The major milestone since our last newsletter has been the Candidate Release of our infrastructure. We are now ready to focus our efforts more fully on the end user programme. The major event in this period has been the completion of our Year 3 review in Brussels on 23 May 2014. All deliverables were accepted, and the formal assessment was ‘excellent progress (the project has fully achieved its objectives and technical goals for the period and even exceeded expectations)’. This is a magnificent result for any Integrated Project, each of which represents significant financial investment and for which expectations are always high, and I take this opportunity once again to express my thanks to all of you who worked so hard to achieve it.

We spent several months planning the review, and this showed on the day. It would be inappropriate for me to single out individuals because it truly was a team effort, but there were some who hardly slept in the hectic days leading up to the review. We are indebted to three end users, Claudio, Daniel and Peter, who did a great job of presenting external clinical and industrial appreciation of the VPH-Share infrastructure. We wish to record our appreciation of the work done by our Project Officer and our Expert Reviewers, who established and maintained a positive and constructive atmosphere throughout the review process.

The major focus of your Project Board in the last period has been on planning for the sustainability of VPH-Share after the project ends in 2015. We asked for an extension of the project until the end of May 2015 to support additional efforts on the implementation of our sustainability plans, including further focus on our end user engagement programme. This has been accepted in principle, and we are requested to respond with to our Project Officer with further details of our future plans by 31st August.

We will have an open demonstration of our infrastructure at VPH2014 on September 9th to 12th in Trondheim, Norway. Many of our team have been successful in the acceptance of abstracts for this event and will be there to present and to support the demonstration. If you are unable to be there, I look forward to seeing you at the final General Assembly in Krakow next year.

Editorial:
Professor Rod Hose
VPH-Share Scientific Coordinator
News

General Assembly Meets in Bonn

VPH-Share held its fourth annual General Assembly in Bonn, Germany on 6th and 7th March 2014. Hosted by exploitation partners empirica, the GA focussed on reviewing the project’s progress from its third year in preparation for the annual review and planning for the final year of the project. Karl Streitmann and Rainer Thiel from empirica welcomed forty VPH-Share members to the Wolfgang Paul Hall, in the University Club building, in Bonn, before the meeting of individual workpackages. Every workpackage was represented, which allowed crucial work to be carried out, to drive forward progress on the VPH-Share infrastructure. The afternoon of the first day saw a meeting of the Project Board and the Review Action Group, chaired by Keith McCormack. There were opportunities throughout the day for further meetings within and between different workpackages, which allowed groups to iron out issues in preparation for the review. The first day culminated in the General Assembly dinner held at Restaurant Matthäus’s, a cozy neighbourhood restaurant, serving a modern take on traditional German cuisine. It was both well attended and enjoyed.

Friday morning saw a plenary session given by Rita Azevedo from TruST, the Translational Research Project. The Dutch project aims to deploy a nationwide IT infrastructure for data and workflow management, targeted specifically at the needs of translational projects – work that ‘translates’ scientific discoveries into practical healthcare solutions. Rita’s presentation was well received and stimulated valuable discussion.

The plenary session was followed by the official business of the General Assembly, which saw a request to the voting members regarding a three month extension of the project. The members were given eight weeks to consult with the other members of their institutions to decide whether they wished to support and/or be actively involved in an extension which would take the end of the project to May 2015. The vote went in favour, allowing the project to approach its European Project Officer to make an official request for a three month extension.

The fifth and final GA is due to return by the GM of the SwissNeuroFoundation and its project of curating an international database of images that are biometrically sound, non-invasive and publicly available.

In an unprecedented move, the reviewers had, in the lead up to the review, requested access to the infrastructure two weeks prior to the review date, in order to test VPH-Share’s services. While this resulted in an intense period of work to fine tune the system, the outcome was a success and the reviewers were happy with progress.

Rod Hose said: “this is a tremendous outcome for an Integrated Project, from which the expectations are high. I wish to record my personal thanks to all of you who worked so hard throughout the year, and particularly during the exceptionally intense period leading up to the review (most unusually our reviewers had requested live access to the system for the two weeks prior to the review). It would not be appropriate for me to single out individuals. But it is fair to say that putting in such great a deal of effort in so many areas, from the completion of technical and managerial deliverables, the development of the core infrastructure, the development of the applications and the integration of complex components, through to the detailed and strategic planning of the review itself. I wish also to thank our review team in Brussels, who came across as just… a Team, and who ensured that the work of the project was professionally presented to the expert reviewers.”

Of the clinical demonstrators he said: “I’m sure that you will all join me in extending special thanks to these individuals, each of whom gave up their time to travel to Brussels to support us at the Review (an even at the practice the day before) and each of whom gave a first class demonstration that really convinced the reviewers that we have developed a usable and valuable infrastructure and that we are serious about engaging with the community.”

The focus for the final year of VPH-Share will be ensuring that there is appropriate planning for sustainability so that its infrastructure and services remain available to the community after the project finishes.

INSINGEO’s First Anniversary Showcase

The Insigene Institute for in silico medicine celebrated its first anniversary with a showcase of its research, held in Sheffield on 8th May 2014. The event, which attracted national media attention, was an opportunity for the leaders of INSINGEO’s research projects to present an overview of their work – using scientific simulation as an approach to investigate disease mechanisms – to an audience of invited delegates from industry and healthcare. Introductory addresses were given by Scientific Director of INSINGEO, Professor Marco Viceconti, Pro-Vice-Chancellor for Engineering at the University of Sheffield, Mike Hounslow, and Medical Director of Sheffield Teaching Hospitals David Throssell.

Excellent Results from Review in Brussels

VPH-Share completed its Period 3 review in Brussels on Friday 23rd May 2014. The assessment from the European Commission Project Officer was that it has made excellent progress and the project should be allowed to continue without modifications.

VPH-Share’s presentation was kicked off by Scientific Director Rod Hose, who briefly described the project’s work during its third period before outlining the review recommendations. He was followed by leaders of all eight workpackages, who summarised their progress during the last 12 months.

The afternoon featured clinical demonstrations from three of VPH-Share’s usecases. Daniel Rüfenacht represented neurIST, Claudio Silvestro RT35, while Peter Elthes from the National Center for Spinal Disorders in Budapest presented MySpine. The demonstrations, which were designed to show that the VPH-Share infrastructure is ready for external users, were very well received.

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The year four review will be held in May 2015.

“FP6 @neurIST, a precursor of FP7 VPH-projects, established a variety of interesting products for clinicians. With the end of the project, interesting but not yet commercial products almost got lost in development. Thanks to VPH-Share, there is now hope for such products to be translated to clinical practice. Furthering clinical neurosciences is the mission of the SwissNeuroFoundation and its project of curating an international AneurysmDatabase. It could not have come at a better time. Our thanks to VPH-Share!”

Daniel Rüfenacht, July 2014

VPH-Share Issue 6

PM 36 Milestones

Milestone 8 (PM30): VPH-Share Parameter Estimation and Uncertainty/ Variation Modeling Strategies Released

Milestone 9 (PM30): Markov Languages Formally Represent Uncertainty and Parameter Variation

Milestone 10 (PM30): Exploitation Framework Available to all Project Partners

Milestone 11 (PM36): VPH-Share Service Bundle Candidate Release – Cloud, Data, Semantics and Access
### Exposure to Aneurysm Community at ICS

VPH-Share was able to publicise its services to the VPH community working on cerebral aneurysms, when it took part in the Interdisciplinary Cerebrovascular Symposium, Intercranial Stent Meeting in Zurich on 2nd June 2014. Organised by the Swiss Neuro Foundation, the three day event brought together key experts, to discuss questions in the field of cerebral aneurysm research. VPH-Share’s involvement was through invitation from Prof. Daniel Rüfenacht from Hirslanden Klinik, one of the organising partners, who earlier in the month had presented at VPH-Share’s third annual review. The event was divided into three themes the first day focused on devices and computational fluid dynamics, day two on disease understanding, while the conference closed with a session on imaging and analysis. Mari-Cruz Villa-Urriol, from VPH-Share’s computational workflows, was invited to represent the project. Her session gave an overview of VPH-Share’s portal and its relevance to using computational workflows for understanding cerebral aneurysms, in particular how the infrastructure could be used for shape analysis of aneurysms, using the @neuvST workflow. Mari-Cruz said: “overall there was a great exposure of VPH-Share and the feedback was really good.”

ICS 2015 will take place in the Gold Coast, Queensland, Australia. For more info see: www.ics2014.org

### RT3S Secures Patient Data via VPH-Share

RT3S (Real-Time Simulation for Safer Stenting) has been successful in its search for patient data, thanks to collaboration with VPH-Share. The project, which has developed a patient-specific probabilistic model for peripheral stent fatigue-fracture, called on members of the VPH community for CTA and MRA datasets.

The RT3S models are designed to reduce the risk of stents fracturing in leg arteries, by calculating their fracture risk. RT3S has developed computer aided planning software - AimoSimul - which allows interactive pre-processing of patient images to obtain 3D geometry of the vessel. It also allows clinicians to virtually deploy the stent on patients’ data to predict the fatigue fracture risk of the device.

RT3S was successfully completed in March 2014 and will now use VPH-Share to ensure its sustainability. It aims to increase both the number of users testing the application and its patient database. The VPH-Share infrastructure will provide the location needed to share data as well as easy access to the software. AimaSimul will be available through the secure VPH-Share portal and users will their Biomed Town details in order to log in.

For more information see: rt3s.eu

### Computational Biomedicine Book Launched

The eagerly awaited Computational Biomedicine textbook was officially launched in London on 16th June 2014 as part of the Computational Life and Medical Sciences Network Symposium 2014. The book, which is the first text for the student reader in the multidisciplinary field of computational biomedicine, was edited by Peter Covenev, Vanessa Díaz-Zuccarini, Peter Hunter, and Marco Vincenzi.

Published by Oxford University Press, the textbook contains contributions by VPH-Share members Rod Hose, Steven Wood, Nic Smith, Maria-Cruz Villa-Urriol and Suheel Varma, as well as founder of computational biomedicine Denis Noble. Chapter eight focuses on computational workflows and features VPH-Share as an example of how workflows can be run. The textbook, which is subtitled Modelling the Human Body works through the stages of computational biomedicine, from the underlying science, through modelling and using workflows, to clinical deployment. Early chapters focus on molecular foundations of computational bioscience and understanding the genotype-phenotype relationship, with the book progressing through image based modelling and modelling cell function and organs. The penultimate chapter is dedicated to issues surrounding privacy and security when sharing patient data.

To order a book, go to: ukcatalogue.oup.com/product/9780199658183.do

### VPH-Share at VPH2014

Plenary, posters and hands-on demonstration at the biannual conference

9th - 12th September 2014, Trondheim, Norway

VPH-Share will be well represented at VPH2014, the bi-annual conference and preeminent gathering of the Virtual Physiological Human community. Rod Hose will give a plenary session, VPH-Share: A Scalable Architecture for Scientific Cloud Computing, at the event, which takes place from 9th-12th September in Trondheim, Norway. He will be supported by four separate papers, from a range of VPH-Share’s workpackages, two posters and an oral workshop: Characterising Uncertainty of VPH-related Multiscale Models. Spiros Koulouzis, Dmitry Yasyurov, Adam Belloum and Marian Lu, represent VPH-Share’s cloud platform workpackage, will present their paper, Data Storage Federation for VPH Applications as part of the session Interoperability infrastructures bridging molecular to organ-level data and models.

A hands-on demonstration of VPH-Share’s services will take place on Friday 12th September. Led by Debora Testi, the session will enable potential users to learn how they can use the VPH-Share infrastructure to share, discover and access biomedical resources. Suheel Varma, Maria-Cruz Villa-Urriol, Emilio Mancini, Enrico Schiele, Pablo Lamata, Nic Smith and Rod Hose are co-authors on the poster VPH-Share: Patient-Centred Multi-scale Cloud-Enabled Computational Workflows, while Suheel will also exhibit an individual poster, Privacy-Preserving Scalable Data Federation.

VPH-Share Presentations will Include:
- Improving the assessment of diastolic performance, A Nasopoulou, M Sohal, A Rinaldi, N Smith, S Niederer, P Lamata
- The VPH-Share plugin for workflow composition and execution, E Coto, J Arenas, A Saglimbeni, D Testi, A Frangi
- Characterising Uncertainty of VPH-related Multiscale Models, J Feher, S Varma, M Sciola, P Morris, R Hose
- Untangling the Complexity of Ageing, Pail Hunter, University of Auckland, Reproducible Modeling: Standards, Databases and Software Tools
- Data Storage Federation for VPH Applications, S Varma, M Sciola, P Morris, R Hose
- Characterising Uncertainty of VPH-related Multiscale Models, J Feher, S Varma, M Sciola, P Morris, R Hose
- The Digital Patient Possible: What are the Roadblocks and How Do We Negotiate Them? Tom Kirkwood, Newcastle University, Unravelling the Complexity of Ageing
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### VPH-Share’s Taverna Training Workshop

31 potential users received hands-on training on how to use the VPH-Share system at the Taverna Training Workshop, which took place from 17th-18th July at the University of Sheffield. Jointly hosted by the Insigneo Institute for in silico medicine and CISTIB, the Center for Computational Imaging and Simulation Technologies in Biomedicine, the workshop provided participants with first-hand experience building biomedical workflows in the medical domain.

The users, mostly students from both Sheffield and Manchester universities, were instructed on how to access and share data, tools and workflows via VPH-Share and how to build cloud applications and wrap tools on the VPH-Share platform.

The aim of the workshop was to equip users with the knowledge of how to develop scientific workflows both locally, on the Taverna Workbench and via the VPH-Share portal.
Data Visualisation

VPH-Share has created a sophisticated infrastructure, capable of managing a rich assortment of datasets. The sophistication of the systems ensures that the creation of wide ranging workflows is made possible. Although not necessarily all publically available, the datasets below are managed through VPH-Share and should the data owners agree, can be made available to users.

24 million citations for biomedical literature from MEDLINE, life science journals, and online books, available through PubMed.

Public
125 million admitted patient, outpatient and accident and emergency records each year in Hospital Episode Statistics.

Public
780 liver samples screened for the human liver cohort, one of VPH-Share’s public and external datasets.

Public
120 angiography datasets available through vFFR3D, a VPH-Share collaborating project, calculating fractional flow reserve.

Restricted Access
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Restricted Access

Datasets managed by the VPH-Share infrastructure

Flagship Workflows

Partners

Public and External

Collaborators

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10
The VPH-Share project presents the data service platform – called Atmosphere Cloud – as a novel solution to the complex challenge of managing and sharing heterogeneous and distributed datasets across research platforms. This paper is structured to provide an overview of the Atmosphere Hybrid Cloud Platform and its capabilities, followed by a detailed analysis of its infrastructure and cloud platform functionalities. The reference section includes a list of authors, locations, and references, providing a comprehensive resource for further research and collaboration in the field of virtual physiological human and medical data sharing.
Heart failure with preserved ejection fraction (HFpEF) has high prevalence involving up to 55% of all patients with congestive heart failure. Cardiac imaging modalities play a central role in the evaluation of systolic and diastolic function, which is crucial in the diagnosis and management of HFpEF. Cardiovascular magnetic resonance (CMR) imaging has emerged over the last years and currently represents the gold standard in the quantification of systolic function. Its role in the characterization of diastolic function has not equally been established. Historically, available techniques for diastolic function quantification such as myocardial tagging remain relatively time consuming, thereby limiting their clinical applicability. Recent advances in deformation quantification based on myocardial feature tracking allow for easy and quick quantification of ventricular and atrial physiology. This report aims to review available CMR modalities for the evaluation of diastolic dysfunction including the latest advancements in the field, with an emphasis on their potential future role and clinical implications.

With the changing population and the concomitant change of the compound of risk factors heart failure with preserved ejection fraction (HFpEF) has increased in prevalence and has developed into a major health problem in the western world[1,2]. Today, HFpEF accounts for up to 55% of all patients with congestive heart failure[3,4]. Studies investigating patients hospitalised for heart failure have further reasons documented that the prognosis associated with HFpEF is similar to that associated with heart failure with reduced ejection fraction with only a minimal mortality difference between both groups[2-5]. According to current consensus statement[6], the diagnosis of HFpEF requires the presence of three obligatory conditions: (1) presence of signs or symptoms of congestive heart failure; (2) presence of normal or mildly abnormal left ventricular (LV) systolic function; and (3) evidence of diastolic LV dysfunction. Cardiac imaging modalities therefore have a central role in the diagnosis of HFpEF with a clear need for easy and comprehensive non-invasive imaging techniques. An impaired diastolic ventricular filling can be caused by three mechanical factors: a decreased relaxation capability of myocytes, an increased stiffness of the ventricular wall, or an impaired atrioventricular conduction of blood flow. Current diagnostic guidelines are based on surrogate of these mechanisms, captured by invasive catheterization with blood pressure recordings, blood tests or echocardiography[6]. A direct assessment of tissue stiffness can further provide a good analysis of the relationship between pressure and imaging data[7], and recent advances in computational techniques have enabled to decouple the combined effects of stiffness and accurate active tension from CMR[8], see figure 1. Nevertheless, these more accurate methodologies rely on invasive pressure recordings.

Currently, echocardiography represents the imaging modality of choice to evaluate and to grade diastolic function including a wide range of corresponding technical approaches[6,9], but has some limitations regarding systolic function assessment[10,11]. On the other hand, cardiovascular magnetic resonance (CMR) imaging has developed into the gold standard for volumetric quantification of systolic function[10,12]. In contrast, the role of CMR in the evaluation of diastolic dysfunction is less well established in clinical routine. Several CMR imaging techniques including tissue phasecontrast[13], elastography[14], MR spectroscopy[15], displacement encoding with stimulated echoes[16] and strain encoded magnetic imaging (SENC)[17] have been introduced with a potential use in the diagnosis of diastolic dysfunction. However, practical obstacles, e.g. the need for a separate sequence acquisition, time-consuming post-processing and image analysis limit their clinical applicability at the present time. Recently, novel techniques have been introduced that may allow for a reliable and less time-consuming evaluation of diastolic function based on clinically available standard cine sequences. This report aims to review the potential of diastolic function assessment with CMR with an emphasis on novel CMR techniques that enable an easy and quick evaluation of diastolic function from routinely available standard steady-state free precession (SSFP) cine CMR images.

Conclusion
CMR imaging gains an incremental role in the evaluation of diastolic dysfunction. Whilst novel relaxation parameters from CMR-FT may offer more accurate assessment of diastolic function, relaxation indices from CMR fractional area change and a reliable evaluation of left atrial contractile function represent interesting techniques to quantify the amount of diastolic dysfunction present in an individual patient. The presented novel CMR techniques promise an evaluation of diastolic function from clinically standard SSFP cine CMR images and require only minimal post-processing efforts underlining their applicability particularly for clinical routine. 4D velocity mapping represents a promising approach to assess intraventricular pressure gradients and might help to characterize impaired relaxation. The role of these techniques in the examination of diastolic dysfunction in HFpEF and patients with asymptomatic diastolic dysfunction however remains to be defined in future prospective clinical investigations.

References (abridged)
What is your role within VPH-Share? I mostly use the orthopaedic modelling workflow, which is being transferred to VPH-Share. Normally, weak features are the validation of the workflow in clinical studies of osteoporotic fractures, and also on an exploration of a broader application of the workflow to clinical data, i.e. to characterise disease-specific traits or population-based variabilities.

What are you working on at the moment? I have multiple active work-fronts: the first is the direct application of our workflow to cohort studies. We are now finalising a small work on coupled musculoskeletal and bone modelling for the vertebrae, whose structural deterioration and weakening is increasingly considered as a hallmark of skeletal fragility. We have just completed a cross-study validation of the workflow on the femur, where femur modelling showed instead to be good at retrospectively or prospectively classifying site-specific (i.e. femoral) fractures, but not general fragility conditions, as made evident by prevalent fractures at various skeletal locations. The main original feature of our femur models is the minimum strength concept, i.e. the consideration of multiple, instead of a single, loading configurations for each bone, then retaining only the minimum calculated strength. This is to allow us to better account for femur-anomaly, but I am convinced that are the validation of the workflow in clinical studies of osteoporotic fractures, and also on an exploration of a broader application of the workflow to clinical data, i.e. to characterise disease-specific traits or population-based variabilities.

I am convinced that the atomisation of VPHOP onto VPH-Share can help us better understand the relative importance of each step and improve them.

The systematic comparison of model performances is a too-often neglected instance in our research community. VPHare may be an answer. Many challenges, and we are still in the process of overcoming some of them. We need to say that the major obstacle is that we at Rizzoli own no computer developers, rather mechanical engineers brought to biomechanics. Ok, we are used to writing our Matlab or C scripts, we want a VPH-Share environment, helped developing MAF, and so on, still it has never been easy to interface with the technically challenging domain of the software and its language. A great help on this can come from Debora Testi and her group in CINECA (formerly RCS).

Workflows

Very true. Very funny. The perils of multiple users are many and annoying. One person’s useful data is another’s annoying angst. Thankfully as well as sharing established workflows, VPHare allows users to build their own, either from scratch or by modifying an existing sequence. By saving the workflow to their individual workspace, users can design the right chain for their experiments, and to possibly improve it. We need to say that the major obstacle is that we at Rizzoli own no computer developers, rather mechanical engineers brought to biomechanics. Ok, we are used to writing our Matlab or C scripts, we want a VPH-Share environment, helped developing MAF, and so on, still it has never been easy to interface with the technically challenging domain of the software and its language. A great help on this can come from Debora Testi and her group in CINECA (formerly RCS).

What has the field of bioengineering changed during your time in working in it and in what direction would you like to see it go? It has been a long journey. Firstly, all has grown tremendously. I wouldn’t say beyond any expectations, since expectations, well, there were many also 15 years ago. Anyway growth remains the first impression. It is unquestionable how bioengineering is nowadays pervading (and attracting resources from) many science domains. I am about to attend the World Congress on Computational Mechanics, where 15 years ago concrete and steel were perhaps already fading, fluids dynamics and composites instead emerging, and few bioengineering works spotted here. Nowadays CFD and composites are still there, concrete and steel have not disappeared yet, but 50% of the conference is bioengineering! Please note, not just computational biomechanics in a strict sense, but extending to transport phenomena for cell nutrition, or multiphase models of tumour growth. What was the key to all this? The orders-of-magnitude increase in the availability of computational resources played a major role, no doubt. But I would like to focus the attention also to the methodological improvements, and to the parallel advancements of experimental testing, that made it possible to validate models against independent measurements. Through verification (checking the numerical accuracy) and validation (checking model results against independent measurements assumed as reference) bioengineering models achieved the strength and reliability necessary to be brought to the bedside. From the very beginning, our lab has been focusing its attention on experimental validation. We’d like to continue pursuing this direction, in a multiscale biomechanical environment.
A group of usecases are helping VPH-Share to test its tools and services. These workflows, mostly from previous VPH projects, have added their tools and services, either in whole or part, to the infrastructure. They will be used to ensure that the system is able to accommodate new users at the end of year four. To understand in more detail what the usecases are about – and what VPH-Share will be able to provide – we take a closer look at VPH-Dare, MySpine and ARTreat.

VPH-DARE
Improving dementia research through in silico models of the brain

Dementia is not a normal part of aging. Decline in memory and thinking have a huge impact on a person’s quality of life and their ability to perform normal daily activities. There are an estimated 35 million people living with dementia in the world today and this is expected to quadruple by 2050. Early diagnosis is key to reducing the number of sufferers. Delaying the onset of the disease by just one year leads to a 10% reduction in cases and has dramatic consequences on the patient’s quality of life, as well as savings for the healthcare system.

The FP7 funded project VPH-Dare@IT aims to ameliorate the huge patient and societal burden of dementia by providing technologies for earlier and differential diagnosis of the condition. It will do so through the development of patient specific, ‘multi-factorial and multi-scale’ in silico models of the brain. “The approach developed within VPH-Dare@IT is multi-factorial and multi-scale in the sense that it describes processes occurring, and interacting, across wide spatial and temporal scales, and integrates information from disparate factors,” said Dr. Zeike Taylor, lecturer in Mechanical Engineering at Sheffield University and work-package leader of VPH-Dare@IT. Two main threads will be integrated to establish this framework: a multi-compartmental model describing fluid transport at various scales within the brain, and a metabolic network model describing genetic and biochemical processes.

Because dementia is not a single disease, but an umbrella term used to describe a number of related symptoms, it is particularly difficult to predict how a patient’s lifestyle will affect their chances of developing the condition and its progression, should they develop it. One of the benefits of the Dare platform is that it will be able to assess a patient’s lifestyle factors and use this information to investigate their effects. “Cognitive impairment in dementia patients has been linked to a plethora of lifestyle, behavioural and environmental factors, including diet, physical activity and smoking.” Said Dr. Taylor. “Although these links are supported by substantial statistical correlations, the linkage mechanisms remain largely unknown. Our hypothesis is that personal lifestyles and environmental factors may chronically affect brain fluid balances, transport and metabolic mechanisms that may precede brain deterioration. The biophysical and biochemical models provide a means of investigating these alterations and linking to lifestyle descriptors through model parameters and boundary conditions.”

VPH-Dare aim to integrate these models into a clinical decision support platform, which will allow doctors to create workflows aimed at personalising treatment for patients with dementia. The single framework will facilitate the analysis of clinical, biological and environmental data, to understand the brain ageing process and the progression of dementia. “Our modelling platform will support clinical dementia research in two ways: discovery of novel biomarkers of disease and extending our basic understanding of dementia. Our clinical decision support strategy will build on the concepts of Disease State Index and Disease State Fingerprint, developed in the precursor PredictAD project. Based on a spectrum of patient-specific biomarkers, these provide a framework for characterising an individual’s disease stage and for computing a so-called risk score for disease. The clinical platform will provide an intuitive and simple interface to this information, suitable for use in clinical environments and by non-technical experts.”

VPH-Share’s portal forms an integral part of VPH-Dare’s work as the former’s infrastructure will be the means by which the latter’s workflows, tools and data are made available. “VPH-Share will provide VPH-Dare@IT with the foundation services needed by its research platform,” said Alberto Biancardi, a software developer who works on VPH-Dare@IT. “It will fully leverage several datasets related to dementia. VPH-DARE aims to gather all of these datasets into a uniform collection by using the VPH-Share data publication capabilities and semantic services. As the VPH-Dare project progresses, more VPH-Share facilities will be used. VPH-Dare@IT is also fostering collaborations that will benefit each project’s community as the one with NeuGRID.”
MySpine
Clinical decision support for low back pain.

Lower back pain is a common problem. The NHS spends more than £1 billion per year on back pain related conditions, which range from problems in the disc space, such as disc herniation, to pain related to joint degeneration, such as osteoarthritis. Increased sitting, inactivity and poor posture are just some of the reasons why 80% of the population will experience low back pain at some point in their lives. Despite this, treatments for spinal disorders are still inadequate. Based on trial and error clinical decisions, treatments may succeed in short term pain relief, but their longer term success needs to be improved.

The MySpine computing platform, which has been developed by the Institute for Bioengineering of Catalonia (IBEC) in Barcelona, in conjunction with six other partners including Sheffield University and the National Center for Spinal Disorders in Budapest, aims to provide in silico virtual assessments for spinal conditions, which will improve the long term success of treatments. “The MySpine models predict the effects of spinal treatments from the least to the most invasive. These are conservative treatments, such as physiotherapy and surgical treatments, such as discectomy and spinal fusion,” explains Dr. Jérôme Noailly from MySpine and Senior Research Associate at IBEC. “Clinicians will be able to use the MySpine platform to simulate how individual patients respond to the various treatments, using this information to anticipate the one which is most effective. “The MySpine platform allows clinicians to perform virtual surgery on the patient model. Either part of the herniated disc material can be removed (discectomy) and/or two vertebrae can be bridged together with an implant (fusion), which improves the patient’s condition in the short term by restricting the motion of a painful intervertebral disc.”

The long term success of spinal treatments relies on a number of factors, which are not necessarily apparent at the time of treatment. A re-intervention – further treatment – may become necessary should the original treatment fail in the long term. If this is the case, the patient can find himself faced with multiple surgeries and uncertain outcomes. Dr Noailly says: “while these treatments are common, they change the biomechanics of the spine. While they succeed in relieving mechanically painful areas, the redistribution of the mechanical loads in the treated spine can also have negative effects. The MySpine calculations aim to anticipate these possible negative effects and understand their origin. The objective is to provide the clinician with additional information to decide when surgery is appropriate.”

The MySpine system relies on patient-specific models for its simulations. The starting point for these are medical images taken from the patient. The information is as unique to the patient as their fingerprint and allows treatments for the first time to be personally tailored. Drs. Peter Paul Varga and Peter Eltes from the National Center for Spinal Disorders in Budapest explain: “currently the diagnosis and treatment of disc degeneration related to low back pain is mainly based on patient symptoms and clinical imagistic data. The most commonly used methods are the MRI (Magnetic resonance imaging) and the CT (Computerized tomography) scans. The MRI allows the estimation of soft tissue structures, whereas the CT images visualise the bony elements, such as vertebral endplates and facet joints. Currently, despite the need for simultaneous examination, these two complementary methods can be run only in parallel and this is where MySpine made its first breakthrough. The MySpine platform does not only allow the fusion of these methods but creates a patient specific 3D geometry as well. This can be created in 15 minutes and the clinician can rotate, move and section the geometry as it is necessary for the diagnostic process.”

As well as predicting the effects of three types of spinal treatment, the MySpine platform aims to also model the effects of aging. This will allow doctors to simulate various treatments at, for example, five year intervals to show how the treated spine will develop over time and which treatment provides the best chance of long term success. “An important aspect of the intervertebral disc models is the ability to simulate water as a model parameter,” says Dr. Noailly. “Because degeneration and ageing are primarily characterized by a loss of water, if we can simulate water composition, we can in turn simulate the effects of degeneration and aging. The disc model also allows the calculation of the redistribution of water contents as a function of both the properties of the disc (e.g. degenerated or health disc) and of the mechanical loads (e.g. baring patient’s weight or during physical activity). These calculations are important for predicting the health of the patient’s spine as they age.”

Developed by researchers, the success of MySpine will rely on whether doctors are capable of using its technology as well as whether hospitals have the necessary computing infrastructure to support its simulations. Drs Varga and Eltes say: “the MySpine platform is far less complex than any of the clinical software already used on a daily basis. It is comparable to the use of a smart phone application. The semiautomatic workflow requires minimal interactions and running a simulation does not require any bioengineering knowledge. The idea that clinical centres will invest financial resources to build, run and maintain their own High Computing Facility to run the workflow is not realistic. Therefore we opted to use VPH-Share which allows the running of the platform from any PC in any clinic, or even from a tablet. We are convinced that the MySpine platform is a ‘disruptive innovation’ and will help the diagnosis, treatment and prognosis of patients suffering from low back pain.”

The MySpine platform allows clinicians to perform virtual surgery on the patient model.
The ARTreat decision support platform aims to provide detailed personalised evidence from population literature. Based on their own experience and must decide which treatment to use – how plaque will develop – and their patient’s disease will evolve and treat it accordingly.

Atherosclerosis is a vascular disease which involves the development of plaque within arteries. The build-up of plaque can cause arteries to harden and narrow which may affect the flow of blood within them. This is dangerous as restricted blood flow can damage organs and stop them functioning properly. Diseases connected with atherosclerosis are the leading cause of death in Europe each year.

Treatment of atherosclerosis traditionally involves either a dose of medication or the insertion of a stent, in order to widen the artery and restore blood flow. However, in the case of stenting, because the treatment can result in changes in blood flow, both locally, i.e. within the treated area and in the wider arterial tree, it is possible that plaque formation may be triggered in new areas. So treatment, which aims to improve the condition, if not correctly chosen can, in effect, spread the disease.

Despite the significance of these effects, cardiologists do not currently have the information to predict how their patient’s disease will evolve – how plaque will develop – and must decide which treatment to use based on their own experience and evidence from population literature. The ARTreat decision support platform aims to provide detailed personalised information before, during and after cardiovascular interventions to reduce the possibility of complications arising and the need for further operations. “The interventional decision support system of the ARTreat platform provides the optimal stent positioning and inflation parameters, that result in the optimal wall shear stress distribution in the artery, after the stent implantation,” said Dr. Themis Exarchos, a researcher at the Foundation for Research and Technology in Greece and member of the ARTreat project. “Depending on the complexity of the analysed arterial segment and the level of detail, the decision support system provides near real-time advice for the positioning of the stent. However in complex cases, requesting high level of detail and very fine mesh, the procedure is performed some time prior to the operation, so that the cardiologist has the information available at the time of the operation.”

The ARTreat tools will help clinicians answer a range of questions: What kind of treatment should I use for this patient? Should I use a stent or not? Which kind of stent should I use?

The ARTreat tools will help clinicians answer a range of questions relevant to their treatment: What kind of treatment should I use for this patient? Should I use a stent or not? Which kind of stent should I use? What is the best position for that stent? How much time do I have in order to conduct the stenting procedure for a patient? Am I prepared well enough to perform this operation?

As well as helping practicing cardiologists, the ARTreat tools have been designed to support those still training. By providing a virtual testing environment, in which cardiology students can practice stenting on virtual patients, the ARTreat platform will allow doctors to refine their skills before using them on breathing patients. Dr. Exarchos notes: “The user interfaces are easy to use by experienced and novice cardiologists. They have been designed following the advised of both, offering all the functionalities of the ARTreat platform in a simple and efficient way.”

The ARTreat platform has been made possible by the development of a three-level 3D model of the cardiovascular system, developed by the project’s partners who span academia and industry and were chosen for their expertise in medical IT and cardiovascular and arterial surgery. The three-level model describes the anatomy of the arterial tree – the branches of arteries round the heart – the patient-specific blood flow and blood particle dynamics and the biological processes that lead to the creation and progression of atherosclerotic plaques. The models are built with patient data including CT scans, intravascular ultrasound, MRI and angiography. It is thanks to the combined information that is generated by this model that cardiologists are able to predict how their patient’s condition will evolve and treat it accordingly.

The ARTreat project was actively funded by the European Commission from 2008-2013. During this time, the project worked to develop its tools, for which its ultimate aim is for them to be deployed and used in hospitals. “The ARTreat platform has been tested in several clinical sites, from partners of the ARTreat consortium, as well as outside the consortium,” said Dr Exarchos. “The questionnaires that have been analysed after the installations show the tendency of cardiologists to become familiar with this new technology of decision support and training, based on advanced VPH models. The plan is to re-validate the models and decision support system in a large population, prior to their introduction in clinical practice.”

The benefits of the ARTreat platform are widespread: improve cardiologists’ skills, provide personalised treatments and minimise future invasive interventions for patients. A small platform, which could make a significant difference.
The Cardiovascular Biomechanics research group of TU/e bring their expertise to VPH-Share by developing a strategy for quantifying uncertainty in model parameters and spatio-temporal variations in boundary conditions. Much of their work is carried out in conjunction with Maastricht University Medical Centre. The two groups have considerable experience in patient-specific cardiovascular modelling and its use in diagnosis and medical decision making. In the Hemodyn project, computational models for patient specific diagnosis and medical planning were incorporated in medical imaging software designed to support pressure and flow computations in peripheral arteries.

In VPH-Share, the group are involved in the tasks dealing with parameter estimation and the calculation of the physiological envelope for simulation and model interpretation. In doing so, they aim to determine the most appropriate range of simulations, particularly in terms of boundary conditions, that should be undertaken to represent the physiological envelope for the individual. A range of sensitivity tests are used to measure the effects of parameter values.

The group are also involved in the employment of VPH-Share Use Cases, by supporting vFFR1D: Virtual Fractional Flow Reserve One-Dimensional Model. By funding a Research Fellow in Catharina Hospital Eindhoven, they aim to replace the invasive procedure used to measure Fractional Flow Reserve with a fluid flow simulation.
A shock of pink greets visitors to Heerstrasse, the cherry tree-lined avenue that adorns the heart of Bonn. The city planted the ornamental Japanese cherry trees in the 1960s, which every spring boast millions of delicate pink flowers. The colourful city played host to VPH-Share’s third General Assembly thanks to the invitation of exploitation partners empirica. Two successful days of work culminated with a celebratory dinner.
Advanced IT Support for Clinical Trials
First CRI Solutions Day

May 26-27, 2014 at Heinrich-Heine University, Düsseldorf, Germany

On May 26-27, the Clinical Research Infrastructures (CRI) Solutions Day took place for the first time, bringing together a large number of representatives from ESFRI infrastructures and EU projects. The event was created to provide an overview of new clinical research tools developed by EU projects. Christian Ohmann (KKS Düsseldorf) opened the conference with an overview of the current developments in clinical trials and translational medicine. Afterwards, the projects TRANSFoRm (Brendan Delaney, King’s College), p-medicine (Norbert Graf, Saarland University), EHR4CR (Brecht Clooshaert, Custodix), ECRIN-IA (Jacques Demotes, ECRIN), as well as BioMedBridges (Stefanie Suhr, BioMedBridges) were presented.

In separate hands-on sessions different tools were demonstrated. In particular:

- for clinical data management (OpenClinica, ObTiMA, VISTA, functional eCRF, mobile eHealth solution),
- for bridging experimental and clinical research data (tranSMART, Molgenis, 12b2),
- for the integration of EHR and care data in clinical trials (Query Workbench, Patient Recruitment Service, Feasibility service, Patient Screening tool, Recruitment and Feasibility tools),
- for imaging (XNAT imaging pipeline, DoctorEye), for biobanking (p-BioSPRE, Biobanking Catalogue, BBMRI Catalogue), and
- for clinical research support (Clinical Trial Information Mediator, Pathology Reviewer, PASTEL).

Since several tools shown at the conference cover the same functionality (for instance, ObTiMA, OpenClinica, and VISTA are data management applications) it was suggested to improve exchange of information already during development and promote joint tool usage. This is a lot easier if tools are built in a modular fashion and standardised interfaces are used.

The keynote speech was held by Norbert Graf (Saarland University) about IT challenges for innovative clinical trials with the focus on challenges in data integration. In the following discussion, possibilities for collaboration, the sharing of deliverables (e.g. common ontology) and sustainability issues were addressed.

Further information: clinical-research-informatics.com/solutiondays.php
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Discussion between p-medicine representatives & BioMedBridges
Breakout session 2
Partners

VPH-Share is an international collaboration between 19 partners, from industry, academia and healthcare.

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