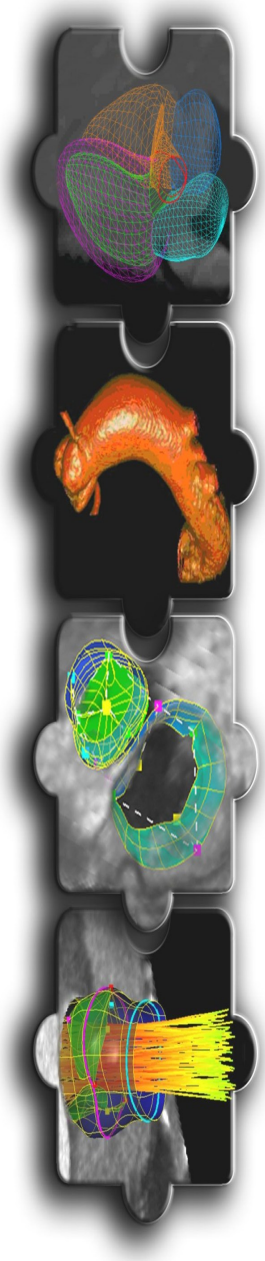
January 2012 - Issue no. 2

Sim-e-Child

# Sim-e-Child Newsletter





www.sim-e-child.org

COOPERATION

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European Commission
Information Society and Media

*Sim-e-Child: a 30-month Specific Targeted Research Project co-funded under the 7th Framework Programme priority "Information Society Technologies"*

*Newsletter edited by William W. McFadden and Mirko De Maldè — Lynkeus*

# An Overview of Sim-e-Child

Now into its final 6 months of work the FP7 STEP Sim-e-Child (SeC) is finalizing the development of a collaborative environment for multi-scale and personalized models of the growing heart and vessels including computational fluid dynamics for blood flow simulations. It operates as an extension of the Health-e-Child (HeC) grid-enabled platform and interconnects the HeC's databases with new data from US multicenter studies, the Johns Hopkins University Hospital (JHU), Baltimore, and the Bambino Gesù Paediatric Hospital (OPBG), Rome .

SeC is extending the VPH work successfully carried out by HeC in cardiology and in developing a Grid-powered eHealth platform in three major ways.

1. With the support of the American College of Cardiology and JHU, SeC is validating HeC's heart modelling capabilities using ongoing clinical US trial databases (the Coarctation Of the Aorta Stent Trial) in collaboration with the OPBG in Italy.

2. The HeC models are being expanded by integrating and enhancing Siemens Corporate Research models of the aorta, aortic valve and mitral valve. The heart valves represent a critical component for the multiscale modelling, simulation, understanding and prediction of the whole heart function, and this work represents the first data-driven modelling of the complete valvular apparatus. Furthermore the final models include blood flow modelling and flow visualization from the Technical University of Munich. The new and comprehensive heart model is applied to congenital aortic disease, thus enriching the portfolio of applications available on the HeC platform.

3. To support these activities, SeC has developed a grid-enabled platform for large scale simulations in paediatric cardiology, by integrating the HeC's Gateway and CaseReasoner (HeC's application for similarity search and decision support) with tools for simulation workflow composition and sharing of scientific experiments. This integration work is leading to the development of a collaborative environment for constructing and validating multi-scale and personalized models of a growing child's heart and vessels. Advanced clinical measurements are being derived, such as blood flow vorticity, wall shear stress, elasticity, distensibility, stiffness, and fluid structure interactions. The models in development will allow the simulation of interventions on morphology, dynamics, and haemodynamics of the aorta to make personalized predictions of optimal therapy.

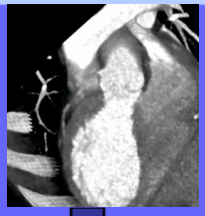
**First Trans-Atlantic platform towards personalized & predictive modelling of congenital heart Disease (CHD)**

**FP7 STREP**
Building upon FP6 IP Health-e-Child
January 2010 to June 2012

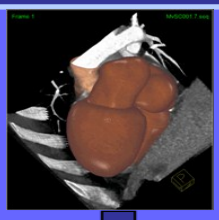
**Technical focus**
Computational **modeling** & **simulation** of cardio-vascular anatomy, function and **haemodynamics**
**Grid-enabled** infrastructure for data management & distributed high-performance computation

**Clinical focus**
Model **validation**
Multi-scale **quantification** of disease extent
**Planning**, **simulation** & assessment of efficacy and safety of **therapies**

**Image Data (CT, MRI, US)**



**Anatomical Model Fitting**



**Haemodynamics Simulation**

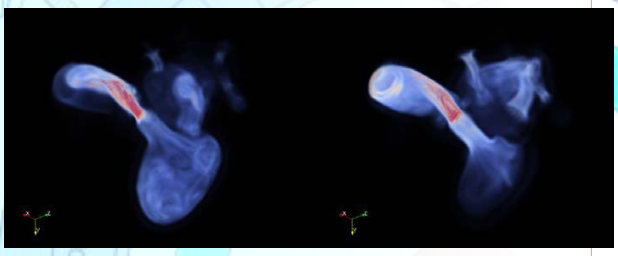

*Sim-e-Child: a 30-month Specific Targeted Research Project co-funded under the 7th Framework Programme priority "Information Society*

# Highlights of 2011

Clinical and Technical Work

In 2011 SeC finalized the development of the first grid-enabled trans-Atlantic platform for large-scale simulations in paediatric cardiology, offering an online collaborative environment for the construction and validation of multi-scale personalised simulations of a growing heart and vessels.

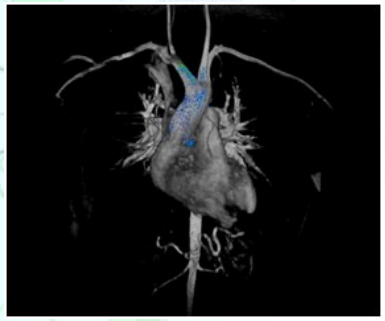

The objectives guiding the progress have been: 1) alignment of clinical protocols on both sides of the Atlantic. 2) alignment of technology and computational methods employed in the joint project, and mobilisation of grid resources in an efficient way without disturbing the involved hospitals routine ICT-function; 3) building of a prototype test platform.



Based on high-quality models of patient-specific geometry and dynamics, SeC's "Cardiac Hemodynamics Computation" is being used to simulate and analyze the blood hemodynamics within a child's heart and the ascending aorta and aortic arch,

SciPort, an online facility for sharing scientific experiments, is providing users with a multi-site, Web-accessible database of SeC's paediatric cardiology data, information and knowledge for translational research and to support the definition, execution and sharing of scientific cardiac modelling and simulations.

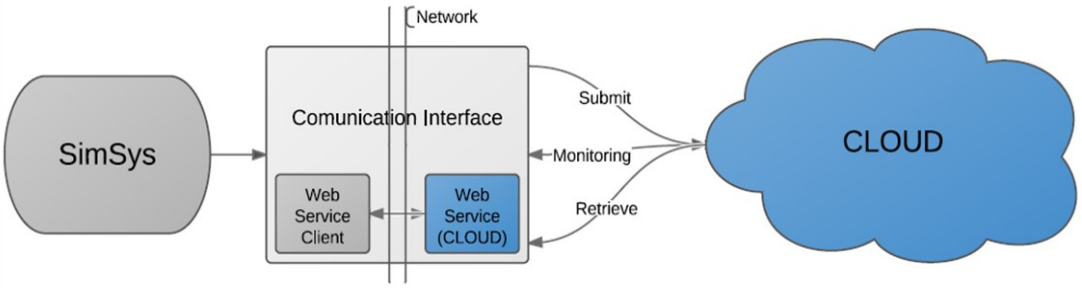
SimSyS (former iKDD) provides workflows for patient-specific cardiac modelling and simulation of the left heart as well as advanced quantitative and qualitative analysis, and experiments validation capabilities.



SimSys in action

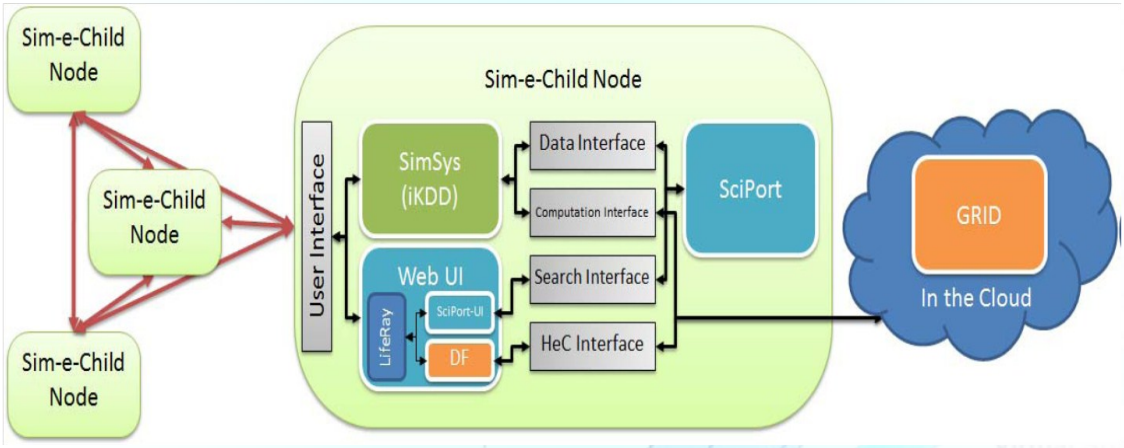
**SimSys client operations**

- Job Submission – sends to the cloud a computation expensive operation
- Job Status – gets the current status of a previously submitted job
- Job Retrieval – retrieves the results of the computation



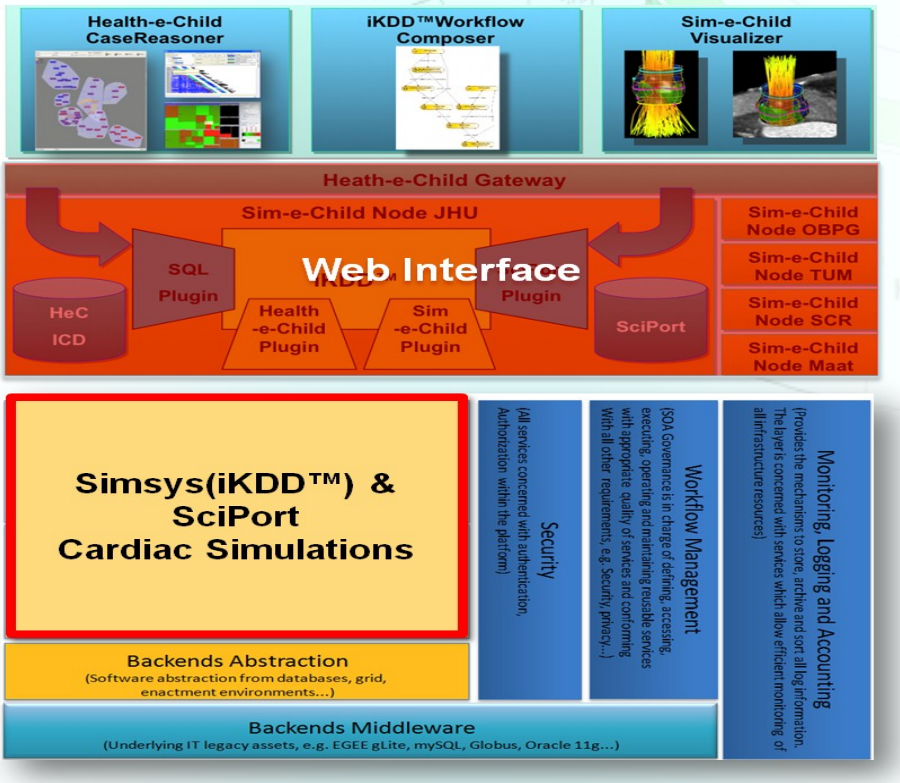
**SeC Grid Platform and Nodes implementation**

Each SeC Node is composed of three core components: the local SimSys and Sciport client applications and the Web User Interface (Web-Portal http://sec-portal.maatg.fr/ ).




Cloud Provisiong is added to the Node, making it into a Grid-Cloud Platform, in order to guarantee:

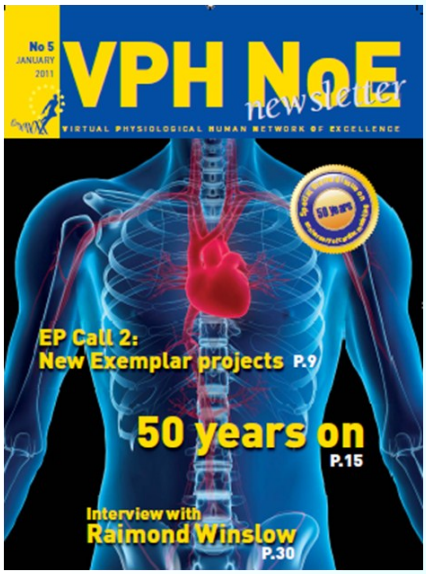
- an elastic infrastructure thanks to the Cloud
- a scalable middleware thanks to the Grid
- operating on demand, so that it only uses what is needed when it is needed, to reduce costs

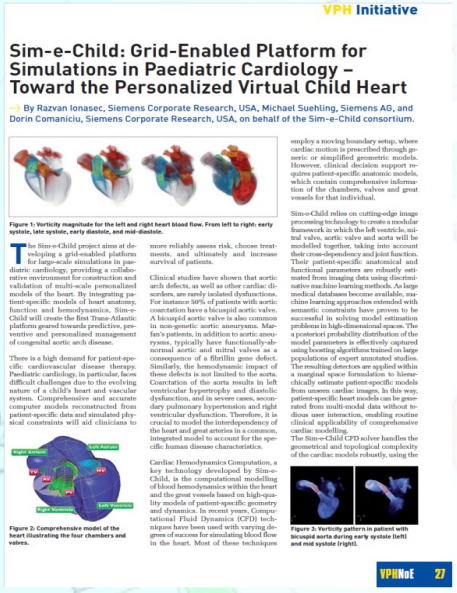


# Dissemination & VPH Community

**VPH-NoE**

Siemens Corporate Research in the US and Siemens AG in Germany produced an article for publication by VPH NoE in 2011.



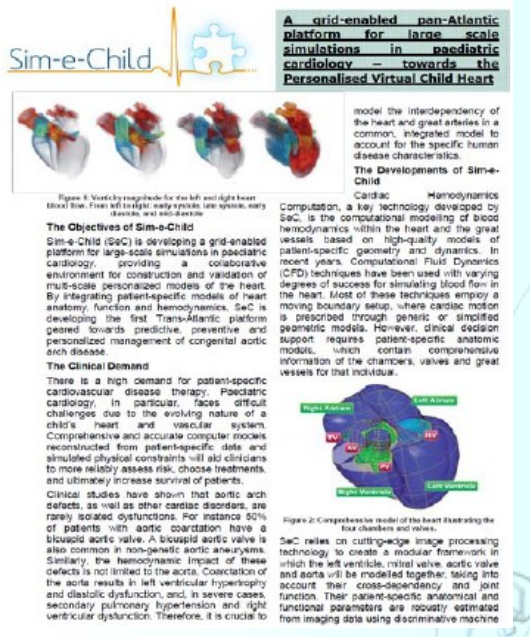


*Patient-specific modelling of whole heart anatomy, dynamics and haemodynamics from four-dimensional cardiac CT images*, Royal Society Interface Focus Journal, June 6, 2011.

This article, a preliminary version of which had first been presented at the Virtual Physiological Human Conference 2010, Brussels 2010, has been highlighted in the cover page of the Royal Society's Interface Focus journal

**ConhIT**

In April 2011 SeC participated at ConHIT in Berlin with a booth and distributed a factsheets tailored for the audience.


Sim-e-Child

**A grid-enabled pan-Atlantic platform for large scale simulations in paediatric cardiology – towards the Personalised Virtual Child Heart**

**The Objectives of Sim-e-Child**

Sim-e-Child (SeC) is developing a grid-enabled platform for large-scale simulations in paediatric cardiology, providing a collaborative environment for construction and validation of multi-scale personalized models of the heart. By integrating patient-specific models of heart anatomy, function and hemodynamics, SeC is developing the first Trans-Atlantic platform geared towards predictive, preventive and personalized management of congenital aortic arch disease.

**The Clinical Demand**

There is a high demand for patient-specific cardiovascular disease therapy. Paediatric cardiology, in particular, faces difficult challenges due to the evolving nature of a child's heart and vascular system. Comprehensive and accurate computer models reconstructed from patient-specific data and simulated physical constraints will aid clinicians to more reliably assess risk, choose treatments, and ultimately increase survival of patients.

Clinical studies have shown that aortic arch defects, as well as other cardiac disorders, are rarely isolated dysfunctions. For instance 50% of patients with aortic coarctation have a bicuspid aortic valve. A bicuspid aortic valve is also common in non-genetic aortic aneurysms. Similarly, the hemodynamic impact of these defects is not limited to the aorta. Coarctation of the aorta results in left ventricular hypertrophy and diastolic dysfunction, and, in severe cases, secondary pulmonary hypertension and right ventricular dysfunction. Therefore, it is crucial to model the interdependency of the heart and great arteries in a common, integrated model to account for the specific human disease characteristics.

**The Developments of Sim-e-Child**

Cardiac Hemodynamics Computation, a key technology developed by SeC, is the computational modelling of blood hemodynamics within the heart and the great vessels based on high-quality models of patient-specific geometry and dynamics. In recent years, Computational Fluid Dynamics (CFD) techniques have been used with varying degrees of success for simulating blood flow in the heart. Most of these techniques employ a moving boundary setup, where cardiac motion is prescribed through generic or simplified geometric models. However, clinical decision support requires patient-specific anatomic models, which contain comprehensive information of the chambers, valves and great vessels for that individual.

Figure 2: Comprehensive model of the heart illustrating the four chambers and valves.

SeC relies on cutting-edge image processing technology to create a modular framework in which the left ventricle, mitral valve, aortic valve and aorta will be modelled together, taking into account their cross-dependency and joint function. Their patient-specific anatomical and functional parameters are robustly estimated from imaging data using discriminative machine learning methods. As large medical databases become available, machine learning approaches extended with semantic constraints have proven to be successful in solving model estimation problems in high-dimensional spaces. The a posterior probability distribution of the model parameters is effectively captured using boosting algorithms trained on large populations of expert annotated studies. The resulting detectors are applied within a marginal space formulation to hierarchically estimate patient-specific models cardiac images unseen by clinicians. In this way, patient-specific heart models can be generated from multi-modal data without tedious user interaction, enabling routine clinical applicability of comprehensive cardiac modelling.

The SeC CFD solver handles the geometrical and topological complexity of the cardiac models robustly, using the embedded boundary and ghost fluid methods within a level-set formulation. Cardiac wall motion specifies the boundary conditions of the blood flow dynamics governed by Navier-Stokes equations. Computations automatically follow regions of interest, accurately capturing critical hemodynamic details through adaptive mesh refinement (AMR) approaches. In addition, simulations that require intense numerical calculations are executed remotely in a distributed fashion on a high-performance computation grid.

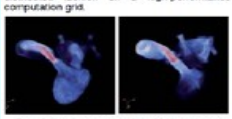


Figure 3: Vorticity pattern in patient with bicuspid aorta during early systole (left) and mid systole (right).

The collection of new and established heart models used by this project is currently undergoing rigorous clinical validation in collaboration with clinical partners in the EU and US.

**Expected Results & Impacts**

SeC is impacting on the way health knowledge is formalized, acquired, understood, represented, analysed, communicated and validated in paediatrics. Thanks to the accrued investments made by the EC in an area such as grid-enhanced computational capacities, where the EU is now a world leader, it will become possible to allow large-scale patient-specific simulations utilizing computationally intensive data-driven models of the full heart and aorta with fluid dynamics and biomechanics. This capacity is based on aligned clinical databases in both the EU and the US, showing that not only the current lack of uniform clinical definitions/formats, which normally impedes electronic representation, transfer, and aggregation of much patient information, can be overcome, but also that testing new potential decision support tools can be performed on a cooperative basis across the Atlantic.

The mix of EU and US research, industrial and clinical partners cooperating in SeC is helping to develop the global health information research infrastructure which is needed for spurring knowledge discovery and translating knowledge faster to benefit patients in terms of both improved quality and safety.

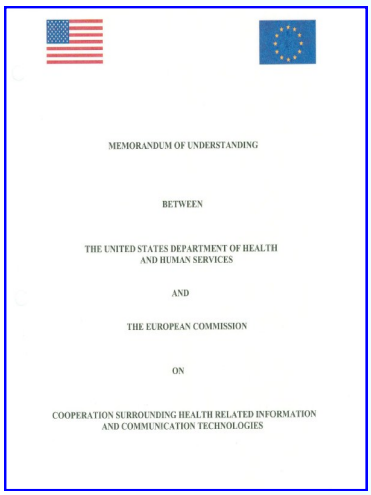
The predictive power facilitated by the Sim-e-Child platform will improve decision making in paediatric cardiology by supporting discovery of new biomarkers and comprehensive patient-specific analysis of complex congenital conditions. Moreover, simulations of cardio-vascular interventions will model morphological changes and their impact on function, and hemodynamics to allow personalized risk assessment, planning and prediction for optimal therapy.

Project Title: Sim-e-Child
Project co-ordinator: Siemens AG
Contact person: Michael Suehling
Email: michael.suehling@siemens.com
Website: www.Sim-e-Child.org
Partners names in full (country)
Siemens AG, (Germany)
Ingenieus Srl, (Italy)
Maut France, (France)
Technische Universität München, (Germany)
Ospedale Pediatrico Bambino Gesù, (Italy)
Siemens Corporate Research, (USA)
Johns Hopkins University, (USA)
American College of Cardiology, (USA)
Total cost: € 7,668,560.00
EC funding: € 993,873.00
Project StartDate: FP7-ICT- 248421

The Project Coordinator Michael Suehling was also a participant in the debate *An EU of opportunities: eHealth activities at European level and the programs of the European Commission*, chaired by EC-Representative Loris Di Pietrantonio.

The following link is to a video of the seminar at conhIT:[www.youtube.com/watch?v=LkRTyNtutP0](www.youtube.com/watch?v=LkRTyNtutP0).


**ARGOS VPH Policy Brief**


MEMORANDUM OF UNDERSTANDING

BETWEEN

THE UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES

AND

THE EUROPEAN COMMISSION

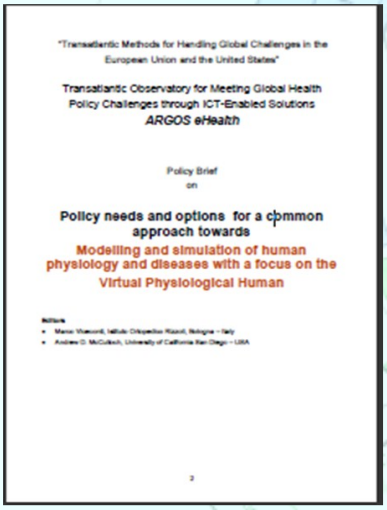
ON

COOPERATION SURROUNDING HEALTH RELATED INFORMATION AND COMMUNICATION TECHNOLOGIES

SeC played a role within the EU/US cooperation. SeC's partners were invited to coordinate the development of a summary of the success stories in EU-US collaboration on VPH research for cardiology for the ARGOS VPH Policy Brief which was put forward as a proposal for the extension of the Memorandum of Understanding (MoU) that had been signed by the Vice-President of the European Commission, Nellie Kroes, and the United States Secretary of Health and Human Services, Kathleen Sebelius, in 2010. ( www.biomedtown.org/argos/reception/brief).

An EU-U.S. session on the implementation of the MoU will take place at the next e-Health week in Copenhagen, in May 2012.

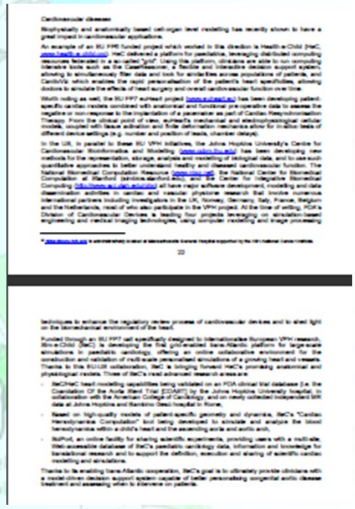
SeC figures therefore in the ARGOS VPH Policy Brief.



"Transatlantic Methods for Handling Global Challenges in the European Union and the United States"

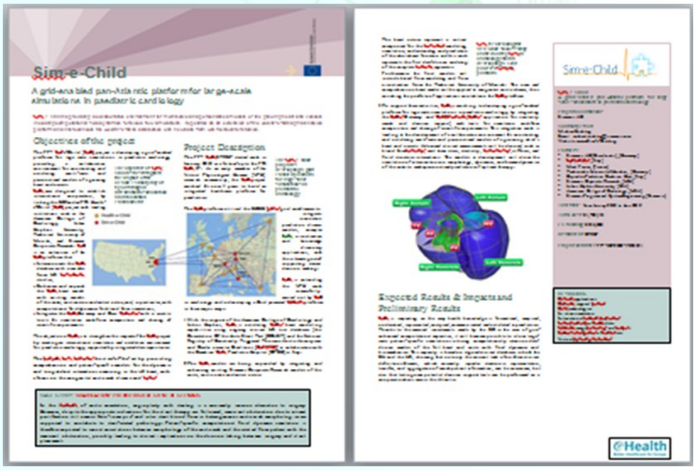
Transatlantic Observatory for Meeting Global Health Policy Challenges through ICT-Enabled Solutions
*ARGOS eHealth*

Policy Brief on

**Policy needs and options for a common approach towards**
**Modelling and simulation of human physiology and diseases with a focus on the Virtual Physiological Human**



SeC developed a 2 pages factsheet for distribution among those present at the signing of the Memorandum of Understanding between the EU and the US related to ICT for Health and at the following workshop on *Ongoing and planned actions* between the US Office of the National Coordinator for Health Information Technology and the European Commission, which took place in April 2011.



## Major Conferences Participation

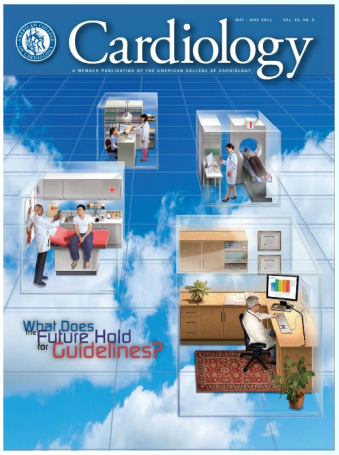
- Pediatric & Adult Interventional Cardiac Symposium (Boston, USA, July 2011)
- SeC's clinical advances were presented in conjunction with the announcement of OPBG's Paediatric Cardiology Digital Repository the completion of which is due in the first half of 2012 at 5 sites across Italy
- ConHIT in Berlin (April 2011)
- Association for European Paediatric Cardiology (Grenada, 18-21 May 2011)
- MICCAI 2011 (Toronto, September, 2011)
- WHO's eHealth pavilion during the ITU Telecom World 2011 symposium (Geneva, October 2011): SeC was featured in a presentation given by David Manset (Maat) and a live demonstration of the SeC simulation platform was also given to visitors: http://www.itu.int/ITU-D/cyb/events/2011/Telecom11/e-health/index.phtml

Geneva, October 2011
Live demonstration of the SeC simulation platform

- A SeC abstract on *Fully-automatic, patient -specific 3D aortic arch modelling for patient treatment with aortic arch anomalies* will be presented at the Society for Cardiovascular Magnetic Resonance (SCMR) 2012 to be held in Orlando, Fl, in February 2012.

### SeC dissemination through ACC

Thanks to the American College of Cardiology (ACC) an article, authored by Allen Everett (JHU), has been published in the *Cardiology Magazine n.3–2011 (May-June)*, a journal regularly sent to over 40,000 ACC members (http://www.bluetoad.com/publication/index.php?p=1&i=70062&ver=swf&pp=1&zoom=0 )




**New Project to Allow for Large-Scale Simulations in Pediatric Cardiology**

The American College of Cardiology (ACC) has partnered with U.S. and international institutions to develop a congenital heart disease modeling platform called Sim-e-Child. The FP7 European Commission funded project is working to develop a grid-enabled platform for large scale simulations in pediatric cardiology, focusing on aortic coarctation and aneurysms.

A key technology developed within Sim-e-Child, is the computational modeling of blood hemodynamics within the heart and the great vessels based on comprehensive models of patient-specific geometry and dynamics. The 30-month program will take advantage of existing MRI imaging in U.S. Food and Drug Administration (FDA) Coarctation Stent Trial (COAST) to develop computer models for stenting of the aorta. It will model what the disease will look like both with and without treatment and personalize therapy for patients. It will also validate newly developed automated volumetric tools for MRI right ventricular volume assessment in tetralogy of Fallot. The results of the right ventricular volume tool validation were presented in May at the Association for European Pediatric Cardiology meeting.

**Allen D. Everett, MD, FACC**, associate professor of pediatric cardiology at Johns Hopkins University and U.S. leader of the project said automobile and aircraft industries have been using modeling for years and by doing the same in pediatric cardiology, the models will help design better therapies.

"It is a wonderful starting point and we wouldn't have been able to do this without the ACC and other partnerships," said Everett. "It's not until you have a lot of information about how the aorta works that you know what will really be the right treatment option. This hopefully will help the field move forward faster. If you have good, routine data there's evidence that you can do more with what you've got with better endpoints."

On the ACC website, Cardiosource (www.cardiosource.org), there is now a link connecting to SeC's website.

120,000 registered users, about half of which are international. So far in 2011, 989,669 visitors and 1,621,246 total page visits.

**Annual ACC Conference 2012, March 24–27, 2012**

A SeC booth will be showing live demos at the forthcoming Annual ACC Conference -McCormick Place in Chicago, Illinois.

Attendees will include cardiovascular professionals, including physicians, scientists, nurse practitioners, physician assistants and nurses, medical students and trainees, technicians, dietitians, administrators and other health care professionals.

ACC 2011

A SeC's abstract , titled *Mri In children and young adults with aortic coarctation repair reveals a high Incidence of re-coarctation*, will be presented within the "Imaging: MRI Applications in Diastology, Pulmonary Hypertension and Congenital Heart Diseas" session on Saturday March 24, 2012.

**A SeC meeting at the Heart House in Washington in June 2012**

ACC is Now working on having in Washington a June meeting at the Heart House to be the final demonstration of the project outcomes:

- ½ day meeting with invited speakers
- Possibly an opportunity for having also a Webinar

# SeC's Left Heart Model Extension

**Personalized complete aortic model estimated from 3D MRI volumes**

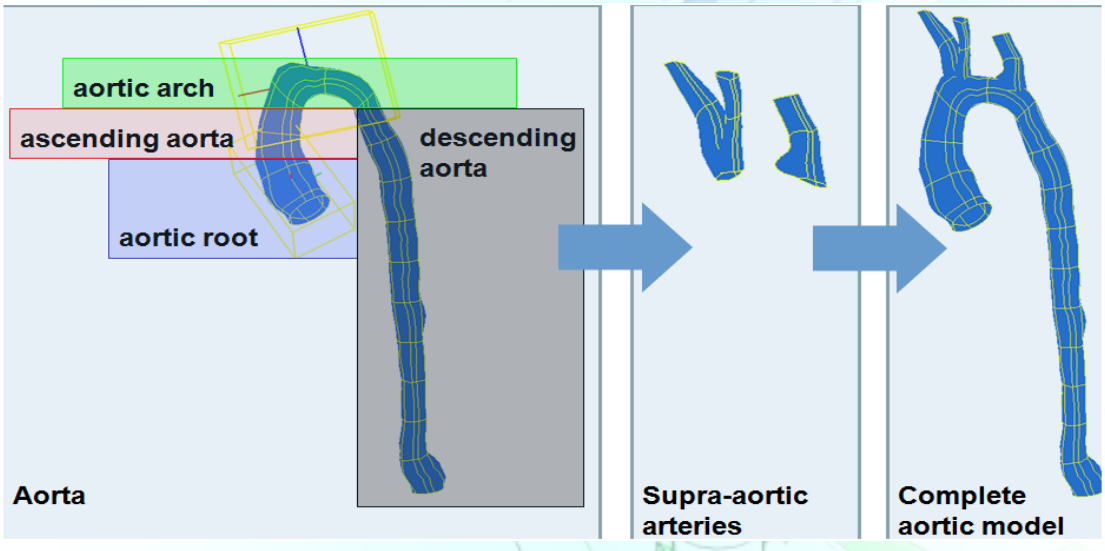
We have developed hierarchical three-stage classification-based method for estimating patient-specific models of the aorta

Hierarchical model representation

- bounding boxes: parameterized by position, orientation and scale include the regions of the aortic root, arch and supra-aortic arteries
- center line: presents the center of the vessel structure
- aortic surface: point-distribution model (PDM)

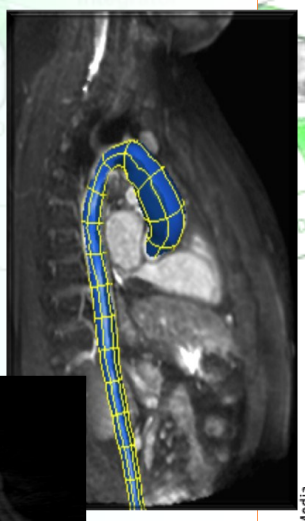
supra-aortic arteries: point-distribution model (PDM)

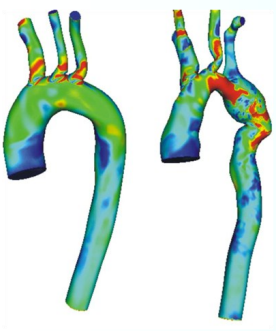
In SeC we employ a part-based aorta model by splitting the whole aorta into four parts: aortic root, ascending aorta, aortic arch, and descending aorta.



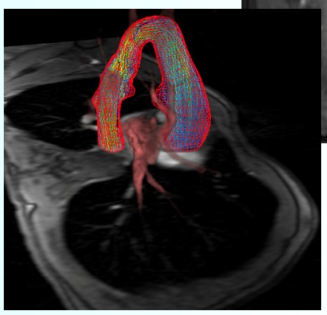

Hierarchical model representation: part-based segmentation approach

Automatic, patient-specific 3D aortic arch model estimation from MRI images provides a better understanding of the geometry of the aortic arch anomaly and might be utilized to evaluate preoperatively the best treatment. Clinicians from JHU and OPBG validated the accuracy of the estimated patient-specific 3D aortic model by comparing manual with model-based derived aortic measurements.





The fully-automated method for personalized aortic model estimation markedly reduced the time necessary to complete volumetric assessment of the aorta.

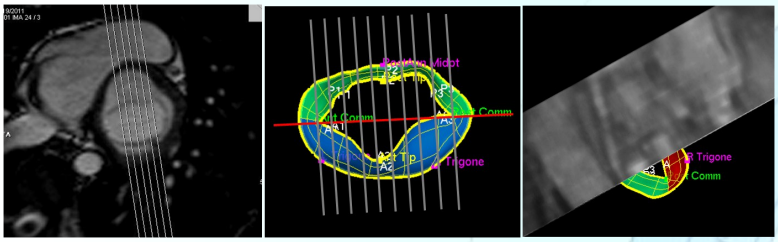


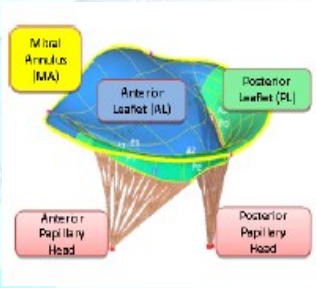
From the results, we have concluded that the aortic measurements automatically derived from our model are reliable, fully-reproducible and faster as compared to manual methods.

*Sim-e-Child: a 30-month Specific Targeted Research Project co-funded under the 7th Framework Programme priority "Information Society Technologies"*

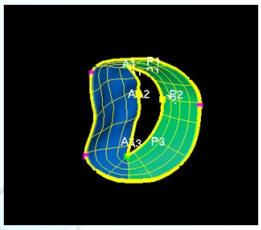
## Personalized mitral valve model estimation

Based on these MRI acquisition protocol adaptations, we developed a novel regression-based method for patient-specific 4D MV model estimation. Based on extensive experiments on simulated data, we first defined the acquisition protocol and optimized it with respect to the number and spatial configuration of the 2D+t MRI slices resulting in reduced acquisition time and 4D MV estimation error. Second, we developed a novel regression-based algorithm to estimate a complete patient-specific mitral valve model from incomplete 2D+t MRI images. The main idea of our algorithm developed consists of learning a regression model from existing mitral valve models from other imaging modalities, CT and Ultrasound, which then can be utilized to estimate personalized MV models from 2D+t MRI images.



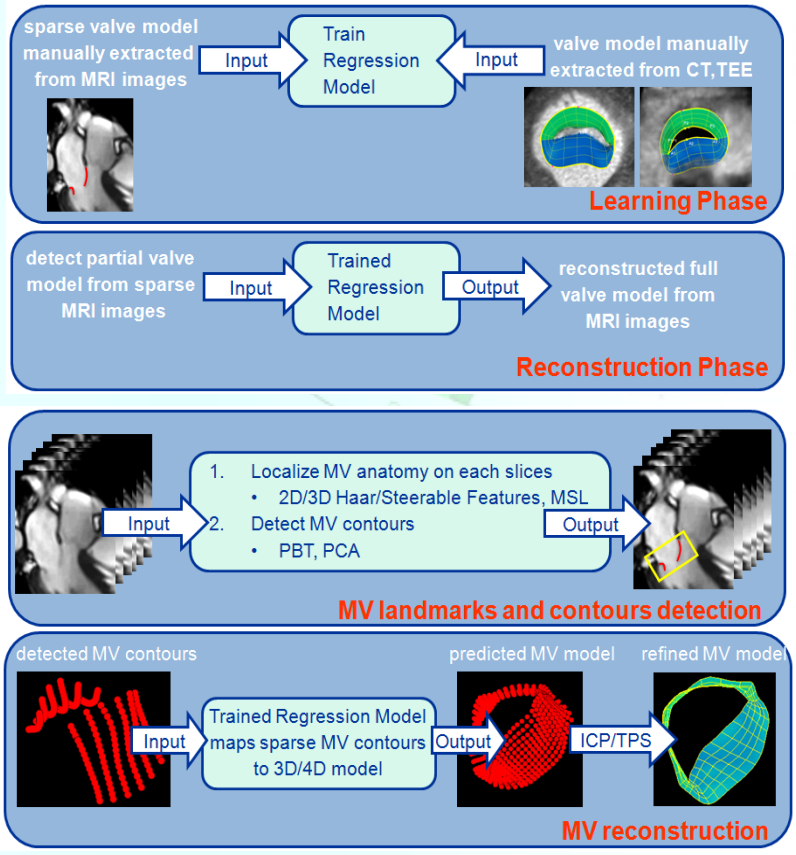



Parallel MRI images are acquired perpendicular to the mitral valve commissures



### Results

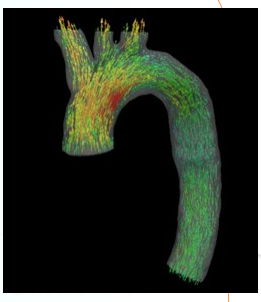
With the results of the inter modality accuracy we prove the applicability of the MV anatomical model across different imaging modalities. In addition, we have shown that a regression model can be learned from one imaging modality (US) and used to estimate a patient-specific MV model in other imaging modality (CT). Finally, the regression model was defined with the best parameter configuration on all available US and CT data (1295 3D volumes). We then applied the learned regression model to estimate patient-specific MV models from the 15 MRI studies acquired according to the developed protocol and evaluate the model estimation accuracy by computing the point-to-mesh distance between the estimated and the associated ground-truth model.



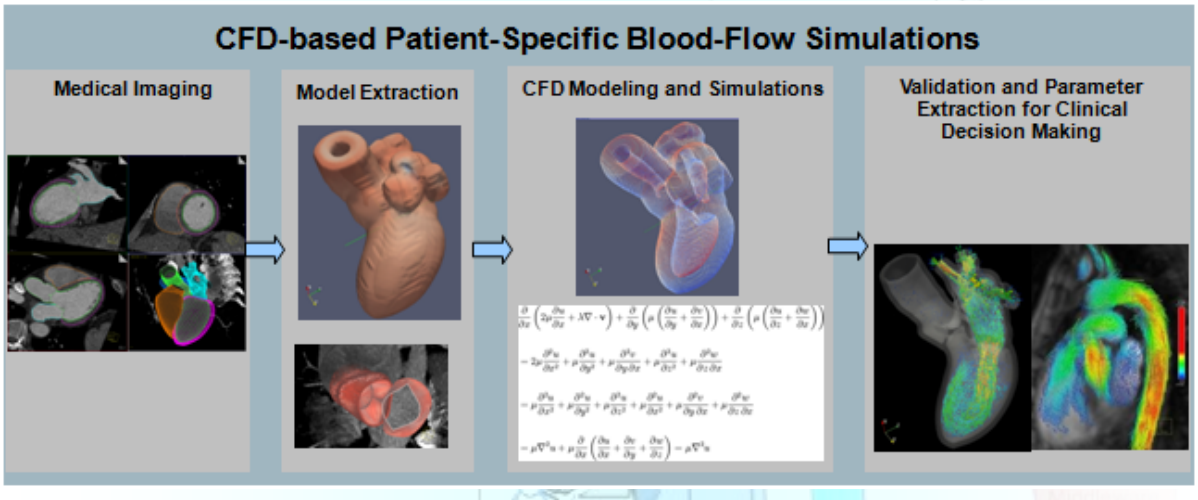

Mitral Valve reconstruction workflow from MRI images

*Sim-e-Child: a 30-month Specific Targeted Research Project co-funded under the 7th Framework Programme priority "Information Society Technologies"*

# SeC's Patient-Specific Haemodynamics Simulation

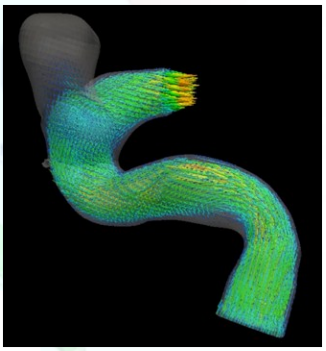


We have developed a unified computational framework for large-scale hemodynamic modelling and simulations to aid diagnostic and therapy decision making. Our method provides a deterministic and streamlined processing pipeline to perform Computational Fluid Dynamics (CFD) simulations from the estimated patient-specific models. The developed method includes an automated approach to segment the inlet and outlet flow profiles over the entire cardiac cycle.




**Result**

With the developed CFD simulation framework we have performed a series of simulations using the geometric constraints of the aortic meshes as static boundary conditions, and the sampled MRI-derived velocity as the inflow profiles. The aortic data was selected from patients with various pathologies, including bicuspid valve, coarctation, artificial valves and stents. We will give here an outline of several observed patterns that correlate with the various pathologies.



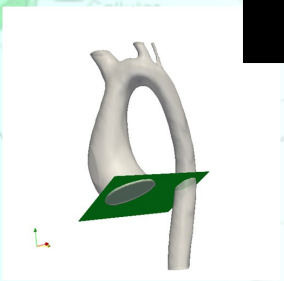
**Validation Approach**

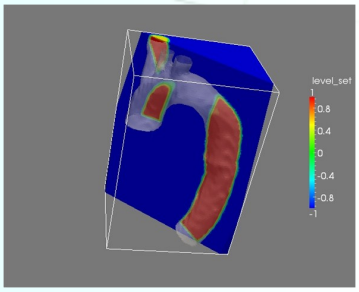
**Comparison at distal descending aorta:**

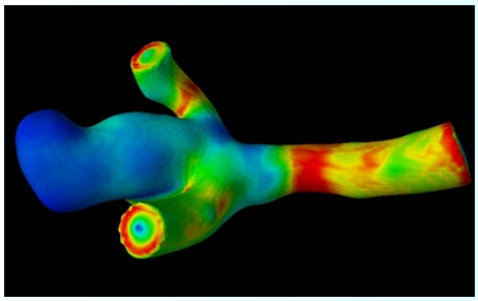
- PC-MR measurement
- CFD simulation

**Baseline parameters (over time):**

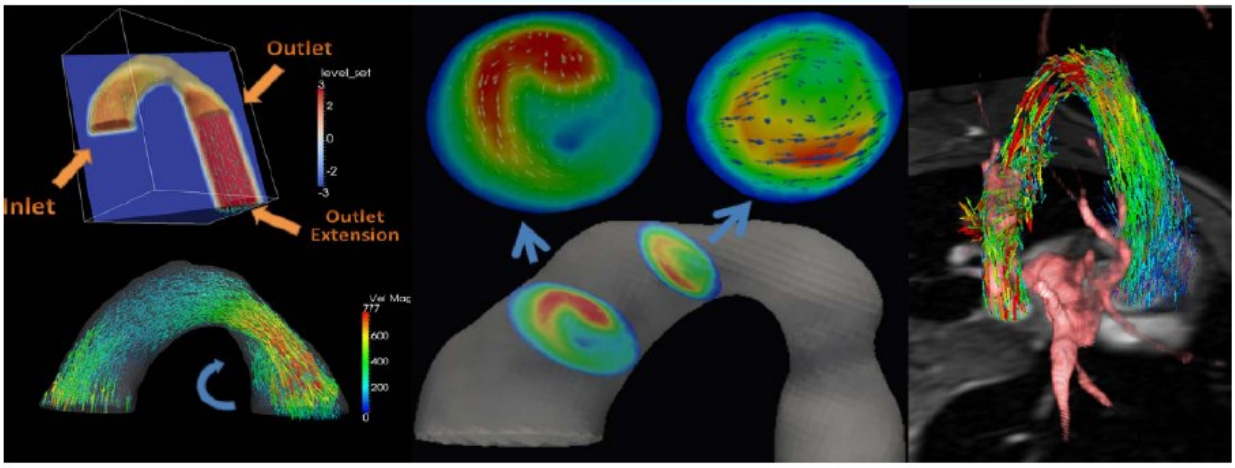
- Blood flow rate
- Max/min velocity values
- Spatial patterns in cross section







Outlet pressures from axisymmetric Windkessel simulation

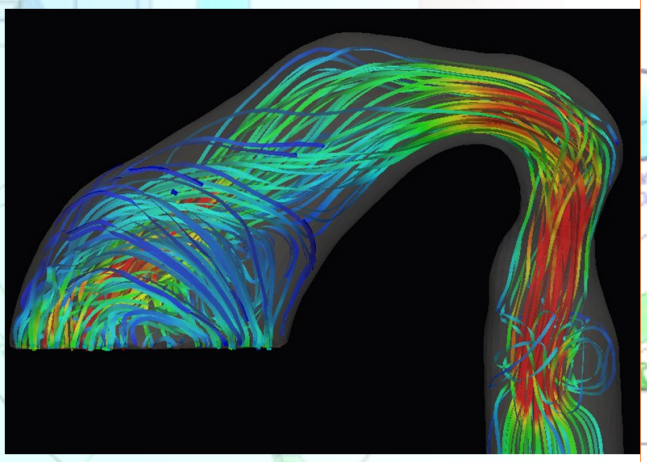



(a) our computational setup: the Lagrangian aortic mesh is embedded in an Eulerian domain using level set. Visible here are a cross-section of the domain, color-coded with the level set values, and the embedded aortic mesh (in transparent yellow) together with its outlet extension (in transparent white). The blood flow velocity field during early systole, simulated using CFD, is also visualized as a vector field. Below, coarctation with vortex formation. (b) Enhanced helical rotation due to bicuspid valve. (c) Simulation results overlaid with anatomical images.

## Motivation

**Clinicians would like to know:**

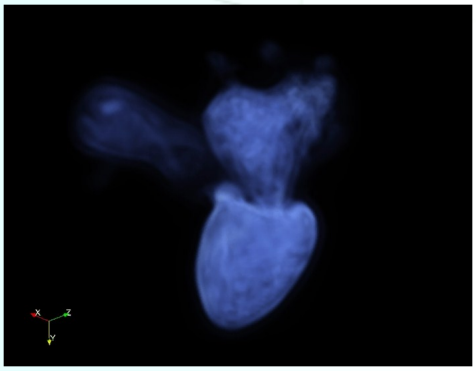
- If procedure will result in unobstructed flow?
- How laminar the flow would be at the mouth of a stent?
- Assess the vorticity in in narrow transverse aortic arch geometry?
- How much energy is delivered to the wall (bicuspid AV)? Relation to dilation?
- Can we provide better indicators that necessitates intervention for aortic aneurisms?
- Why does high blood pressure stay two years after stenting?



Heart with bicuspid aortic valve produces enhanced helical pattern, due to the blood jet that hits aortic wall in the lower ascending aorta.

**Simulation:**

- Provide patient-specific biomarkers
- Enhance diagnosis
- Predict therapy (e.g. material properties)
- Based on standard cardiac MR imaging



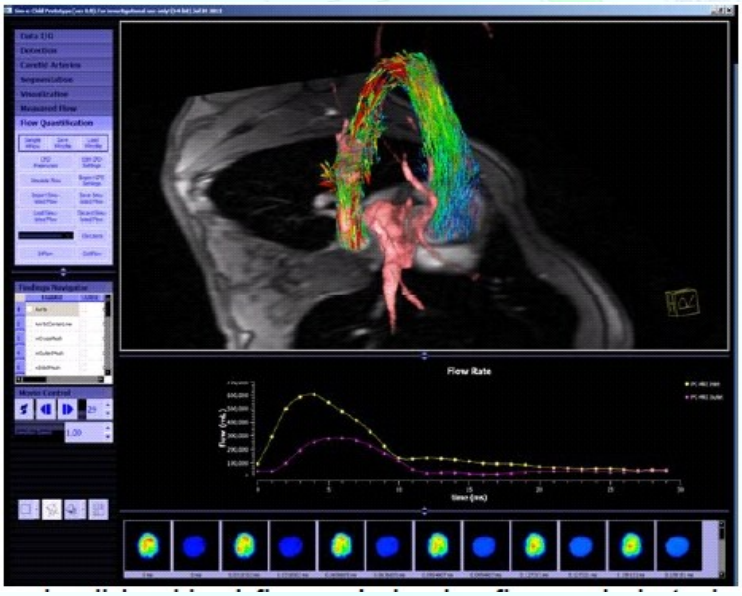
Vorticity magnitude

# SeC's Validation Studies

5 studies have been planned as examples of the clinical objectives for the final 6 months of the project. The timeframe of the project will not allow for the completion of all of them and they have therefore been designed to evolve as clinicians gain more experience with SeC's tools.
Before the end of the first quarter of 2012 the five studies will have been refined, focused and prioritised by all the relevant partners to ensure that by the end of the project, in June 2012, one at least will be completed and the remaining ones will be emblematic of SeC's potential future clinical exploitation activities after the end of the project.
For the time being, the studies should therefore not be considered to be set in stone or to be indicative of work that will be necessarily carried out with EC funding and within the time limits of the project.

## Impact of Aortic Coarctation stent implantation to the hemodynamics of the ascending aorta

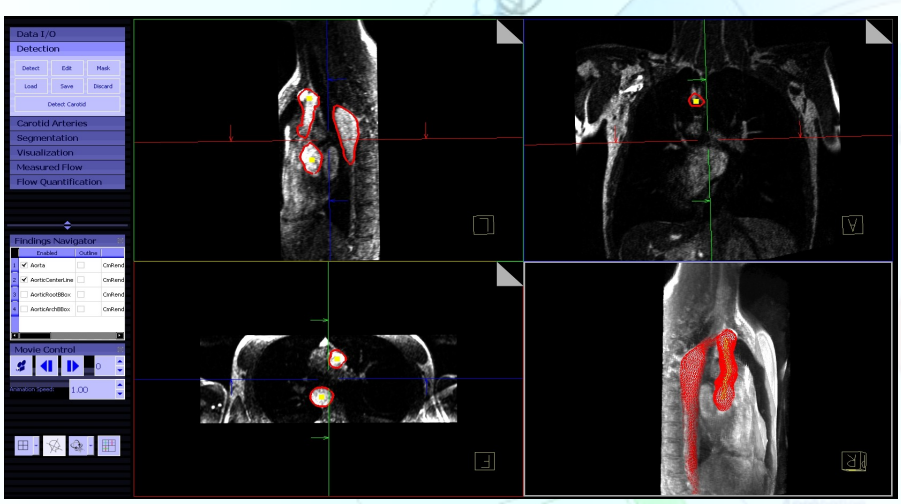
Treatment options for aortic coarctation include surgical approaches, transcatheter balloon angioplasty with or without stent placement. Stent therapy results in significant angiographic improvement and gradient reduction with a low rate of acute procedure-related adverse events and no mortality. Long-term outcomes seem to be comparable or superior to the surgical approach (Holzer R. et al, Cath and Card Int, 2010, 76:553-563). Nevertheless, aortic wall complications such as aortic aneurysms and/or dissection may develop, despite successful outcome of the aortic arch repair, either percutaneous or surgical. The impact of stent on blood patterns in different segments and morphologies of the aortic arch, and precisely in the progression of the dilatation of the ascending aorta, is still being debated. Understanding how the stent placement could change the blood pattern could be useful in identifying precociously patients with high-risk aortic wall complications and then improve timing of interventions.




SeC's SimSys visualizing blood flow and showing flow analysis tools during an aorta workflow

# Coarctation: Prediction of the risk of stent re-stenosis

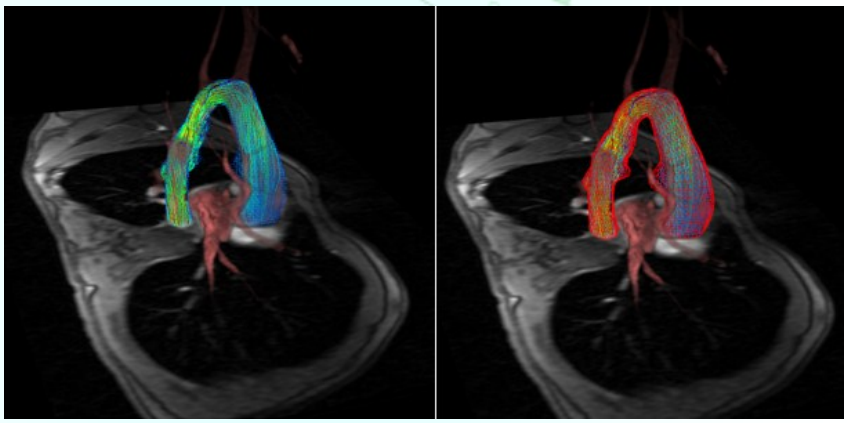
Treatment of aortic coarctation consists of either surgical repair or angioplasty with stenting. Stenting is a minimally invasive alternative to surgery, however very little data are available on the real incidence of recurrent obstruction, aortic wall complications or blood pressure recordings. Despite the right indications to the stent placement (coarctation length/location/morphology/ distance from the subclavian artery, patient's weight) are followed, recurrent obstructions due to intimal proliferation still occur. This seems to be related to the vascular health impairment due to the increase of the aortic stiffness in the stented section. Moreover, non-linear pre- and intra stent flow in some aortic arch morphology could be the cause of the stent-related pathology. The use of patient -specific computational fluid dynamic simulation could indicate if there is a correlation between morphology of the aortic arch and the related flow pattern with the recurrent obstruction. This information could support clinical decision making when choosing between surgery and stent placement.




An example of how from MR images (unenhanced, free-breathing, T2-prepared, segmented 3D SSFP sequence of the whole chest, used at OPBG Hospital in paediatric patients) can be obtained a patient-specific aortic arch model

## Prediction of Stenting Success

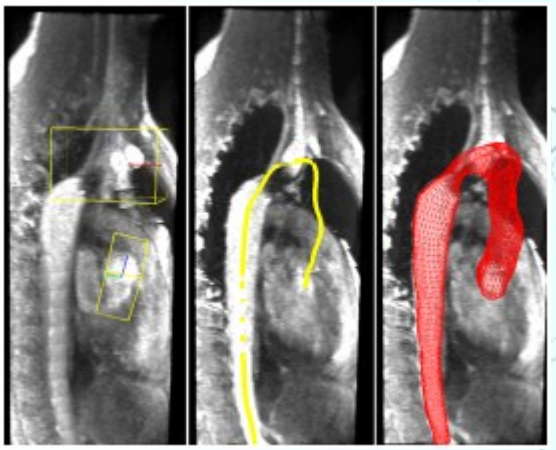
Presently other than baseline aortic diameter there is no predictor of aortic stenting efficacy. Likely factors determining outcome that have not been evaluated are aortic distensibility abnormalities because of intrinsic coarctation wall abnormalities and scar burden from previous surgical repairs in re-coarctation. There are no non-invasive means to determine these aortic wall properties to make stenting efficacy predictions. A long-term validation effort will be to assess the ability of pre-intervention MRI measures of aortic flow, wall distensibility and scar burden to predict stenting acute and medium term (1 year) hemodynamic efficacy.



Examples of an estimated patient-specific flow (left) and its aortic model (right)

# The prediction of the risk of ascending aortic dilatation and aneurysm formation in bicuspid valve patients

The most frequent finding associated with the bicuspid aortic valve (BAV) is the dilatation of the proximal ascending aorta (AA) secondary to abnormalities of the aortic media. Changes in the aortic media are present independently of the valve functionality and, consequently, AA dimensions increase and the related aortic dissection seem not to be connected with hemodynamic abnormalities. However, the abnormal shear stress related to BAV leads to valve calcification, aortic incompetence, further aortic root and proximal AA dilatation. In addition, surprisingly Debl K et al (Clin Res Cardiol 2009, 98:114-120) pointed out that the aortic arch and descending aorta diameters were identical in subjects with BAV and tricuspid aortic valve. Therefore, a potential explanation of such finding might be that these aorta segments are subject to less hemodynamic stress as compared to AA which may not reach a threshold necessary for progressive dilatation. Understanding the progression of this complex disease will help to precisely define late survival, identify earlier high-risk groups, and improve timing of interventions.



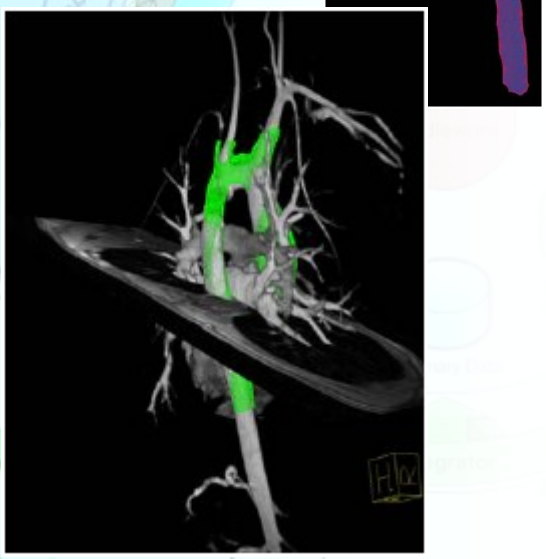




Image: 3D Aortic arch geometry automatically determined from MR images by Sim-e-Child software

## Assessment of Cardiac Remodelling

Ventricular-aortic coupling as a marker of stenting efficacy: Aortic coarctation results in left ventricular hypertrophy and hypertension. Despite a surgical resection of the coarctation segment without residual aortic arch obstruction, many patients are still hypertensive and left ventricular hypertrophy persists. As a long-term validation, clinicians will be examining ventriculo-aortic coupling modelling aortic valve and proximal aortic function, left ventricular mechanics coupled with flow to predict an optimal therapeutic outcome. It is hypothesized that a failure to reverse ventricular hypertrophy and strain post stenting is a prognostic marker of a poor near term (2 years) hemodynamic outcome.

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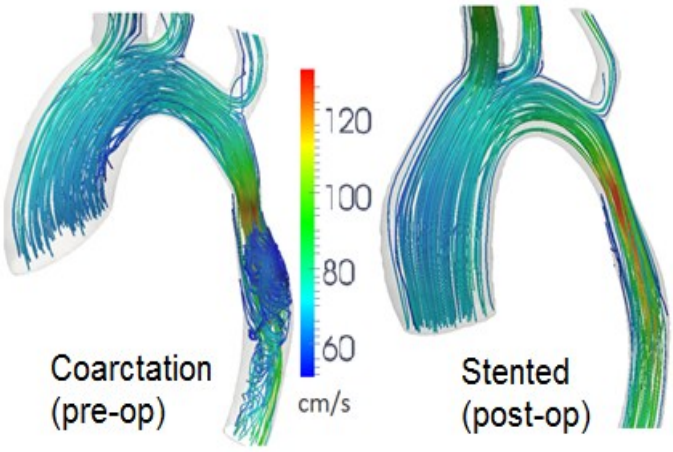
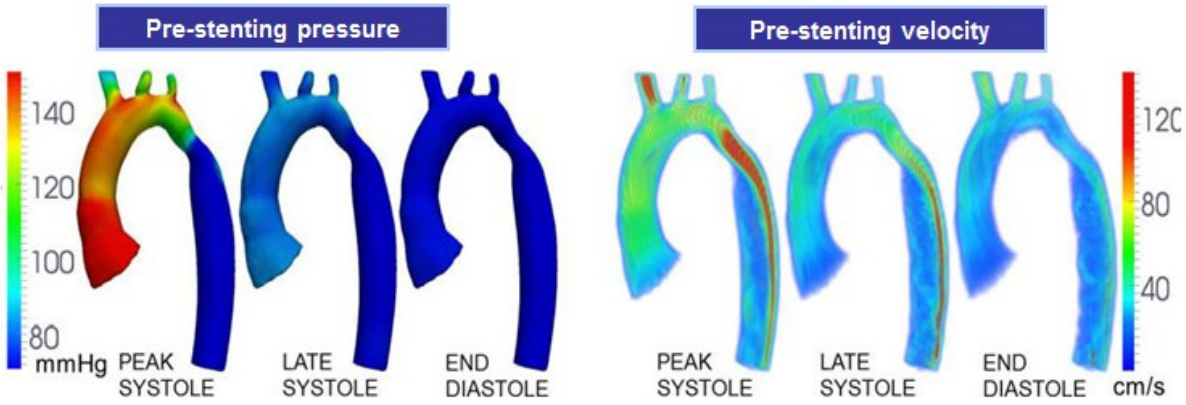
## Exemplary results

- Pre- and post-operative flow streamlines
  - Pre-op: Complex flow patterns typically associated with stenosis
  - Post-op: After stent implantation, flow is improved, characterized by lack of recirculation




## Example of Current Clinical Validation

- Comparison of simulated pressure values with cardiac catheterization pressure measurements in pre- and post stenting cases




- Next step: Simulate stenting outcome (e.g. changes in pressure gradient) by "inserting a virtual stent" in pre-operative image data

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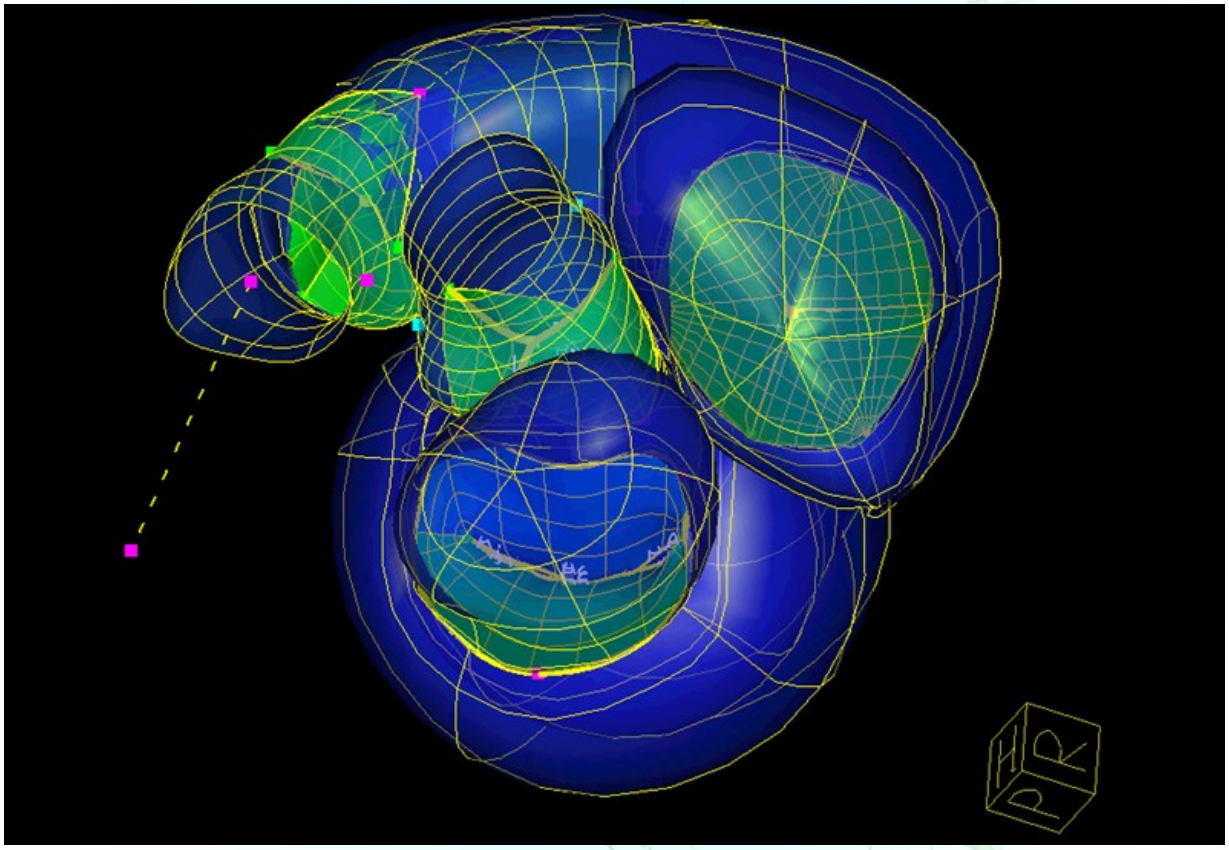

Sim-E-Child's comprehensive heart model

# SeC's Publications up to December 2011


Amodeo A, Brancaccio G, Michielon G, Filippelli S, Ricci Z, Morelli S, Gagliardi MG, Iacobelli R, Pongiglione G, Di Donato RM., *Pneumatic pulsatile ventricular assist device as a bridge to heart transplantation in pediatric patients*, Artif Organs. 2010 Nov;34(11):1017-22.

Barcudi S, Sanders SP, Di Donato RM, de Zorzi A, Iacobelli R, Amodeo A, Gagliardi MG, Borgia F, Pongiglione G, Rinelli G., *Aberrant left innominate artery from the left descending aorta in right aortic arch: echocardiographic diagnosis*, J Am Soc Echocardiogr. 2010 Feb;23(2):221.e5-7.

Brancaccio G, Amodeo A, Ricci Z, Morelli S, Gagliardi MG, Iacobelli R, Michielon G, Picardo S, Parisi F, Pongiglione G, Di Donato RM., *Mechanical assist device as a bridge to heart transplantation in children less than 10 kilograms*, Ann Thorac Surg. 2010 Jul;90(1):58-62.

Carotti A, Albanese SB, Filippelli S, Ravà L, Guccione P, Pongiglione G, Di Donato RM., *Determinants of outcome after surgical treatment of pulmonary atresia with ventricular septal defect and major aortopulmonary collateral arteries*, J Thorac Cardiovasc Surg. 2010 Nov;140(5):1092-103.

Cavallini M, Di Zazzo G, Giordano U, Pongiglione G, Dello Strologo L, Capozza N, Emma F, Matteucci MC., *Long-term cardiovascular effects of pre-transplant native kidney nephrectomy in children*, Pediatr Nephrol. 2010 Dec;25(12):2523-9.

Comaniciu, D., *Patient-Specific Modelling of Whole Heart Anatomy, Dynamics and Hemodynamics from 4D cardiac CT Images*, Interface Focus 2010 - (invited publication-submitted)

De Caro E, Smeraldi A, Trocchio G, Calevo M, Hanau G, Pongiglione G., *Subclinical cardiac dysfunction and exercise performance in childhood cancer survivors*, Pediatr Blood Cancer. 2011 Jan;56(1):122-6.

De Caro E, Spadoni I, Crepaz R, Saitta M, Trocchio G, Calevo MG, Pongiglione G., *Stenting of aortic coarctation and exercise-induced hypertension in the young,* Catheter Cardiovasc Interv. 2010 Feb 1;75 (2):256-61. Erratum in: Catheter Cardiovasc Interv. 2010 Jun 1;75 (7):1143.

Everett, A., Development and validation of a novel automated learning based algorithm for quantification of MRI right ventricular volume in Tetralogy of Fallot, submitted abstract for the 45th Annual Meeting of the Association of European Paediatric Cardiology, to be held in Granada, Spain in May 2011.

Gagliardi MG, Papavasileiou L, Pongiglione G, Rescue treatment by percutaneous closure of interatrial septal defect or PFO in infants with berlin heart, Catheter Cardiovasc Interv. 2010 Sep 17

Grbic S., Ionasec R., D. Vitanovski, Ingmar Voigt, B. Georgescu, , N. Navab, D. Comaniciu, *Complete Valvular Heart Apparatus Model from 4D Cardiac CT*, Medical Image Computing and Computer Assisted Intervention (MICCAI), Beijing, China, September 20-24 2010.

Ionasec R., Georgescu B., Navab N., Comaniciu D., *Patient-Specific Modelling of Whole Heart Anatomy, Dynamics and Hemodynamics from 4D cardiac CT Images*, BMT – 2010, Rostock2010

Vitanovski D., Razvan Ioan Ionasec, A. Tsymbal, B. Georgescu, M. Huber, Joachim Hornegger, D. Comaniciu, *Cross-modality Assessment and Planning for Pulmonary Trunk Treatment using CT and MRI imaging*, Medical Image Computing and Computer Assisted Intervention (MICCAI), Beijing, China, September 20-24 2010.

Mihalef, V., Ionasec, IR., Sharma, P., Georgescu, B., Huber, M., Comaniciu, D., *Patient-Specific Modelling of Whole Heart Anatomy, Dynamics and Hemodynamics from 4D cardiac CT Images*, Virtual Physiological Human Conference 2010, Brussels 2010.

Carotti A, Albanese SB, Filippelli S, Ravà L, Guccione P, Pongiglione G, Di Donato RM, *Determinants of outcome after surgical treatment of pulmonary atresia with ventricular septal defect and major aortopulmonary collateral arteries.*, J Thorac Cardiovasc Surg. 2010 Nov

Gagliardi MG, Papavasileiou L, Pongiglione G., *Rescue treatment by percutaneous closure of interatrial septal defect or PFO in infants with Berlin heart*., Catheter Cardiovasc Interv. 2011 March

Tuo G, Volpe P, Bondanza S, Volpe N, Serafino M, De Robertis V, Zannini L, Pongiglione G, Calevo MG, Marasini M., *Impact of prenatal diagnosis on outcome of pulmonary atresia and intact ventricular septum*., J Matern Fetal Neonatal Med. 2011 Jun

Ionasec R., Suehling M., Comaniciu D., *Sim-e-Child: Grid-Enabled Platform for Simulations in Paediatric Cardiology Toward the Personalized Virtual Child Heart* – VPH NoE 2010

Voigt, T. Mansi, V. Mihalef, R. Ionasec, A. Calleja, E. Mengue, P. Sharma, H. Houle, B. Georgescu, J. Hornegger, D. Comaniciu: *Patient-Specific Model of Left Heart Anatomy, Dynamics and Hemodynamics from 4D TEE: A First Validation Study*, Sixth International Conference on Functional Imaging and Modeling of the Heart, FIMH 2011, May 25-27, 2011.

V. Mihalef, R. Ionasec, G. Georgescu, I. Voigt, M. Suehling, D. Comaniciu: *Patient-specific modelling of whole heart anatomy, dynamics and haemodynamics from four-dimensional cardiac CT images*, Royal Society Interface Focus Journal, June 6, 2011.

Vitanovski, D., Tsymbal, A., Ionasec, A., Greiser, A., Schmidt, M., Mueller, E., Lu, X., Funka-Lea, G., Hornegger, J., Comaniciu, D., *Accurate Regression-based 4D Mitral Valve Surface Reconstruction from 2D+t MRI Slices*; in Machine Learning in Medical Imaging, MICCAI Workshop 2011.

Ralovich, K., Ionasec, R. I., Mihalef, V., Georgescu, B., Everett, A., Navab, N., and Comaniciu, D., *Computational Fluid Dynamics Framework for Large-Scale Simulation in Pediatric Cardiology*; in Computational Biomechanics for Medicine VI (CBM6), MICCAI Workshop, 2011.


**Submitted Papers:**


B. Leonardi, D. Vitanovski, A. Everett, Ph. Spevak M. Suehling, I. Razvan, L. Mantione, G. Pongiglione, *Automatical patient-specific 3D aortic arch model estimation for patient treatment with aortic arch anomalies* (forthcoming in a major scientific journal)

ISBI 2012: *Personalized Learning-based Segmentation of Thoracic Aorta and Main Branches for Diagnosis and Treatment Planning*, D. Vitanovski, K. Ralovich, R. Ionasec, Y. Zheng, M. Suehling, W. Krawtschuk, J. Hornegger and D. Comaniciu

ISMRM 2012: *Modeling and Simulation Framework for Hemodynamic Assessment of Aortic Coarctation Patients*, K. Ralovich, V. Mihalef, P. Sharma, L. Itu, D. Vitanovski, R. Ionasec, M. Suehling, A. Everett, G. Pongiglione, N. Navab, and D. Comaniciu.

# Sim-e-Child Fact Sheet

## Sim-e-Child in figures

| | |
|---|---|
| **Project Identifier** | **FP7-ICT-2009-4 (248421)** |
| **Timeframe** | **January 1, 2010 to June 31, 2012** |
| **Total cost** | **€1.86m** |
| **European Union funding** | **€0.99m** |
| **Number of partners** | **11** |
| **Number of Workpackages** | **6** |
| **Number of Deliverables** | **20** |
| **Total estimated funded efforts** | **223 person months** |
| **Total estimated unfunded effots** | **55 person months** |

## Sim-e-Child Partners

1. **Siemens AG (Siemens)**
2. **Lynkeus Srl (Lynkeus)**
3. **maat France (MAAT)**
4. **Technische Universität München (TUM)**
5. **I.R.C.C.S. Ospedale Pediatrico Bambino Gesù (OPBG)**
6. **Siemens Corporate Research, Inc. (SCR)**
7. **Johns Hopkins University (JHU)**
8. **American College of Cardiology Foundation (ACCF)**
9. **Siemens Program and System Engineering Srl (PSE)**

## Who's who in Sim-*e*-Child

| | |
|---|---|
| **Chairperson of the Governing Board:** | **Michael Sühling (Siemens)** |
| **Chairperson of the Scientific Committee:** | **Dorin Comaniciu (SCR)** |
| **Project Manager:** | **Edwin Morley-Fletcher (Lynkeus)** |
| **Chairperson of the Ethical and Legal Committee:** | **Gerard Martin (ACC)** |

## Sim-*e*-Child Workpackages and Workpackage Leaders

| | | |
|---|---|---|
| **WP1** | **Project Management** | **Siemens** |
| **WP2** | **Interoperability Requirements Analysis** | **Siemens** |
| **WP3** | **Clinical Protocol and Data Alignment, Ethical Clearance and Monitoring** | **OPBG** |
| **WP4** | **Simulation and Collaboration Platform Development** | **Maat** |
| **WP5** | **Development and Assessment of Personalized Child Heart Models** | **Siemens Cooperate Research** |
| **WP6** | **Dissemination** | **Lynkeus** |

**www.sim-e-child.org**

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