Coronary artery disease (CAD)

- Atherosclerotic plaques build up in the coronary arteries
- Can lead to ischemia and infarction
- Leading cause of death worldwide (8.1 million in 2013)\(^1\)

Methods to diagnose CAD in clinic:

- **Conventional coronary angiography**:
  - Identify and measure the degree of stenosis in a coronary artery
  - Fluoroscopy
- **Nuclear stress test**:
  - Assess myocardial perfusion
  - Radioactive tracer injection
  - Treadmill or pharmacological agent
- **Echo stress test**:
  - Assess wall motion abnormalities
  - Treadmill or pharmacological agent
  - Qualitative

Ultrasound-based cardiac strain imaging

Radiofrequency (RF)-based speckle tracking performs better than envelope-based tracking for small tissue deformation as they contain signal phase information\(^1,2\)

2. Ma et al., Ultrasonics, 2013
2-D Myocardial Elastography (ME)

- Tracking of Radiofrequency (RF) signals in axial and lateral direction
- Transmural myocardial strain imaging
- Angle-independent
- Multi-sector and ecg-gating

- Validation against tagged MRI (tMRI) in humans in vivo
- Associated with reduced blood flow in Left Anterior Descending artery (LAD) in canines in vivo
- Can be performed during free breathing in a single heart cycle

Objectives

- Assess the performance of single heartbeat Myocardial Elastography to distinguish normal vs ischemic patients
- Investigate the sensitivity of Myocardial Elastography to the territories perfused by the coronary arteries

Myocardial Elastography: Patient population

- 49 patients for nuclear stress test
- 15 patients with ischemia
- 17 patients for coronary angiography
- 66 patients recruited in total
- 34 normal patients
- 15 patients with coronary occlusion: 1 vessel: N = 6, 2 vessels: N = 2, 3 vessels: N = 7
- 36 normal patients
- 2 normal patients

\*Konofagou et al., Ultrasound Med Biol, 2002
\*Lee et al., Phys Med Biol, 2007
\*Lee et al., Ultrasound Med Biol, 2008
\*Lee et al., Phys Med Biol, 2012

\*Grondin et al., Ultrasound Med Biol, 2017
Myocardial Elastography: RF signals acquisition and beamforming

Diverging wave emission

Reception of RF signals

Verasonics ultrasound system
- 2.5 MHz phased array (ATL P4-2)
- 64 elements
- 2000 Hz acquisition frame rate

Delay-and-sum parallel beamforming

\[ A(x, y) = \sum_{i=1}^{64} RF_i(\Delta t(x, y)) \]

Myocardial Elastography: 2D displacement estimation

RF signals at time \( t \)

RF signals at time \( t+1 \)

- Motion estimation rate: 500 Hz
- 10:1 linear interpolation of RF lines in the lateral direction to improve lateral displacement
- 1-D cross-correlation\(^1\) (window size: 5.9 mm, 90% overlap)
- 1-D kernel in a 2-D search\(^2\)

\(^{1}\text{Luo et al., IEEE TUFFC, 2010}\)
\(^{2}\text{Konofagou et al., Ultrasound Med Biol., 1998}\)

Myocardial Elastography: End-systolic strain estimation

Displacement accumulation during systole

- 2-D displacements are accumulated from end-diastole to end-systole
- The left ventricle is manually segmented and automatically tracked throughout the systolic phase

Cumulative Strains

- 2-D Green-Lagrange strains are computed using a least squares estimator implemented with Savitzky-Golay filters\(^1\)
- Radial strains are computed with the origin of the polar coordinate system at the centroid of the myocardium

\[ \text{Strain} = \frac{L - L_0}{L_0} \]

\(^{1}\text{Luo et al., IEEE TUFFC, 2008}\)
\(^{2}\text{Luo et al., IEEE TUFFC, 2004}\)
Mean radial strain in each territory

- Computation of mean end-systolic radial strain ($\bar{\varepsilon}$) in all the territories

$$\bar{\varepsilon}_T = \bar{\varepsilon}_{LAD} + \bar{\varepsilon}_{LCX} + \bar{\varepsilon}_{RCA}$$

- Computation of mean end-systolic radial strain in each territory perfused by a coronary artery

LV: Left ventricle  
RV: Right ventricle  
LAD: Left Anterior Descending artery  
LCX: Left Circumflex artery  
RCA: Right Coronary Artery  
T: Total cross-section

End-systolic radial strains

Normal subject

Patient with reduced perfusion in inferior wall

Mean radial strain in normal vs. ischemic patients

Grondin et al., Ultrasound Med Biol, 2017
Results: Mean radial strain in normal subjects and CAD patients

Conclusion

- Myocardial Elastography can differentiate normal subjects from CAD patients determined by angiography or nuclear stress test
- Radial strains are lower in territories perfused by occluded arteries or with perfusion defect than in normal territories

Ongoing work:
- Improve quality of strain estimation using coherent compounding
- Validate ME against nuclear imaging (SPECT and PET) in a large cohort of patients

Cardiac arrhythmia mapping

- Cardiac arrhythmia is experienced by ~5.8 million people in the US
- Underlying or contributing cause of death for ~1/5 deaths in the US
- ECG cannot always accurately locate arrhythmias
- Endocardial mapping to locate the arrhythmia is invasive and can be time consuming
- Electromechanical Wave Imaging (EWI) 

Ultrasound based technique
High frame rate (≥ 500 frames per second)
Electromechanical activation of the heart

- Heart is an electromechanical pump
- Needs to be electrically activated in order to contract
- Action potentials propagate along the myocardium and specialized pathways

Sinus node
Atrioventricular node
Bachmann's Bundle
Right bundle branch
Left bundle branch
LA: Left atrium
RA: Right atrium
LV: Left ventricle
RV: Right ventricle

Objectives

- Investigate the relationship between the electromechanical and the electrical activation of the canine heart in vivo
- Demonstrate that 3D-rendered EWI can predict arrhythmia origin location

Hypothesis: Local onset of myocardial shortening imaged by ultrasound is caused by local electrical activation

Methods

Six canines (24.1 ± 0.4 kg), open chest

- Electrical mapping system
- 64 electrodes Basket catheter
  - Endocardial electrical measurement
  - Endocardial pacing
- DAQ National Instruments
- 2 electrodes sutured onto the LV
  - Epicardial pacing in Anterior or Lateral regions
- Ultrasound RF data are acquired simultaneously with endocardial potential during sinus rhythm, endocardial or epicardial pacing
- Electrical delay (<100ms)

Cordeiro et al., Am J Physiol Heart Circ Physiol, 2004
Methods: Electromechanical wave imaging flowchart

1. RF channel data acquisition
   - L = 2.5 MHz
   - Frame rate = 2000 Hz

2. Delay-and-sum beamforming

3. Axial motion estimation
   - 1-D cross-correlation
   - window size = 4.2 mm
   - 50% overlap
   - frame / frame = 1

4. Interframe axial strain estimation
   - least squares estimator implemented with a Savitzky-Golay filter

5. Electromechanical activation time

6. Single view (4-Ch) activation map

7. 4-view activation map

8. Activation map interpolated on ellipsoid

Results: Lateral epicardial pacing activation maps

Electrical activation vs. EWI activation

Electrical activation

Electrical activation

EWI activation

EWI activation

Electrical activation

EWI activation

Methods: Validation against electroanatomical mapping

LV/RV = left/right ventricle
LA = left atrium

LV = left ventricle
RV = right ventricle

LA = left atrium

LA = left atrium

RV = right ventricle

LV = left ventricle

LA = left atrium

Results: Validation in all four chambers

Left Ventricle

Right Ventricle

Right Atrium

Left + Right Atrium

EWI as a treatment planning tool

Premature ventricular contraction (PVC) patient

Methods: 3D rendering of EWI

a) High frame rate acquisition at 2000 fps

b) Strain estimation and segmentation

c) Axial strain curves and isochrones

d) Multi-2D co-registration and 3D rendering
Cardiac Resynchronization Therapy (CRT) patient

<table>
<thead>
<tr>
<th>Without CRT</th>
<th>With CRT</th>
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<tbody>
<tr>
<td>LV</td>
<td>LV</td>
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<tr>
<td>POST</td>
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<td>LAT</td>
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<tr>
<td>SEPT</td>
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</tbody>
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LVEF at baseline = 20 - 25%
- QRS without CRT = 186 ms
- MR without CRT = 58 %
- QRS with CRT = 118 ms
- MR with CRT = 98 %

MR: Myocardial Resynchronization

7 yo. female WPW patient before and after ablation

12-lead ECG prediction
- Boemerma et al. algorithm correctly predicted the left lateral AP
- Amura et al. algorithm did not succeed in accurately localizing the AP and predicted it to be right lateral

Validation with Electrode intracardiac map
- 3D-rendered EWI capable of localizing AP before ablation and characterizing the electromechanical activation pattern after successful ablation in pediatric patients

3D-rendered EWI can localized accessory pathways

Double-blinded study in a cohort of 15 WPW pediatric patients for the first time (1 patient excluded for poor echocardiographic windows)

- EWI accurately predicted the AP location before ablation in 100% cases
- 12-lead ECG analysis correctly predicted 78.6% (11/14) of AP locations
Conclusions

• Electrical and electromechanical activation are well correlated ($R^2 = 0.64-0.82$)
• EWI can identify PVC and quantify response to CRT
• 3D-rendered EWI accurately predicted the AP location before ablation with higher accuracy (100%) than 12-lead ECG (78.6%)

Ongoing and future works:
- Real-time implementation of EWI
- Treatment planning and assessment
- Single-heartbeat 3D EWI of the full heart

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Thank you!
Methods: Study design

N = 15 pediatric patients (aged 7-17, 50% male) imaged with EWI before ablation
1/15* excluded → N = 14: 6 scanned after ablation

* Poor acoustic windows

12-lead ECG blinded Boersma¹, Arruda³ algorithms
Location predictions
Blinded EWI isochrones generation
Predictions compared to ground truth:
intracardiac mapping and successful ablation site

¹Boersma et al., J Cardiovasc Electrophysiol, 2002
²Arruda et al., J Cardiovasc Electrophysiol, 1998
³Melki et al., JACC Clinical EP, 2019

17 yo. female fasciculoventricular AP before ablation

²Melki et al., JACC Clinical EP 2019