Myocardial Elastography and 3D Electromechanical Wave Imaging of the Heart

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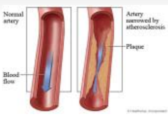
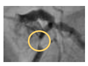
Coronary artery disease (CAD)

- 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]

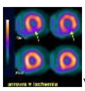


- Methods to diagnose CAD in clinic:

Conventional coronary angiography:
Identify and measure the degree of stenosis in a coronary artery
- Catheter insertion
- Fluoroscopy



Nuclear stress test:
Assess myocardial perfusion
- Radioactive tracer injection
- Treadmill or pharmacological agent



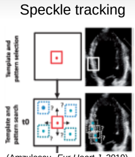
Vesely et al, *J Nucl Med*, 2008

Echo stress test:
Assess wall motion abnormalities
- Treadmill or pharmacological agent
- Qualitative

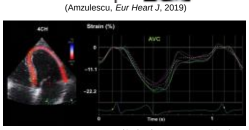
[1]Roth et al., *N Engl J Med*, 2015

Ultrasound-based cardiac strain imaging

Speckle tracking

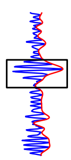


(Amzulescu, *Eur Heart J*, 2019)



(Smiseth, *Eur Heart J*, 2015)

Ultrasound signal



Radiofrequency signal
Phase and amplitude information

Envelope detected signal
Amplitude information only

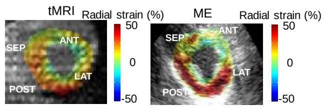
Radiofrequency (RF)-based speckle tracking performs better than envelope-based tracking for small tissue deformation as they contain signal phase information[1,2]

[1]Ma et al., *Ultrasonics*, 2013 [2]Li et al., *Ultrasound Med Biol*, 2015

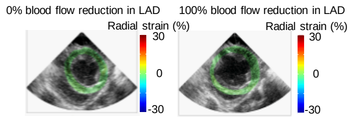
2-D Myocardial Elastography (ME)

- Tracking of Radiofrequency (RF) signals[1] in axial and lateral direction[2]
- Transmural myocardial strain imaging
- Angle-independent
- Multi-sector and ecg-gating

- Validation against tagged MRI (tMRI) in humans *in vivo*[3]



- Associated with reduced blood flow in Left Anterior Descending artery (LAD) in canines *in vivo*[4]



- Can be performed during free breathing in a single heart cycle

[1]Konofagou et al., *Ultrasound Med Biol*, 2002
[2]Lee et al., *TUFFC*, 2007
[3]Lee et al., *Ultrasound Med Biol*, 2008
[4]Lee et al., *Phys Med Biol*, 2011

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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

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Myocardial Elastography: Patient population

66 patients recruited in total

- 49 patients for nuclear stress test
  - 15 patients with ischemia
  - 34 normal patients
- 17 patients for coronary angiography
  - 15 patients with coronary occlusion (1 vessel: N = 6; 2 vessels: N = 2; 3 vessels: N = 7)
  - 2 normal patients

34 normal patients + 2 normal patients → 36 normal patients

Grondin et al., *Ultrasound Med Biol*, 2017

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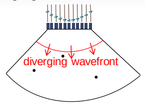
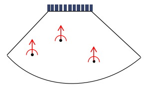
Myocardial Elastography: RF signals acquisition and beamforming

Diverging wave emission

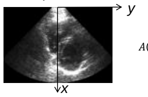
Reception of RF signals





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

Delay-and-sum parallel beamforming

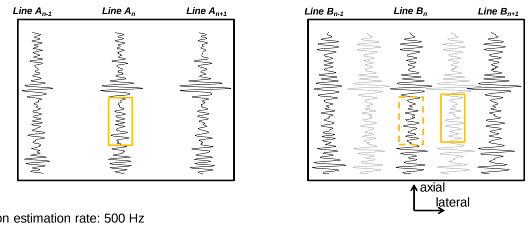


$$A(x,y) = \sum_{i=1}^{64} RF_i\,(\Delta t(x,y))$$

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]

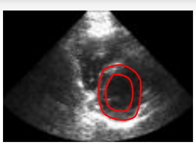
[1]Luo et al., *IEEE TUFFC*, 2010

[2]Konofagou et al., *Ultrasound Med Biol*, 1998

Myocardial Elastography: End-systolic strain estimation

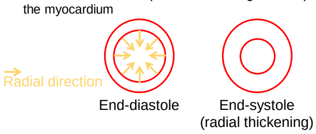
Displacement accumulation during systole

- 2-D displacements are accumulated from end-diastole to end-systole
- The left ventricle is manually segmented and automatically tracked[1] throughout the systolic phase

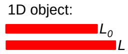


Cumulative Strains

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



1D object:



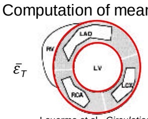
$$Strain = \frac{L - L_0}{L_0}$$

[1]Luo et al., *IEEE TUFFC*, 2008

[2]Luo et al., *IEEE TUFFC*, 2004

Mean radial strain in each territory

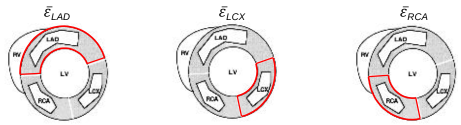
- Computation of mean end-systolic radial strain ($\bar{\varepsilon}$) in all the territories



Lauerma et al., *Circulation*, 1997

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

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



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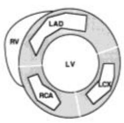
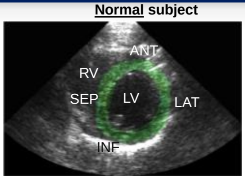
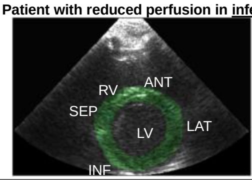
End-systolic radial strains

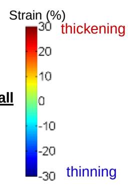
Normal subject





Patient with reduced perfusion in inferior wall





ANT: Anterior
SEP: Septal
INF: Inferior
LAT: Lateral

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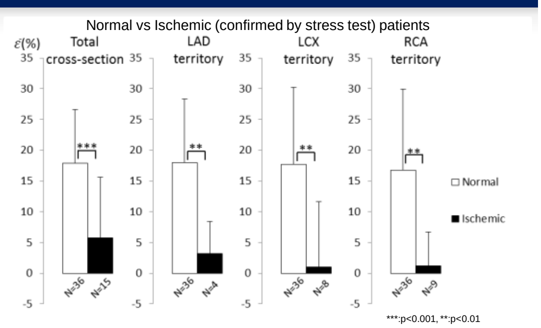
Mean radial strain in normal vs. ischemic patients



Grondin et al., *Ultrasound Med Biol*, 2017

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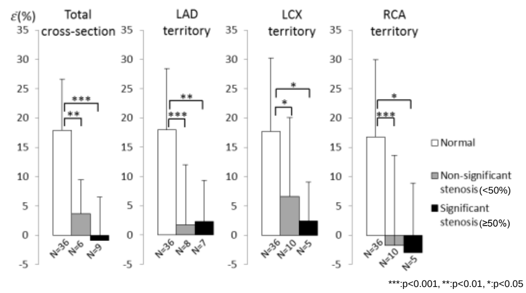
Results: Mean radial strain in normal subjects and CAD patients

Normal vs CAD (confirmed by angiography) patients



***:p<0.001, **:p<0.01, *:p<0.05

Grondin et al., *Ultrasound Med Biol*, 2017

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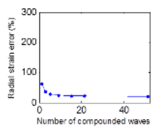
Conclusion

- 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[1,2]
- Validate ME against nuclear imaging (SPECT and PET) in a large cohort of patients



[1]Sayseng et al., *IEEE TUFFC*, 2018

[2]Grondin et al., *IEEE TUFFC*, 2017

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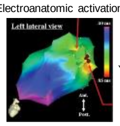
Cardiac arrhythmia mapping

- Cardiac arrhythmia is experienced by **~5.8 million people** in the US[1]
- Underlying or contributing cause of death for ~1/5 deaths in the US[2]
- ECG cannot always accurately locate arrhythmias
- Endocardial mapping to locate the arrhythmia is invasive and can be time consuming

Electroanatomic activation map

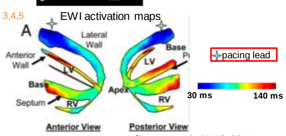


Yamada *et al*, *Europace*, 2009

- Electromechanical Wave Imaging (EWI)[3,4,5]

Ultrasound based technique
High frame rate (≥ 500 frames per second)

EWI activation maps



[1]Tang *et al.*, *Appl Health Econ Health Policy*, 2014
[2]Thom *et al.*, *Circulation*, 2006
[3]Pernot *et al.*, *Ultrasound Med Biol*, 2007
[4]Provost *et al.*, *PNAS*, 2011
[5]Provost *et al.*, *Heart Rhythm*, 2013

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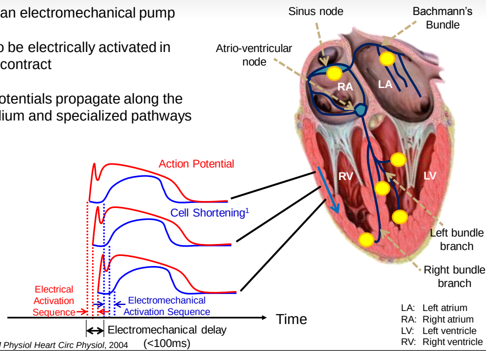
Electromechanical activation of the heart

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



[1]Cordeiro et al., *Am J Physiol Heart Circ Physiol*, 2004

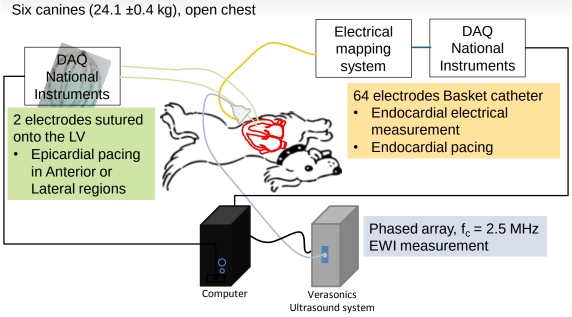
Objectives

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

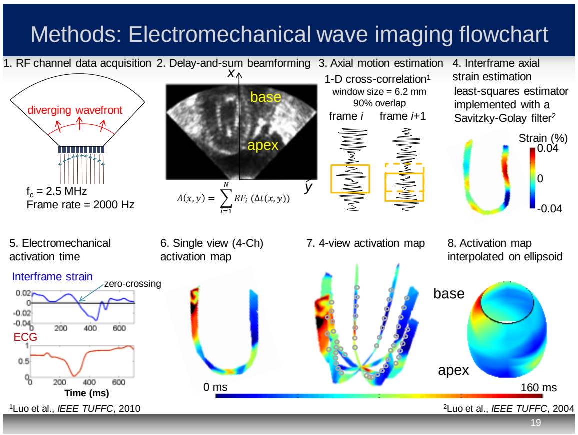
- Investigate the relationship between the electromechanical and the electrical activation of the canine heart *in vivo*
- Demonstrate that 3D-rendered EWI can predict arrhythmia origin location

Methods

Six canines (24.1 ±0.4 kg), open chest



➡ Ultrasound RF data are acquired simultaneously with endocardial potential during sinus rhythm, endocardial or epicardial pacing


Methods: Electromechanical wave imaging flowchart
1. RF channel data acquisition
diverging wavefront
fc = 2.5 MHz
Frame rate = 2000 Hz
2. Delay-and-sum beamforming
base
apex
A(x, y) = Σ RFi (Δt(x, y))
3. Axial motion estimation
1-D cross-correlation1
window size = 6.2 mm
90% overlap
frame i
frame i+1
4. Interframe axial strain estimation
least-squares estimator implemented with a Savitzky-Golay filter2
Strain (%)
0.04
0
-0.04
5. Electromechanical activation time
Interframe strain
zero-crossing
ECG
Time (ms)
6. Single view (4-Ch) activation map
7. 4-view activation map
8. Activation map interpolated on ellipsoid
base
apex
0 ms
160 ms
1Luo et al., IEEE TUFFC, 2010
2Luo et al., IEEE TUFFC, 2004
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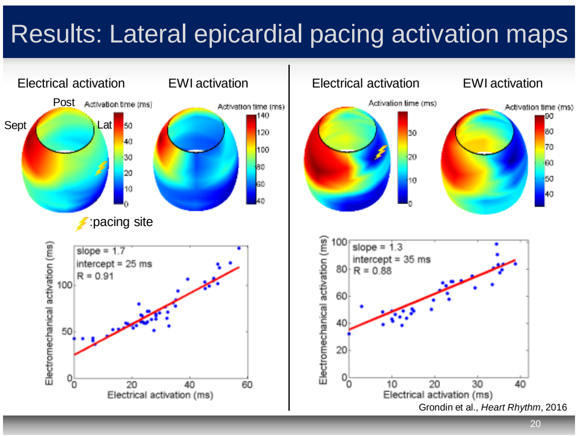
Results: Lateral epicardial pacing activation maps
Electrical activation
EWI activation
Electrical activation
EWI activation
Post
Sept
Lat
Activation time (ms)
:pacing site
slope = 1.7
intercept = 25 ms
R = 0.91
slope = 1.3
intercept = 35 ms
R = 0.88
Electromechanical activation (ms)
Electrical activation (ms)
Grondin et al., Heart Rhythm, 2016
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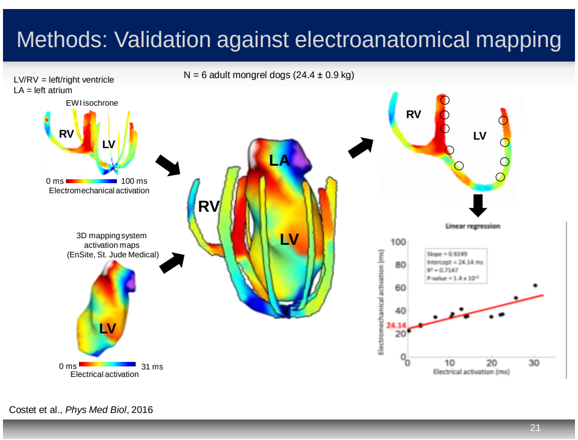
Methods: Validation against electroanatomical mapping
LV/RV = left/right ventricle
LA = left atrium
N = 6 adult mongrel dogs (24.4 ± 0.9 kg)
EWI isochrone
RV
LV
0 ms
100 ms
Electromechanical activation
3D mapping system activation maps (EnSite, St. Jude Medical)
LV
0 ms
31 ms
Electrical activation
LA
RV
LV
RV
LV
Linear regression
24.14
Electrical activation (ms)
Costet et al., Phys Med Biol, 2016
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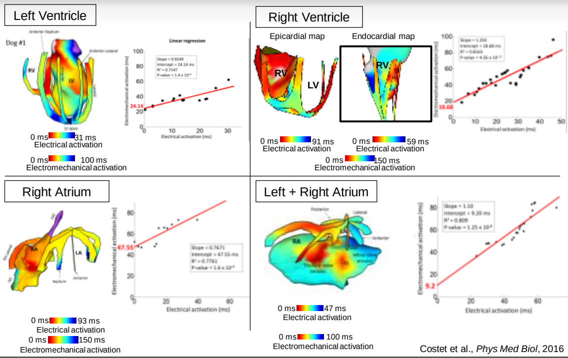
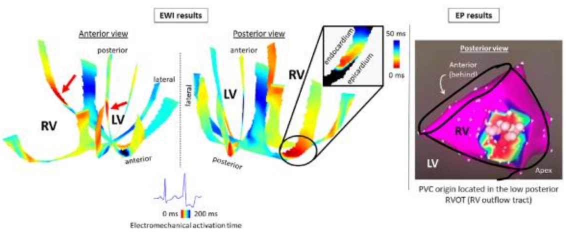
Results: Validation in all four chambers



Costet et al., *Phys Med Biol*, 2016

EWI as a treatment planning tool

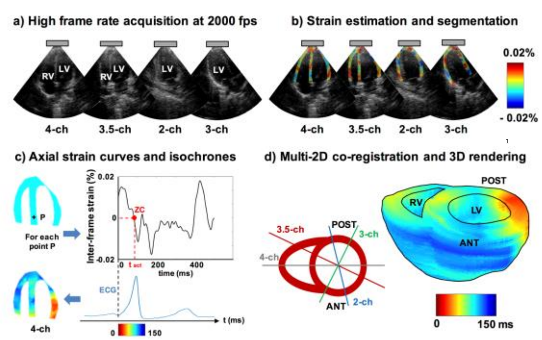
Premature ventricular contraction (PVC) patient



Early activation

Costet et al., *Ultrasound Med Biol*, 2018

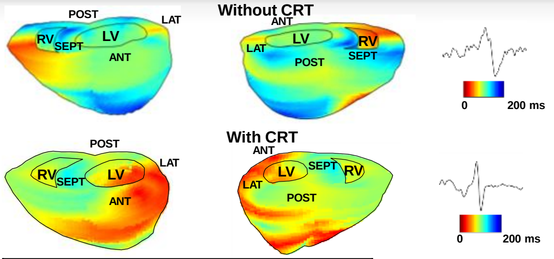
Methods: 3D rendering of EWI



Melki et al., *JACC Clinical EP*, 2019

[1]Nauleau et al., *Med Phys*, 2017

Cardiac Resynchronization Therapy (CRT) patient



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

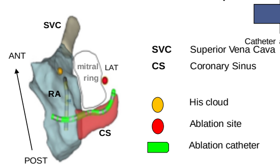
Grubb et al., *JACC*, 2018

7 yo. female WPW patient before and after ablation

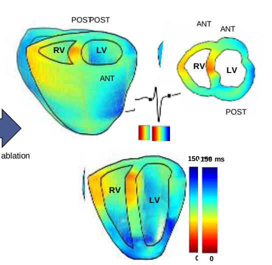
12-lead ECG prediction

- Boersma et al. algorithm correctly predicted the left lateral AP
- Arruda et al. algorithm did not succeed in accurately localizing the AP and predicted it to be right lateral

Validation with EnSite intracardiac map



Sinus rhythm after ablation of the AP

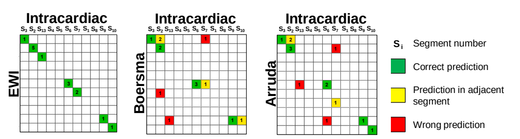


Melki et al., *JACC Clinical EP*, 2019

→ 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

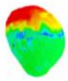
Melki et al., *JACC Clinical EP*, 2019

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

In vivo EWI activation times of a human during normal sinus rhythm



2D matrix array : 32x32 elements

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Thank you!

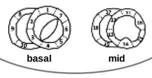
Methods: Study design

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
Boersma[1], Arruda[2]
algorithms

Location predictions



Blinded EWI
isochrones generation

Predictions compared to ground truth:
intracardiac mapping and **successful ablation site**

[1]Boersma et al., *J Cardiovasc Electrophysiol*, 2002
[2]Arruda et al., *J Cardiovasc Electrophysiol*, 1998

Melki et al., *JACC Clinical EP*, 2019

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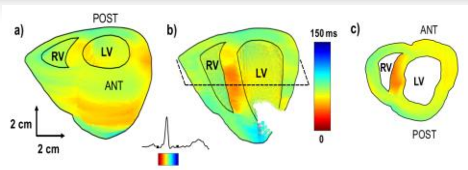
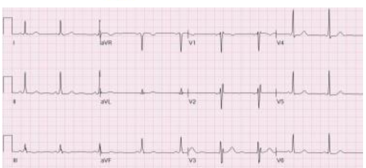
17 yo. female fasciculoventricular AP before ablation





Melki et al. JACC Clinical EP 2019