Quantification of Right Ventricular Function in Pulmonary Hypertension using Cardiac PET Images

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Motivation and Goals

Motivation:
- 3 year survival 48% without treatment and 55% with current therapy.

Long term goal:
- To understand the risk factors and causes of pulmonary hypertension (PH), understand disease progression, and develop therapies.

Immediate goal:
- Develop an automatic tool with optional operator intervention for defining RV region of interest in 3D cardiac images:
  - Used to quantify RV cardiac function.
  - Used to quantify RV molecular function.

http://www-sop.inria.fr/asclepios/projects/Health-e-Child/DiseaseModels/content/cardiac/tofSimul_inroduction.php
Introduction – Literature Review

- Advanced PH is associated with RV hypertrophy and dysfunction. 1,2

- Previous work investigated use of SPECT for imaging advanced disease. 1,2,4
  - Limited understanding of PH and its relation to RV function.
  - Manual segmentation of the RV.

- Early RV disease may be better detected and understood with SPECT and PET imaging. 1
  - Perfusion?
  - Metabolism?

- Automatic quantification of left ventricular (LV) function using FlowQuant. 3
  - RV function not currently measured for PET images.

Brief Overview of PET and SPECT

- Injected tracer – trace amounts of specific molecule that interacts physiologically.
- Specialized camera detect radiation and reconstruct 3D image **volume** of tracer concentrations.
Introduction – Model properties

- Automatically register RV ROI with optional operator intervention:
  - Accommodate all RV anatomies (normal, hypertrophic)
  - Minimum control points and degrees of freedom
Defining Model Shape

- 12 control points (13 degrees of freedom).
  - Initially estimated based on LV shape.
  - Automatically optimized
  - Adjustable by operator (GUI)
Sampling points interpolated in pseudo-cylindrical coordinate system:

- 16 slices by 18 sectors = 288 sampling points.
- Radii interpolated for each slice and sector.
Graphical Representation

3D Mesh

Horizontal Long Axis (HLA) slice

Polar Map

Short axis (SA) slices
Global Contour Optimization

- Minimization of a cost function
  - \( C = C_{\text{intensity}} + C_{\text{constraints}} \)

- Maximization of sampled image intensity
  - \( C_{\text{intensity}} = \sum_{p \in \text{ROI}} \frac{I_{\text{max}}}{I_{\text{max}} - I_p} \)
    where \( I_{\text{max}} \) is the maximum image intensity and \( I_p \) is the image intensity of pixel \( p \)

- Constraints on RV shape and size
Model Validation and Characterization

- Model Appropriateness
  - Manual adjustment of control points

- Automation Performance

- Operator Dependent Variability
  - 2 operators x 2 runs each
  - Tracer uptake reproducibility
  - Sampling point position variability

- Cavity Volume and EF Accuracy (PET vs. CMR)
Model Validation-Results

- **Model appropriateness - 20 Images** (5 non-PH, 5 PH, 5 normal rat, 5 PH rats*)
  - 14 passed, 6 failed
  - Low image intensity in normal rats

- **Automation performance - 14 Images that passed model evaluations:**
  - 7 complete automation
  - 13 successful automatic fitting of the free wall

* PH induced by treating with monocrotaline (MCT)
Model Validation - Operator Variability

- 2 operators
  - Expert and Novice
- 2 runs each:
  - separate days
  - anonymized
  - Randomized order

Inter-Operator Uptake

\[ y = 1.01x - 0.255 \]
\[ r^2 = 0.91 \]
\[ n = 114 \]

RPC: 8.2 (11%)

<table>
<thead>
<tr>
<th></th>
<th>RV (current)</th>
<th>LV (Klein et-al)</th>
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<tbody>
<tr>
<td>Intra Operator Variability</td>
<td>Op 1 (expert)</td>
<td>5.6</td>
</tr>
<tr>
<td>Op 2 (novice)</td>
<td>6.4</td>
<td>1.2</td>
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Inter Operator Variability | 8.2 | 1.8 |
Cavity volume and EF accuracy - Results

- (PET vs. CMR)

![Graphs showing Cavity Volume and EF comparisons between PET and CMR](image-url)
Results Summary

- Complete automation not achieved due to:
  - Image Intensity (low around the atrium)
  - Spillover from LV
  - A wide range of RV anatomies
  - RV bifurcation into PA and RA

- Nevertheless, semi-automated tool can be used for current research.
Discussion and Limitations

- **Operator reproducibility**
  ◦ Did not include animal images.
  ◦ Limited demographics.

- **Cardiac function accuracy (PET vs. CMR)**
  ◦ Small number of patients.
  ◦ Limited demographics.

- **Only used $^{18}$F labeled tracers.**
  ◦ Lower quality images not included.
  ◦ Did not include SPECT image.
Conclusions

- Developed, validated, characterized, and demonstrated a spline model that sufficiently registers the RV region of interest semi-automatically.
  - First of its kind
  - Sufficient for current and future research of PH in animal models and clinical studies.

- Future Work
  - Improve Automation
  - More Validation
  - Development and evaluation of kinetic modeling for quantification of physiologic function.
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