VPH concepts in Health-e-Child

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Maat-G, president of HealthGrid
On behalf of the Health-e-Child Consortium

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ISGC 2009 - Taipei
Motivation

- Health-e-Child is about severe, complex paediatric diseases
  - due to **low incidence** only few experts can rely on personal experience for diagnosis and treatment
  - textbook diagnosis may not reflect **latest medical knowledge**
  - cause and/or progression of the **disease are little understood**
  - treatment is severe and **complex** too
  - incentives to **invest** in paediatric research are **low**
- Clinical demand for integration and exploitation of heterogeneous biomedical information
  - vertical dimension – **multiple** traditional and emerging **data** sources
  - horizontal dimension – **multiple sites**
- Need for generic and scalable solutions
  - offer decision support in diagnosis, therapy and follow-up
  - provide complex integrated disease models
  - ubiquitous access to knowledge repositories in clinical routine
  - connect stakeholders in clinical research
Introduction

• Motivation for VPH models
  • Understand anatomy, morphology, physiology and pathology
  • Support patient management

• VPH models in Health-e-Child
  • focus on organ level models
  • focus on disease and even patient-specific models
Health-e-Child

Links between Models and Imaging Data

Data genericity

- Lab experiments
- Clinical research
- Clinical routine

Model complexity

- Patient-Specific Computational Models: HeC models
- Image Tools: Segmentation, Registration
- Estimation: from data to models
- Multi-scale generic models: Physiome project
- Interpretation: from models to data
Progress in Medical Image Acquisition (I)

SIRETOM (1974)

Siemens SOMATOM Sensation 64 (2004)

Courtesy of CT Clinical Innovation Center, Mayo Clinic, Rochester, MN
Progress in Medical Image Acquisition (II)

• 3D+t is becoming standard in CT, MR and echo
• PET, SPECT, Doppler etc. are adding information about function (wall motion, wall thickening, wall strain, blood flow, myocardial viability, myocardial perfusion) and metabolism
Progress in Image Processing

- Manual 2D measurements to approximate e.g. LV volume, ejection fraction and stroke volume → still standard in the 90s
- Today 4D anatomical models can be extracted automatically from CT data

Right Ventricular Volume Determinations in Children: Normal Values and Observations with Volume or Pressure Overload. T. P. GRAHAM et al., *Circulation* 1973;47;144-153
HeC Disease Focus: (Post-op) Tetralogy of Fallot

- Complex condition of 4 heart defects:
  - Requires surgery in first year
- Occurs in 1 of 2500..20000 live births
Re-intervention Procedure

- Initial surgery can lead to the destruction of the Pulmonary valve
- This leads to regurgitation of the blood back into the Right Ventricle and loss of function
- When function reaches a certain level (perhaps years after initial surgery), valve implantation is performed
- Percutaneous Pulmonary Valve Implantation (PPVI) is a novel technique to replace the valve without surgery

Melody™ Transcatheter Pulmonary Valve from Medtronic
Research Goal: Predicting the Best Timing for Pulmonary Valve Replacement

• The timing for reintervention and the various surgical reconstruction possibilities of the right-ventricular outflow tract are still controversial and evolving
• Decision when to reintervene depends on many factors
  • Extent of pulmonary regurgitation, residual or recurrent pulmonary stenosis, RV dilation and deterioration of ventricular function
  • Anatomy of RVOT, RVOT aneurysms, potential complications and sequelae
  • Clinical parameters, ECG, exercise testing (e.g. age of patient, prolonged QRS duration)
Step 1: Anatomical RV Model from Cardiac MR

- Anatomical model of right ventricle (RV) created from HeC data (based on 30 isotropic volumes from GOSH)

- Semi-automatic initialisation of model based on detection library from Siemens Corporate Technology

- Multi-sequence view for model editing

→ Fast, accurate 4D quantification of RV volumes (ES, ED) from which RV ejection fraction and further measurements can be easily derived
Step 2: Anatomical 4D Model of Pulmonary Trunk and Valve

- Generate a full dynamic model of the pulmonary trunk and valves in high resolution CT data.
- Current protocol in GOSH for ToF patients includes 1 isometric volume at end-diastole (the standard 4D short axis stack does not include pulmonary trunk).
- Fit prior model to the isometric MRI volume.
- Track the model based on a dynamic long-axis.
Anatomical Model of the Pulmonary Trunk

- Measurements
  - RVOT, Valve and Bifurcation Diameter
  - Pulmonary Trunk Volume
  - Diameter vs. RVOT length

- Morphology and dynamics determine suitability for PPVI

Type I  Type II  Type III  Type IV  Type V

S. Schievano et al., Variations in Right Ventricular Outflow Tract Morphology Following Repair of Congenital Heart Disease: Implications for Percutaneous Pulmonary Valve Implantation
Step 3: Disease-specific models: Method

• Describe each pathology
  • In computer science and bio-mechanical terms
  • Sources: HeC cardiologists / Bibliography

• Clinical pathological features → Model parameters

<table>
<thead>
<tr>
<th>Anatomical parameters</th>
<th>Biomechanical parameters</th>
<th>Electrical parameters</th>
<th>Boundary conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardium thickness</td>
<td>Contractility</td>
<td>Conductivity</td>
<td>Atrial pressures</td>
</tr>
<tr>
<td>Ventricle dilation,</td>
<td>Tissue stiffness,</td>
<td>Diffusion anisotropy,</td>
<td>Arterial pressure,</td>
</tr>
<tr>
<td>…</td>
<td>…</td>
<td>…</td>
<td>Regurgitation, …</td>
</tr>
</tbody>
</table>

**Anatomical parameters**
- Myocardium thickness
- Ventricle dilation, ...

**Biomechanical parameters**
- Contractility
- Tissue stiffness, ...

**Electrical parameters**
- Conductivity
- Diffusion anisotropy, ...

**Boundary conditions**
- Atrial pressures
- Arterial pressure, Regurgitation, …
Example: Right-ventricle overload

<table>
<thead>
<tr>
<th>Right-ventricle overload</th>
<th>Normal heart</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Geometrical parameters</strong></td>
<td></td>
</tr>
<tr>
<td>Degree of the super-ellipsoid: 2.5</td>
<td>Degree of the super-ellipsoid: 2.5</td>
</tr>
<tr>
<td>RV passive volume: 114 mL</td>
<td>RV passive volume: 65 mL</td>
</tr>
<tr>
<td>Ventricle passive volume ratio: 1.58</td>
<td>Ventricle passive volume ratio: 0.90</td>
</tr>
<tr>
<td>Fibre orientations: +60° to -60°</td>
<td>Fibre orientations: +90° to -90°</td>
</tr>
<tr>
<td><strong>Boundary conditions</strong></td>
<td></td>
</tr>
<tr>
<td>Right atrium pressure: 12.8 mmHg</td>
<td>Right atrium pressure: 7.5 mmHg</td>
</tr>
<tr>
<td>Left atrium pressure: 15 mmHg</td>
<td>Left atrium pressure: 15 mmHg</td>
</tr>
<tr>
<td>Pulmonary artery pressure: 30 mmHg</td>
<td>Pulmonary artery pressure: 30 mmHg</td>
</tr>
<tr>
<td>Aorta pressure: 60 mmHg</td>
<td>Aorta pressure: 60 mmHg</td>
</tr>
</tbody>
</table>

**Increased pre-load**

→ ventricle dilated without increase of myocardium mass. Higher end-diastolic volume (128 mL/m² with respect to 70 mL/m² in normal children (Graham et al., 1973)), just like the volume ratio between right and left ventricle (2.3 versus 1 (Graham et al., 1973)).

**Longer major axis** of the super-ellipsoid (+29%)

Stretching of the myocardium → synthetic fibre directions are made more horizontal

Conservation of mass → thinning of the right-ventricular myocardium (-20%).

*The mass of the simulated pathological geometry is then almost equal to the one of the synthetic normal heart.*
**Example: Right-ventricle overload**

<table>
<thead>
<tr>
<th>Right Ventricle (RV)</th>
<th>Left Ventricle (LV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV EDV = 158.84 mL</td>
<td>LV EDV = 82.61 mL</td>
</tr>
<tr>
<td>RV ESV = 73.40 mL</td>
<td>LV ESV = 31.96 mL</td>
</tr>
<tr>
<td>RV SV = 85.44 mL</td>
<td>LV SV = 50.65 mL</td>
</tr>
<tr>
<td>RV EF = 53.79 %</td>
<td>LV EF = 61.31 %</td>
</tr>
</tbody>
</table>

**Clinical observations**
- Increased RVEF/LVEF ratio (+17%, 0.99 in healthy children → 1.17 in RVO subjects)
- Normal RVEF (Graham et al., 1973),
- Increased RV EDV and ESV (Helbing et al., 1995)

**Simulations**
- RVEF/LVEF ratio increased: 0.88 for RVO (0.77 for normal heart) → +14%
- RVEF not significantly increased (53.79% / 48.76%). However, the simulated ejection fraction is still low in comparison with ground-truth measurements (54% versus 70%).
- RV EDV and RV ESV significantly higher, with a volume ratio equal to 1.9 at end diastole and to 2.3 at end systole (0.9 and 1.3 in the simulated normal heart). These results are in line with clinical measurements.
Step 4 Patient-specific electromechanical models for Tetralogy of Fallot patients

• Method:
  • Adjust the generic disease-specific electromechanical model to patient anatomy and function
    1. Use a 3D anatomical representation (mesh) of the patient heart from clinical images (cineMRI)
    2. Adjust electromechanical parameters to simulate the cardiac function

• Use motion (time-sequence) to validate
  • 3D+t segmentation vs simulation
Electromechanical simulation

Volumetric mesh at time 0

Simulated fibres
(+60° on the endocardium to
-60° on the epicardium)

Visual adjustment of simulation
(Segmentation / Simulation)

Simulated beating heart + fibres
Colors: contraction

Simulated beating heart + fibres
Colors: strain anisotropy
Patient-specific electromechanical models

- Electromechanical simulation provide:
  - Qualitative assessment of RV motion (including twisting)
  - Quantitative indications of parameters not easily available in a clinical environment
    - Pressure and PV diagrams
    - 3D strain and stress

- Simulations of normal heart, RVO, HCM and DCM publicly available from INRIA
Step 5: Therapy Planning (Preliminary Results)

Volume Curves

LV: Left Ventricle
RV: Right Ventricle

Ejection fractions

<table>
<thead>
<tr>
<th>Ventricle</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left Ventricle</td>
<td>61%</td>
</tr>
<tr>
<td>Right Ventricle</td>
<td>41%</td>
</tr>
</tbody>
</table>

Dyskinetic area

Supported by:
- IRCCS Giannina Gaslini, Genua, Italy
- Great Ormond St. Hospital, London, UK
- Necker Enfants Malades, Paris, France

Radial displacement of each vertex
(in red: outwards motion, in blue: inwards motion)
Reference frame: end diastole
Therapy Planning (Preliminary Results)

• **Rationale:**
  • Use EM models and soft-tissue intervention platforms to simulate different PVR therapies (Percutaneous, RV surgery ...)

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*Image of 3D cardiac models.*
Preliminary Results of Therapy Planning

<table>
<thead>
<tr>
<th>Simulated pre-op ejection fractions</th>
<th>Simulated post-op ejection fractions</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV</td>
<td>LV</td>
</tr>
<tr>
<td>59 %</td>
<td>61 %</td>
</tr>
<tr>
<td>RV</td>
<td>RV</td>
</tr>
<tr>
<td>40 %</td>
<td>59 %</td>
</tr>
</tbody>
</table>
Step 6: Using Models for Case Based Reasoning

Current Patient Data

Knowledge Base

Hospital 1
Hospital 2
Hospital N

“Do I Operate”

Search

Unhealthy

Healthy

Action

Unhealthy

Healthy
## Summary

<table>
<thead>
<tr>
<th>Model</th>
<th>Usage</th>
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<tbody>
<tr>
<td>Anatomical RV Model</td>
<td>4D quantification of RV volumes, ejection fractions etc.</td>
</tr>
<tr>
<td>Anatomical 4D Model of Pulmonary Trunk</td>
<td>Morphology determines suitability for pulmonary valve replacement</td>
</tr>
<tr>
<td>Disease-specific models</td>
<td>Disease Understanding</td>
</tr>
<tr>
<td>Patient-specific electromechanical models for Tetralogy of Fallot</td>
<td>PV diagrams, 3D strain and stress</td>
</tr>
<tr>
<td>Soft-tissue intervention platforms</td>
<td>Simulation of the effects of pulmonary valve replacement</td>
</tr>
<tr>
<td>Search of Models (Case Based Reasoning)</td>
<td>Clinical Decision Support</td>
</tr>
</tbody>
</table>
Outlook (1): 3d-Knowledge Browser and @neuLink

1. Ocular pathology in congenital heart disease.

PURPOSE: To describe the ocular findings in subjects with congenital heart disease (CHD). METHODS: In a prospective study, the same observer examined 246 congenital heart disease subjects and 246 control subjects. RESULTS: The average age of the congenital heart disease subjects was 17 years (range: 1 month to 80 years) and the control subjects was 17 years (range: 1 month to 80 years). The congenital heart disease subjects were divided into six groups: atrial septal defect, ventricular septal defect, bicuspid aortic valve, mitral valve prolapse, coarctation of the aorta, and other congenital heart defects. CONCLUSIONS: The results of the study demonstrated that ocular findings in congenital heart disease subjects were similar to the control subjects. The most common finding was myopia, followed by strabismus and astigmatism.


The existence of Kussmaul syndrome as a distinct entity has been thrown into doubt by a recent study conducted on the family originally reported by Kussmaul. In this study, Kussmaul syndrome was not identified in any of the family members. The results of this study do not support the existence of Kussmaul syndrome as a distinct entity. However, further research is needed to clarify the role of Kussmaul syndrome in the pathogenesis of pediatric diseases.
Outlook (2):

Super Peta-scale Infrastructure for Distributed e-health And biomedical Research

http://spider.healthgrid.org
Welcome to Berlin (Germany)
28th June – 1st July 2009

Invitation to HealthGrid 2009
Organization and Contact Persons:

**TMF** (Germany) – S.C. Semler, M. Freudigmann, M. Jacobi

**HealthGrid HQ** (France) – Y. Legré et al.

e-mail: contact-hg2009@healthgrid.org


Conference Chair:
Martin Hofmann-Apitius (Fraunhofer SCAI / Germany)
Thank you for your attention!