted to Association of Coloproctology of Great Britain & Ireland 32nd Annual Meeting 2021
5. A manuscript is being written and will be submitted for peer review soon.

PhD Studentship:

From this work, a new PhD studentship has been allocated to extend this work to upper GI and a project entitled, "biofluid spectrometry as an alternative non-invasive tool for the diagnosis of oesophageal adenocarcinoma (OAC)" is ongoing. A clinical Fellow (surgical registrar) is working on this project. OAC and Barrett's oesophagus carry a significant burden of morbidity to the patient and to the health economy. OAC is often diagnosed at a late stage and is thus related to a high mortality rate. It is evident there is a need for a reliable, cost effective and non-invasive method of diagnosing OAC in its early stages. Spectroscopic analysis of biofluids may fulfil these requirements and therefore warrants further study for this clinical application.

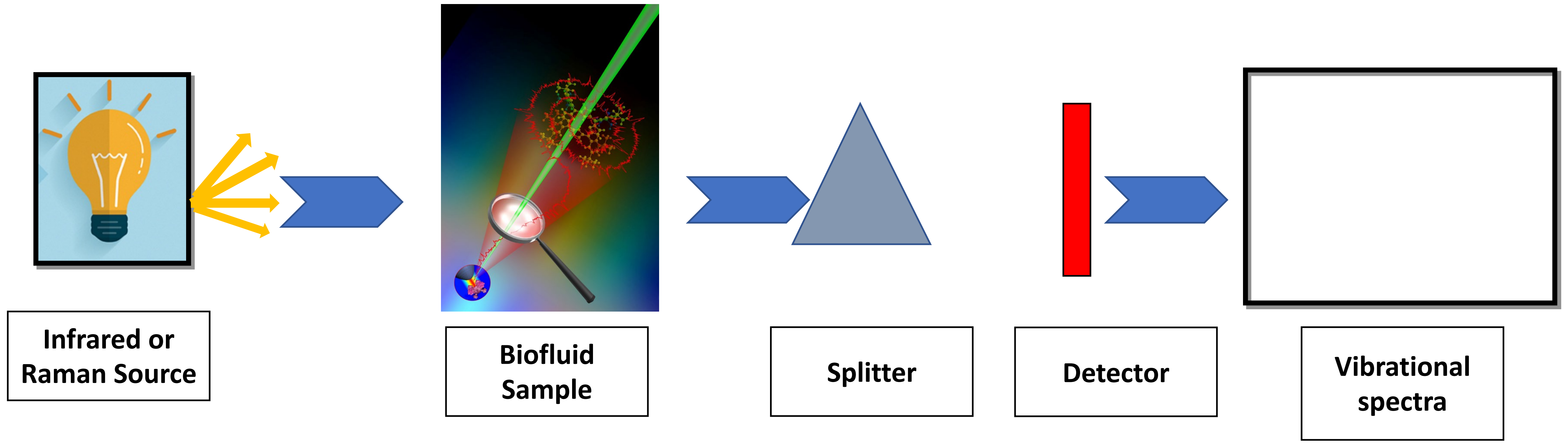
Follow on funding:

1. We secured small research pump priming grants funding of £10K from The Royal College of Surgeons of Edinburgh. This funding was for the clinical nurse time and retrieval/collection of liquid biopsies from the patients.
2. Knowledge gained from these studies was used to apply for Innovate UK funding with an industrial partner (Glyconics) and secured funding for the development of a Cloud-based real-time screening capability for the presence of the COVID-19 virus in nasopharyngeal swabs using Mid-InfraRed spectroscopy.
3. Secured funding for a project entitled Infrared Spectroscopy and Artificial Intelligence to disrupt the status quo in Cervical Cancer Screening form Canadian Cancer Society/Canadian Institutes of Health/Brain Canada Spark Grants: Novel Technology Applications in Cancer Prevention and Early Detection. This will involve use of IR and Raman spectroscopy to detect high-risk HPV in urine and be a disruptive technology to detect cervical intraepithelial neoplasia 2 or worse disease (CIN2+).

PROJECT: NON-INVASIVE SPECTROSCOPIC METHODS TO DIAGNOSE COLORECTAL NEOPLASIA

What's Next?

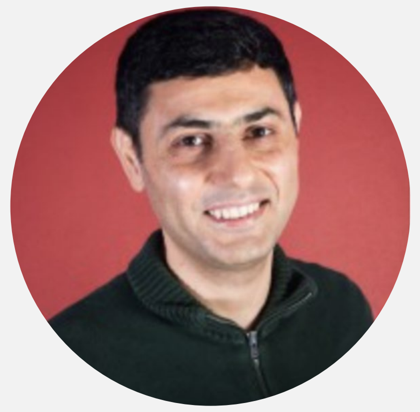
Our ultimate goal is to take "developed technologies from "lab to bedside" to address healthcare challenges. We plan to further progress our early stage programme of activity by using Infrared and Raman spectroscopy of biofluids, which is relatively a new technology, being evaluated for clinical applications. This technology facilitates unique fingerprints of biofluids, yielding specific signatures for disease biomarkers. To date, spectroscopy of biofluids in large cross-sectional studies have shown high sensitivity and specificity in dementia, brain cancers and endometrial cancers. Early proof of concept studies have demonstrated enormous potential in number of diseases.
In addition, we have shown that spectroscopy can also differentiate between microbes based on the signatures of their chemical properties. We have developed a number of new collaborations to explore use of spectroscopy to analyse liquid biopsies (saliva, blood serum and urine) for exploring oncology, gynaecology, urology, upper and lower GI, breast, oral and lung cancers disease.
This subject area is rapidly increasing.



Spectral analysis of biofluids

> *"Raman spectroscopy facilitates unique fingerprints of biofluids, yielding specific signatures for disease biomarkers and potentially transforming non-invasive early detection of cancer.*

MAIN PROJECT INVESTIGATORS



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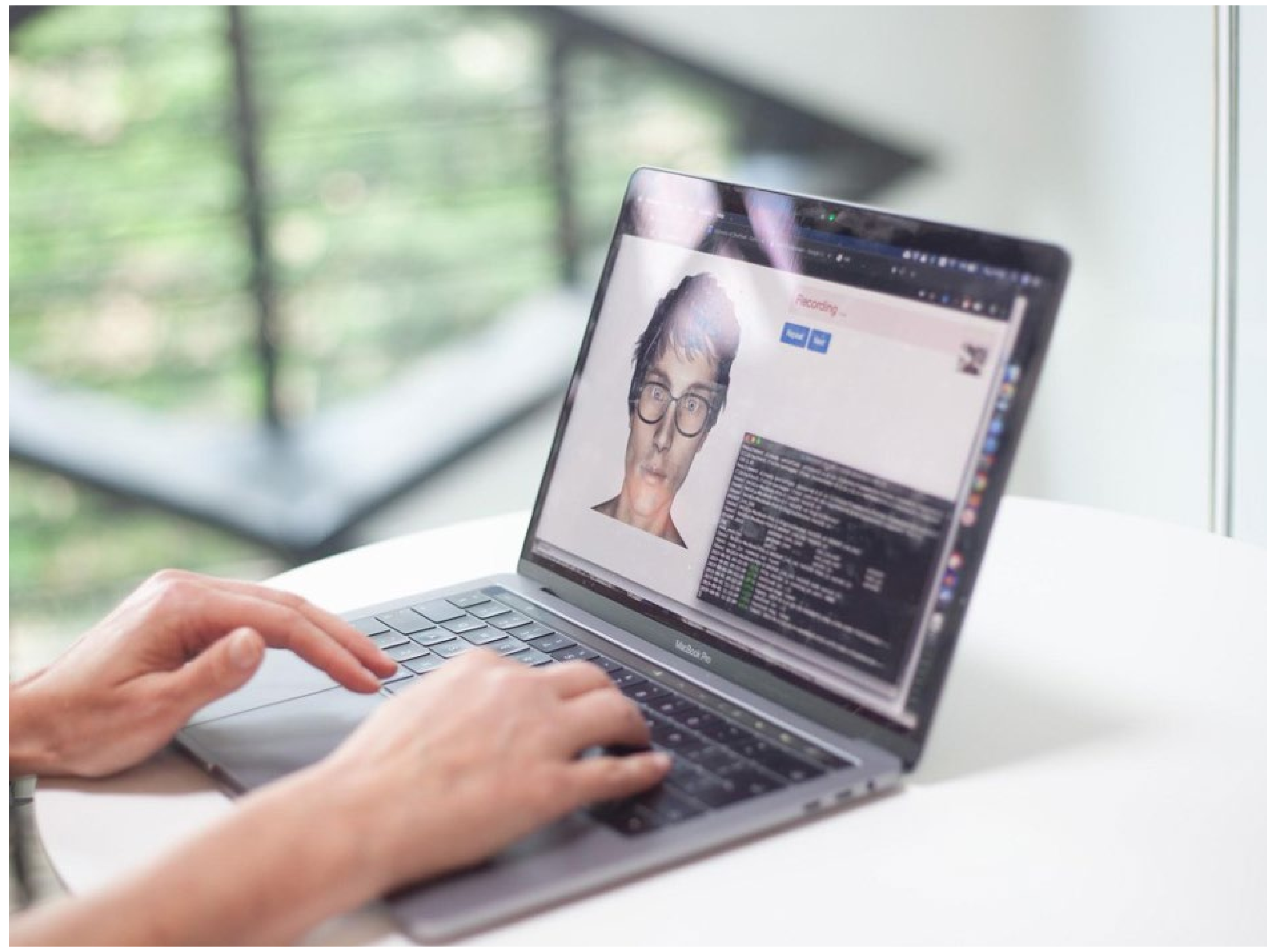
PROJECT

COMPutational Assessment of Stroke Survivors Prototype (COMPASS-proto)

1ST SEPTEMBER 2019 — 29TH FEBRUARY 2020



Why is this Important?

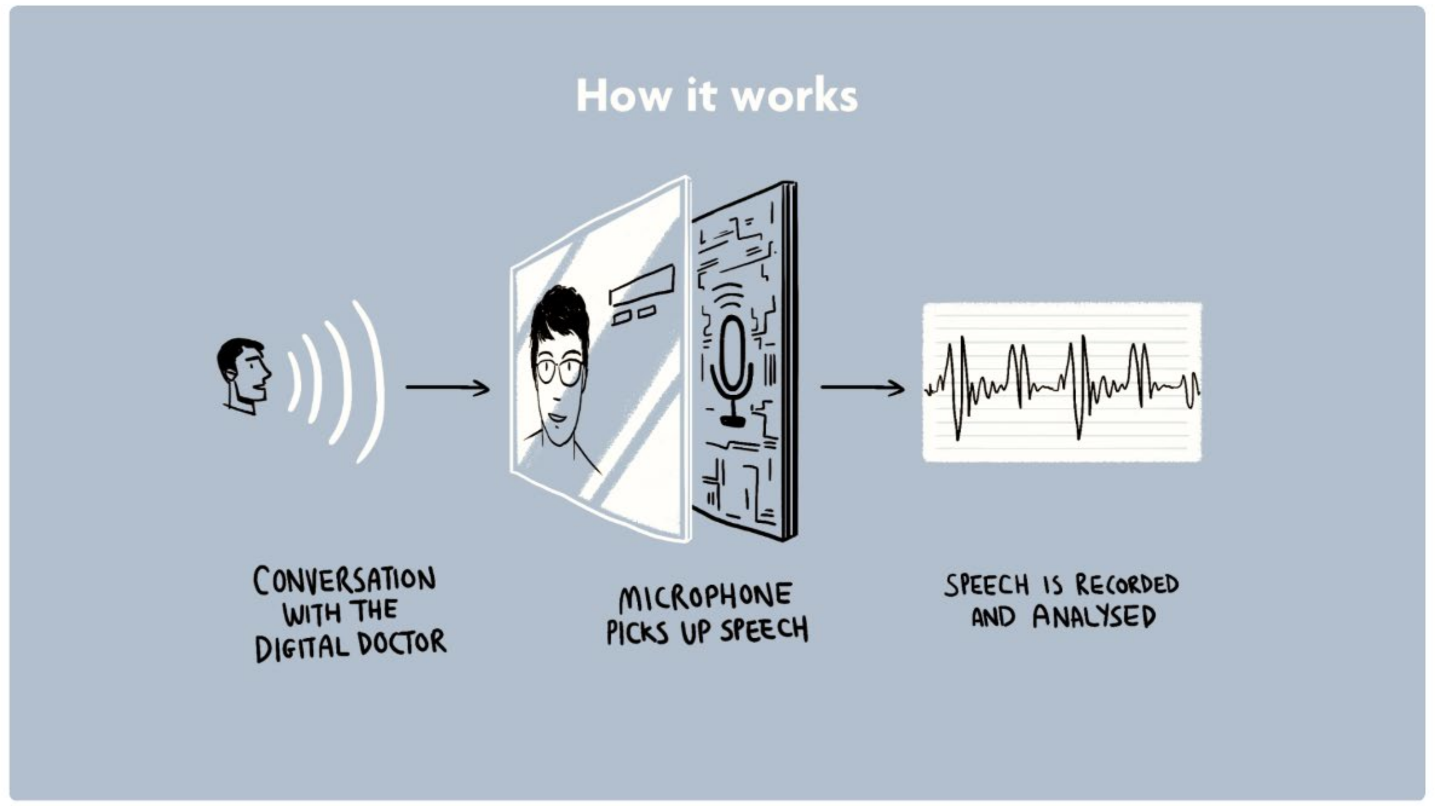
Stroke affects 152,000 UK citizens every year. Over 50% of stroke survivors have cognitive impairment. Currently 850,000 people live with dementia in the UK and stroke is one of the biggest risk factors. National guidelines promote early cognitive testing on all people who have had a stroke. However, current pen-and-paper based tests are not always appropriate for stroke survivors who often have motor, visual or language difficulties. Currently, assessments typically take place in hospital settings, are costly and often inconvenient for patients. In addition, longitudinal follow-up is required to detect emerging cognitive impairment.

This project aims to create an easy-to-use cognitive assessment tool specifically designed for the needs of stroke survivors. It will be based on our stratification tool COCOA (COmputational COgnitive Assessment), developed for detecting early signs of dementia.

PROJECT: COMPUTATIONAL ASSESSMENT OF STROKE SURVIVORS PROTOTYPE (COMPASS-PROTO)

The tool uses automatic analysis of conversations that patients have with an on-screen digital doctor. The patients' speech is analysed for signs of cognitive decline using speech recognition and machine learning classification.

The home-based testing tool can facilitate addressing the needs for "improved care pathways", "improved access to health services", and "efficient, cost effective healthcare systems". Web-based interface technology is applied for developing the tool.



Changing diagnostic pathways: There is an urgent need to ensure quicker access to specialist assessment for those most likely to benefit. We have developed CognoSpeak™, a tool that uses the automatic analysis of conversations that patients have with an on-screen virtual agent. Patients' speech is examined for signs of cognitive decline using automatic speech recognition, diagnostic feature identification and classification involving machine learning.

Speech and machine learning technologies are used to help clinicians with diagnosis. From clinical points of view, the system can help in continuous assessment of mental health, early diagnosis from multiple sources and recovery monitoring tracking cognitive impairment of stroke survivors.

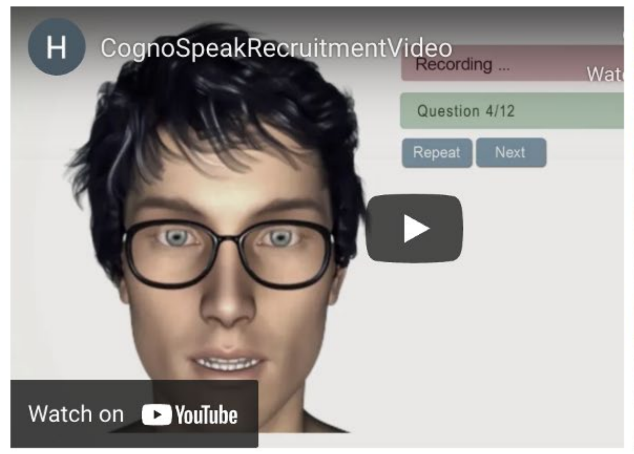
What was Achieved?

The stages of the study included data gathering, developing questions, developing the web-based tool, applying speech recognition and machine learning and speech analysis algorithms, publishing results, as well as applying for the follow-up funding.

The CognoSpeak system (www.cognospeak.org) asks a few conversational questions as well as the standard fluency and picture description cognitive tests. In the first stage of the study, the previous questions of the digital doctor were modified to capture more diagnostic features of people with stroke, targeting vascular cognitive impairment, especially executive dysfunction. Consulting our specialist in stroke, a new complex picture description question, a question of naming months of year in reverse, a question of describing steps of making a cup of tea were added to help in identifying signs of executive dysfunction questions. To identify their mood, two standard questionnaires (Ph9 and GAD7) were set for participants on the website as well a question about their future plan.

In order to track and monitor cognitive impairment over time, a number of predefined versions of the questions/tests were designed. The slight changes in the tests could reduce the effect of memorising

A person with memory problems using CognoSpeak™



PROJECT: COMPUTATIONAL ASSESSMENT OF STROKE SURVIVORS PROTOTYPE (COMPASS-PROTO) FAST HEALTHCARE CALL FAST DIGITAL HEALTH FOR REMOTE MONITORING AND SELF-MANAGEMENT

questions. The conversations were video and audio recorded online and then were transferred automatically to a server to be analysed.

Due to the effect of pandemic on our study, data collection was slow. So far two survivor patients and seven healthy survivors have had the online recordings at their home. Since the number of data gathered is limited, we have not completed yet processing and analysing the results of speech recognition and MI algorithms. As the number of data gathered increases, the recordings will be manually transcribed for the gold standard of automatic speech recognition.

Meanwhile we focused on more analysis of our previous data sets and published (or are publishing) a number of papers.

The FAST Healthcare funding helped us to provide the prototype of COMPASS and apply for follow-up funding for the whole project. We successfully gained funding for the project from three sources: £125k from Rosetrees Trust International Prize matched by £48k from The University of Sheffield Knowledge Exchange and £17k from NIHR Clinical Research Network. The project covers three years of study from March 2020 till Feb 2023.

The list of publications:

Mirheidari, B., Blackburn, D., O'Malley, R., Venneri, A., Walker, T., Reuber, M., & Christensen, H. (2020). Improving cognitive impairment classification by generative neural network-based feature augmentation. Proc. Interspeech 2020, 2527-2531.

Pan, Y., Mirheidari, B., Reuber, M., Venneri, A., Blackburn, D., & Christensen, H. (2020). Improving detection of Alzheimer's Disease using automatic speech recognition to identify high-quality segments for more robust feature extraction. Proc. Interspeech 2020, 4961-4965.

O'Malley, R. P. D., Mirheidari, B., Harkness, K., Reuber, M., Venneri, A., Walker, T., ... & Blackburn, D. (2021). Fully automated cognitive screening tool based on assessment of speech and language. Journal of Neurology, Neurosurgery & Psychiatry, 92(1), 12-15.

Walker, G., Morris, L. A., Christensen, H., Mirheidari, B., Reuber, M., & Blackburn, D. J. (2021). Characterising spoken responses to an intelligent virtual agent by persons with mild cognitive impairment. Clinical linguistics & phonetics, 35(3), 237-252.

What's Next?

In the following months we are focusing on data gathering over time to monitor and track the signs of cognitive decline. We will be improving our MI and speech technology methods and publish the results of analysis on data.

The findings of the study will help us to demonstrate applicability of our system to help clinicians in diagnosing cognitive impairment and keeping track of patients' states over time.

"Our tool uses automatic analysis of conversations that patients have with an on-screen digital doctor to assess for cognitive decline.

Multiple workshops have helped us design CognoSpeak™. We have worked with people with memory concerns, their care-partners and families as well as with GPs, nurses, occupational therapists, neurologists and psychiatrists.

MAIN PROJECT INVESTIGATORS

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PROJECT

Using iKOALA To Sustain Physical Activity for Long-Term Self-Management of Osteoarthritis

1ST NOVEMBER 2019 — 30TH SEPTEMBER 2020

Why is this Important?

The societal burden of Osteoarthritis is considerable, with 8.75m people having sought treatment. Osteoarthritis accounts for 98% of knee replacements and individuals with musculoskeletal conditions report lower quality of life than individuals with diabetes/cancer. Physical activity and exercise are proven to be beneficial for pain, function and quality of life for Osteoarthritis. However, delivering supervised interventions is resource intensive and gains made during structured programs often decline once complete.

Smartphone apps provide a promising opportunity to allow flexible rehabilitation options that move beyond available digital structured programmes Although these programmes are highly effective, they are of a fixed duration and lack flexibility, personalisation and social support which can empower patients to take control of their care.

We assembled an interdisciplinary team, combining knowledge in physical activity, behaviour change, rehabilitation and human-computer interaction to develop the intelligent Knee Osteoarthritis Lifestyle App (iKOALA). The aim of the project was to involve both potential app users and physiotherapists as co-creators of the app,

PROJECT: USING IKOALA TO SUSTAIN PHYSICAL ACTIVITY FOR LONG-TERM SELF-MANAGEMENT OF OSTEOARTHRITIS

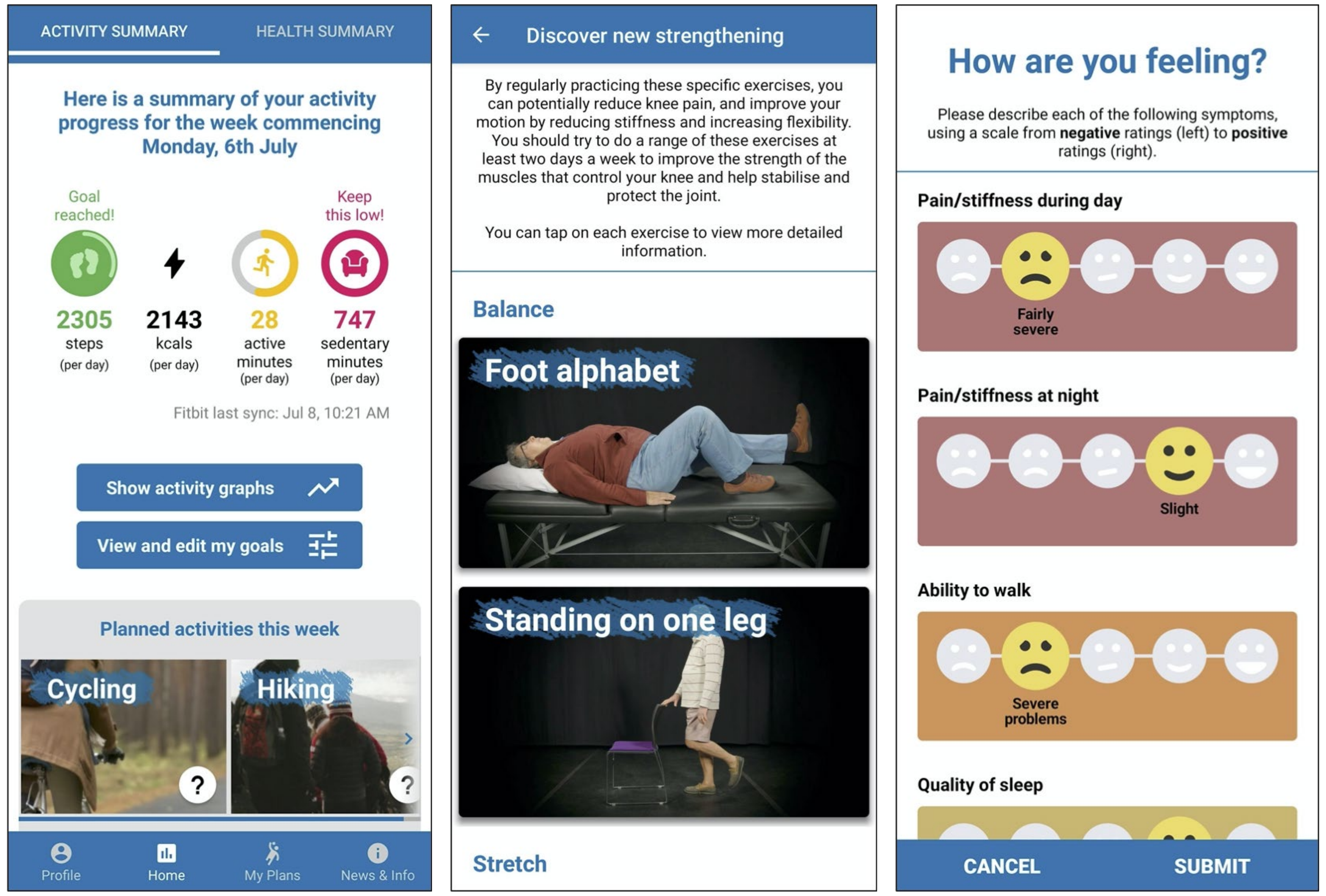
to ensure it met clinical and patient needs. We hoped to capitalise on the potential for data capture through the app, to produce a highly tailored product that responded to users' preferences and capabilities to provide tailored feedback and intelligent activity recommendations.

What was Achieved?

Funding from the FAST Healthcare Project allowed us to formalise a new collaboration amongst members of the Bath University team with Professor Nicola Walsh from UWE. Prof Walsh is a Professor of Knowledge Mobilisation and Musculoskeletal Health and brought unique experience of musculoskeletal rehabilitation and innovative treatment models to the project team. Funding from the Network also allowed us to employ a software engineer, Mr Victor Ceballos Inza, to undertake the app development.

We followed an established methodology for developing health interventions called the "Person Based Approach". Initially, we rapidly reviewed information from the academic literature and clinical guidelines relating to physical activity and Osteoarthritis to determine appropriate evidence to incorporate into our app. Alongside this process we conducted focus groups with individuals with knee problems to determine the needs of potential app users. Physiotherapists were also individually interviewed to establish which physical and psychosocial factors were deemed important to account for in providing activity options from a clinical perspective. Potential app users highlighted uncertainty regarding the risks/benefits from activity and uncertainty regarding appropriate sources of information. App users highlighted symptom tracking as a key feature and social support as an important factor in motivation for activity. Both app users and physiotherapists emphasised the importance of tailored options accounting for individual capabilities and preferences.

Combining the information from users/clinicians and the academic evidence, we undertook an intensive period of app development, incorporating desired features and established behaviour change techniques. Features included feedback from linked wearable activity trackers; information and intelligently tailored physical activity options form user preferences and symptoms. Broader self-management aspects include rehabilitation exercise content, symptom tracking and alerts, weight management tools and education resources. Crucially, for long-term maintenance, the app includes forum features, fostering social relatedness among users.



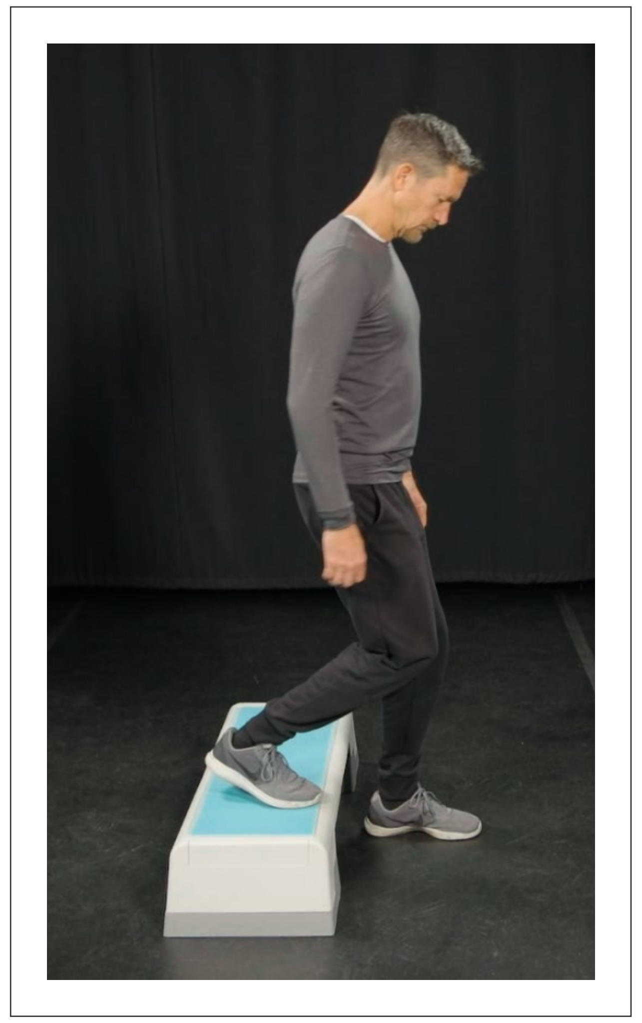
PROJECT: USING IKOALA TO SUSTAIN PHYSICAL ACTIVITY FOR LONG-TERM SELF-MANAGEMENT OF OSTEOARTHRITIS

Following initial development, we undertook "think aloud" interviews with potential app users to assess app usability and perceived usefulness and made ongoing improvements based upon feedback based upon short exposures to the app. We also undertook interviews with physiotherapists to validate the perceived appropriateness of the content and features of the app. From these ongoing evaluation activities we were able to establish that the app is positively received by potential users and deemed to be appropriate, safe and beneficial by clinicians. We are currently assessing the "real world" efficacy of the app in a longer user deployment and evaluation phase.

What's Next?

The funding from the Fast Healthcare Network has allowed us to produce a fully functioning Android prototype iKOALA app. The app has been informed by best evidence and co-created with potential users and with clinical input. The app has undergone extensive ongoing evaluation and has been positively received by both potential users and physiotherapists.

We now hope to move to the next stages of translating the research innovation that has been made possible by the FAST network to a deployable product for enabling widespread impact. In order to do this, we hope to undertake larger and longer evaluations of the app and seek to develop a scalable version of the app with a commercial partner. We hope the iKOALA app could be used directly by interested individuals or potentially integrated with in person clinical care. In the future, we hope that the principles and innovations within the iKOALA app could be applied to other conditions.



> ***"By combining information from users and clinicans with academic evidence, we have developed an innovative app which can provide individuals with Osteoarthritis a personalised tool to help them be active and better manage their condition.***

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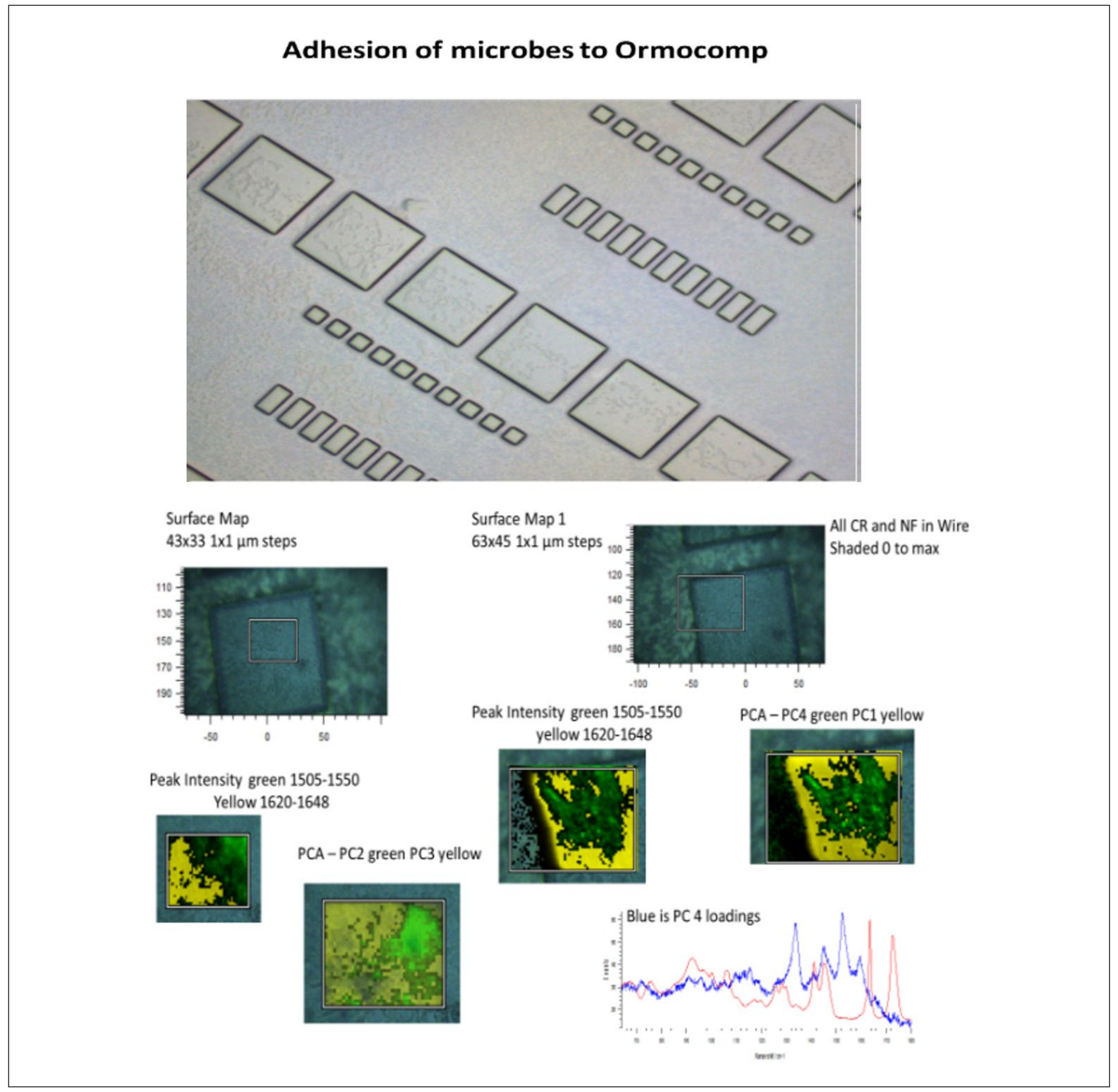
PROJECT

Advancing the understanding of Biofilms with Raman Spectroscopy

1ST AUGUST 2019 — 30TH JANUARY 2020



Why is this Important?

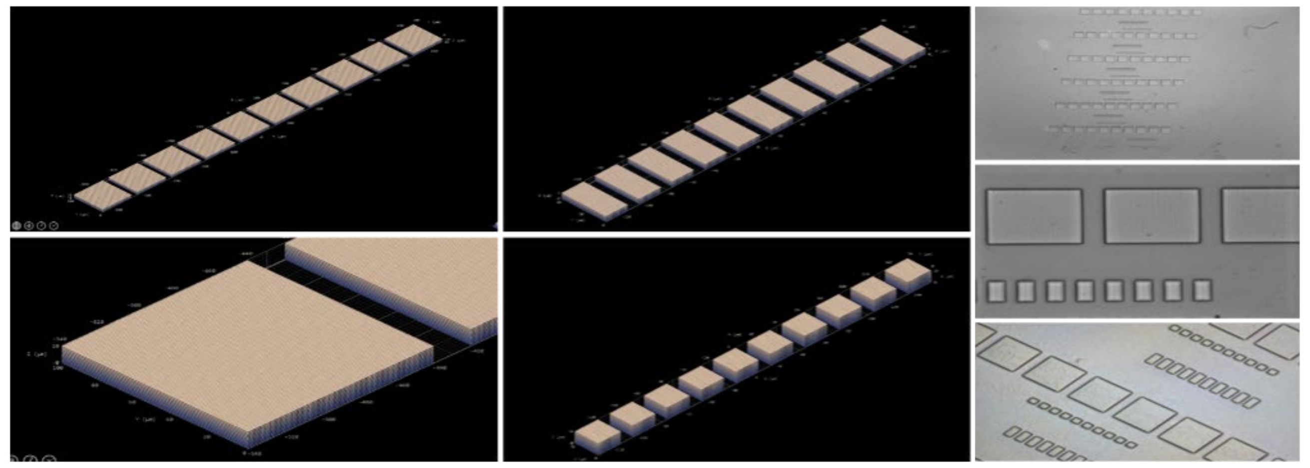
This study was to investigate Raman micro-spectroscopy - combined with chemometric analysis to understand the dynamics of biofilm accumulation in a 3D construct developing an in-vitro model to study antimicrobial resistance (AMR). Biofilms are a big problem for hospitals as many bacterial infections that form biofilms are more difficult to treat. Biofilms are a structured consortium of microbial cells encased in a matrix of extracellular polymeric substances (EPS) and once established; no current antimicrobial therapy can fully eradicate the biofilms. One cause of the recalcitrance of mature biofilms to antimicrobials is attributed to the EPS matrix, a highly hydrated mixture where chemical species including proteins, polysaccharides and DNA which may prevent the antimicrobial from reaching the bacterial cells embedded in the matrix. 3D scaffolds using OrmoComp®, a polymer which have been widely used for cell culture experiments and combined this with a recently developed semi-dry-surface biofilm model were fabricated. Staphylococcus aureus ATCC 25923 was grown onto the scaffolds using a batch phase at 5% Tryptone soy broth followed by long dehydration over 288hrs. The 3D in vitro model biofilms were investigated with Raman micro-spectroscopy combined with chemometric analysis

PROJECT: ADVANCING THE UNDERSTANDING OF BIOFILMS WITH RAMAN SPECTROSCOPY

to understand the dynamics of EPS accumulation in biofilms. The potential of Raman imaging to identify matrix components along with their spatial distribution within biofilms, which will be useful in devising ways to weaken biofilms and increase their susceptibility to antimicrobials, has been investigated.

What was Achieved?

We successfully fabricated scaffolds suitable for biofilm formation: Designing of different scaffolds using two-photon polymerization direct laser writing (DLW) and direct ink writing (DIW) methods. Figure 1:



AutoCAD file depiction of array of large and single square ridges (100X100X10µm)

Figure 1: Fabrication of 3D scaffolds by using **OrmoComp®**, a commercially available inorganic-organic hybrid polymer using **Direct Laser Writing (DLW)**, Initially, square and rectangular ridges of different dimensions were fabricated using **AutoCAD** followed by **Photonic Professional GT (Nanoscribe GmbH)**.

In addition, we obtained Raman spectra of the scaffolds to establish baseline data and compared it with the spectral peaks of nucleic acid and proteins that act as biomarker peaks in biofilm formation.

Spectra of bacteria were also obtained on the scaffolds confirming the attachment of bacteria on Ormocomp (Figure 2). Investigation of bacteria-scaffold attachment EPS depositing of Staphylococcus aureus Gram-positive biofilm using Raman spectroscopy was performed and biofilm development and interaction with scaffold surface was investigated.

In this study, it was demonstrated that Confocal Raman Microspectroscopy could be used to visualise S. aureus semi-dry biofilm distribution indirectly by carotenoid mapping. 3D Raman mapping of polymer and biofilm complexes might be helpful in understanding host environment and biofilm relationships starting with, but not limited to, biofilm formation, mechanical stability and survival. These kinds of chemical imaging methods have significant potential in exploring EPS distribution and by connection, to studying the effects of therapeutics. In future studies, Raman Microspectroscopy may be employed to single and multiple microorganism biofilms at different culture time points to develop a comprehensive spectral database for biofilm types/states/maturities. This approach would be valuable in rapid identification and classification of biofilm infections and may lead to the development of biomarkers indicating the presence of biofilm. Volume mapping at different time points of biofilm growth under different experimental conditions will also allow us to explore effects on EPS distribution to elucidate the mechanisms of antimicrobial resistance and on developing ex vivo tissue engineered models of biofilms using single and multiple microorganisms, where they may be studied in biologically more relevant environments. This might be helpful in developing new strategies for AMR and in particular, in medical implant research.

A number of other micro-organisms were analysed and Raman spectra obtained.

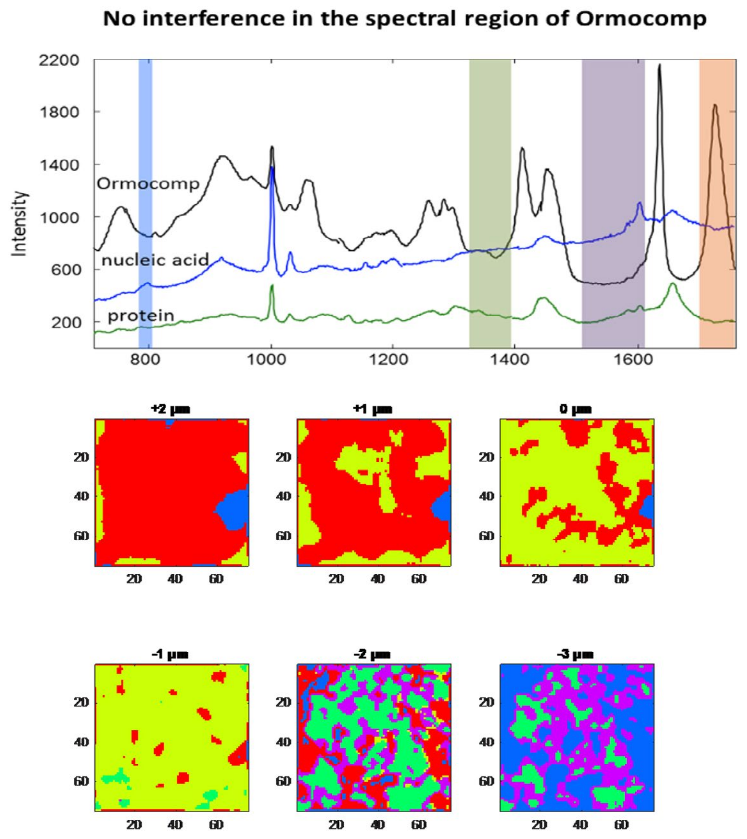


Figure 2: Raman spectra of Ormocomp and its comparison with spectral peaks of bacteria. On right, adhesion of bacteria on substrate is clearly visible

PROJECT: ADVANCING THE UNDERSTANDING OF BIOFILMS WITH RAMAN SPECTROSCOPY

What's Next?

Our ultimate goal is to take developed technologies from lab to bedside to address healthcare challenges.

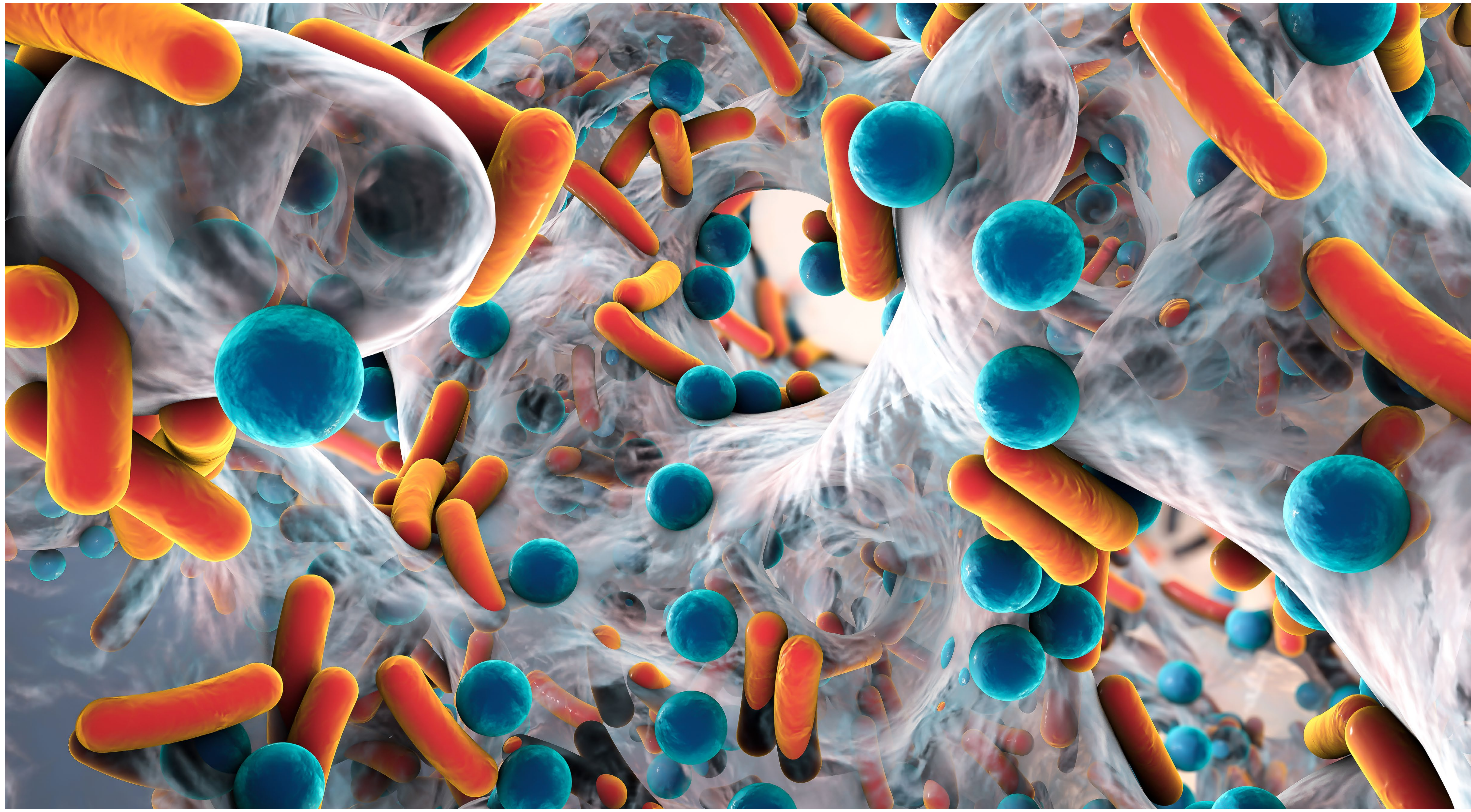
We plan to further progress our early stage programme of activity in AMR and extend spectroscopic techniques combined with Artificial Intelligence (AI), Neural Network (NN) and Machine Learning (ML) for tackling a broader number of major medical healthcare challenges.

To achieve this, we will:

1. Organise a one day workshop by inviting key players in this subject area and develop at least one platform research proposal.

2. Link up with experts in AI, NN and ML.

A paper has been submitted to Royal Society Journal: Interface.



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DermNet

PROJECT

Early detection of skin cancer by using mobile devices at point of care

1ST NOVEMBER 2020 – 30TH APRIL 2021

Why is this Important?

Although melanoma affects only a small number of individuals, it is responsible for a large number of deaths. In America, it is estimated that 207,390 cases of melanoma will be diagnosed in 2021, and the number of new cases will increase by 5.8%[13]. Diagnosing melanoma is difficult. Available applications currently track the mole as it changes without providing any automated opinions. A system, such as the one we are currently developing, can aid dermatologists in clinical decision making. This could potentially help to reduce the strain on already overburdened healthcare systems.

Currently, the annual ISIC[14, 15] demonstrates the current state-of-the-art in skin lesion diagnoses. However, concluding this is difficult as the techniques are varied. We demonstrate a firm baseline by comparing off the shelf networks under the same settings allowing for a fair comparison between models.

The project focuses on using Electronic Health Records (EHR) and combining them with Artificial Intelligence (AI) to create an automated framework for early skin lesion diagnoses. Our method include global pattern in deep learning model training. It leverages dermosopic images and anatomic sites to make an informed decision of lesion diagnoses, focusing on melanoma detection. We then demonstrate this technology by integrating the trained AI model onto a mobile device to demonstrate a point of care application of these techniques. To improve the reception of our techniques with dermatologists, who give gold standard feedback, we use explainable AI methods to demonstrate how the AI are making the decisions.

What was Achieved?

FAST Healthcare helped to establish collaboration between Manchester Metropolitan University, AGH University of Science and Technology, and The Dermatology Centre. We completed the following two key pieces of research (Figure 1):

13 Society, A.C., 2021 American cancer society. Cancer statistics center; https://cancerstatisticscenter.cancer.org

14 Noel Codella, Veronica Rotemberg, Philipp Tschandl, M. Emre Celebi, Stephen Dusza, David Gutman, Brian Helba, Aadi Kalloo, Konstantinos Liopyris, Michael Marchetti, Harald Kittler, Allan Halpern: "Skin Lesion Analysis Toward Melanoma Detection 2018: A Challenge Hosted by the International Skin Imaging Collaboration (ISIC)", 2018; https://arxiv.org/abs/1902.03368

15 Tschandl, P., Rosendahl, C. & Kittler, H. The HAM10000 dataset, a large collection of multi-source dermatoscopic images of common pigmented skin lesions. Sci. Data 5, 180161 doi:10.1038/sdata.2018.161 (2018).

PROJECT: EARLY DETECTION OF SKIN CANCER BY USING MOBILE DEVICES AT POINT OF CARE

1.

We curated all ISIC datasets by removing the duplicates and overlapping images. We followed ISIC's guidelines on their duplicate image lists. However, following our own duplicate checks, we found the reported duplicate totals did not tally with those reported by ISIC. Thus, we performed a full dataset analysis, checking for duplicates both within and between datasets on ISIC 2016 – ISIC 2020. Image hash techniques and UMAP[16] were used to curate and visualise the data distribution. We are currently writing a research paper to report this analysis and benchmark the curated dataset with popular deep learning algorithms.

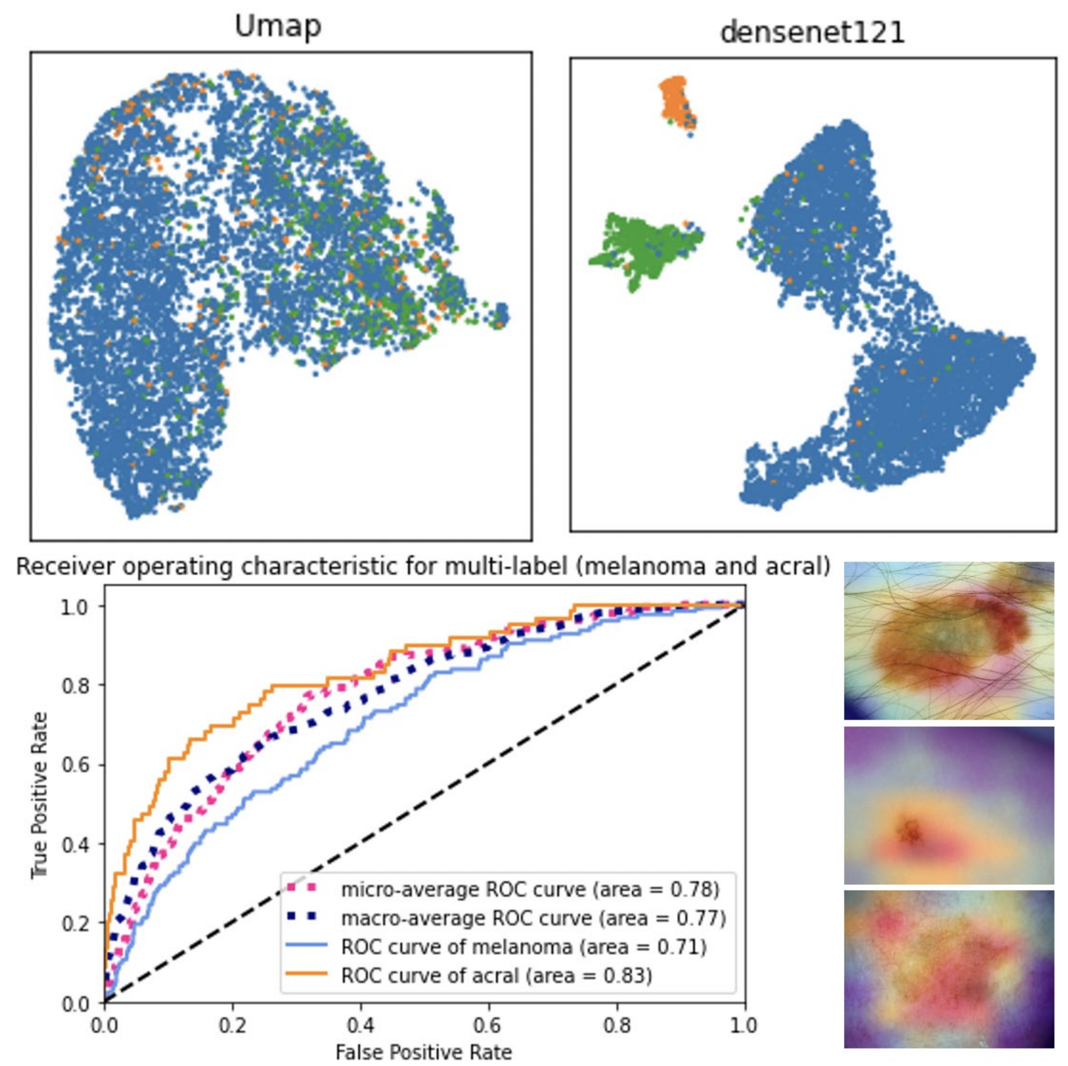

Figure 1

Deliverables: A journal paper in preparation, to be submitted to Special Issues on Image Analysis in Dermatology, Medical Image Analysis.

2.

We performed three experiments to evaluate the anatomic sites of the skin lesion in melanoma detection. First, we used the performance of the deep learning networks in detecting the anatomic sites of the skin lesion (trunk, head and acral). We obtained high accuracy using DenseNet121 and EfficientNetB0, with GradCAM visualisation[17] showing that the model used surrounding skin to make its decision. We then studied the accuracy of the neural network in detecting melanoma on full HAM10000, and study the effect of anatomic sites by removing acral from the full dataset. We found the anatomic sites play a role in melanoma prediction. Finally, we performed a test on multi-class classification on both the prediction of melanoma skin and anatomic sites, where we found it was a more challenging task when compared to one versus all network.

Deliverables: A conference paper to be submitted to CVPR 2021 ISIC Workshop.

We have developed a Melanoma Artificial Intelligence Application (MAIA) (see Figure 2). Due to social distancing, we will not be able to run the usability study.

Figure 2

Additionally, two early career researchers and a PhD student were involved in this project. This project provided opportunities to train young researchers in research and expand their national / international network.

What's Next?

This project achieved the majority of its objectives apart from the usability study of the MAIA mobile app due to COVID-19 pandemic. The next stage is to port our best performing models onto mobile devices, which will lead into a short evaluation where clinicians will test the system in a clinical setting and give their feedback on its performace. We are discussing with Dr. Matthew Harries from the Dermatology Centre Manchester, on the potential to provide advice and feedback on the app. We will seek further funding (such as Pfizer, British Skin Foundation and larger scale international collaboration grant) to support further development of MAIA.

> ***By combining Electronic Health Records with photos from phones and AI for analysis we have created an automated framework for early skin lesion diagnoses.***

16 McInnes, L., Healy, J. and Melville, J., 2018. Umap: Uniform manifold approximation and projection for dimension reduction. arXiv preprint arXiv:1802.03426.
17 Selvaraju, R.R., Das, A., Vedantam, R., Cogswell, M., Parikh, D. and Batra, D., 2016. Grad-cam: Why did you say that?. arXiv preprint arXiv:1611.07450.

MAIN PROJECT INVESTIGATORS

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COLLABORATORS

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PROJECT

Human Factors resources for FAST healthcare

1ST FEBRUARY 2021 – 31ST MARCH 2021

Why is this Important?

Many novel health technologies are developed without sufficient understanding of the needs, values, and practices of the intended users. Focusing on the engineering challenges, human factors work is often considered an afterthought, if at all. As a result, healthcare solutions are developed that solve the "wrong" problem or do not meet a particular need for healthcare workers and miss valuable opportunities to create greater impact. The interfaces themselves may be difficult for users to use, which lead to users developing workarounds or not even using the device as current methods are easier. Human factors is a research field that investigates users' needs within the correct context to improve understanding and improve the impact of technology. Within healthcare, this requires undertaking evaluation within relevant contexts such as clinics, hospitals, surgical theatres, and patients' homes and then iteratively developing technologies to address users' needs that are systematically evaluated at each stage.

One of the biggest issues faced by engineering groups is that human factors are only introduced towards the end of development when user testing commences and issues are identified, at which point the cost to make changes is high. The aim of this project is to provide FAST engineers with human factors resources which include mixed method approaches to better understand the needs of healthcare professionals and patients and identify barriers end users face in a given context. These resources will present what mixed methods are available, when these methods should be applied, and how to use each of these methods. Incorporating human factors within FAST healthcare will improve product development and user satisfaction for products, by designing them to address an identified user need. By providing this information, specifically for working within the context of healthcare, engineering teams will be able to include human factors approaches earlier in the development process.

PROJECT: HUMAN FACTORS RESOURCES FOR FAST HEALTHCARE

What was Achieved?

To achieve this a website is being developed that includes a handbook of human factors mixed methods and evaluation techniques best suited for healthcare product development and aimed at FAST engineers. This resource will be a reference that can be utilised during the initial stages of development so that engineers can include human factors to their product development process. The resource is designed to explain how these mixed methods and evaluation techniques are conducted, and provides examples and additional supporting documentation. Each section will also include a supporting video as a 'quick reference' to each method.

A suggested process map is also included detailing when each method or evaluation should be conducted and how each of these leads to improved outcomes of product development. Doing so allows the FAST engineers to include these items into their timelines, and ensures that human factors is not overlooked.

What's Next?

This project has received additional support from the Wellcome/EPSRC Centre for Interventional and Surgical Sciences (WEISS) (Wellcome Trust [203145Z/16/Z]), who develop innovative engineering solutions for clinicians to improve patients' wellbeing. This additional support will carry this work forward to develop a richer resource for both FAST and WEISS engineers. With the additional support we plan on extending the website and its resources to include new methods and supplementary materials and documentation as they are developed. We also propose to present this work at a symposium planned for June 2021, to further showcase the website and highlighting the importance of incorporating human factors early when developing healthcare products.

If FAST and WEISS engineers understand the added value of including human factors, and the mixed methods that can be used to identify users' needs and barriers, projects moving forward should have shorter roll-out times. This will result in less time being spent on iterating design concepts or resolving late user interaction issues, which should lead to improved clinical practices to benefit patients.

You can find out more about how to include human factors in your research at www.ucl.ac.uk/interventional-surgical-sciences/human-factors-engineers

> ***Human factors help bring the users' needs to the forefront when designing novel health technologies, improving the chances of engineering solutions improving clinical outcomes.***

FAST HEALTHCARE NETWORKS PLUS

ANNUAL REPORT MARCH 2021

Conclusions

The EPSRC FAST Healthcare NetworksPlus has been able to support an enormously diverse range of projects from helping children with asthma to be more active to improved early detection of cancer. What are the top level things that we can learn from this?

CONCLUSIONS

Conclusions and Future Directions

The EPSRC FAST Healthcare NetworksPlus was set up with the aim of taking a systems-based engineering approach to enable improved patient treatment at lower cost through appropriate technological and medical advances. The Network has brought together researchers from a diverse range of backgrounds through our workshops to set out clinically-motivated research challenges and it has allowed new research teams to form to carry out initiator projects to build momentum.

By taking systems-based engineering as our common theme, the Network has a portfolio of projects covering some of the most pressing health conditions that individuals face in their lives: cardiovascular disease, cancer, osteoarthritis, stroke, asthma and even anti-microbial resistance. Engineering and physical sciences researchers have been able to make a difference in all of these areas, but only through effective collaboration with clinicians. In addition, the importance of engaging with the people who will be expected to use whatever is developed at the earliest stage is essential for long-term success, and this has been a persistent theme from the first workshop onwards.

Although the projects have been clinically very diverse, some common themes have emerged.

One is the opportunity that technology and AI is affording to allow people to be more precisely treated as unique individuals. The ability to collect personalised data and then compare this with what is known at population level opens up new possibilities for greater effectiveness of treatment at lower cost. This does not always need new physical technology: often we can use the data that is already generated around us or the hardware that currently exists for getting new data.

Another area is the power of longitudinal monitoring to understand an individual's condition over time. This creates new challenges for data management, data security and personal privacy; therefore a system-based engineering approach is essential, but the opportunities for optimising treatment of conditions like cardiovascular disease are significant.

And this provides a direction for where the FAST Healthcare NetworksPlus goes next.

In the main, medicine is largely reactive. We develop a new symptom and seek treatment. Our focus in FAST has been on optimising this. However, there has long been a desire to move towards a preventative approach where we try and keep people healthier for longer by assisting them to understand their general wellbeing and advising on appropriate actions that could be taken to ensure a higher standard of wellbeing for longer. Just as precision medicine is all about understanding people as individuals, the same is true for this emerging area of 'precision health'.

The University of Cambridge has therefore set up a new Strategic Research Initiative: the **Precision Health Initiative**. Precision health will need to place the lived experience of real people at its heart if it is to make a difference to society broadly. This new initiative will therefore build on the multidisciplinary experience of FAST but aims to draw in new communities of researchers from the social sciences in particular, and still with a strong systems-level understanding. This new initiative will launch in early 2022, and we hope that you will find further opportunities for collaboration as a result.

How to Connect

If you would like to find out more about any of the projects supported by the FAST Healthcare NetworksPlus, please either contact the relevant researchers directly, or e-mail info@fast-healthcare.org.uk and we can put you in contact with the right people.

You can also see videos about projects, read our extended workshop reports and find out more about the FAST Healthcare NetworksPlus at www.fast-healthcare.org.uk.

To find out more about the new Precision Health Initiative at the University of Cambridge, please see www.precisionhealth.cam.ac.uk or contact Professor Andrew Flewitt (ajf@eng.cam.ac.uk).

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Thanks are also due to all of the participants at our workshops for sharing their thoughts and to the speakers for the direction that they helped to give.

Finally, we would like to thank all of the members of the Network – we hope that you have found being part of this a real benefit to your research and we look forward to continued collaboration in the future.