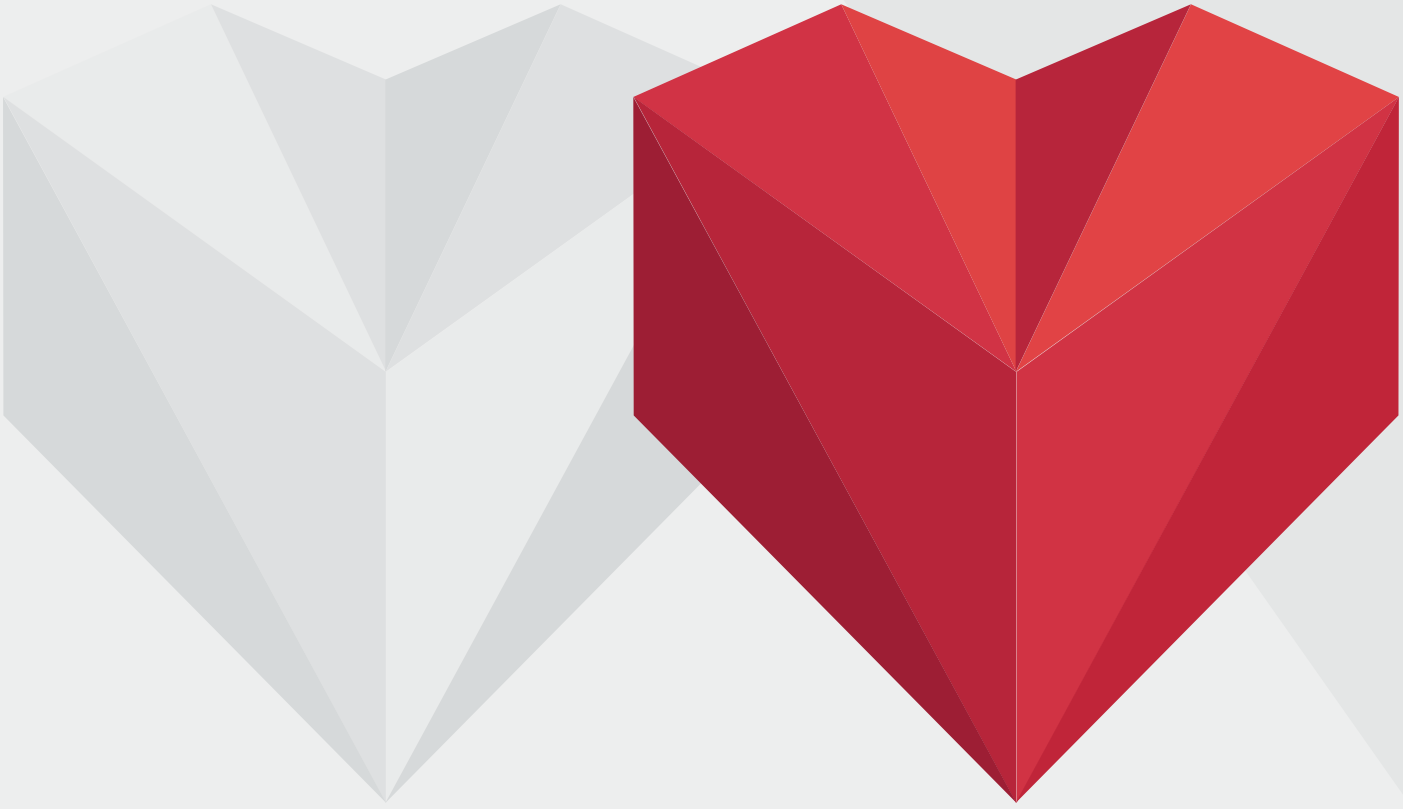
CARDIOPROOF PROJECT

Newsletter

Issue #1 October 2014

European Commission

eHealth
Better Healthcare for Europe



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EDITORIAL

by Edwin Morley-Fletcher
Project Coordinator

It is my pleasure to welcome you to this first newsletter for Cardioproof. We have had a busy first year and yet we still have much to achieve as we get into the core of this fascinating project. As project coordinator I am proud of the way that the consortium has built productive working relationships as well as considerable momentum in our work, and both of these will stand us in good stead for the forthcoming challenges.

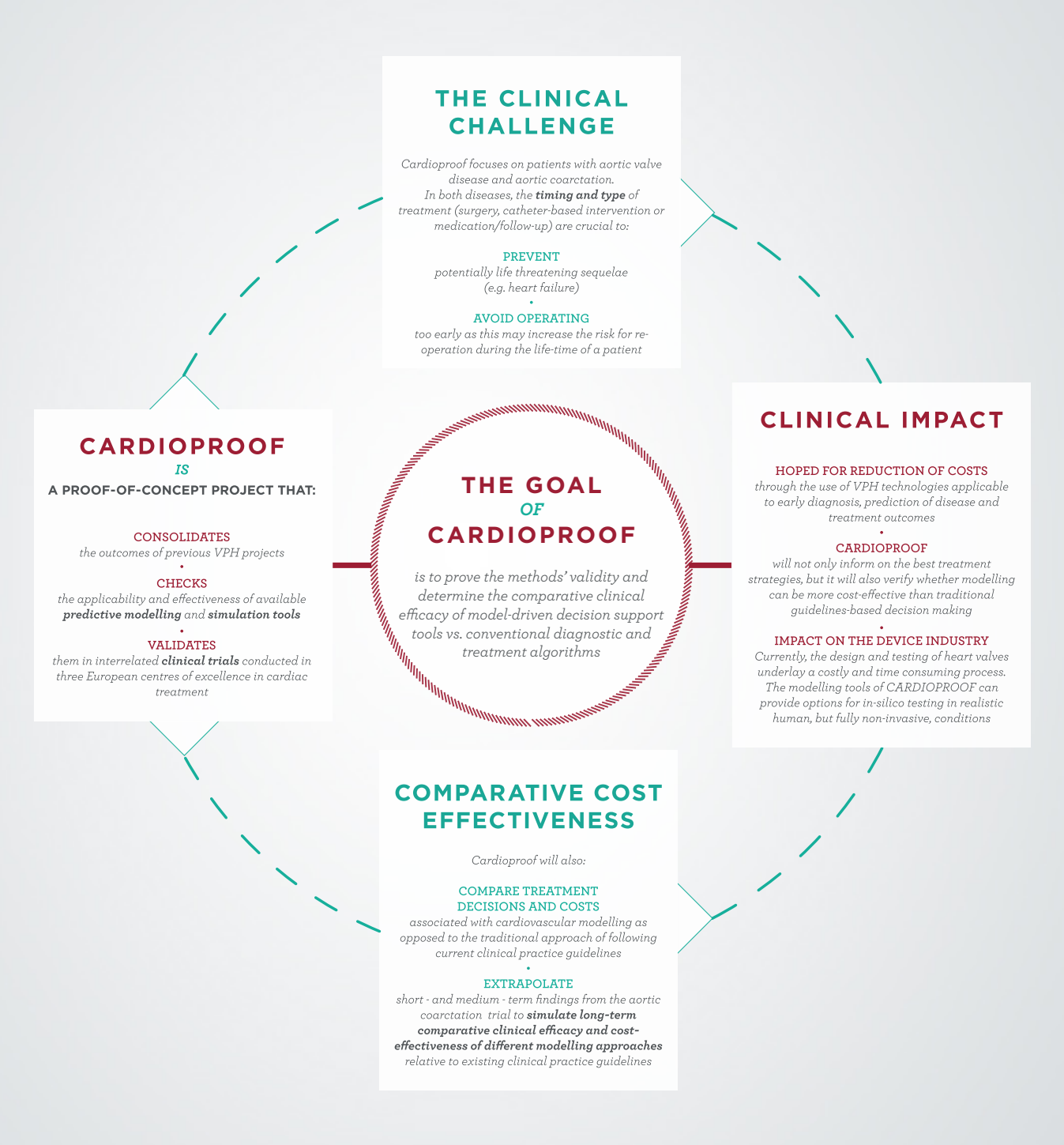
If asked to explain Cardioproof in a single sentence I usually respond with something such as the following: *The raison d'être for Cardioproof is to test computational modelling in clinical use.* We are seeking to apply and upgrade methods that have been developed in previous research projects, but more than this we wish to create a working end-to-end proof of concept that can be used to validate the use of Virtual Physiological Human (VPH) based modelling approaches in a clinical setting.

This translation from research tool into a routine clinical environment is challenging and substantially bounded. Despite increasing interest from the medical community to apply VPH concepts to the field of cardiovascular (CV) diseases, limited results have been achieved so far. Cardioproof seeks to address the main hurdles to this translation which are due to a lack of sufficient *Validation*, insofar as data of methods validity in clinical studies is sparse and yield, if at all, only low evidence levels; *Comparative effectiveness* of the methods, which is still unknown (do they result in different treatment decisions? i.e. comparative clinical efficacy; what is the comparative effect on costs e.g., cost-to-diagnosis, cost-to-treatment)?; *Usability and interoperability,* since software application and data management do not comply with clinical requirements (too complex, and too labour and time consuming).

Therefore, using modelling methods developed in previous projects (i.e., reuse of methods), Cardioproof's primary objectives are to conduct validation trials in patients with aortic valve disease (AVD) or aortic coarctation (CoA) that reflect a real-world approach by covering and comparing the complete spectrum of cardiovascular treatments to *prove* the validity of model based CV trials, and *assess* the validity of Computational fluid dynamics (CFD) models of the LV and the aorta including fluid structure interaction; Biomechanical-electrophysiological models of the LV and Lumped heart models.

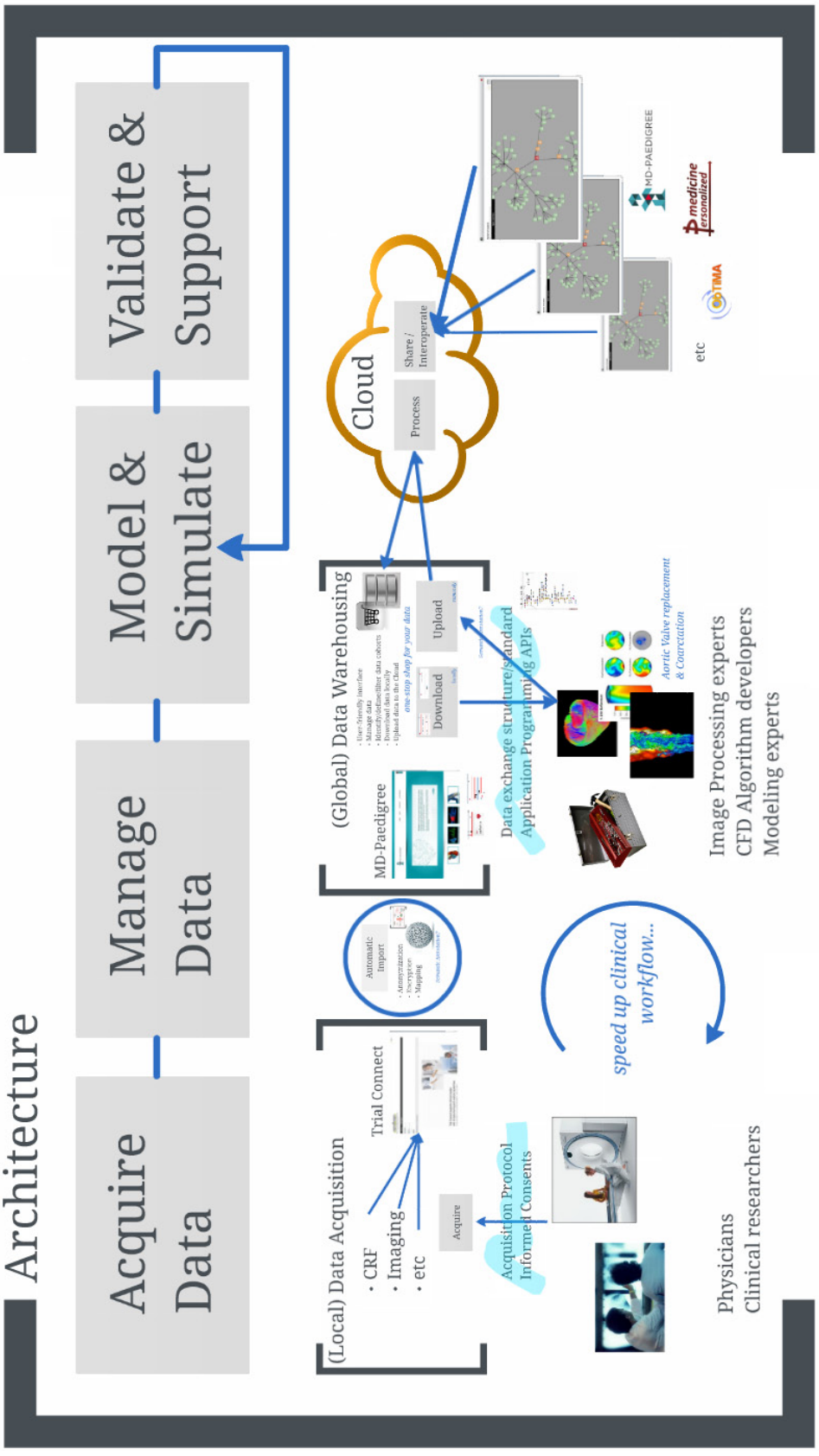
While the particular context for Cardioproof is paediatric cardiology, this project may be seen as a proof of concept for computational modelling as a clinical decision support tool for medicine in general. We wish to use this proof of concept to assess the advanced VPH modelling techniques we will be applying. In making these assessments we will investigate not just the validity, usability and effectiveness of these techniques when compared to the traditional methods, we will also be assessing the relative cost-effectiveness. This end-to-end proof of concept combined with the wide range of outcome analyses is ground-breaking for EC funded research and, as a result, we hope will show the way for other such studies in future.

CARDIOPROOF CONCEPT & GOALS



A visualisation of concept and goals of Cardioproof.

CARDIOPROOF ARCHITECTURE



A functional representation of Cardioproof's architecture

Cardioproof Internal Review

Almerico Bartoli & Callum MacGregor - Lynkeus

Reviewer Profile

Ornella Milanesi
Independent Clinical Reviewer

Andrea De Gaetano
Independent Technical Reviewer

On 17th & 18th September 2014 Cardioproof held our yearly Internal Review in Rome, kindly hosted by the Bambino Gesù paediatric hospital (OPBG). The Internal Review is an opportunity for the partners to present their work over the course of the previous year both to each other and to two independent external reviewers. The reviewers this year were: for the clinical side **Ornella Milanesi**, Head of the Paediatric Cardiology Dept. of Padova Hospital and of the University Heart Centre for Congenital Cardiac Diseases, and, for the technical side, **Andrea Di Gaetano**, Coordinator of the BioMathLab of the National Council for Research in Italy. Our esteemed reviewers then provided valuable feedback and criticism, which will enable the partners to maintain their high standards of achievement. Some of the topics touched upon during the review, which deserve to be highlighted beyond other issues already dealt with in this Newsletter, are the following:

Giacomo Pongiglione
OPBG

Retrospective prediction as a means of validation

Giacomo Pongiglione, head of the Cardiology Dept. of OPBG, highlighted the need to use retrospective prediction for comparison of the effect of current treatments with those which could have been adopted by making use of the predictive models. This is because patient involvement in Cardioproof must interfere neither with the patients' regular course of care nor with standard therapy. Patients are assessed by routine methods as defined by the current clinical guidelines including clinical information, laboratory blood testing and diagnostic imaging. In this way, modelling approaches are being used to predict the effect of stenting patients with significant coarctation of the aorta. The validity of this approach will be demonstrated comparing the predicted results with the 'real' post interventional state.

Virtual patients

The Project Coordinator, **Edwin Morley-Fletcher,** also showed the intention of dedicating some effort to a special challenge: trying to make use also of virtual patients (artificial computer-defined patients, presenting a "long tail" of relevant parameters in the explored disease areas, in order to better validate, on a much larger amount of stratified cohorts of virtual cases, the models under trial. The ambition is to have this way Cardioproof being a pioneering example of in silico clinical trial.

Anja Hennemuth,
Fraunhofer MEVIS

Predicting Haemodynamical effects

Anja Hennemuth, who is leading the work at Fraunhofer MEVIS, described their work to provide computational models to predict the haemodynamical effects of treatments of aortic coartation. This aims to provide a clinically applicable framework for planning and assessment of therapies for this condition.

Felix Ritter
Fraunhofer MEVIS

Patient journeys and clinical workflows

Ashley Waring and Felix Ritter presented Fraunhofer MEVIS's work, conducted in collaboration with the clinical partners, to analyse the clinical workflows and patient journeys in current clini-

cal practice. Amongst other things, this work will be used as the basis for making a user interface that is efficient and intuitive for the clinicians, helping them work faster and with fewer errors.

Gernot Plank
MUG

The software pipeline
Gernot Plank explained how his group at the Medical University of Graz (MUG) has been defining a technical standard that allows enable the data exchange between the various stages of the computational pipeline to take 4D image data and use it to create computer models. It is these models that, in turn, allow the Computational Fluid Dynamics (CFD) analyses to be made. This work is crucial as it is the software glue that binds the work in the modelling and simulation work packages.

Paul Groenenboom
ESI Group

Integration of the computational models of the morphology and the 4D MRI data
Paul Groenenboom described how at the ESI Group they have been defining another technical standard, which allows exchanging data between the morphology of the ventricle and aortic valve, using the segmentation of the images acquired by the clinical partners and related MRI (magnetic resonance imaging) information. This helps in the haemodynamical modelling of the ventricle and aortic valve.

Olivier Ecabert
Siemens

Computational tool for computing internal pressure in the aorta from 4D Flow data
Siemens' **Olivier Ecabert** reported on a novel method developed to compute the relative pressure within the aorta non-invasively from MRI data. This technique has been applied to three patients from the Cardioproof project, delivering sound results even with imperfect data. Moreover, the whole pipeline will be validated using the coarctation cases, also acquired within the project, which include invasive pressure measurements. This means that it will be possible to directly compare the simulated pressures with the measured ones.

CARDIOPROOF 's Bootstrapped Infrastructure

By Sébastien Gaspard, David Manset, Jérome Revillard

David Manset
gnúbila

One of the central pillars of Cardioproof is the technical infrastructure that enables the safe hosting, transmission and analysis of the patient data on which the project relies. gnúbila, with consultation from clinical and technical partners, has put in place the first version of the infrastructure for the Cardioproof project. This infrastructure has been built on top on the ongoing FP7 project MD-Paedigree, as an extension to it, in order to make best use of time, effort and funding.

Sébastien Gaspard
gnúbila

Installed on top of the existing MD-Paedigree infrastructure, the current solution provides two nodes that have the ability to host science gateways, central services and a web portal. The Cardioproof project shall add at least one node to this infrastructure. Most of the solution is provided by functionality and resource implemented for MD-Paedigree, bootstrapping on these existing components has provided a significant cost reduction in terms of hardware infrastructure, software evolution and maintenance. Both projects benefit from this arrangement, as any improvements coming from either project are shared with the other.

In Cardioproof, the data infrastructure and information system is based on gnúbila's FedEHR product. As the BARC study "Big Data Survey Europe" from 2013[1] states, organizations are taking a serious view on big data, recognizing the critical success factors and issues associated with handling enormous data volumes. Like medical imaging in the 80's, big data is indeed about to reorganize medical practice. Big data not only is a major challenge for ICT and health care professionals, but also is a great opportunity. The use of massively available medical data may allow clinicians to simulate potential outcomes and so prevent patients from undergoing ineffective treatments or improve on current treatment. In other words, accumulating and using data to develop a greater understanding of pathophysiological processes will result in significant healthcare improvements.

Jérome Revillard
gnúbila

Developed in collaboration with renowned medical centres in Europe, FedEHR is a patient-centric Electronic Health Records (EHR) big data solution. FedEHR stands for Federated Electronic Health Record. It leverages cloud elasticity to provide a scalable vendor-neutral database, which is able to cope with massive multi-modal and heterogeneous medical information, data and knowledge integration. FedEHR grew from leading edge technologies developed and tested in computationally and data intensive environments at the European Organization for Nuclear Research (CERN[2]). Over the last 7 years, FedEHR has matured and extended its range of application to a number of fields of medical science, from advanced biomedical research, to translational and clinical medicine. FedEHR has been installed in reference hospitals internationally, including Necker Enfants Malades in Paris, France, the Great Ormond Street Hospital in London, UK, Ospedale Bambin Gésu in Rome, Italy, and the Johns Hopkins University hospital in Baltimore, USA. The solution also was awarded at major events from its inception, including the Gold Medal at the International Inventions Exhibition in Geneva[3] in Switzerland, in May 2007; the Technology Transfer Award from CNRS,[4] in December 2010; and, as part of MD-Paedigree, the Best Exhibit Award of Europe's largest ICT conference, ICT 2013[5], last November 2013.

1 http://www.pmone.com/fileadmin/user_upload/doc/study/BARC_BIG_DATA_SURVEY_EN_final.pdf

2 Health Surveillance. How Knowledge Transfer Changed Biology, Medicine and Health Care. D. Manset. WILEY, 2014. In Press.

3 Gold Medal at the International Inventions Exhibition in Geneva http://cds.cern.ch/record/1035139 "MAAT Gknowledge took a gold medal for MammoGrid, a GRID-based mammogram analysis system to be implemented in the Extremadura region in Spain".

4 Technology Transfer Award from CNRS https://gnubila.fr/en_GB/awards-recognitions

5 Best Exhibit Award at ICT 2013 http://ec.europa.eu/digital-agenda/en/news/meet-winners-best-exhibitors-ict-2013 MD-Paedigree.

Structural Overview

The system is composed of two main components:

a. A **backend**, composed by all the Web Services being the ground of the platform with the addition of external applications;

b. A **frontend**, offering a user-friendly web interface allowing user communities to easily interact with the platform.

Cardioproof's backend has been inherited from MD-Paedigree and is the foundation of the system. Its Service Oriented Architecture (SOA) comprises a range of components interacting with each other and with external entities. Most of the platform features are exposed as Web Services, allowing an easily decoupling of the user interface rendering from the business logic. The user Interfaces can offer powerful features by aggregating the Web Services. The main entry point to the system is the frontend, and has been built by extending the MD-Paedigree front end. It exposes all the Cardioproof applications and tools through a common and simple web-based interface.

Patient Centric Data Structure

In accordance with the latest data modelling concepts in the literature, Cardioproof implements a storage model that is fully centred on patients. All data that is stored in the system is organised around a data structure representing a patient model. The current description of FedEHR architecture provides an evolutionary structure of data starting from the patient. Currently, the data structure is oriented around medical concepts of medical events and clinical variables. These abstract models can be refined and specialised using metadata definitions created from physicians' descriptions of diseases and exams or from normative works.

The New Patient Cart

The first need expressed during the project was to be able to easily choose a patient to add to a cohort of study. To respond to this, the first version of Patient Cart portlet has been designed and implemented. This development is to add ability to select patients in all the existing interfaces that show, sort, or list patients on criteria, and to send these patients to the Patient Cart. In the future, this will allow users to generate, share, and save patient cohorts into the system.

The Query System

FedEHR provides an inter-site query system presented as an SQL query for end users. These queries are managed by a query management system, which generates a result set that can be downloaded in a variety of formats and also includes a graph visualisation tool. Stored data is not useful without a query system. Inherited from MD-Paedigree, the Query System has been updated to be able to enrich Cardioproof Patient Cart to add the management of patient lists.

Access Rights

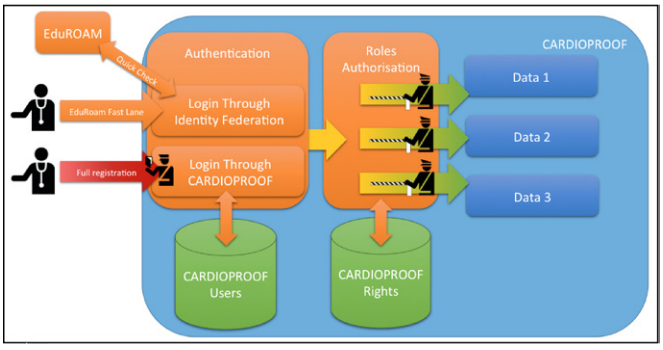
The Cardioproof/MD-Paedigree system also includes a RBAC (Role Based Access Control) mechanism for data security. For each patient medical event, the access can be defined based on roles given or not to the users. The provider of the data decides what access is given to whom and is able at any moment to review and alter the access to data provided to a particular user. Roles can be given to groups that can be multiplied as needed. A group can be assigned to member of a whole hospital, a special service or represent inter-hospital group. to member of a whole hospital, a special service or represent inter-hospital group.

Data Importers

Data importers have bee developed to import data from routine systems, while adding metadata information from images and measurement and textual information from annotations. They also are able to normalise the data and pseudonymising it using a 3 part storage mechanism. In the process, some ontological information such as ICD or SNOMED can be added in order to provide a uniform concept-based query capacity This means that there is a common human readable data structure at each node.

Our Current infrastructure

Basing the Cardioproof infrastructure on that already in place for MD-Paedigree has helped to jumpstart



Cardioproof Access Rights Architecture

data collection by avoiding the delays incurred from waiting for additional hardware to be installed.

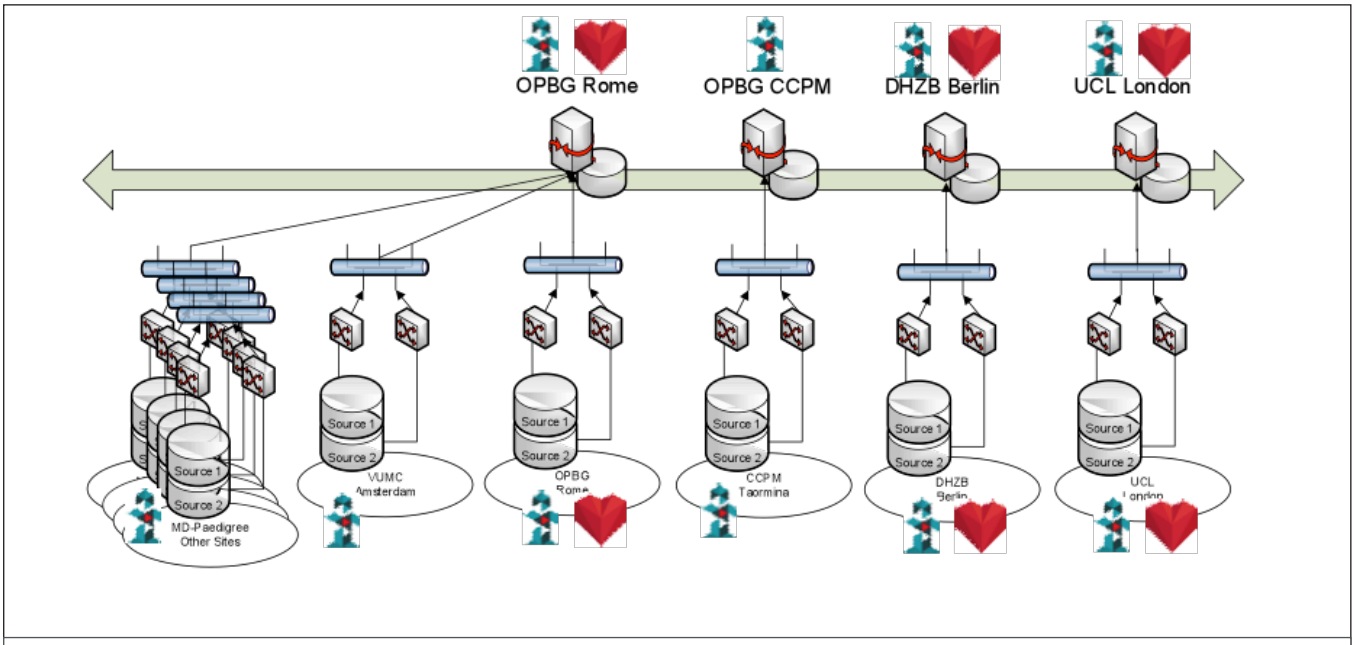
The Rome Gateway has been updated to allow Cardioproof data to be stored. The DHZB Gateway has been installed in Rome and is waiting for migration to the system in Berlin when available.

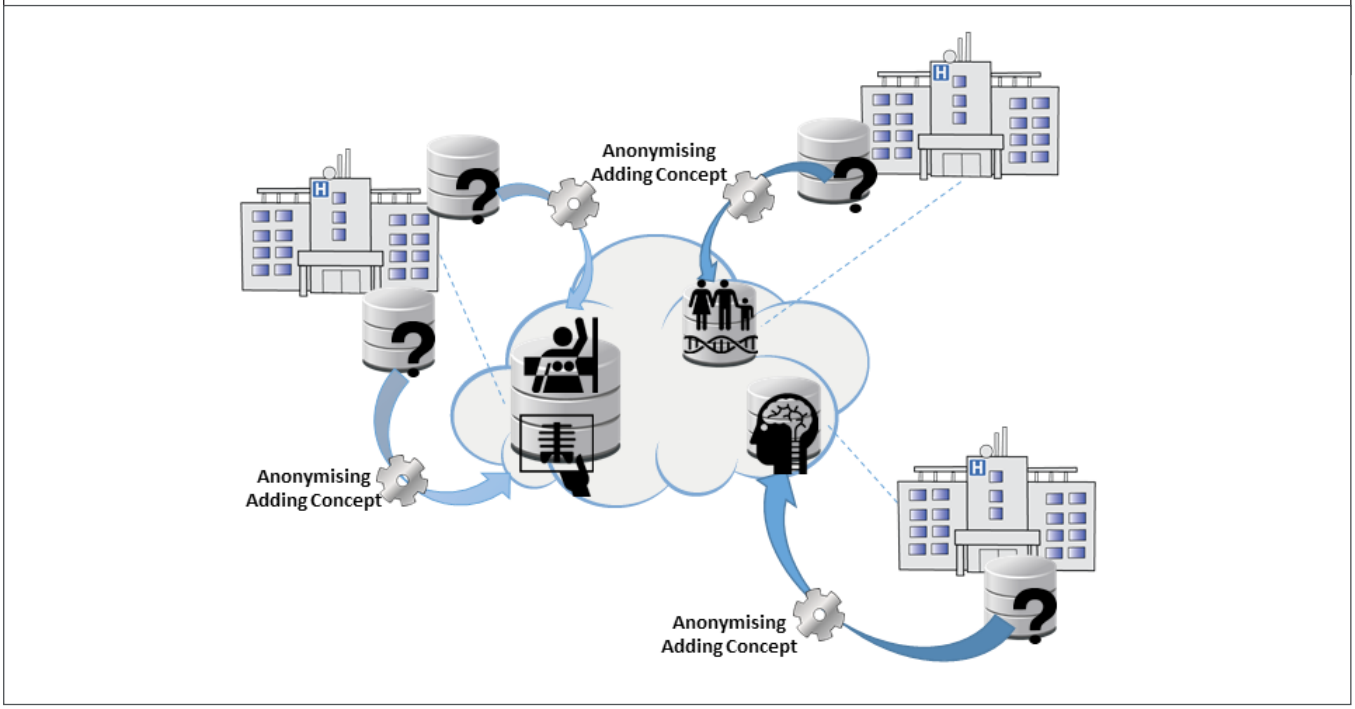
Next Steps

At least two further Nodes are planned for Cardioproof, one in London at UCL, and one in Berlin at DHZB. Once the hardware has been installed pre-configured virtual machines will be taken and installed on site. The added nodes mean that the system will have multiple physical nodes in three different countries, all collaborating to share data.

As you can see, Cardioproof has benefited substantially from the existing infrastructure that has enabled us to achieve the current advanced status. With the proposed updates the Cardioproof's infrastructure will go from strength to strength.

The planned MD-Paedigree & Cardioproof infrastructure





Importing data into Cardioproof

Virtual Stenting

By Hanieh Mirzaee

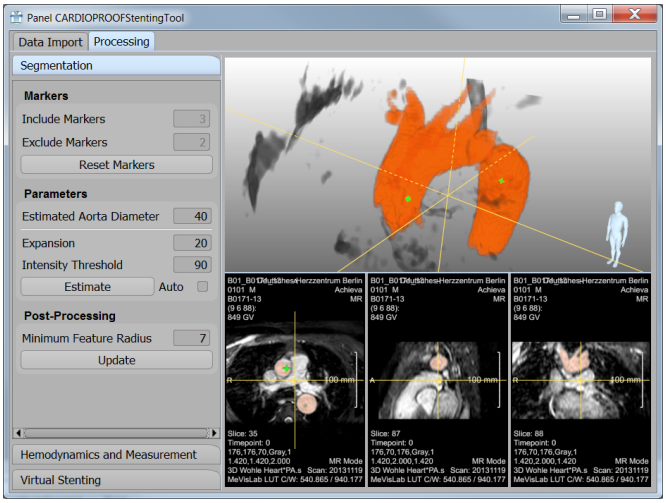
Hanieh Mirzaee
Fraunhofer MEVIS

Motivation

Aortic coarctation is a narrowing of the aorta in the region of the transition between the aortic arch and the descending aorta where the fetal ductus arteriosus is joined. It occurs in about 7% of all congenital heart defects. The high afterload induced by the stenosis can lead to ventricular dysfunction and thus a major therapy goal is to remove the pressure gradient. According to the AHA Guidelines, balloon angioplasty with stenting is a minimally-invasive recommended therapy for patients with a systolic pressure gradient of more than 20 mmHg (Feltes, et al. 2011). optimal stent placement is however a non-trivial task. Care must be taken with respect to several associated complications such as occlusion of the subclavian artery, (Waltham et al. 2005), stent migration, formation of aneurysms, and aortic dissection, (Godart 2011), to name a few. and associated complications to avoid include the occlusion of the subclavian artery (Waltham, et al. 2005) as well as a stent placement that causes stent migration or the formation of aneurysms or aortic dissection (Godart 2011). It is therefore desirable to simulate treatment options prior to the intervention in order to decide on an optimal stent placement that would result in reasonable changes in diameter and acceptable post-interventional hemodynamics provided by the guidelines.

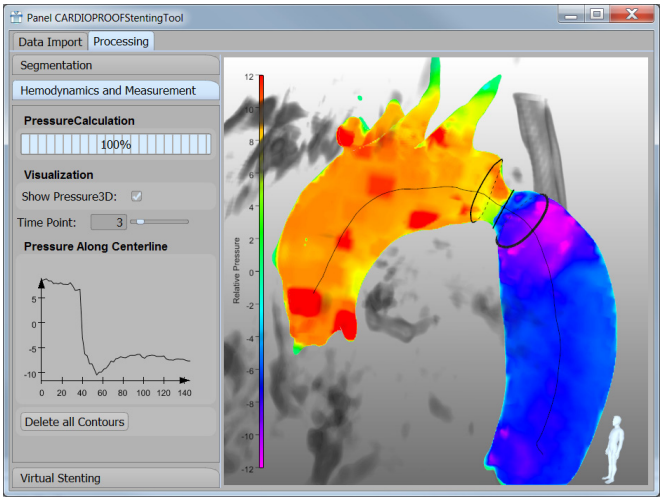
Pipeline

Our prototype works with arbitrary 3D datasets of the patient's anatomy and 4D PC MRI data of the patient's blood flow. The software enables the extraction of the vessel geometry using an interactive approach that combines the watershed transformation with manual correction tools. The extracted anatomy is then fused with the pre-processed PC MRI data that contains the blood flow velocity information for one heart cycle. With these data blood flow as well as pressure differences can be visualized and quantified. (Hennemuth, et al. 2011) (Drexl, et al. 2013) (Meier, et al. 2013). In order to explore intervention strategies, it is then possible to interactively change the aorta anatomy through simulating a stenting procedure.



Interactive Segmentation

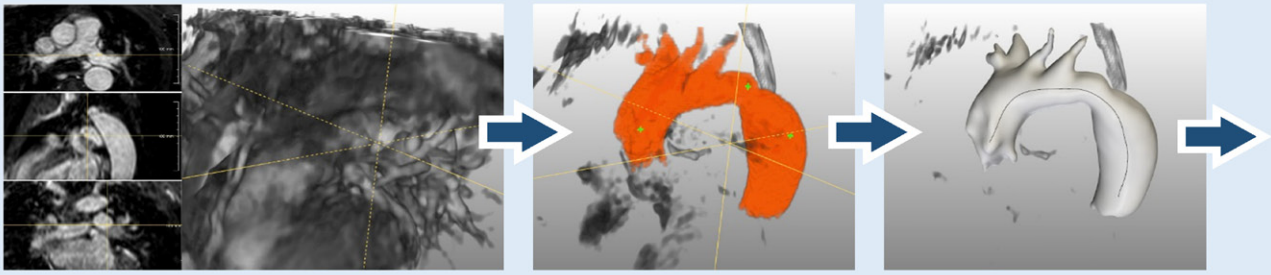
The extracted anatomy is converted into a high quality surface mesh and the centreline of the vessel is computed. The user selects pre-, post- and stenosis locations by interactively placing cross-sectional contours on the vessel surface. Hemodynamic data is provided as contextual information. A pressure map and the pressure curve along the centreline allows for a detailed qualitative and quantitative analysis of the pressure gradient.



Pressure Exploration

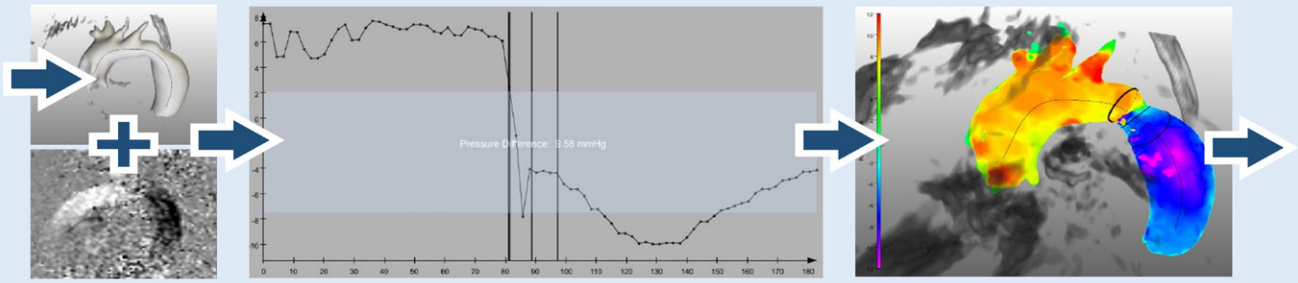
All necessary parameters (e.g. stent length, balloon diameter) are derived from these contours. The vessel segment affected by the stent is deformed accordingly. The user can interactively alter the suggested

Geometry Extraction



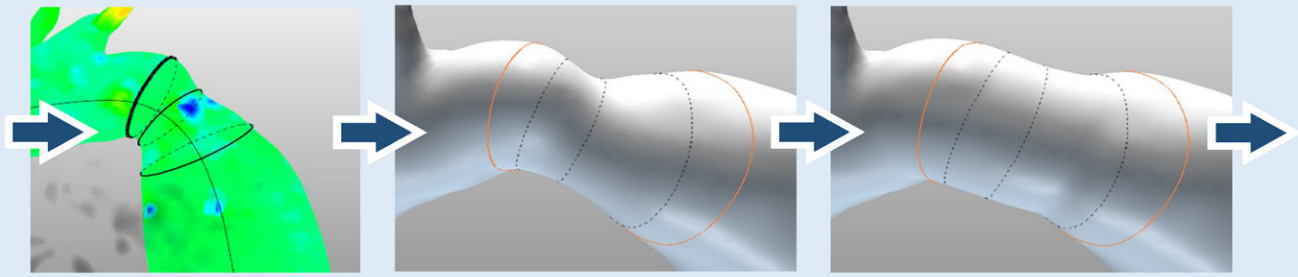
Whole Heart Image Data (2D / Volume) | Segmentation | Mesh & Centerline

Hemodynamic Assessment



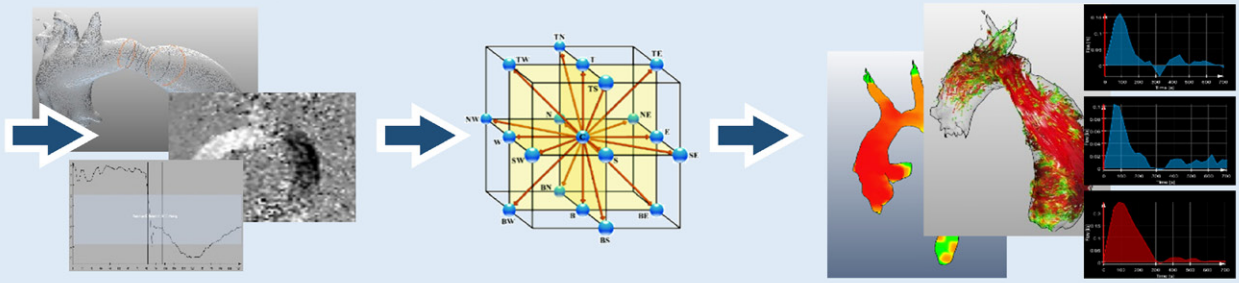
Masked Flow Data (4D PC MRI) | Pressure along Centerline | Pressure Map (MIP)

Virtual Stenting



Contour Placement | Before... | ...after Virtual Stenting

Simulation (work in progress)



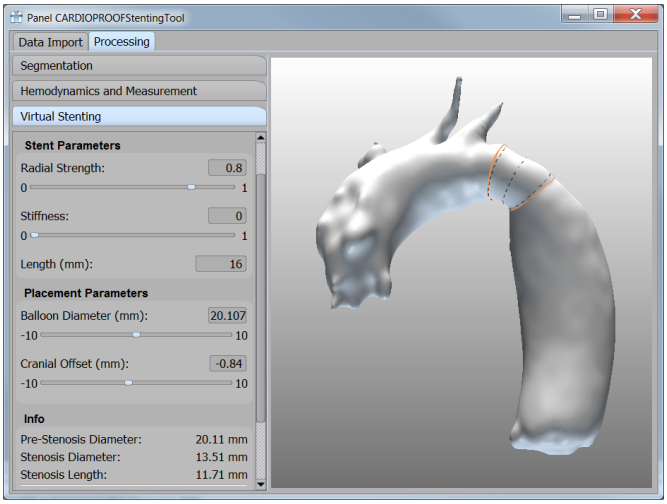
Domain & Boundary conditions | Lattice Boltzmann Simulation | Comparative Flow Analysis

Overview of the processing pipeline

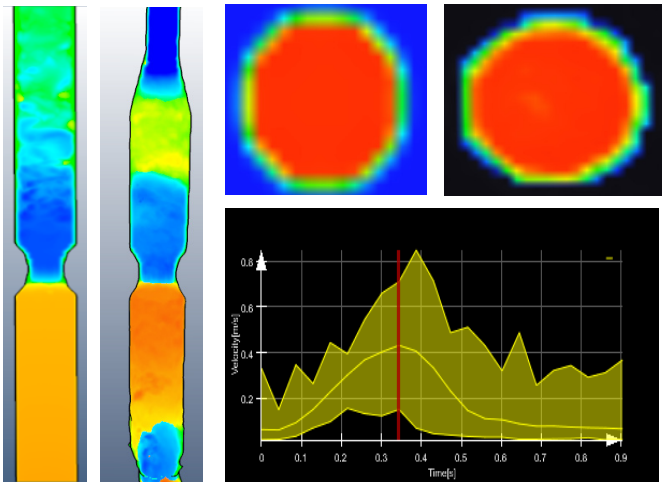
deformation by changing the stent parameters (stiffness, radial force), relocating the stent or change its diameter. The resulting geometry as well as the inflow conditions derived from the 4D PC MRI data are then used as input information for a simulation of the hemodynamic situation after stenting.

Outlook

Computational fluid dynamics (CFD) simulations in this pipeline provide one of its kind data quantifying hemodynamics for patients with coarctation of the aorta. After the virtual treatment of the vascular geometry a mesh-less CFD approach based on the lattice Boltzmann method is applied to simulate the velocity field after a treatment. Based on this field the pressure values are computed and ultimately the pressure gradients are visualized. Our preliminary results on a stenosis phantom data depicted below indicate a good agreement between simulation and measured 4D PC MRI data.



Virtual Stenting



Stenosis Phantom model. Left: comparison of pressure maps between simulation results (left) and 4D PC MRI measurements (right). Right top: comparison of velocity at a location inside the stenosis, measured data (left) vs. simulated data (right). Results are provided at the time of peak systole

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Drexl, J., Mirzaee, H., Harloff, A., Hüllebrand, M., Hennemuth, A., Hahn, H.. (2013). *A Software Tool for the Computation of Arterial Pulse Wave Velocity from Flow-sensitive 4D MRI Data. CinC – Computing in Cardiology Conference 2013.*

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Usability Engineering, Data Infrastructure, and Information System Design & Development

By Ashley Waring

Ashley Waring
Fraunhofer MEVIS

Motivation

A major component within the Cardioproof project is the analysis of clinical requirements including data, content of use, clinical workflow, and data requirements gathered by other work packages. This data is then used with the goal of analysing and solving usability and workflow-related problems, which prevent the application of modelling and simulation methods in clinical practice.

Dedicated contextual research was required to create workflows, interpret clinical routines, understand individual responsibilities of stakeholders, and understand stakeholder interactions with others, medical devices, and software programs. Utilizing user centred research and evaluative techniques aid in understanding the users needs and requirements on a much deeper level, allowing for thoughtful, effective, and highly useful solutions.

Contextual Research: Analysing Processes in the Field

Contextual research is a type of research that involves the researcher going into the users' environment in order to observe first hand how the workflow is influenced by various users and products. This immersive technique also allows for observations of users behaviours in a specific context to evaluate needs and determine users roles in the system. Within CARDIOPROOF, the hospitals of the clinical project partners in London, Rome, and Berlin were visited to conduct contextual research and understand clinical requirements.

Stakeholders - Who is Involved?

Stakeholders are described as the key players affecting and who are affected by the workflow. As three separate medical institutes are collaborating for CARDIOPROOF, the stakeholders from each needed to be studied with respect to protocols, workflows, and experiences. Since each location is a different size and has slightly different protocols, each procedure and who conducts what was noted. An example of this task difference is in London, where clinical fellows have traineeships of two years and often write clinical reports. In the other two locations, fellows are either not present or are not present long enough to gain the experience necessary to write clinical reports. This means that the senior level cardiologists in London can fill their time by seeing additional patients or other tasks instead of report writing (although they do review the fellow's work before submission). This easily could impact the cardiologist's workflow and number of patients he or she sees on a given day.

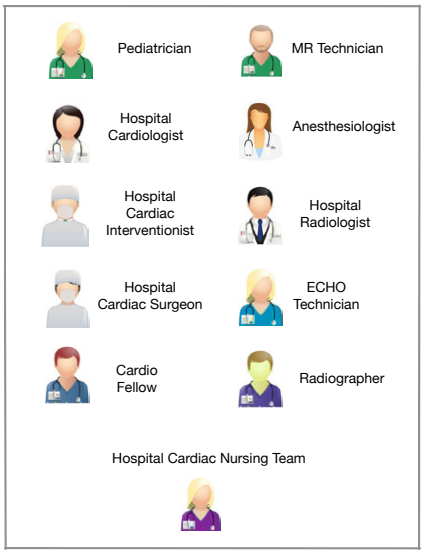


Figure 1: Stakeholders

Workflows – Where to Integrate New Tools?

The workflow analysis is a step-by-step description of the tests and treatments patients go through when being treated for aortic coarctation and aortic valve disease in the CARDIOPROOF project. This means that surgeries, interventions, MRI's, Echo's, and segmentation procedures along with other events were observed, noting the timing and individuals taking part in each.

Workflows were then illustrated for each of the three locations. Variations in workflow were then noted as well as consistencies. This resulted in a fourth workflow,

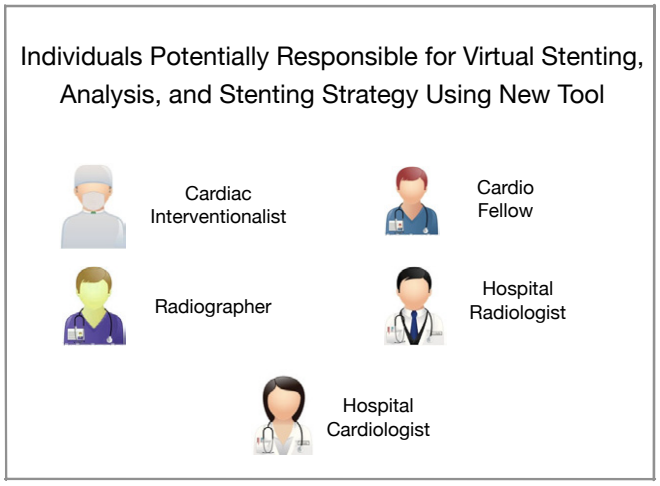


Figure 2: Potential Users of New CARDIOPROOF Tool

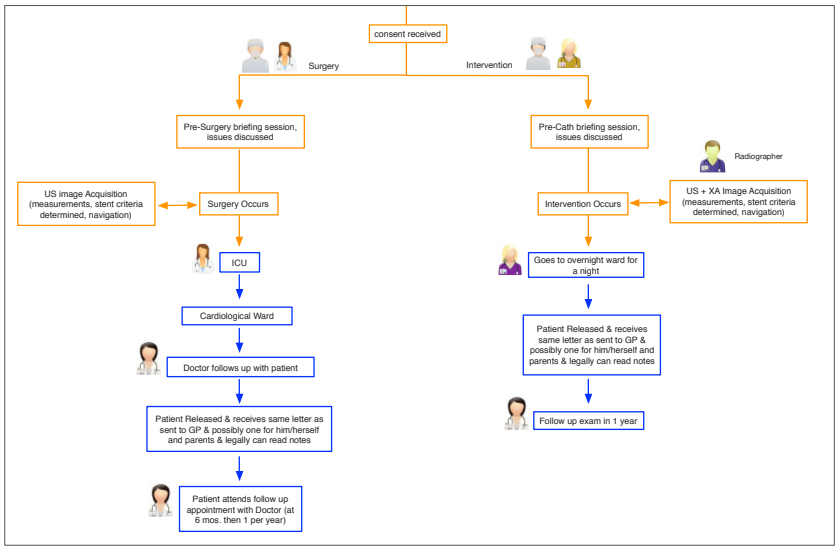


Figure 3: Workflow Section: End of Patient Process

which displays the general process and highlights areas where differences in workflows occur. This iteration also helped to identify opportunities where new software tools could be integrated into the workflow. A section of this fourth workflow can be seen in the image below (Fig 3). This section of the workflow shows the end of the treatment process, explaining the events that occur once it's decided that a surgery or intervention will take place. It also shows the individuals involved in this part of the process (hospital cardiologist, interventional cardiologist, cardiac surgeon, nurse(s), radiographer, and an anaesthesiologist). The red arrows identify where additional software features developed by the CardioProof project could be used.

To determine specifics on usage (ie. who will do the analysis, who would do the virtual stenting, and who reviews the results to make final conclusions about stenting strategy) additional research and discussions with stakeholders must be conducted. It is likely based on current workflows that different stakeholders may complete the same tasks in the different locations. This could potentially impact the user interface of the virtual tool based on preferences and needs of the various users. These potential tool users are seen in Figure 2.

Identifying Web Tool Needs

Following the development of the workflow, conversations regarding the current and future software tools took place. These discussions included analysing existing software solutions with experts and led to identifying where improvements and new solutions could take place and key information required for new web tool development. Following this task, a wireframe of the new web tool was developed (Fig 4) and can be be considered in the development prototypes, as shown in Figure 5 below.

Figure 4:
Prototype of Patient Selection Web Tool

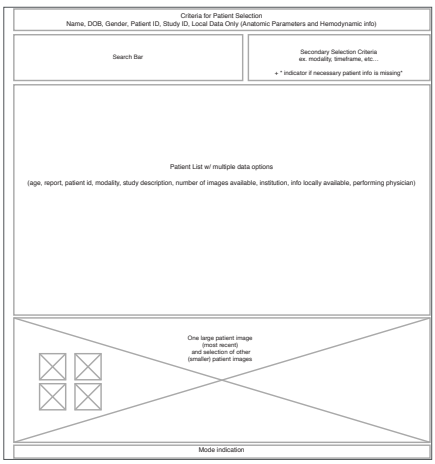


Figure 5:
Wireframe of Patient Selection in Web Tool

Proof of model-based cardiovascular prediction in clinical settings

by Marcus Kelm
and Leonid Goubergrits

Marcus Kelm
DHZB

What is the project motivation?

The rapid development of modelling and hardware tools promises an ability of a patient specific modelling of blood flow in a human blood circulation. Thanks to EU-funded projects, such as Virtual Human Project or e-Heart, the first modelling tools are available. We aim to prove the ability of modelling tools to work in clinical settings by a validation of modelling predictions for two groups of patients: patients with an aortic valve disease and patients with a narrowing of the aorta called coarctation that is a congenital heart disease.

What clinicians are expecting from modelling?

We are expecting more precise and differentiated

Leonid Goubergrits
DHZB

diagnoses based on non-invasive imaging data such as Magnetic Resonance Imaging. This would enable clinicians to avoid or reduce invasive catheterization procedures. Modelling of blood flow could also provide additional new hemodynamic information, for example the distribution of wall shear stress – a force with which blood flow acts on the vessel wall. Furthermore, we are expecting virtual treatment tools allowing the prediction of the post treatment situations and thus improving treatment procedures. Finally, we are hoping for an improvement of a long-term outcomes and hence quality of life and life expectancy for patients. The following clinical example (see below) shows our aims such as opportunities of modelling tools.

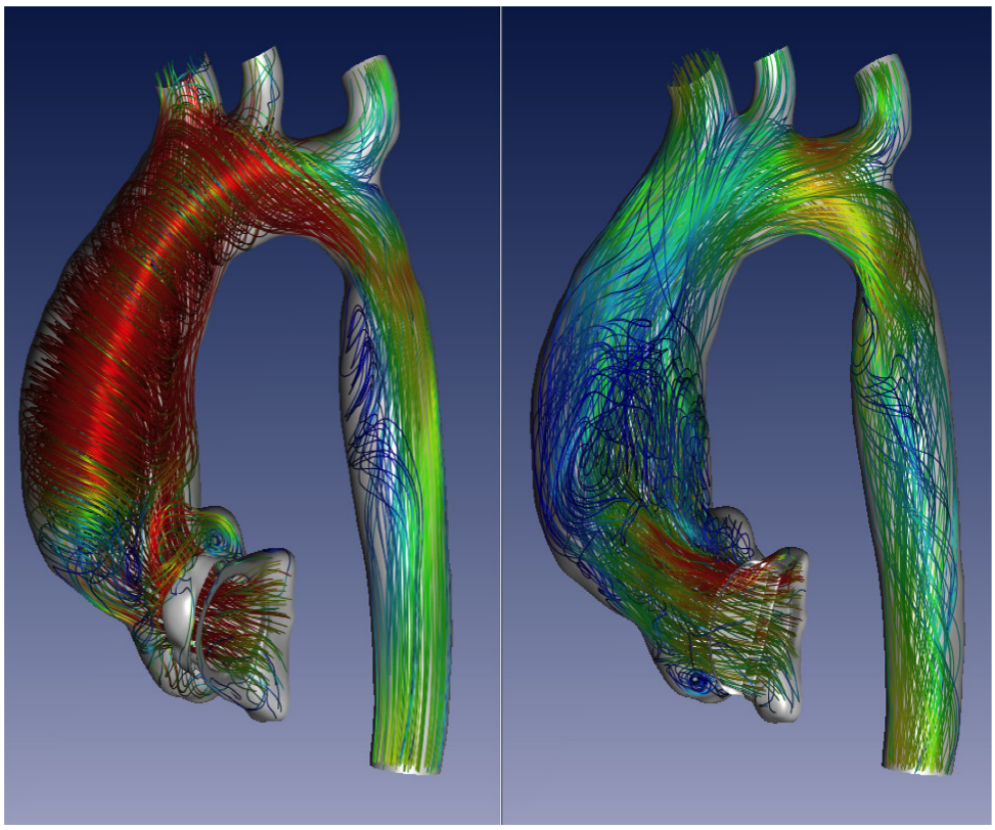


Fig. 1: A comparison of haemodynamics after the virtual valve replacement procedure using one biological and a one mechanical valve prosthesis. Path lines are colour coded by a velocity magnitude.

A clinical example - how modelling may improve clinical practice

by Titus Kühne

Titus Kühne
Cardioproof Principal Investigator, DHZB

A 23 year old female patient with a native bicuspid aortic valve (congenital heart disease) and with a dilated ascending aorta. This is associated with aortic valve disease and the proposed treatment is an aortic valve replacement.

The choice of a proper valve replacement is challenging. When biological valves are used they could fail several years after implantation due to lower durability, whereas mechanical prostheses have better durability but require life-long medication which reduces blood clotting.

Younger paediatric patients will not be suitable for such medication and the choice of a proper valve replacement is also limited by the fact that they will still grow. Using a computer model of the patient's cardiac system, we performed two virtual valve replacements, one using a biological heart valve and one using a mechanical heart valve prosthesis.

Then we analysed the post treatment haemodynamics and compared both possible treatments (see Figure above): the valve replacement using biological valve prosthesis causes, according to the modelling software, an ascending aorta entrance jet directed toward the lateral wall that forms a strong secondary flow (swirl) associated with high velocity magnitudes near the wall. In contrast, the mechanical valve forms a jet located at the centre of the ascending aorta with lower velocities near the aortic wall. Higher velocities near wall are associated with higher force acting on the aortic wall that is supposed to promote an aortic dilatation. In this light, the mechanical valve seems to be the favourable treatment solution.

Physics developments and protocol optimisation at GOSH

by Vivek Muthurangu

Vivek Muthurangu
UCL/GOSH

Great Ormond Street Hospital (GOSH) is the biggest paediatric hospital in the UK and the Cardiac Unit is the biggest paediatric congenital heart disease unit in Europe. Our centre for cardiovascular imaging at GOSH performed 1000 clinical scans and 500 research scans in 2013-2014 with a projected 50% increase in numbers for 2014-2015. In the MR (Magneto Resonance) Physics Development Group we augment the work of the Imaging Service at GOSH by significantly reducing scan times for routine imaging and increasing the numbers of children who can be scanned without anaesthesia.

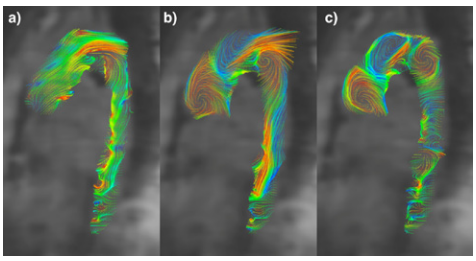
The Cardioproof protocol is extremely long with significant additional scanning required over and above routine clinical imaging. This may prolong scans times to over 1.5 hours, which is unacceptable to most patients in our population. Therefore, we have made a significant attempt to speed up the protocol by developing new accelerated sequences.

4D flow

4D flow is one of the foundations of the Cardioproof project as it allows modelling of blood flow in the heart and aorta. Unfortunately, current scan times for this sequences can take up to 20 minutes and unless used in conjunction with a respiratory navigator are unsuitable for assessment of intracardiac and myocardial velocities. Therefore, we have put a significant amount of work into developing rapid methodologies for acquiring 4D flow data in the aorta and ventricles.

Vascular 4D flow

We have developed a 4D flow sequences that can acquire the whole aorta with a true isotropic spatial resolution of 2.0-2.5 mm and a true temporal resolution of 40-50ms in between 2-4 minutes (representing a 5-10x acceleration). This has been achieved using a combination of a non-Cartesian stack of spiral k-space filling strategy and 3D parallel imaging. Furthermore, we have implemented fast online GPU reconstruction so that data is quickly accessible to the operator. An example in a repaired coarctation is shown below.



Streamlines calculated from 4D flow data in a patient with repaired coarctation a) early systole, b) early diastole, c) late diastole. Streamlines colour coded for vorticity.

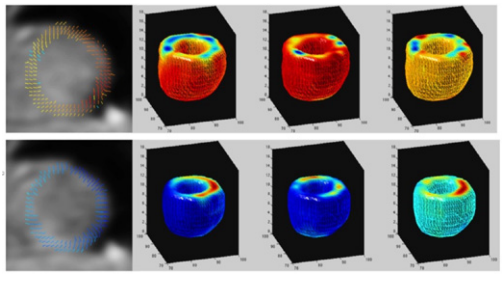
Myocardial 4D flow

Assessment of myocardial velocities is not possible without some form of respiratory compensation. Respiratory navigation is extremely time consuming and therefore we have vastly accelerated our imaging in order to acquire 4D myocardial and intracardiac velocity data in a single breath hold. This utilises the same technology as the vascular 4D flow acquisition but also add temporal encoding (UNFOLD) to further accelerate the acquisition. An example is shown below.

Rapid 2D flow acquisition

The Cardioproof protocol requires several 2D flow acquisitions that in congenital heart disease are usually acquired using time consuming free breathing acquisitions. We have developed a new breath hold 2D flow sequence that uses the same technologies as described above to acquire extremely high temporal resolution flow data within a short breath hold. This has significantly reduced up total acquisition time.

The recent introduction of all these techniques (and other techniques previously developed) has now enabled us to perform the whole Cardioproof protocol in less than 1 hour, making it feasible within our clinical environment and with our specific patient population.



Example data from a healthy volunteer. Top; peak S wave, bottom; peak E wave. A) 2D vector plots from the mid slice, b) Longitudinal velocity, c) Radial velocity, d) Tangential velocity. The colours represent the veolcities, with reds representing shortening/contraction/clockwise rotation, and blues representing lengthening/expansion/anti-clockwise rotation

The quantities analysed in Cardioproof

by Gernot Plank

Input quantities

a. EASI 12 lead ECG ϕ, (t)
b. Left ventricular pressure $P_{LV(t)}$
c. Aortic pressure $p_{AO}(X_c,T)$
d. Left Ventricular Volume $V_{LV}(t)$
e. Enddiastolic Anatomy $\Omega_{NYO}(t_{EO})$

Input data from clinical partners

a. MRI anatomy / segmentation
b. 4D MRI flow
c. Cine MR + pressure derived compliance
d. 4D VEC MRI

Computed Output quantities

a. Displacement u(x,t) in Ω_{NYO}
b. Strain ξ(x,t) in Ω_{NYO}
c. Stress δ(x,t) in Ω_{NYO}
d. Work W(x,t) in Ω_{NYO}
e. $V_{LV}(t)$
   . Flow $dV_{LV}/dt(t)$
   . Stroke volume SV
   . Left Ventriculare Ejection Fraction LVEF
f. Left Ventriculare Pressure $P_{LV}(t)$
g. Rate of change in pressure $dP_{LV}/dt(t)$
h. ECG ϕ, (t)

Outputs

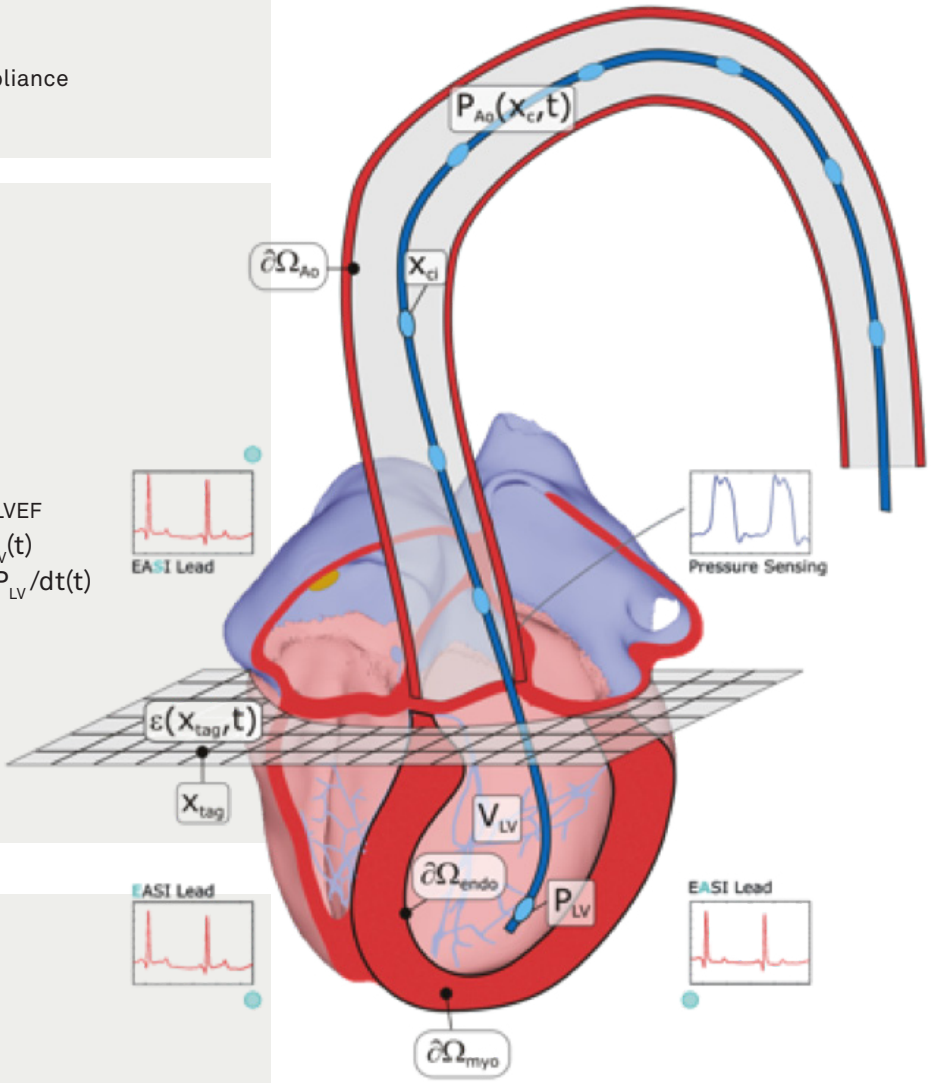
a. Flow
b. Wall shear stress
c. Pressures

Validation Quantities

a. Displacement $u(\delta\Omega_{undor}t)$
b. Strain $\xi(x_{log??}t)$

Validation against gold standards

a. 4D MRI flow (path lines)
b. Catheter measured pressures



Partner profile

Lynkeus is an independent strategy consultancy, founded in 2000, which works to identify and promote the best cutting-edge technological solutions to complex socio-economic problems in a variety of areas related to technological applications in public policies, with a particular focus on European Framework Programme Integrated Projects in e-Health.
www.lynkeus.eu

The **Deutsches Herzzentrum Berlin** (German Heart Institute Berlin, DHZB) is one of Europe's largest Heart Institutes. The research activities of the DHZB cover almost all emerging fields of cardiac diagnostic and therapy, which is reflected by more than 120 peer reviewed publications annually. One major research focus is on non-invasive cardiovascular imaging of patients in all age groups (from infancy to late adulthood).
www.dhzb.de

The **University Collecge of London (UCL)** is a large academic university associated with one of the largest paediatric hospitals in Europe – Great Ormond Street Hospital for Children NHS Foundation Trust (GOSH). UCL has one of the largest cardiovascular imaging (echocardiography and MRI) departments. The cardiovascular MR department is renowned for its research excellence and forms a crucial part of the UCL Institute of Cardiovascular Science research strategy.
www.ucl.ac.uk

The **Bambino Gesù Paediatric Hospital (OPBG)** is a health care and research institution, specialised in paediatric and developing ages, part of the Italian National Healthcare System and widely recognised as referral centre for all paediatric specialties at national and international level. Thanks to its organization, structures, technologies and highly qualified health care professionals, it guarantees total coverage for all health care needs, including emergencies.
www.ospedalebambinogesu.it

Fraunhofer MEVIS, Institute for Medical Image Computing (FME) was founded in 1995 as an independent non-profit research and development centre in the neighbourhood of the University of Bremen and is now part of Fraunhofer-Gesellschaft. The research focuses on computerassistance for medical diagnosis and therapy based on modern imaging, quantitative image analysis and visualisation, computer-aided teaching and training.
www.fraunhofer.de

Siemens AG is a global electronics and electrical engineering company, operating in industry, energy, healthcare, and infrastructure & cities. Innovation is Siemens' major growth and productivity driver. Its Corporate Technology (CT) division (3,000 researchers, >55,000 active patents) is a world leader among technology company research networks.
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ESI is a world leading software company with more than 1000 employees around the world, that specialises in the numerical simulation of prototype and manufacturing process engineering in applied mechanics. The key to ESI's success is the use of realistic material physics, providing "as good as real" virtual solutions, in order to replace the lengthy trial and error processes on real prototypes.
vjc@esi-group.com

The **Medical University of Graz (MUG)** comprises 16 Research Institutes, 23 Clinical Departments and a Center for Medical Research equipped with highly specialized core facilities as well as lab and office space. The Computational Cardiology Lab (CCL) at the Institute of Biophysics develops integrated multi-scale computer models of bio-electric and mechanic activity of the heart.
www.medunigraz.at

Gnúbila France (ex maatG) is a consulting firm delivering ICT solutions and professional services axed on Grid and Cloud computing with a special emphasis on e-Health and Health Information Systems. Gnúbila France justifies of a rich expertise in the establishment and execution of multi-partner collaborations, which it has capitalized upon its involvement in several international initiatives.
www.maatg.fr

LSE Health and Social Care is a research centre within the London School of Economics & Political Science that brings together diverse disciplinary perspectives and cutting edge methods to tackle current and future challenges to health and social care in the UK, Europe and beyond. The Centre's unique research base contributes to the LSE's established world presence and reputation in health policy, health economics and demography.
www.lse.ac.uk

Upcoming events

EVENT	WHEN	WHERE
Myocardial Velocity & Deformation Imaging 2015	February 5th-6th, 2015	Heverlee, Belgium
IHIC 2015 – 15th International HL7 Interoperability Conference	February 9th -11th, 2015	Prague, Czech Republic
ACC'15 – 64th Annual Scientific Session & Expo	March 14th-16th, 2015	San Diego - CA, USA
SERVICE COMPUTATION 2015 – 7th International Conferences on Advanced Service Computing	March 22nd – 27th, 2015	Nice, France
ICCFDM 2015 - XIII International Conference on Computational Fluid Dynamics and Mechanics	April 13th – 14th, 2015	Venice, Italy
E-health week 2015	May 11th -13th, 2015	Riga, Latvia
EuroPCR - Official Congress of the European Association of Percutaneous Cardiovascular Interventions	May 19th-22nd, 2015	Paris, France
AEPC 2015 - 49th Annual Meeting of the Association for European Paediatric and Congenital Cardiology	May 20th-23rd, 2015	Prague, Czech Republic
iCi 2015 - Imaging in Cardiovascular interventions	June 24th, 2015	Frankfurt, Germany
CSI 2015 - Catheter Interventions in Congenital and Structural Heart Disease	June 25th -27th, 2015	Frankfurt, Germany
FIMH 2015 – 8th International Conference on Functional Imaging and Modeling of the Heart	June 25th -27th, 2015	Maastricht, The Netherlands
MCCSIS 2015 – 9th Multi conference on Computer Science and Information Systems	July 21st – 24th, 2015	Gran Canaria, Spain
Medinfo 2015 – 15th World Congress on Health and Biomedical Informatics	August 19th 23rd, 2015	Sao Paulo, Brasil
EMBS - 37th Annual International Conference Of The Ieee Engineering In Medicine And Biology Society	August 25th-29th, 2015	Milan, Italy
ESC 2015 – European Society of Cardiology Congress	Aug 29th– Sep 2nd, 2015	London, United Kingdom
Personalized Medicine 2015 - 3rd International Conference on Predictive, Preventive and Personalized Medicine & Molecular Diagnostics	September 1st -3rd, 2015	Valencia, Spain
PICS-AICS 2015 – Paediatric and Adult Interventional Cardiac Symposium	September 18th-21st, 2015	Las Vegas, USA
MICCAI 2015 - 18th International Conference on Medical Image Computing and Computer Assisted Intervention	October 5th-9th, 2015	Munich, Germany
AEPC 2016: 50th Annual Meeting of the Association for European Paediatric and Congenital Cardiology	May 31st-June 4th, 2016	Rome, Italy
As part of the AEPC 2016 edition, two dedicated slots are being planned. One Mannheimer lecture on 'Innovation in Paediatric Cardiology' by Dr Anthony Chang and a special session on the 'Future of Decision Support Systems in Paediatric Cardiology', led by Prof. Giacomo Pongiglione, where Cardioproof outcomes will be a key topic .		

NEWSLETTER INFORMATION

Subscription
The Cardioproof newsletter is published annually by the Cardioproof consortium and is distributed free of charge. All issues of the newsletter will be available on our website. For subscription to the newsletter please go to www.cardioproof.eu

Disclaimer
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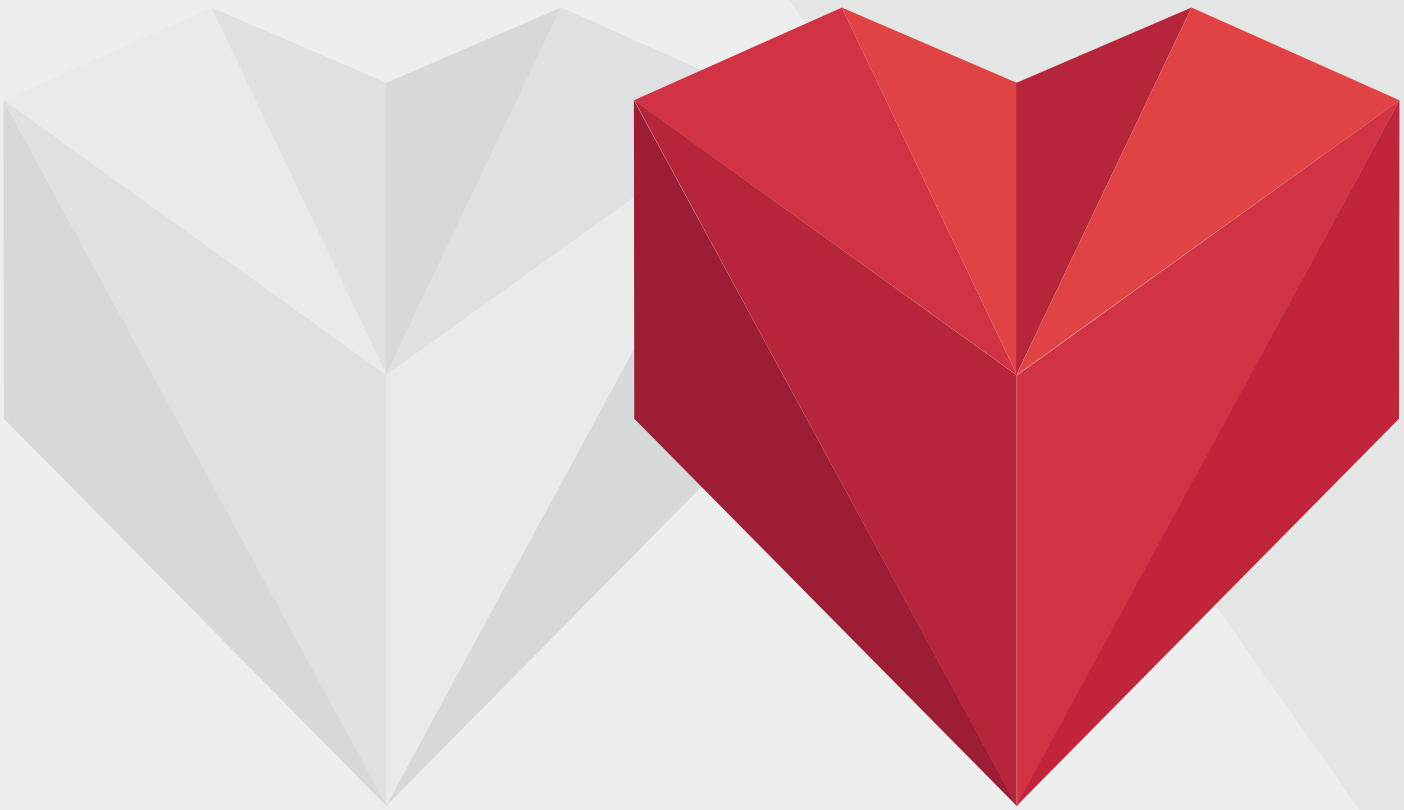

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