Patient-Specific Multi-Scale Modeling of Heart Disease

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Computational modeling for predicting performance of engineering designs in service is now routine in many industries ...

And is increasingly used for implanted cardiovascular devices ...
But we need to analyze the device interacting with heart tissues in vivo and it’s effect on cardiac physiology ...

And we need ways to include the effects of individual variation and human diversity ...
We need ...

Predictive, mechanistic, integrative, *patient-specific* computational models of cardiac electrical, mechanical, hemodynamic and metabolic function.
Heart Failure

- Condition in which the heart is unable to pump enough blood to meet the metabolic demands of the body
- Chambers enlarge, excess fluid backs up into the lungs and systemic circulation leading to edema, shortness of breath, cough, exercise intolerance ...
- 5 million Americans with heart failure
- 5-year mortality is 50%
- Highly heterogeneous syndrome
- There are multiple etiologies and co-morbidities, including arrhythmia

Cardiac Resynchronization Therapy (CRT) for Dyssynchronous Heart Failure (DHF)

- Up to 40% of HF patients have conduction defects such as left bundle branch block (LBBB) resulting in ventricular mechanical dyssynchrony
- CRT using biventricular pacemakers can improve synchrony between LV and RV contraction
  - improves quality of life*
  - reduces mortality*
  - 30-40% of patients do not respond to CRT, especially those with myocardial infarcts
  - No accepted clinical predictor of CRT outcomes

*Cleland, 2005
**Electrophysiology**

- Markov Models of Channel Kinetics
- Systems Model of Excitation-Contraction Coupling & Signaling
- Constitutive Models of Anisotropic Myocardial Properties
- 3D Finite Element Model of Ventricular Anatomy
- Microstructural Model of Myofilament Lattice
- Lumped Parameter Model of Circulation

**Biomechanics**

**Echocardiographic Responses to CRT**

8 Male Patients with DHF received CRT
NYHA class III HF
EF < 40%
QRS ≥ 120ms
Follow up at 3-6 mths

<table>
<thead>
<tr>
<th>BiV1</th>
<th>BiV3</th>
<th>BiV5</th>
<th>BiV6</th>
<th>BiV8</th>
<th>BiV2</th>
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<td>LVESV reduction (6 months) (%)</td>
<td>59%</td>
<td>16%</td>
<td>15%</td>
<td>12%</td>
<td>7%</td>
<td>-2%</td>
<td>-12%</td>
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Echo responder
Echo non-responder
Clinical non-responder
The Decrease in LVESV at 6 Months Did Not Correlate with Baseline Electrical, Functional, Hemodynamic or Anatomic Measurements
“With four parameters I can fit an elephant, and with five I can make him wiggle his trunk.”
— Attributed to John von Neumann by Enrico Fermi in 1953

Add Pacemaker Stimulation to Simulate Resynchronization Therapy
How does CRT Affect Ventricular Mechanical Efficiency?

Computed Reduction in Septal Myocardium Performing “Negative” Work May Predict CRT Response
Ventricular Fibrillation Leads to Sudden Death

- Ventricular fibrillation is chaotic heart rhythm and major cause of ~700,000 sudden cardiac deaths per year in US and Europe (Cobb et al, JAMA 2002)
- ICD misfirings may increase future VF risk and cause significant depression
- Ablation therapy may reduce the need for ICD
- Can be due to focal triggers and/or reentrant spiral waves (rotors)

Non-invasive Model-Based Assessment

Model Predictions

Clinical Validation

Ho et al, J Cardiovasc Electrophysiol, 2017
From Individual Patients to Populations
3D Models from Cardiac MR Imaging

Ventricular Shape Atlases (MESA Study)

Top 4 Left Ventricular Shape Modes

- ED Mode 1
  LV size

- ED Mode 2
  sphericity
  valve orientation

- ED Mode 3
  sphericity
  valve orientation

- ED Mode 4
  wall thickness
  valve orientation

Top 3 Bientricular Shape Modes

- 5th Percentile
- Average Shape
- 95th Percentile

Mode 1

Mode 2

Mode 3

From 1,991 asymptomatic subjects in the Multi-Ethnic Study of Atherosclerosis
Summary

• Patient specific computational models have potential to improve the diagnosis, device therapy and medical management of heart failure and ventricular fibrillation

• Population based models may identify new biomarkers of disease progression in acquired and congenital heart diseases