



# Imaging to Enhance the Treatment and Understanding of Atrial Arrhythmias

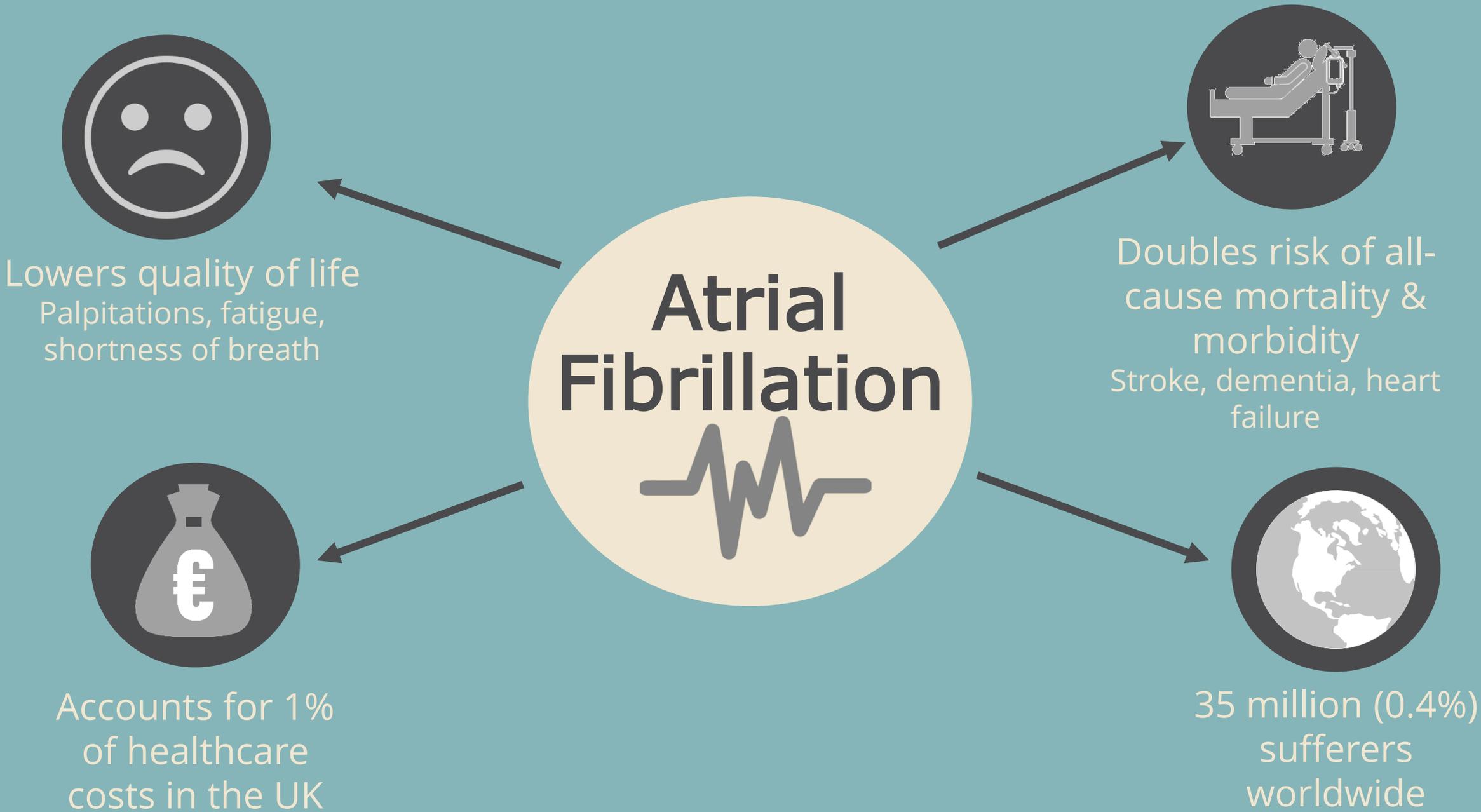


Marta Varela

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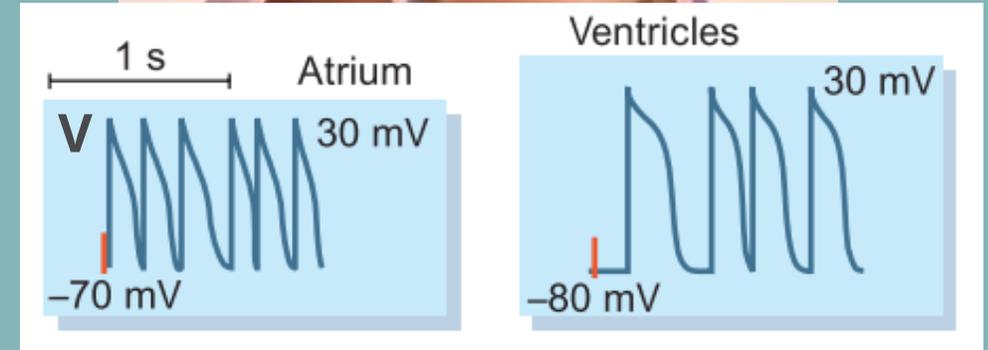
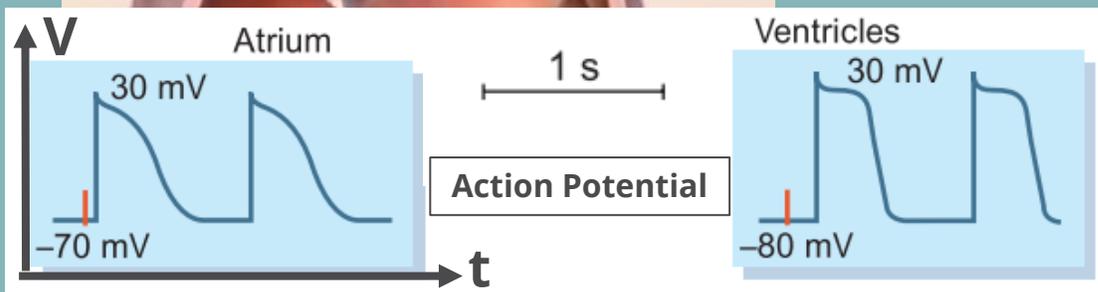
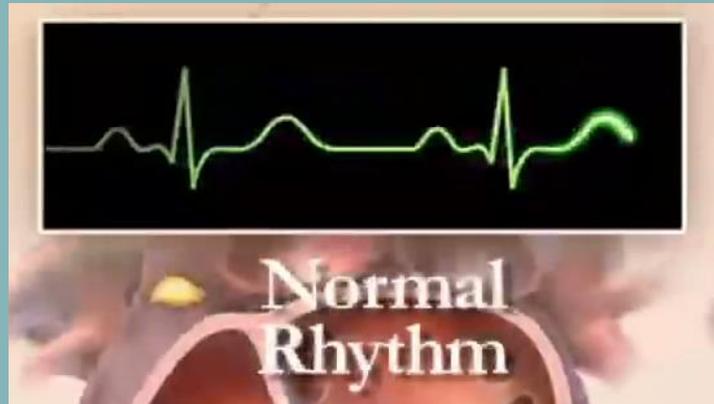
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Source: Kirchhof et al, *Guidelines for the Management of AF*, 2016

# What is Atrial Fibrillation?



- Regular, long, spaced action potentials
- Efficient contraction

- Fast, short, irregular action potentials
- Decreased pumping efficiency
- Higher likelihood of clot formation

# Treatment

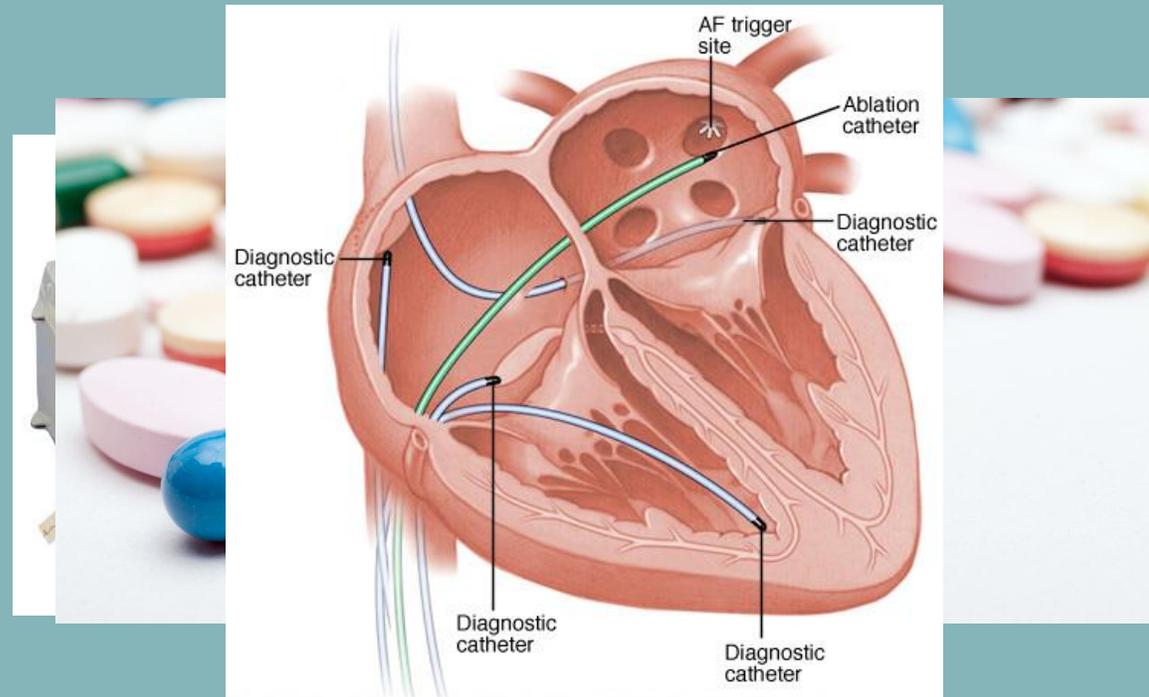
## Cardioversion

## Anti-Arrhythmic Drugs

## Catheter Ablation

## Rate Control & Stroke Prevention

- Does not treat AF; only reduces risk of adverse events
- Ensures heart rate is appropriate and stable
- Minimises likelihood of formation of clots



<sup>1</sup> Kuppahally et al, Int Arch Med, 2009

<sup>2</sup> Calkins et al, Circ Arrhythmia EP, 2009

# Why is treatment so ineffective?

## AF mechanisms are unclear.

- Ectopic foci, anatomical re-entry, rotors, ...?

## Better treatments

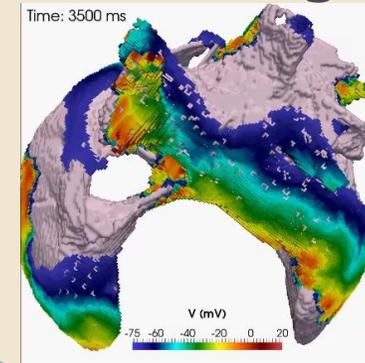
## Treatment is not personalised.

- Lack of powerful biomarkers to guide treatment.
- Imaging (e.g. MRI) common, but often interpreted subjectively.

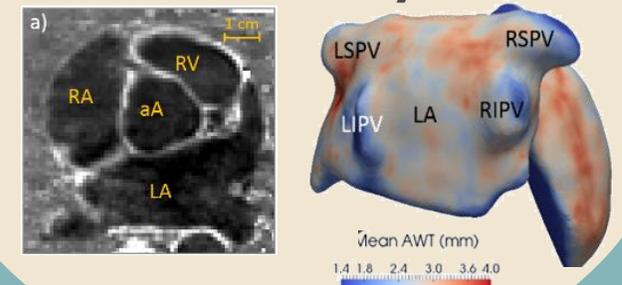
Mechanistic hypothesis testing

Imaging-based predictors

## Biophysical Modelling

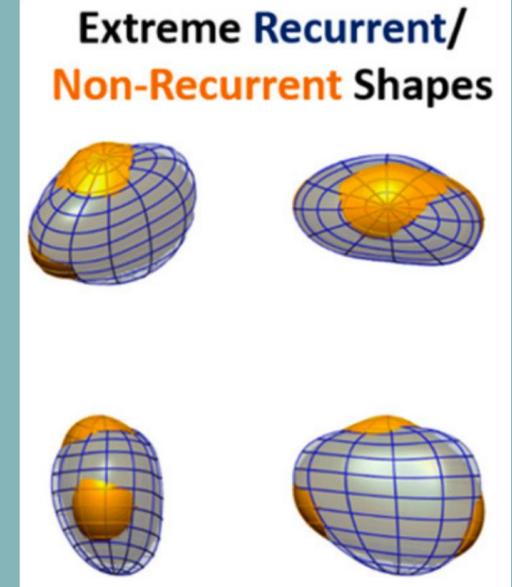
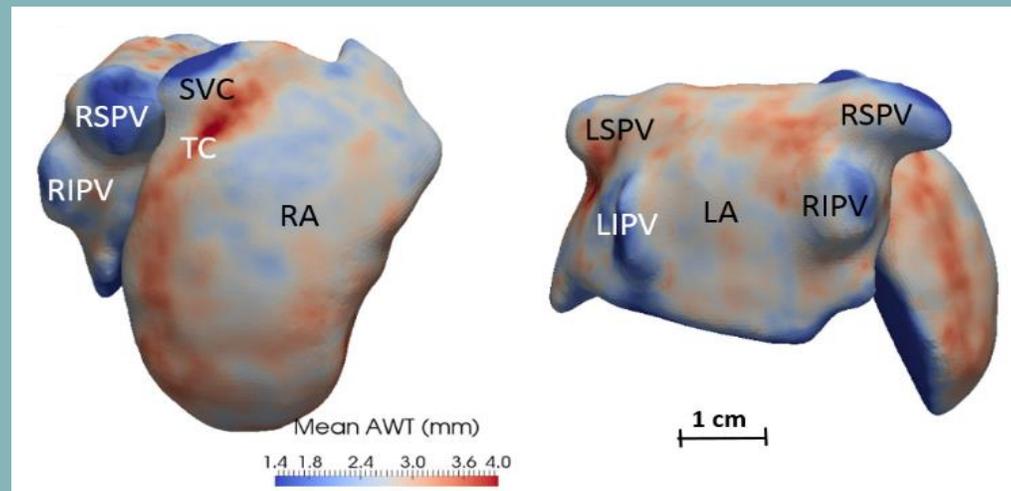
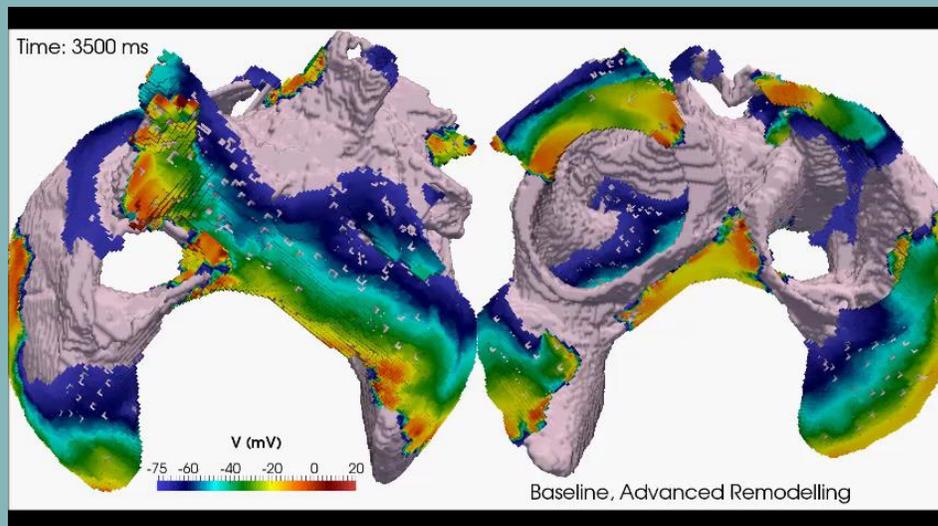


## Imaging & Data Analysis



# Today

1. In Silico Testing of Anti-Arrhythmic Drugs for AF
2. Role of Atrial Wall Thickness in AF Mechanisms
3. Can Atrial Shape Predict Outcomes in AF?



# In Silico Testing of Anti-Arrhythmic Drugs for AF



RESEARCH ARTICLE

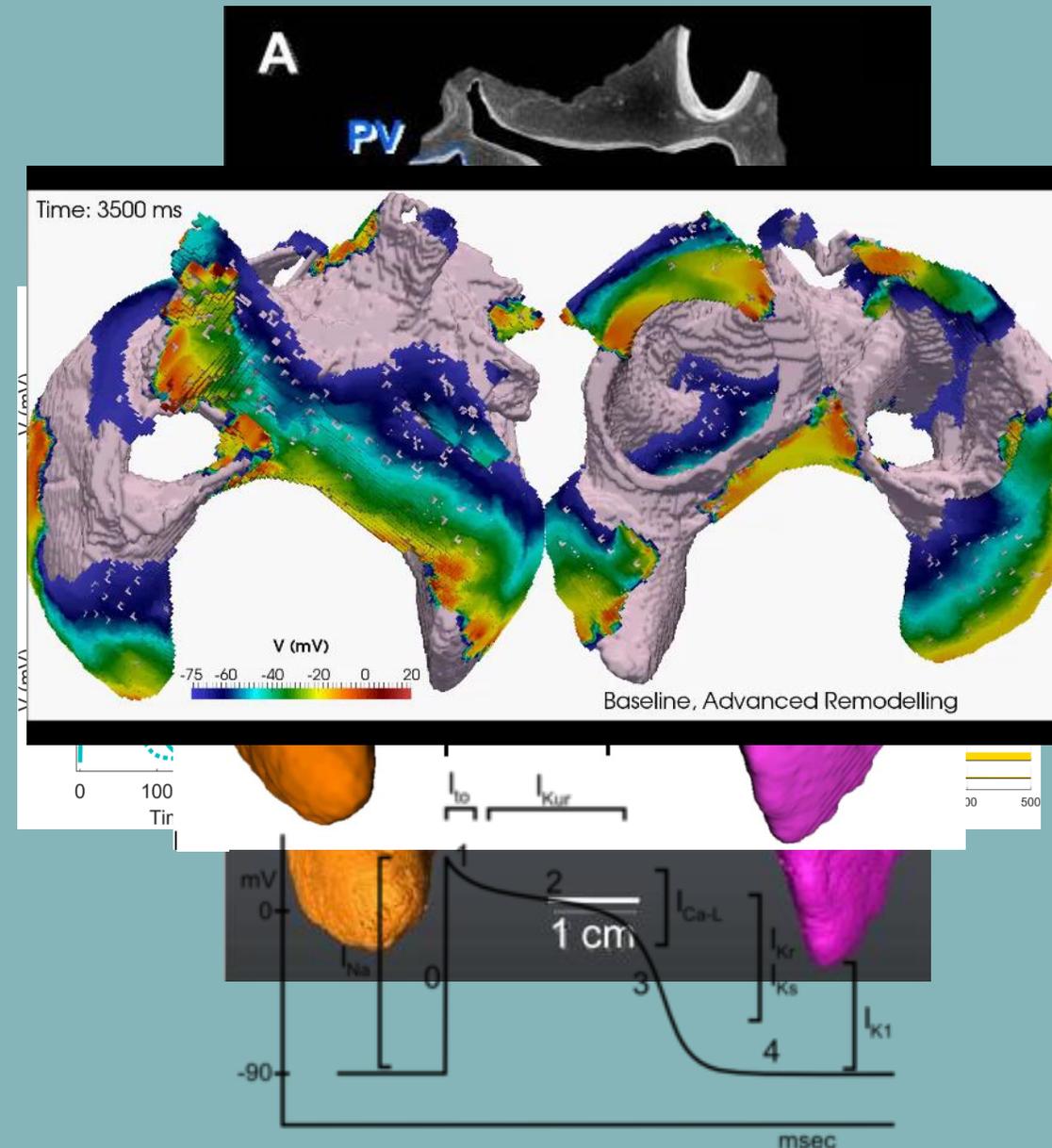
Atrial Heterogeneity Generates Re-entrant Substrate during Atrial Fibrillation and Anti-arrhythmic Drug Action: Mechanistic Insights from Canine Atrial Models

Marta Varela<sup>1</sup>, Michael A. Colman<sup>2</sup>, Jules C. Hancox<sup>3</sup>, Oleg V. Aslanidi<sup>1\*</sup>

# Creation of Biophysical Model of AF

1. Segment and label atrium from high-resolution microCT images
2. Compute myofibre orientations
3. Assign appropriate electrophysiological properties
4. Create ectopic foci in the pulmonary veins, as seen clinically
5. Solve the equations for the propagation of the electrical potential numerically in a super-computer

## Biophysical Model of AF

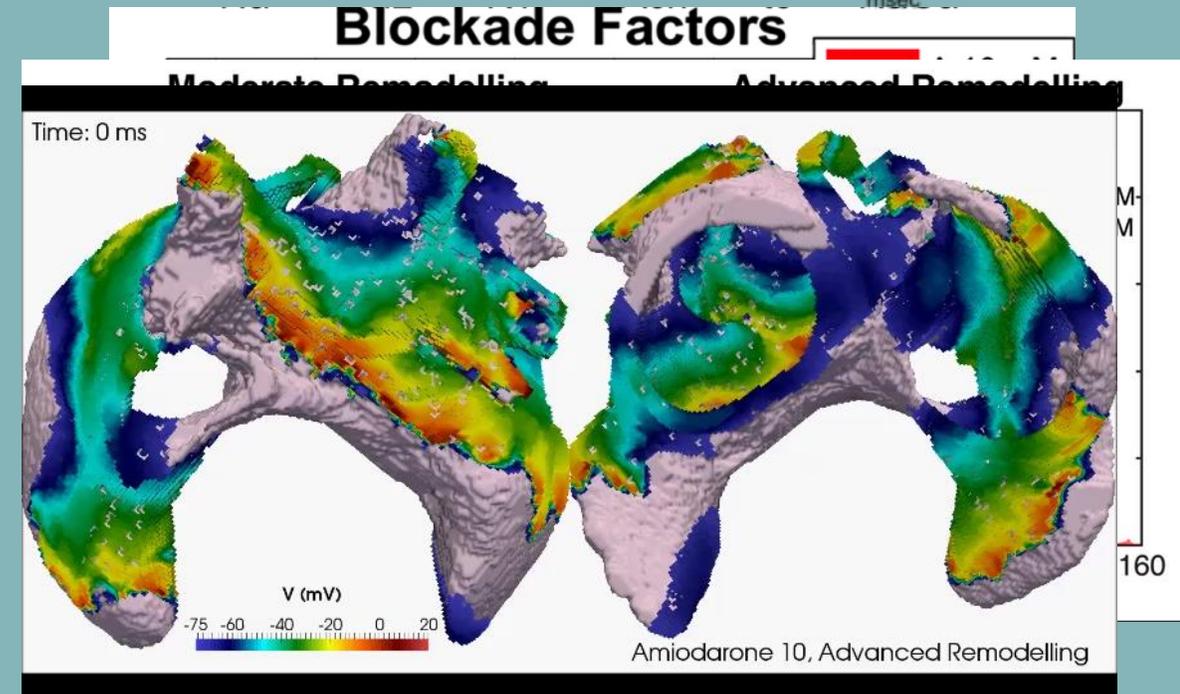
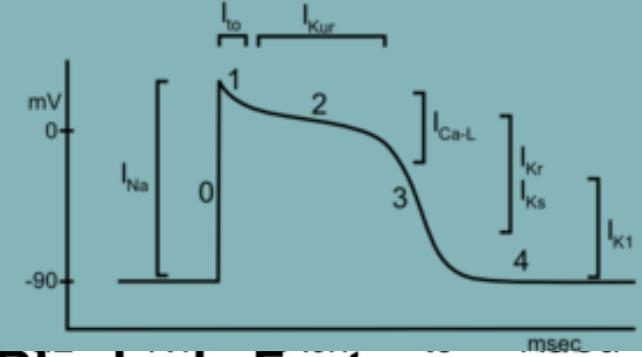


Varela et al, LNCS, 2013

Aslanidi et al, IEEE TMI, 2013

# In Silico Testing of Drugs

- Alter the properties of the ionic currents, mimicking the action of anti-arrhythmic drugs
- Mimic the administration of drug in the AF scenario
- Determine which drugs lead to AF termination
- What characteristics do successful drugs have?



**Conclusion:** The most successful drugs extend the duration of the action potential (APD) without increasing atrial APD heterogeneity.

# Role of Atrial Wall Thickness in AF Mechanisms



IEEE TRANSACTIONS ON MEDICAL IMAGING, VOL. 36, NO. 8, AUGUST 2017

1607

## Novel MRI Technique Enables Non-Invasive Measurement of Atrial Wall Thickness

Marta Varela,\* Ross Morgan, Adeline Theron, Desmond Dillon-Murphy, Henry Chubb, John Whitaker, Markus Henningson, Paul Aljabar, Tobias Schaeffter, Christoph Kolbitsch, and Oleg V. Aslanidi

### ORIGINAL RESEARCH ARTICLE

Front. Physiol. 04 October 2018 | <https://doi.org/10.3389/fphys.2018.01352>

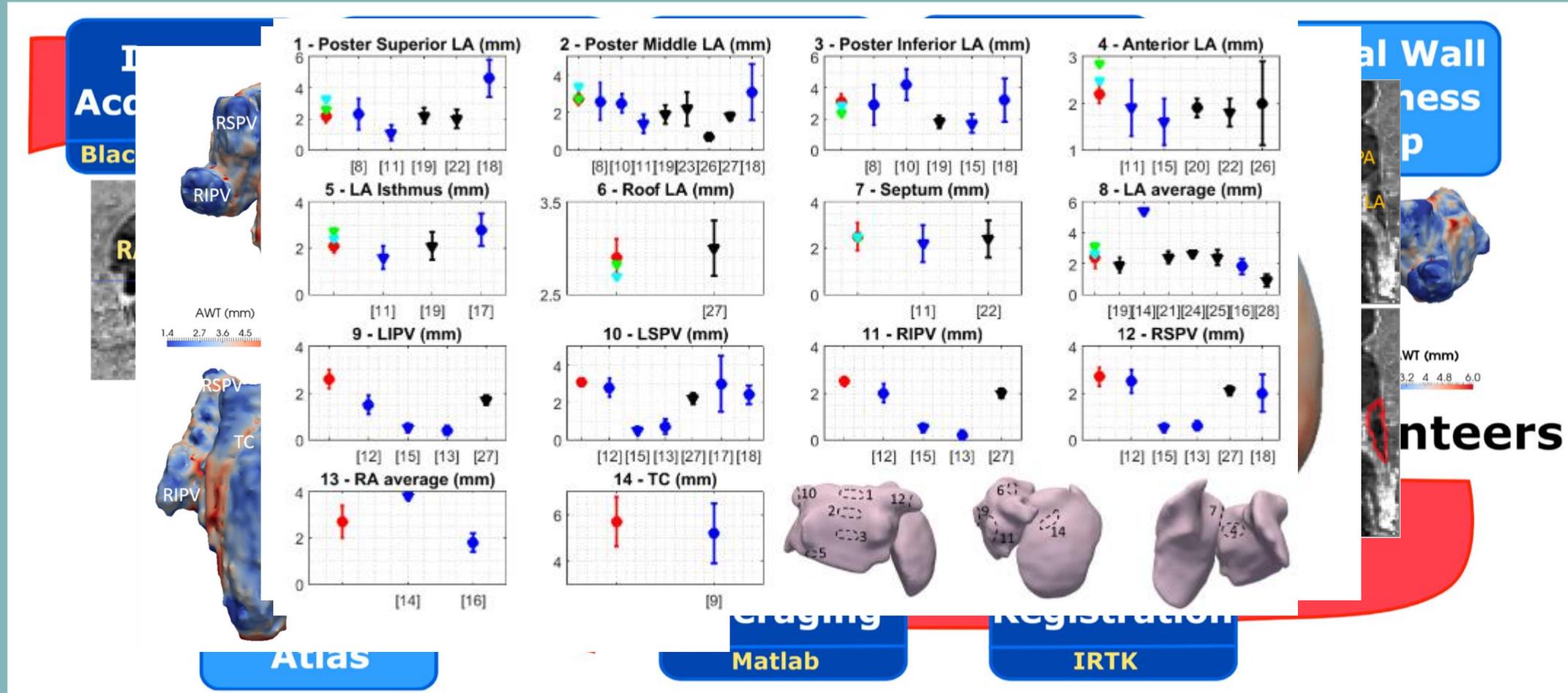


## Image-Based Computational Evaluation of the Effects of Atrial Wall Thickness and Fibrosis on Re-entrant Drivers for Atrial Fibrillation

 Aditi Roy,  Marta Varela and  Oleg Aslanidi\*

Department of Biomedical Engineering, School of Biomedical Engineering & Imaging Sciences, King's College London, King's Health Partners, St Thomas' Hospital, London, United Kingdom

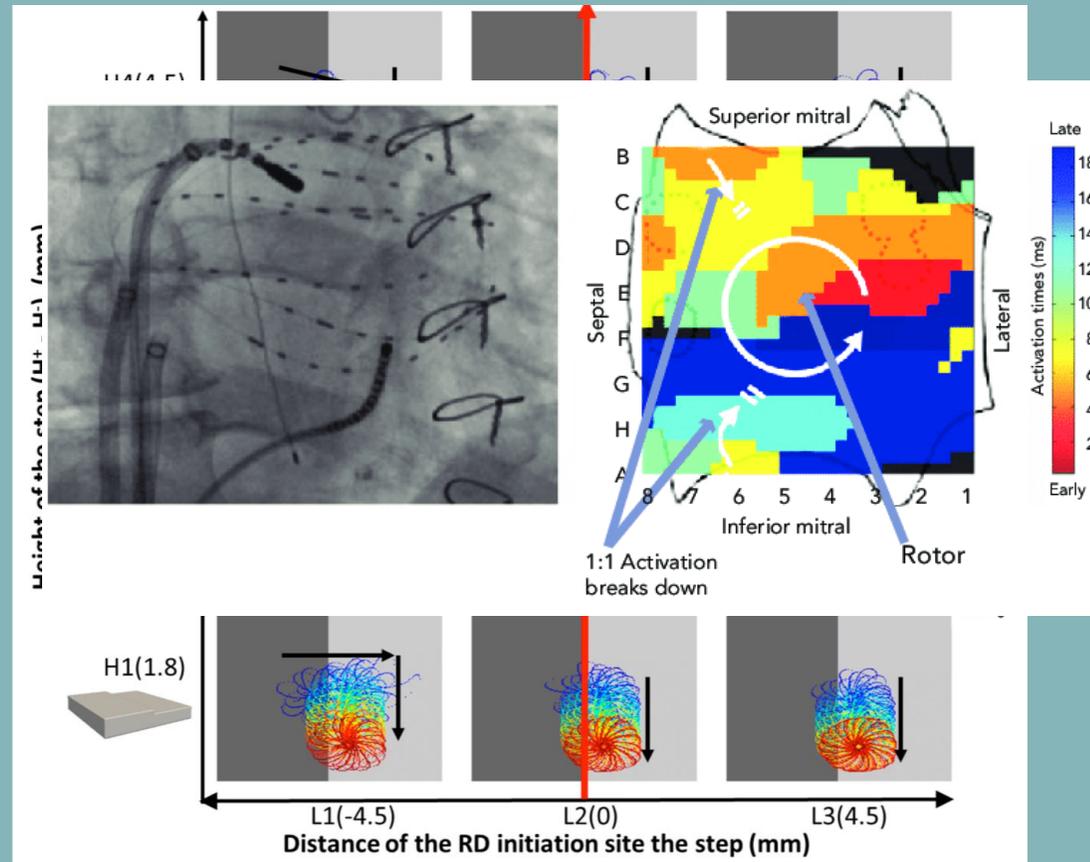
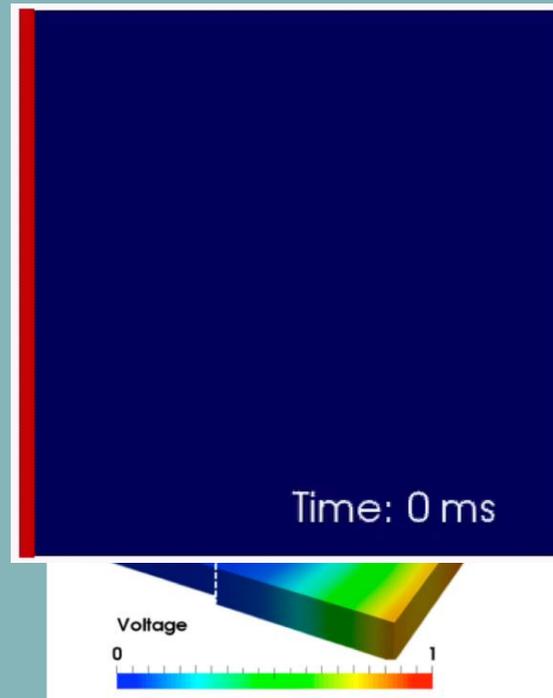
# Imaging Atrial Wall Thickness



# Does wall thickness affect the dynamics of rotors ...

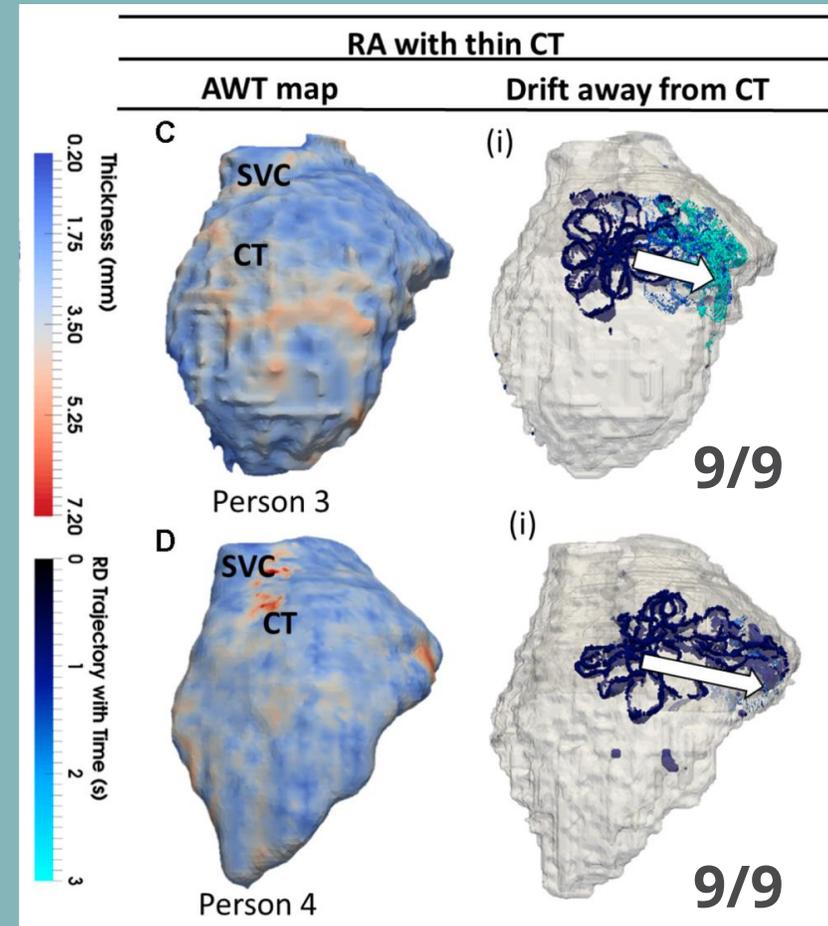
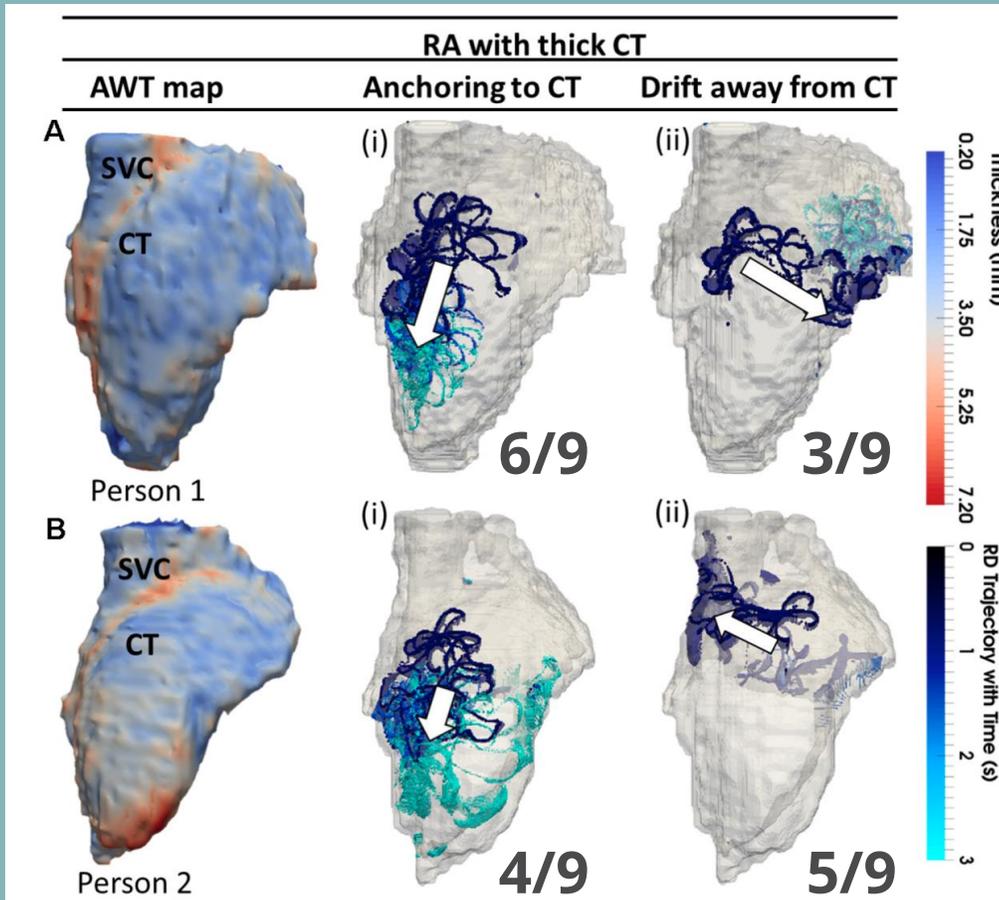


Aditi Roy



Yes. Rotors drift towards and then along gradients in wall thickness.

# ... for realistic wall thickness gradients?



Yes. Rotors drift towards and along the crista terminalis, a well-known location for right atrial arrhythmias.

# Can Atrial Shape Predict Outcomes in AF?

ORIGINAL RESEARCH ARTICLE

Front. Physiol., 14 February 2017 | <https://doi.org/10.3389/fphys.2017.00068>



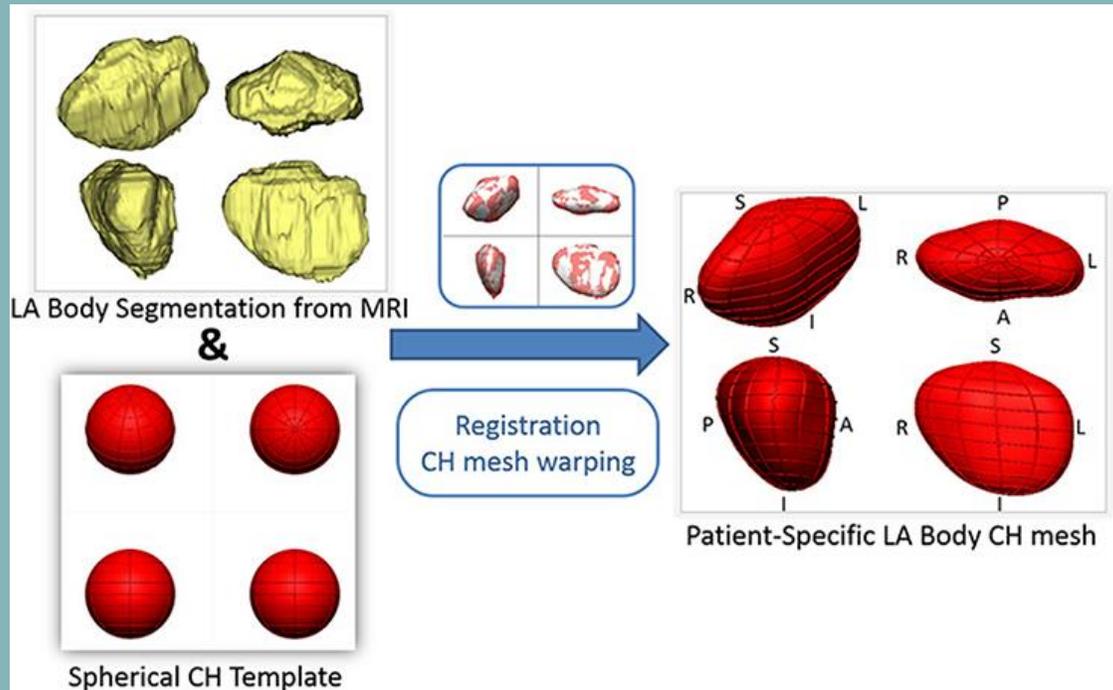
## Novel Computational Analysis of Left Atrial Anatomy Improves Prediction of Atrial Fibrillation Recurrence after Ablation

 Marta Varela<sup>1</sup>,  Felipe Bisbal<sup>2</sup>,  Ernesto Zacur<sup>1,3</sup>,  Antonio Berruezo<sup>4</sup>,  Oleg V. Aslanidi<sup>1</sup>,  Lluis Mont<sup>4</sup> and  Pablo Lamata<sup>1\*</sup>

# Study Design

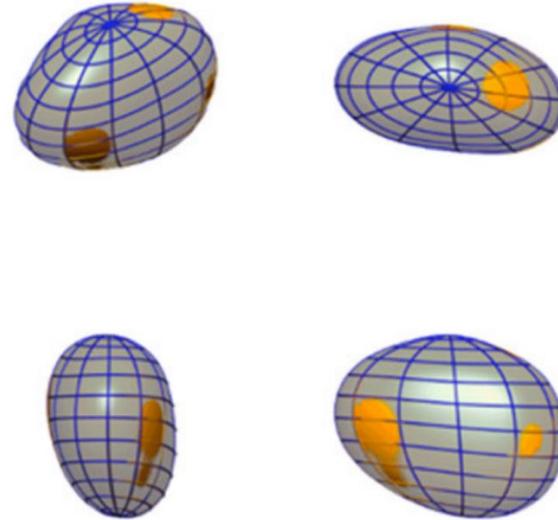
- **Hypothesis**
  - Patients whose atria have remodelled and changed shape and size have a poorer outcome.
- Left atrial (LA) volume, diameter and “sphericity” have been used as predictors of outcome, but have a poor predictive value.
- **Aims**
  - Do a computational analysis of LA shape.
  - Understand which shape features are most predictive of outcome.
- **Patients**
  - 144 AF patients undergoing catheter ablation.
  - AF recurrence follow-up for 2 years.

# Data Analysis

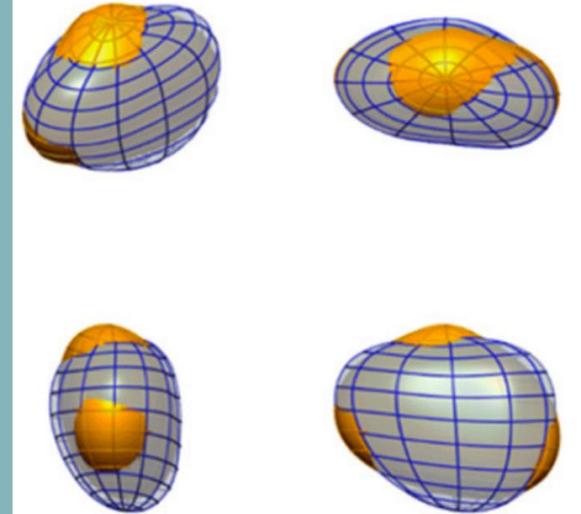


- Register LA meshes to same common space.
- Compute statistics on these meshes.

## Observed Recurrent/ Non-Recurrent Shapes

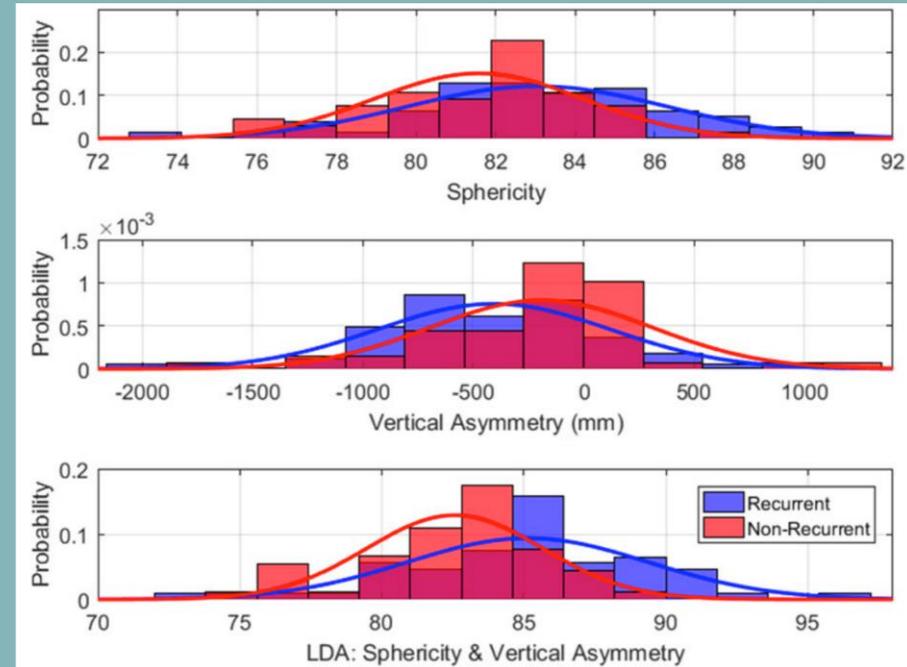
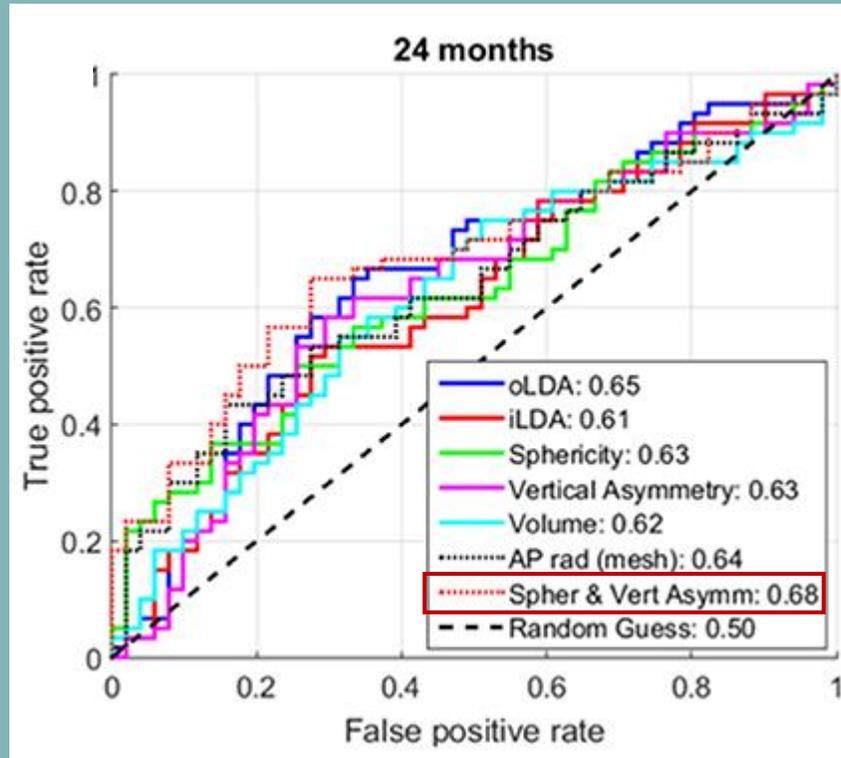


## Extreme Recurrent/ Non-Recurrent Shapes



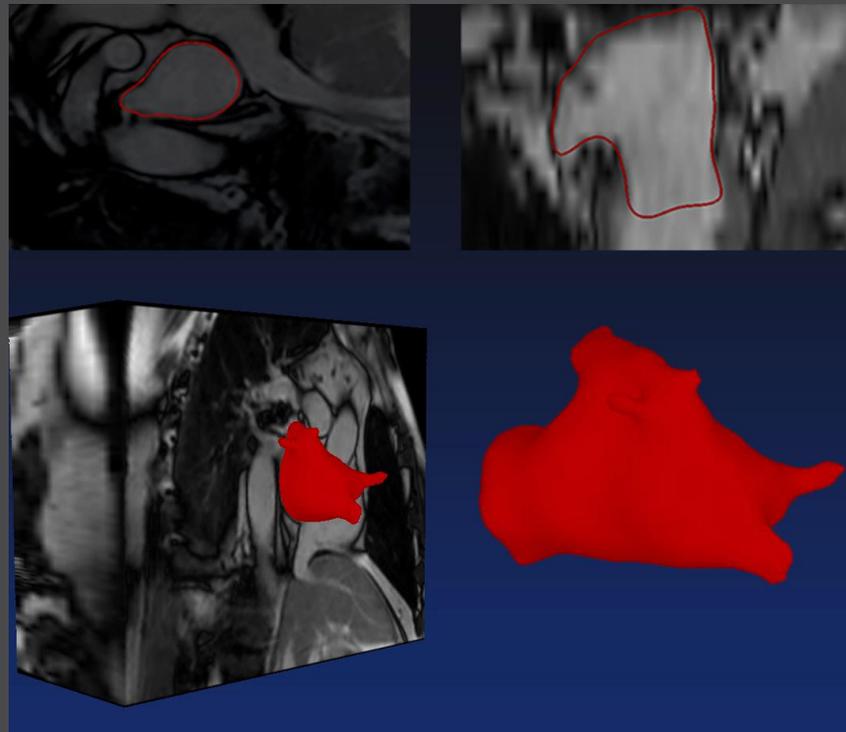
- Find the principal modes of shape variation (PCA).
- Find the combination of modes that optimally separates recurrent/non-recurrent atria.
- Artificially amplify the differences between recurrent and non-recurrent shapes.

# Conclusions



- Computational shape analysis produces novel predictors of outcome, but with comparable predictive power to existing ones.
- Computational analysis gives novel insights.
- Information on atrial shape averaged across the cardiac cycle...

# Future Plans: Outcome predictors using atrial deformations



# The atria deform...

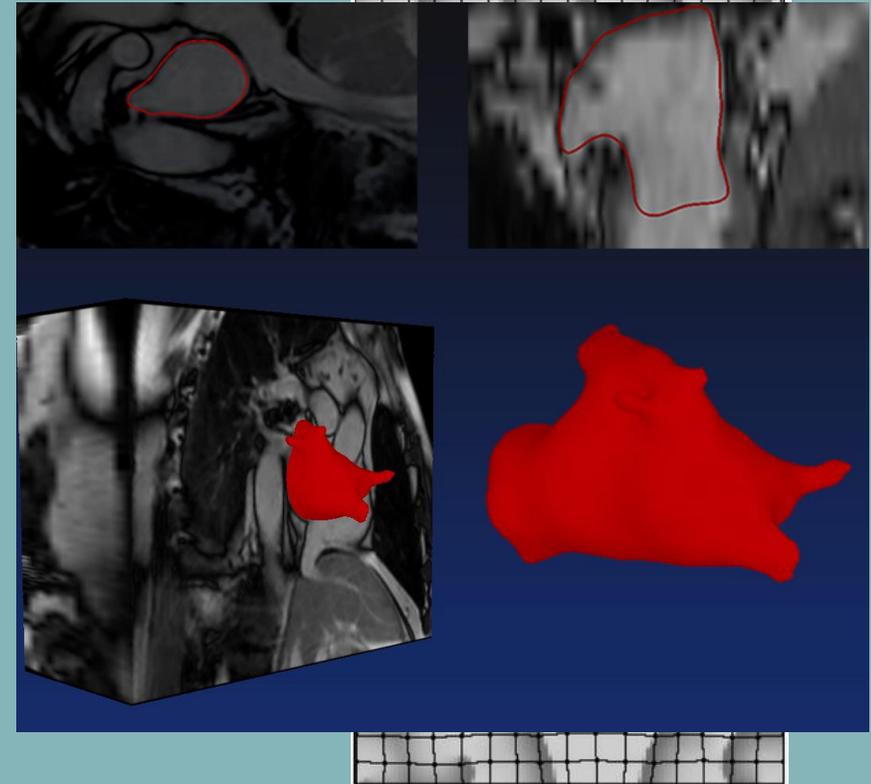
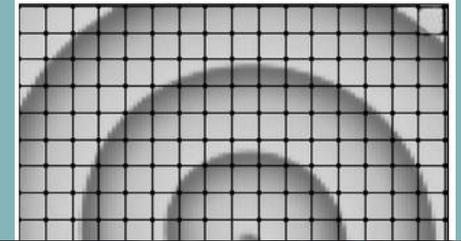
## Novel Deformation Biomarkers

- Acquire high-resolution CINE-MRI in AF patients.
- Estimate atrial deformations (strain, strain rate).
- Build deformation-based predictor of outcome.

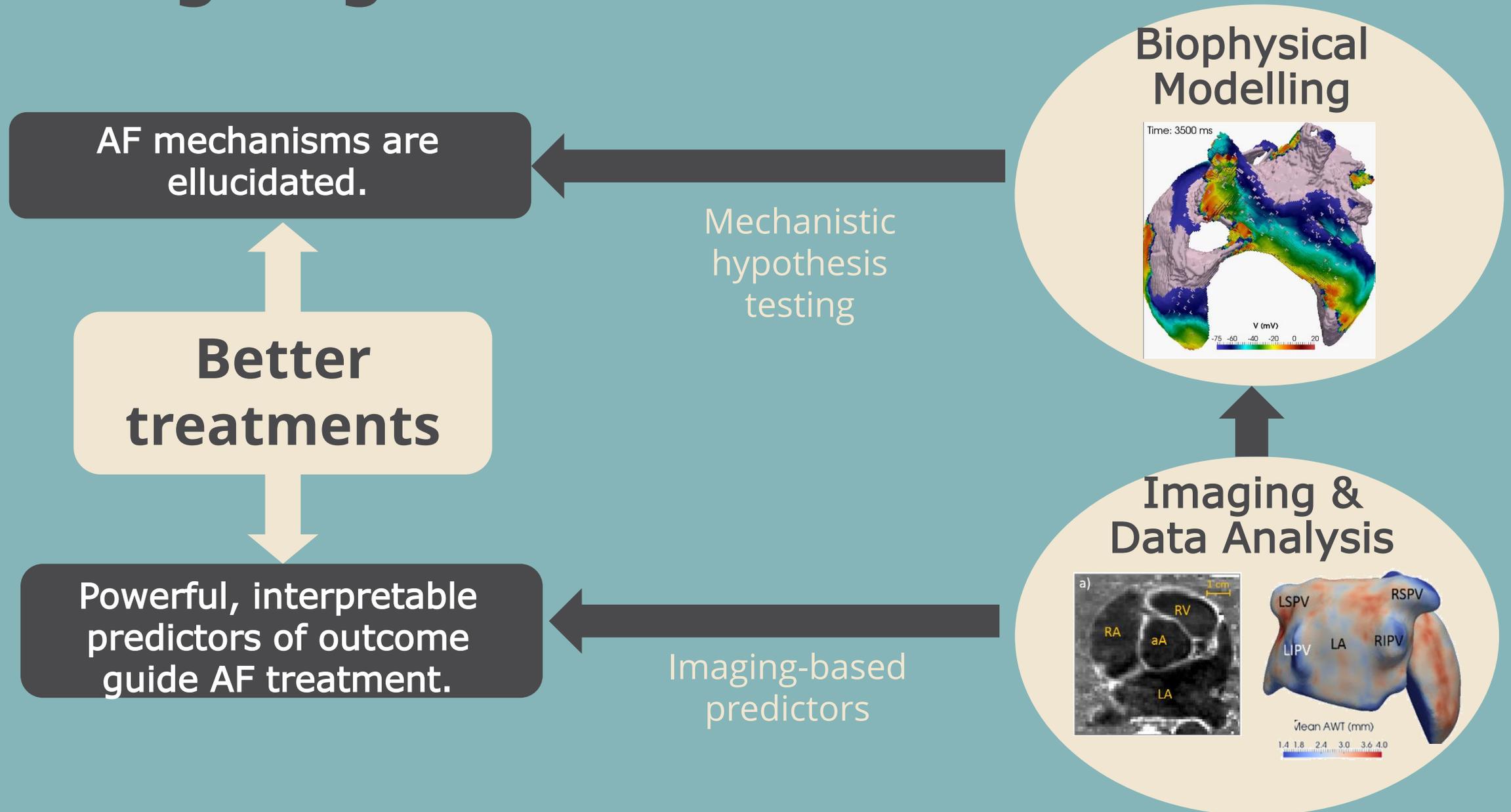
## Understanding Mechanisms

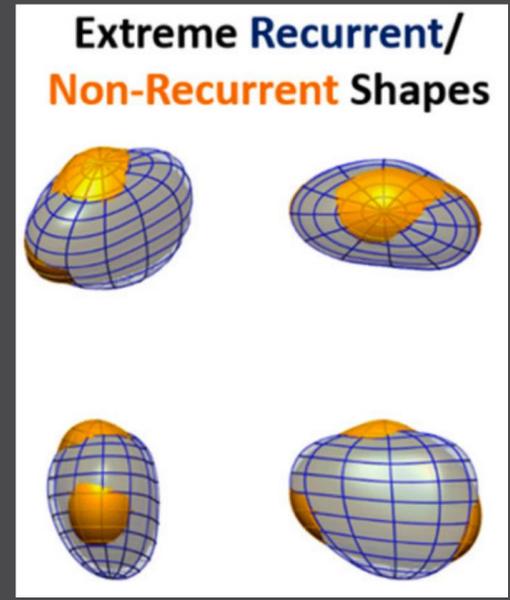
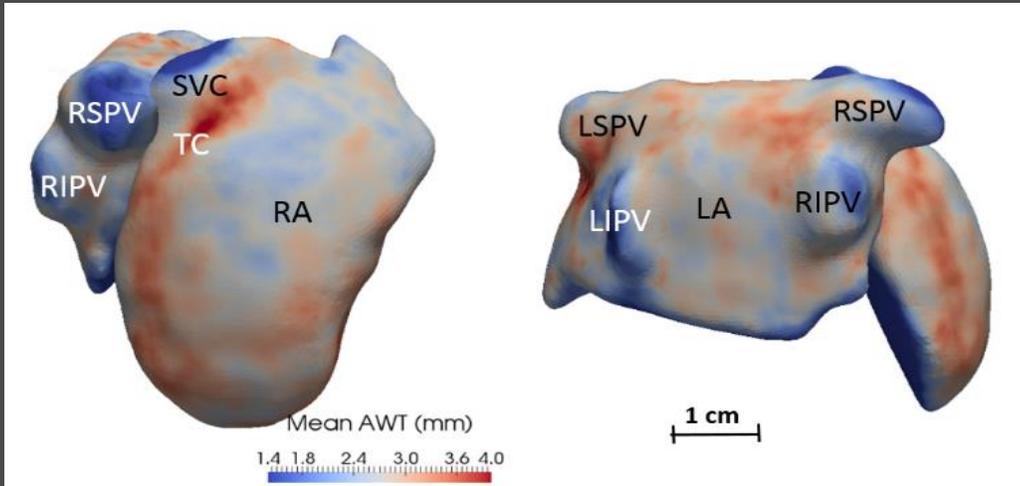
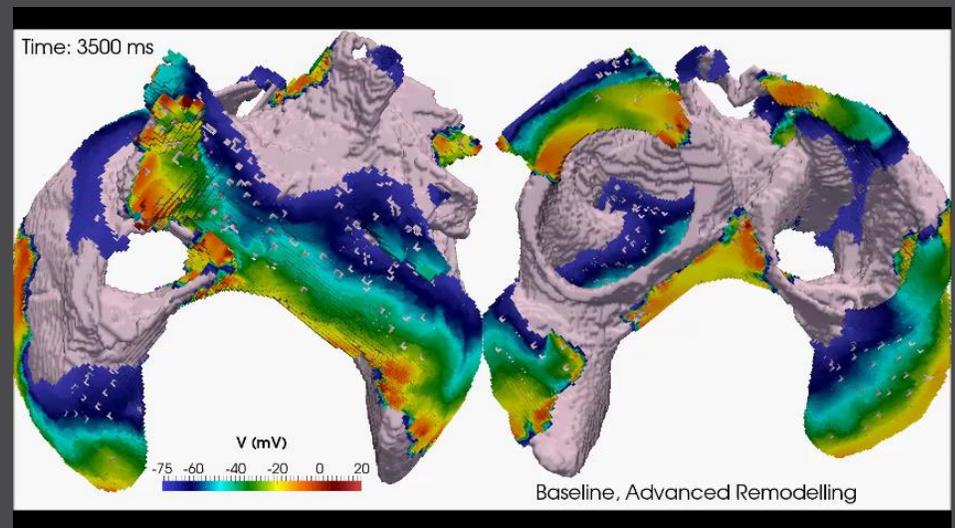
- Create dynamic models of the propagation of the electrical signal.
- **Hypothesis:** Some types of deformation help sustain AF.

No deformations



# Designing Better Treatments





Thank you!

Questions?

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# Mechanisms of AF

**Unclear at the moment.** Several hypotheses:

1. **Ectopic foci:** Rogue atrial cells behave like pacemakers
2. **Re-entry:** Electrical signal can propagate in several stable closed loops
  - Anatomical re-entry
  - Spiral waves/rotors
3. **Rotor Breakup:** Mother rotor continuously gives off transient rotors
4. **All of the above!**

**Atria remodel to perpetuate AF: "AF begets AF."**

