Impact Objectives

- Deliver innovative technologies to support improved medical device design and patient diagnosis and treatment in the field of personalised cardiovascular medicine
- Train Early Stage Researchers through both their individual projects and network-wide activities

Making the CaSE for collaboration

*Project coordinators **Dr John Fenner** and **Dr Andrew Narracott** outline the background of this initiative – which is developing new personalised solutions for cardiovascular support – while director of R&D at collaborating organisation **LifeTec Group**, **Dr Marco Stijnen**, explains the key role that industry partnership plays in the project*

Clockwise from top left: Dr John Fenner, Dr Andrew Narracott and Dr Marco Stijnen

Could you explain the origins of VPH-CaSE, and how the research projects within it were chosen?

JF: VPH-CaSE is built on the foundations of collaborations between individual research groups and the success of a previous Marie Curie Training Network, MeDDiCA. Dr Andrew Narracott and I led the funding proposal from the University of Sheffield, UK, with strong support from the network of academic and industrial beneficiaries. Identification of the focus for the 14 individual research projects that form the foundation of the network research programme required a collaborative approach that could exploit clusters of research activity. Synergies between research interests were identified, as well as clinical and industrial targets for translation of the research outcomes.

VPH-CaSE has brought together influential institutions, both at an academic and industrial level. Can you outline how this collaboration is mutually beneficial?

MS: This project involves work in different specialities; from experiments on slaughterhouse hearts, to numerical simulations, to application of interventions on healthy or diseased human hearts. At LifeTec Group, we are working on improving knowledge about the heart in an experimental environment, and we can learn a lot from the simulation work that is being done at University College London (UCL), UK, for example. In return, the development of the numerical work will benefit from our experimental results, because it provides important information such as input for those models, which is hard to find in clinical settings. Not only are we collaborating on understanding the healthy heart, but jointly we are trying to mimic diseased hearts so that other institutions, such as Eindhoven University of Technology (TU/e), Netherlands – who are working on devices to support a failing heart – will also benefit from validation studies. This interconnectivity ensures the different projects receive valuable feedback from each other.

How important do you consider initiatives like this to be for Early Stage Researchers?

AN: It is very important for researchers to develop a balanced set of skills to ensure they have access to the best opportunities in a competitive job market. VPH-CaSE focuses primarily on ensuring researchers receive excellent training in core scientific and technical skills, but recognises that broader skills are also essential for their future employment. VPH-CaSE researchers benefit through development of these skills during their progression through the network training programme, and are able to evidence this to future employers through specific activities such as outreach events, or website and newsletter editorial roles.

As the project nears its conclusion, what will be its main outcomes?

JF: We will release an excellent cohort of individuals into the world of biomedical development to pursue the next stage of their careers in either academia or industry. Their track record in scientific publication will contribute to both their own careers, and support the future research of their host institutions. For industrial members of the network in particular, this activity will also result in novel products (software and hardware) and intellectual property for future exploitation.

How do you see this field developing in the near future?

AN: The state of the art continues to develop rapidly, driven by new technology and fundamental techniques, applied to clinical problems. VPH-CaSE develops physics-based approaches to provide a mechanistic description of physiology and pathology and inform the development of medical devices tailored to individual patients. Big data techniques, machine learning approaches and uncertainty analysis are increasingly being applied within healthcare research to improve understanding of outcomes across patient cohorts and develop empirical models to aid clinical decision making. The combination of mechanistic and data-driven approaches has the potential to extend *in silico* techniques to the level of full clinical trials, reducing the costs and risk associated with device development and delivery of healthcare.

Personalised care in a heartbeat

***VPH-CaSE**, a highly translational and collaborative project consisting of Early Stage Researchers working with industry and clinical partners, aims to advance the state of the art in personalised cardiovascular support*

Transfer of practical knowledge and data integration between distinct research areas is considered to be one of the biggest challenges in biomedicine, and one that hinders the development of technologies in critical care and diagnostic medicine. Work being undertaken within the Virtual Physiological Human (VPH) Initiative is attempting to integrate the huge amount of information generated in clinical research. At the same time, it is translating results into a framework of methods and techniques that allow investigation of the human body as a whole.

The team behind the VPH-CaSE programme

Dr John Fenner and Dr Andrew Narracott at the University of Sheffield, UK, were inspired to apply this approach to the training of Early Stage Researchers within a cardiovascular research programme based on VPH's core values. The result was VPH-CaSE (VPH – Cardiovascular Simulation and Experimentation for Personalized Medical Devices). This programme is a collaborative endeavour aiming to unite research interests and clinical and industrial targets. Crucially, it also aims to translate research into practice and train the next generation of researchers.

The network consortium identified 14 projects run by Early Stage Researchers (ESRs) with the potential to make waves in the field of personalised cardiovascular support and diagnosis, as well as promote effective and transparent communication at all levels of clinical research. VPH-CaSE builds on previous research of the consortium partners, who together have a successful track record of EU-funded research programmes, supported by strong international collaborations.

SUCCESS THROUGH COLLABORATION

VPH-CaSE researchers are exploring three key areas, namely cardiac tissue function and cardiac support; pathology and intervention of cardiovascular haemodynamics; and image-based diagnosis and imaging quality assurance. When designing novel clinical methods, ethical issues and the interests of patients are pivotal to the research, with industry providing a valuable perspective on commercial considerations. 'VPH-CaSE deals with all these aspects. Research is undertaken within an appropriate ethical framework with an open access policy to scientific publication, with all activity overseen by the network as a whole in the form of the Steering Committee, which includes representation of both academia and industry,' explains Narracott.

To the VPH-CaSE team, collaboration is essential for success. The project recognises the need to build a diverse skill set in its young researchers. Tailoring novel therapeutic methods and readying them for application in a clinical context requires a multidisciplinary approach. Traditionally, most researchers worked in exclusive niches, without focusing on translational skills, but Narracott thinks the broader approach of this project is crucial. This is particularly true of healthcare technology, as new developments require the support of the industries that will ultimately produce the new devices in question.

In partnering with non-academic institutions, VPH-CaSE is providing the ESRs with the skills required to thrive in a competitive environment. So far, this idea has been supported by the mobility of participating researchers in the form of collaborative secondments, as well as the critiques of their progress during network meetings.

REAL WORLD OUTCOMES

With this in mind, researchers within the programme are given the opportunity to reach further and explore their given project from an industrial and clinical perspective. This involves visiting organisations operating in their field, such as the CERMEP preclinical and clinical *in vivo* imaging centre, and EDAP-TMS, a 'global leader in therapeutic ultrasound'. This approach is expected to yield positive outcomes, not just for the personal development of the ESRs themselves, but also in terms of their output.

In fact, some of the partner organisations are already reaping the benefits of their young collaborators. 'In many cases VPH-CaSE projects represent an important step in ambitious research programmes that require the effort of multiple PhD programmes to support clinical translation,' explains Fenner. Such projects tend to be those that are addressing more fundamental questions,

and numerical analysis is a central element, supported by partner ANSYS. 'However, in some instances, techniques are being directly applied to existing clinical technologies within the project activity, supported by the hosting of VPH-CaSE researchers within the software company Therenva and phantom designer Leeds Test Objects,' he continues.

slaughterhouse. Not only does PhysioHeart provide an excellent platform upon which to test devices and therapies for heart disease, it also has the wider societal benefit of reducing the need for animal testing. In short, this project epitomises the good that can come out of collaborative projects such as VPH-CaSE.

"Research is undertaken within an appropriate ethical framework with an open access policy to scientific publication, with all activity overseen by the network as a whole"

Broadly speaking, however, the true impact of the project for heart disease patients will only be realised when findings from the project are translated together with clinical network partners.

NETWORK TRAINING

Throughout its course, VPH-CaSE is based around network-wide training activities, in which both clinical and industrial partners are invited to evaluate the progress of the 14 projects. The latest training activities saw encouraging improvements in the participants' communication and experimental skills. Of particular note was the network event in Eindhoven last October, which was a defining moment for the project so far. Each of the ESRs presented their work to an audience of their peers and senior representatives from the academic, industrial and clinical sectors, and the positive response from an external European Commission reviewer was encouraging and suggested the network was achieving its ambitions. Overall, the network event focused on bridging the gap between theoretical and applied knowledge, and involved participation in various ultrasound and circulatory experiments.

One other notable feature from the Eindhoven event was a demonstration by LifeTec Group (a member of the VPH-CaSE Consortium). LifeTec Group has developed PhysioHeart, a platform consisting of an isolated beating heart harvested from a

COMMUNICATION IS KEY

Dissemination is an important aspect of VPH-CaSE, and its integrated communication and engagement strategy extends its impact beyond mere research outputs. Heart disease is one of the biggest killers in the world, and as such it is something that touches the lives of practically everyone. The team behind VPH-CaSE see it as their responsibility to communicate their work to the wider public in a way that is accessible and understandable. They want non-scientists to feel as enthusiastic about the groundbreaking work they are undertaking as they do themselves.

As part of this effort, the ESRs are encouraged to publish newsletters and video material describing their individual work on the project's website, as well as via open access publishing routes, and within institutional repositories. They are also involved directly in the development of editorial policies for their scientific content. Furthermore, participation in events such as Sheffield's Festival of Life and UCL's Women in Engineering Taster Day provide opportunities for more hands-on dissemination to the general public.

VPH-CaSE will pave the way for a generation of researchers capable of using their careers to make a difference within their chosen discipline, and it will also contribute towards novel products for future industries. Fenner and Narracott want to see a cohort of VPH-capable scientists who are able to work in industry, clinical and academic settings, and are equally comfortable communicating their results with the public as with their fellow scientists. The project impact will be showcased to the scientific and clinical community as part of the final training activity in London, UK, in the summer of 2018.

VPH-CaSE Outputs

Further details of VPH-CaSE activities across all 14 research projects are provided in the Outputs section of the project website (www.vph-case.eu), which details Outreach, Deliverables, Newsletters and Publications.

Project Insights

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CONTACT

John Fenner
Andrew Narracott
Project Coordinators

E: j.w.fenner@sheffield.ac.uk
E: a.j.narracott@sheffield.ac.uk
W: www.vph-case.eu

PROJECT COORDINATOR BIOS

Dr Andrew Narracott has an MPhys in Physics and a PhD in Medical Physics from the University of Sheffield, UK. He has 17 years' experience of research projects with a biomedical engineering focus. These projects have addressed numerical simulation and experimental validation of cardiovascular mechanics and haemodynamics, with strong focus on national and international academic and industrial collaboration, including a six-month fellowship at the RIKEN Institute, Tokyo, Japan. He is Director of Operations for the Insigneo Institute for *in silico* medicine (www.insigneo.org).

Dr John Fenner obtained his PhD in laser-tissue interactions from the University of Glasgow, UK. Shortly thereafter, he pursued development of a 3D laser scanner for characterising artificial heart valves in the lab, leading to an increased interest in imaging, quality assurance and radiation physics. His enthusiasm for modelling led to involvement with the Virtual Physiological Human, providing an opportunity to work on real-world problems in collaboration with creative groups like those found in VPH-CaSE.