VPH concepts in Health-e-Child

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Barcelona, Spain
September 18th, 2008
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
Links between Models and Imaging Data

Data genericity

Lab experiments

Clinical research

Clinical routine

Model complexity

Estimation: from data to models

Multi-scale generic models

Physiome project

Patient-Specific Computational Models

HeC models

Image Tools

Segmentation
Registration

Interpretation: from models to data
Progress in Medical Image Acquisition (I)

SIRETOM (1974)

SOMATOM Sensation 64 (2004)

Courtesy of CT Clinical Innovation Center, Mayo Clinic, Rochester, MN
• 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:
  - Ventricular septal defect,
  - Pulmonary (or RV outflow tract) obstruction,
  - Overriding aorta and
  - Hypertrophy of RV.
- 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 Research

- 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

*Manual annotations in diastole and systole*

*HeC application for semi-automatic annotations*
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\(^1\) 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

\(^1\) Great Ormond Street Hospital, London
Anatomical Model of the Pulmonary Trunk

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

• Morphology determines suitability for PPVI

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, Regurgitation,</td>
</tr>
</tbody>
</table>

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Health-e-Child

Information Society Technologies
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>
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</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>
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<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>

End-diastolic Volume Ratio: 1.92

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

- Biomechanical parameters adjusted from disease-specific values
  - Simulation qualitatively compared with the images
  - Adjustment based on the LV apparent motion
  - Only global contractility parameters are modified
    - Maximum contraction
    - Speed of contraction and relaxation
- Other parameters are kept at their normal values
- Myocardium fibres are simulated
  - Interpolated from $+60^\circ$ on the endocardium to $-60^\circ$ on the epicardium w.r.t. the horizontal
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
Simulation Results for a Concrete Patient

<table>
<thead>
<tr>
<th></th>
<th>Measured ejection fractions</th>
<th>Simulated ejection fractions</th>
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<tbody>
<tr>
<td>LV</td>
<td>61 %</td>
<td>59 %</td>
</tr>
<tr>
<td>RV</td>
<td>41 %</td>
<td>40 %</td>
</tr>
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</table>

LV: Left ventricle  
RV: Right ventricle
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
Step 5: Therapy Planning (Preliminary Results)

<table>
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<th>Ejection fractions</th>
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Note: Ejection fractions are calculated as a percentage of the end-diastolic volume.

**Volume Curves**

- **LV:** Left Ventricle
- **RV:** Right Ventricle

**Dyskinetic area**

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 ...
Preliminary Results of Therapy Planning

Pressure-Volume Loops

Preoperative simulation

Postoperative simulation

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

Current Patient Data

Hospital 1

Hospital 2

Hospital N

"Do I Operate"

Search

Knowledge Base

Unhealthy

Healthy

Unhealthy

Healthy
### Summary

<table>
<thead>
<tr>
<th>Model</th>
<th>Usage</th>
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<tr>
<td>Anatomical RV Model</td>
<td>4D quantification of RV volumes, ejection fractions etc.</td>
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<tr>
<td>Anatomical 4D Model of Pulmonary Trunk</td>
<td>Morphology determines suitability for pulmonary valve replacement</td>
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<tr>
<td>Disease-specific models</td>
<td>Disease Understanding</td>
</tr>
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<td>Patient-specific electromechanical models</td>
<td>PV diagrams, 3D strain and stress</td>
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<tr>
<td>for Tetralogy of Fallot</td>
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<td>soft-tissue intervention platforms</td>
<td>Simulation of the effects of pulmonary valve replacement</td>
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<td>Search of Models (Case Based Reasoning)</td>
<td>Clinical Decision Support</td>
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Thank you for your attention!