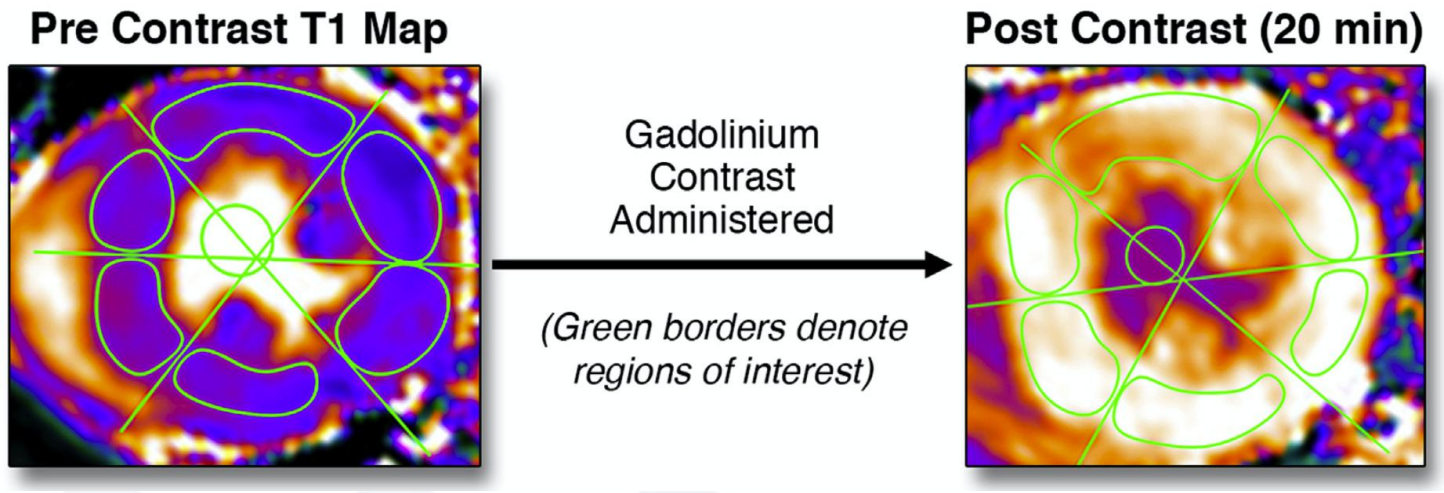
Heart rhythm disease institute

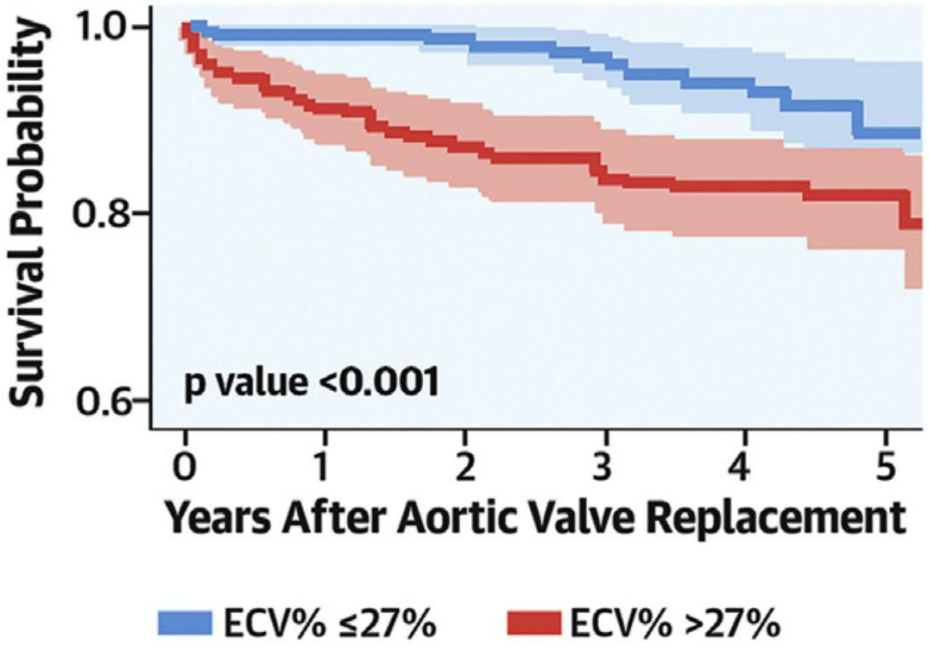
Increased extracellular volume in the ventricles after aortic valve replacement is not associated with a change in conduction velocity: a computational study

Vladimír Sobota, Christoph M. Augustin, Edward J. Vigmond, Sarah Nordmeyer, Jason D. Bayer

Extracellular Volume (ECV)



$$ECV = (1 - haematocrit)\frac{\frac{1}{post\ contrast\ T1\ myo} - \frac{1}{native\ T1\ myo}}{\frac{1}{post\ contrast\ T1\ blood} - \frac{1}{native\ T1\ blood}}$$



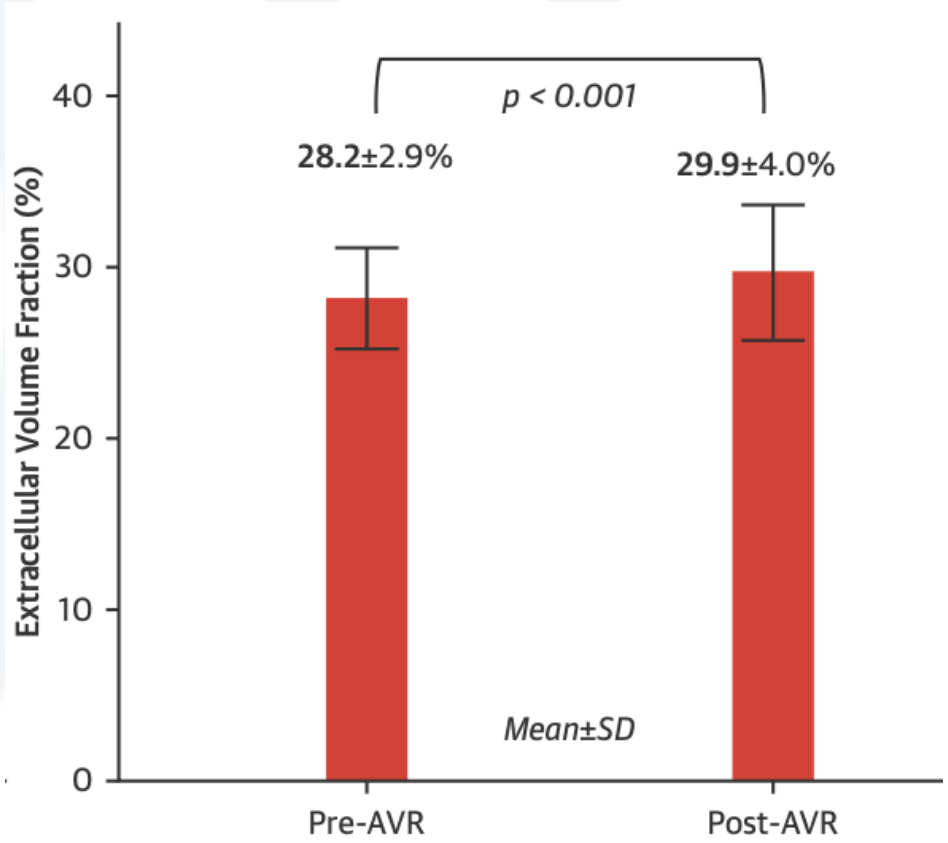
ECV is a predictor of mortality in AS patients

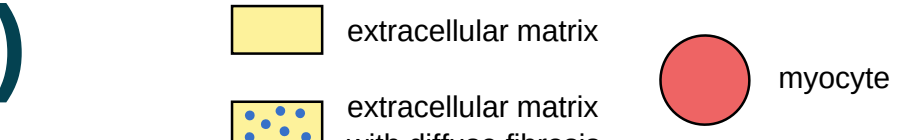
Haaf et al. *J Cardiovasc Magn Reson* 2016

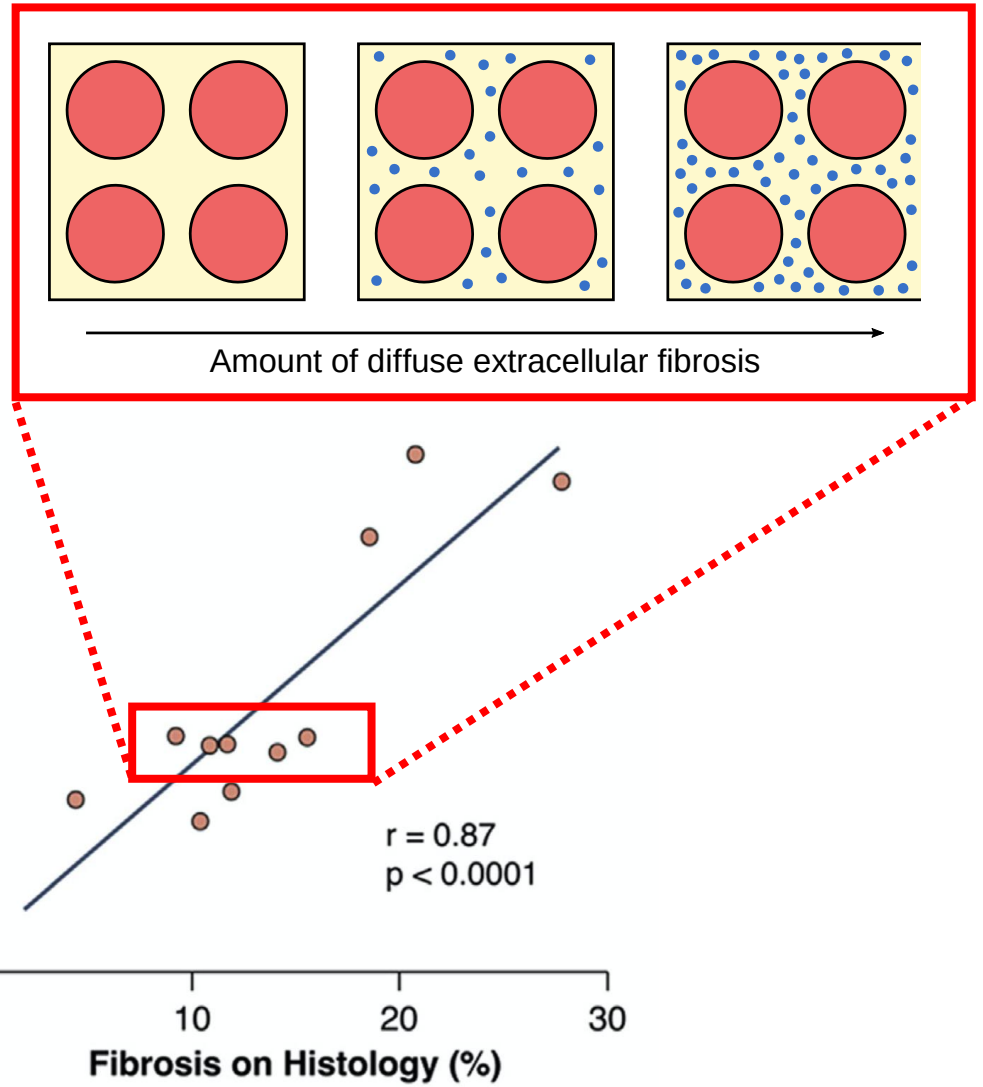
Chin et al. *JACC Cardiovasc Imaging* 2017

Kwak et al. *JACC* 2021

EXTRACELLULAR VOLUME (ECV)



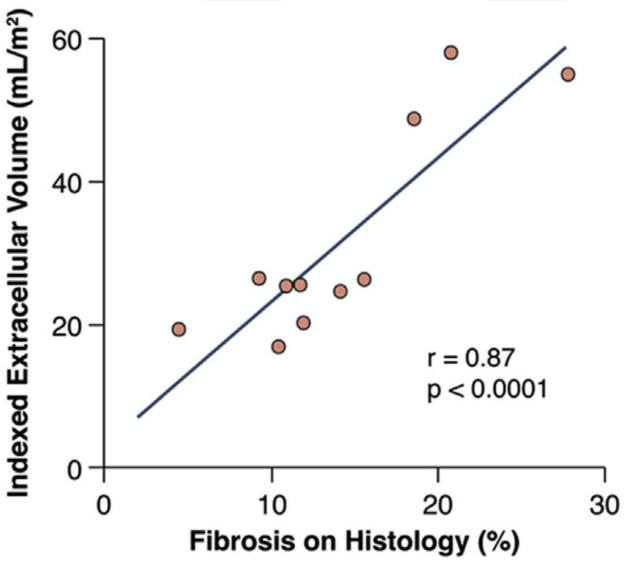


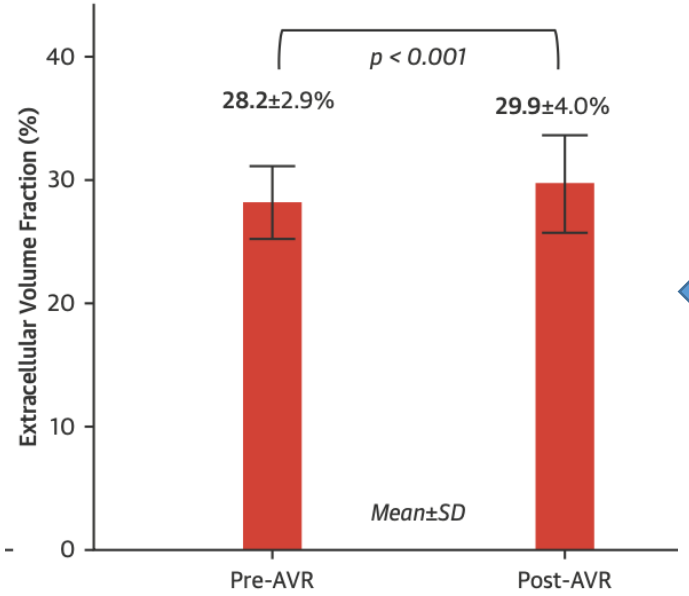


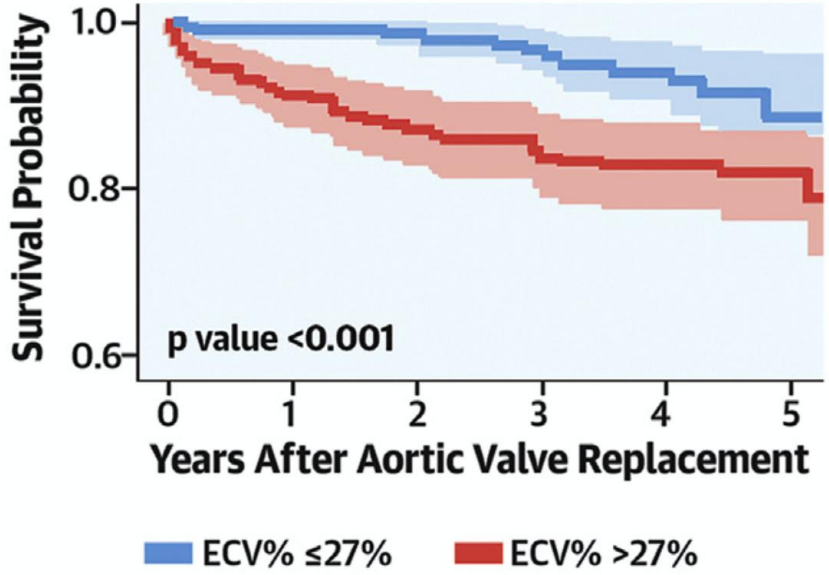
Treibel et al. 2018

Chin et al. *JACC Cardiovasc Imaging* 2017

HYPOTHESIS







Chin et al. *JACC Cardiovasc Imaging* 2017

Treibel et al. *JACC* 2018

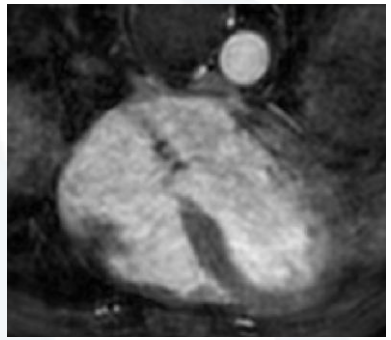
Kwak et al. *JACC* 2021

↑ ECV after AVR suggests that the reversed ventricular remodeling is associated with an ↑ in diffuse fibrosis and possibly ↑ risk of mortality.

If ECV ≈ diffuse fibrosis, there should be a noticeable decrease in conduction velocity in ventricles after AVR.

VIRTUAL HEART MODELS

Patient data

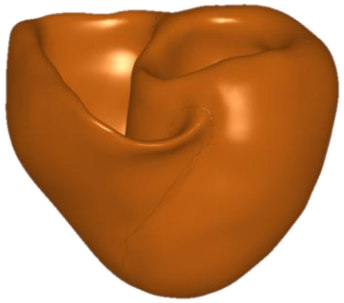


MRI

Extracellular volume

ECG

Personalized heart model

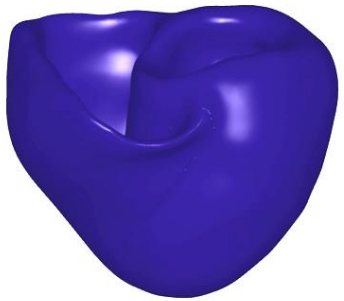


3D geometry

Fibrosis

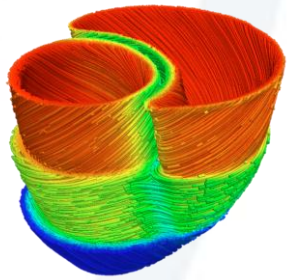
Electrophysiology

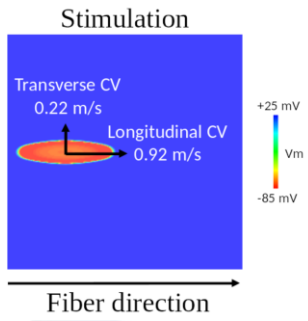
Simulation of electrical activity

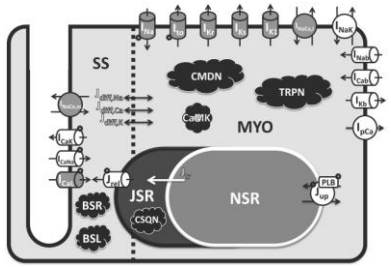


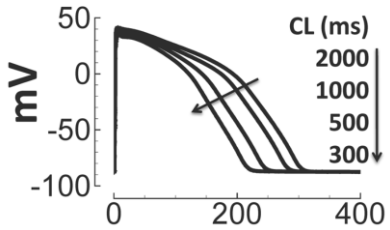
Conduction velocity

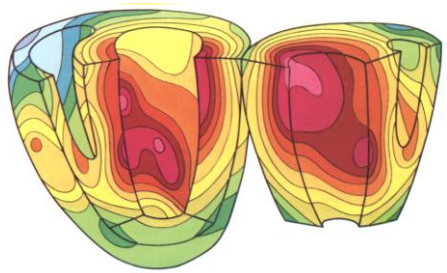
QRS

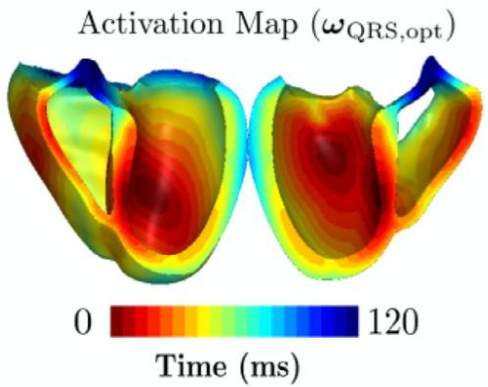












O'Hara et al. *PLoS Comp Biol* 2011

Bayer et al. *Ann Biomed Eng* 2012

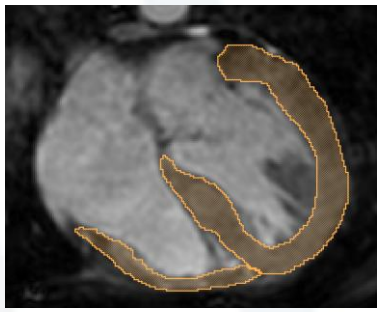
Durrer et al. *Circulation* 1970

Gillette et al. *Med. Image Analysis* 2021

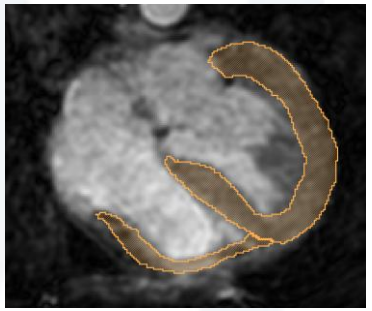
METHODS – GENERAL IDEA

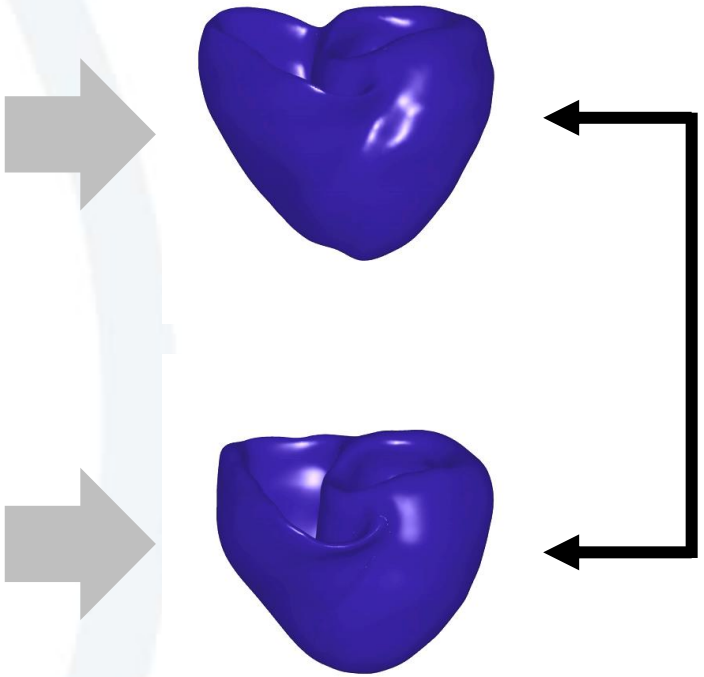
Use virtual heart models to estimate tissue parameters and conduction velocity in ventricles before and after AVR

Before AVR



After AVR





Conduction velocity difference → **Correlation with ECV**

Patients with:
- QRS ≤ 110 ms
- no scar on LGE MRI

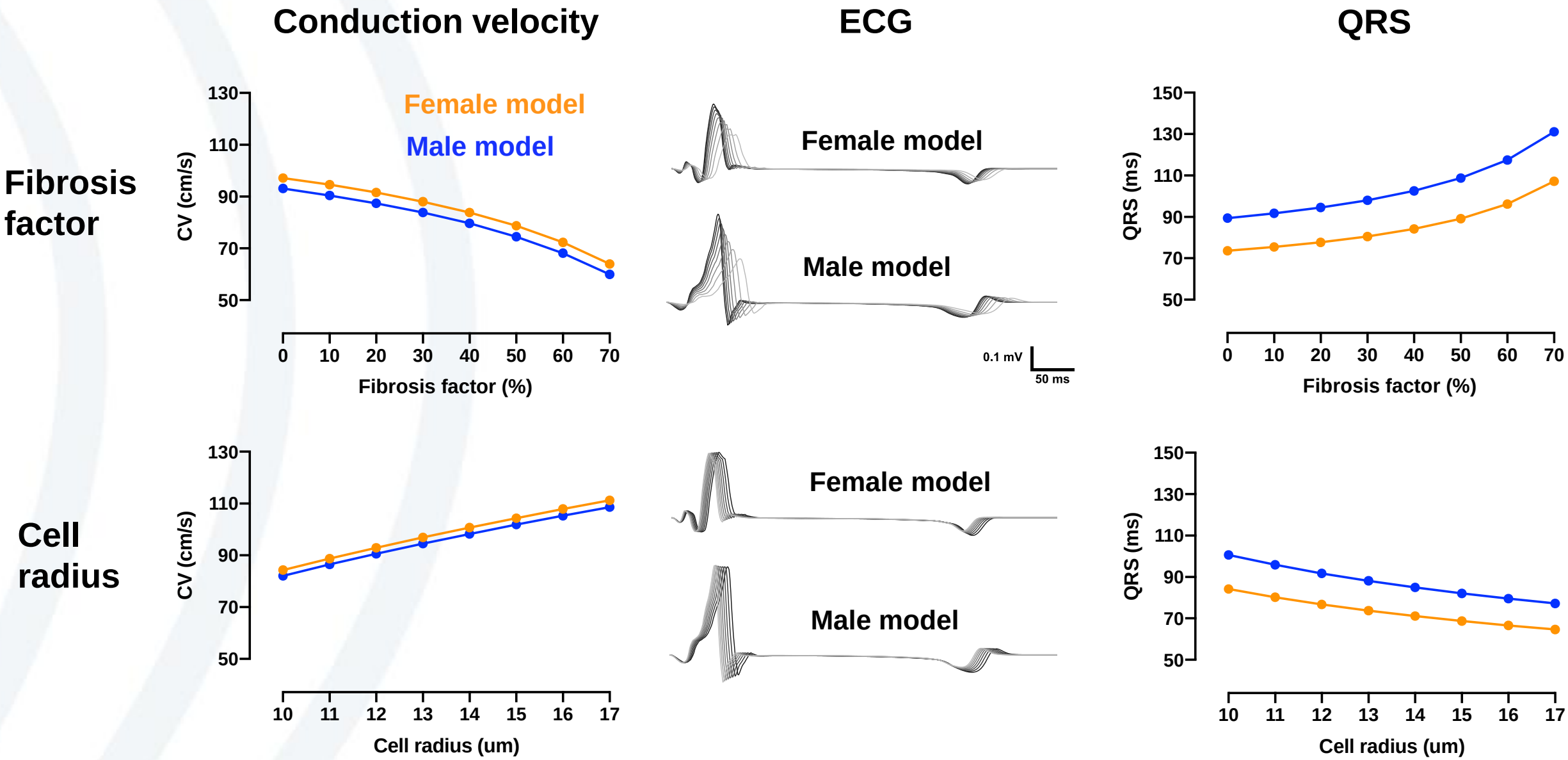
MRI quantification of **hypertrophy**

ECV quantification of **fibrosis**

ECG QRS duration to be fitted

Cell radius (R)
+
Fibrosis factor (F)
↓
Conduction velocity (CV)

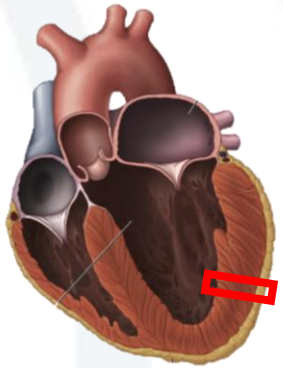
THE EFFECT OF R AND F ON QRS AND CV

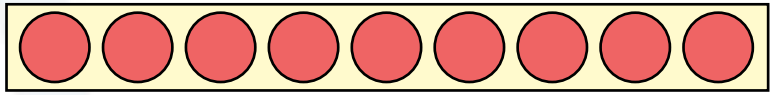


PERSONALIZATION OF TISSUE PARAMETERS

Step #1: Cell radius (R)

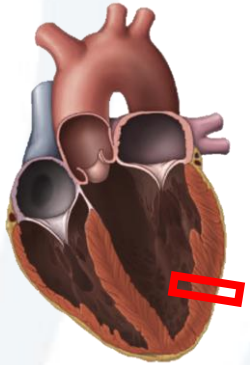
Before AVR

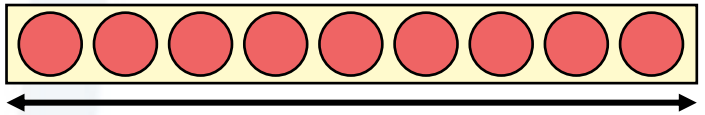




$W_{before} \approx N_{cell} * 2R_{before}$

After AVR



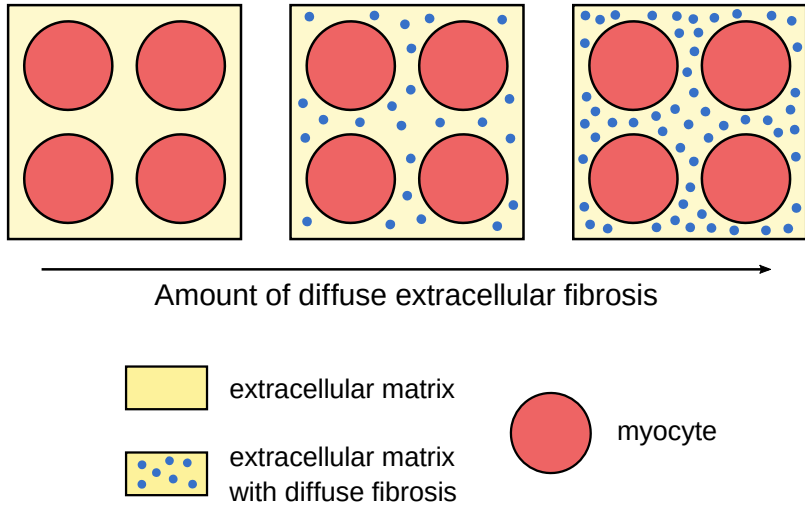


$W_{after} \approx N_{cell} * 2R_{after}$

$$k = \frac{R_{before}}{R_{after}} \approx \frac{W_{before}}{W_{after}}$$

For each model, find R ∈ [9.6,17.8] μm such that $QRS_{model} \leq QRS_{patient}$

Step #2: Fibrosis factor (F)

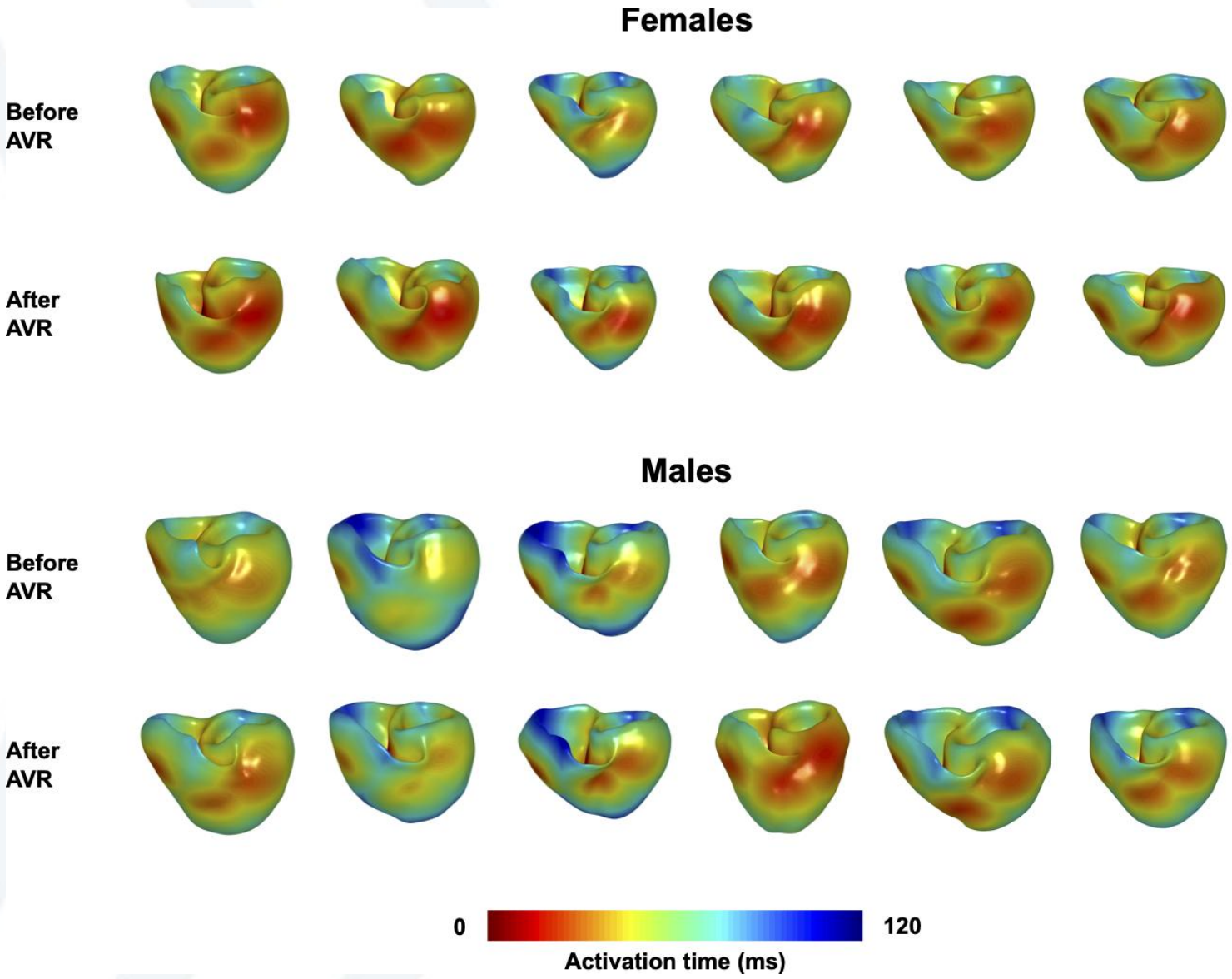


For each model, find F ∈ [0,1] that minimizes the error between QRS_{model} and $QRS_{patient}$

S1 = 600 ms
pacing until stable QRS duration

Aurigemma et al. *Circ Cardiovasc Imag* 2013

BI-VENTRICULAR MODELS



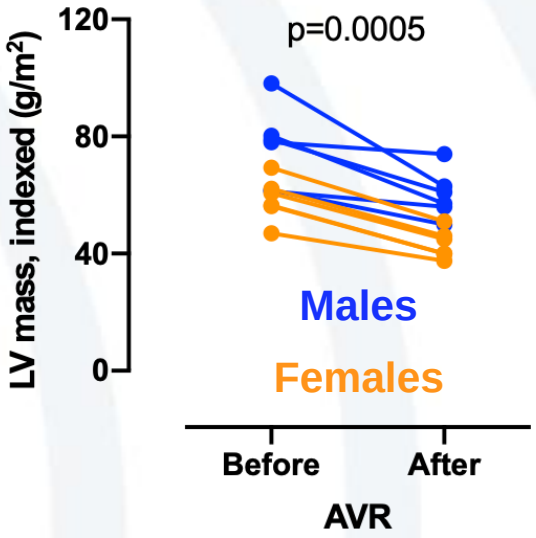
CHARITÉ
UNIVERSITÄTSMEDIZIN BERLIN

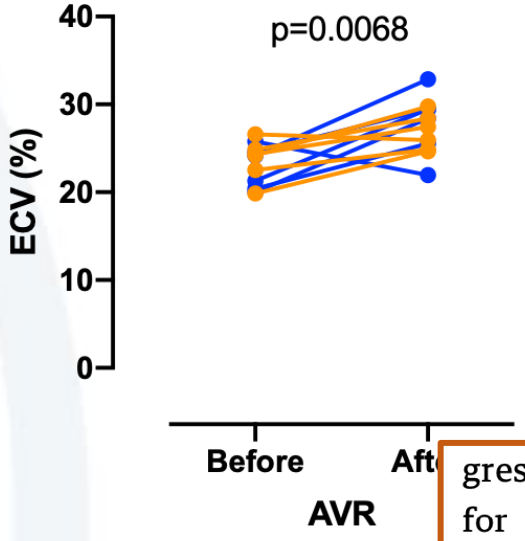
Supercomputer Joliot-Curie

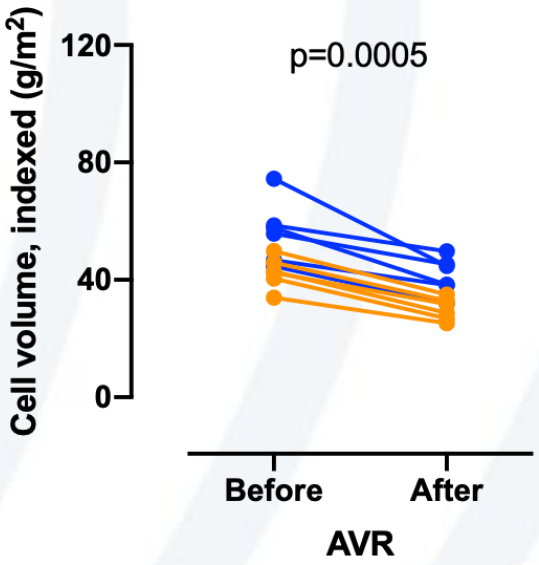
≈ 300 000 core-hours

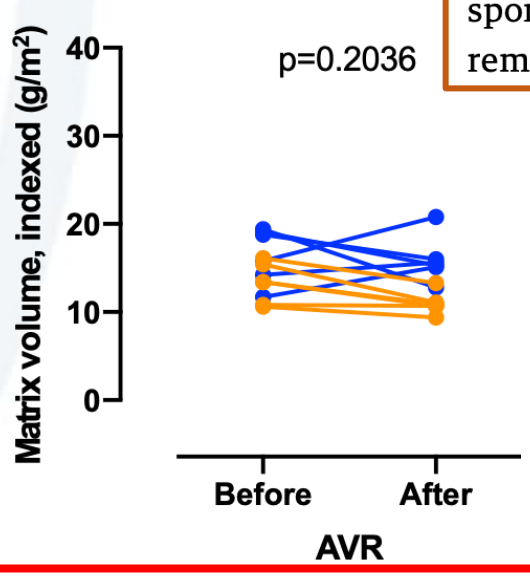
≈ 4.3 years of computing
using an equivalent
8-core computer

RESULTS - VENTRICULAR REMODELING





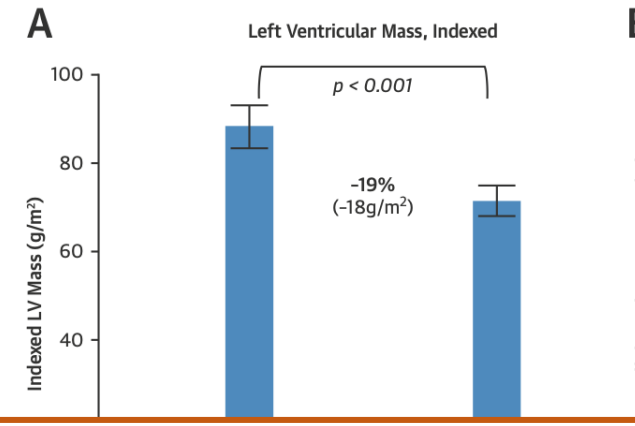


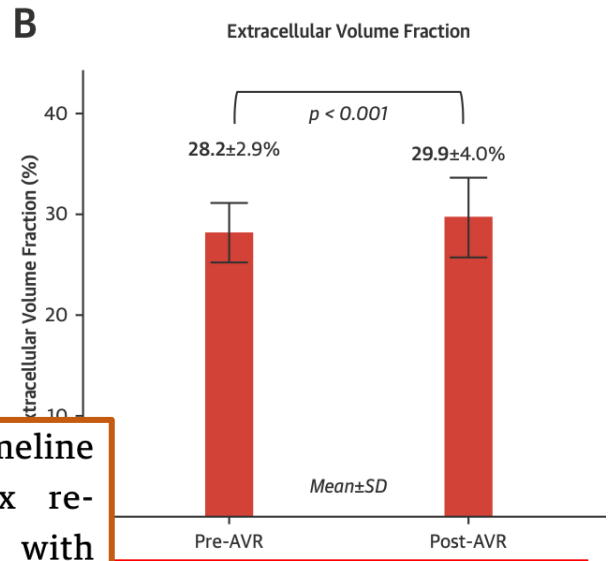


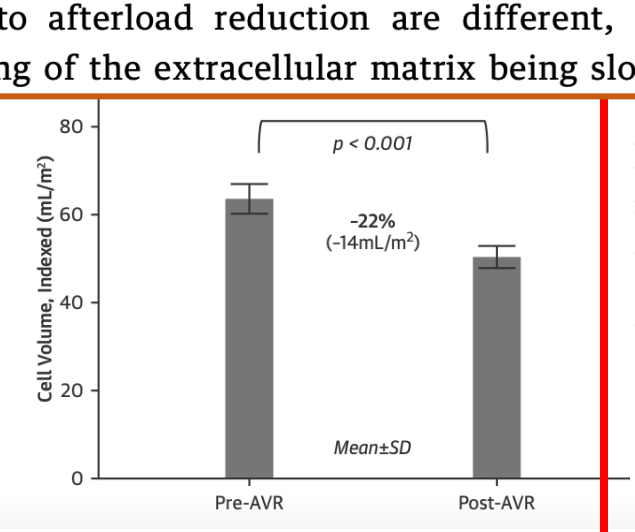
LV mass * (1-ECV)

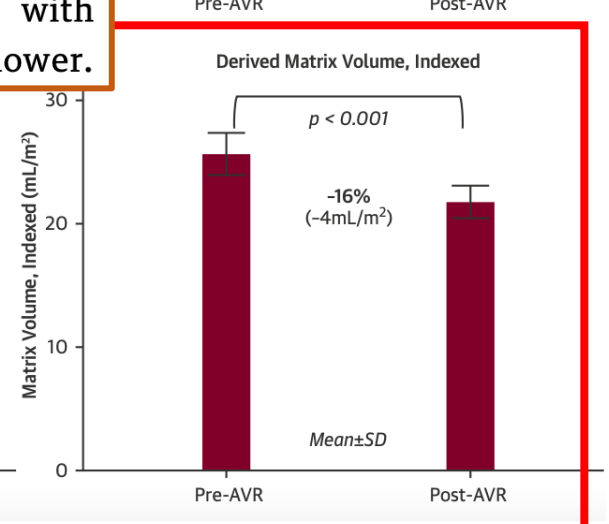
LV mass * ECV

gresses (30), this study suggests that the timeline for cardiomyocyte and extracellular matrix responses to afterload reduction are different, with remodeling of the extracellular matrix being slower.



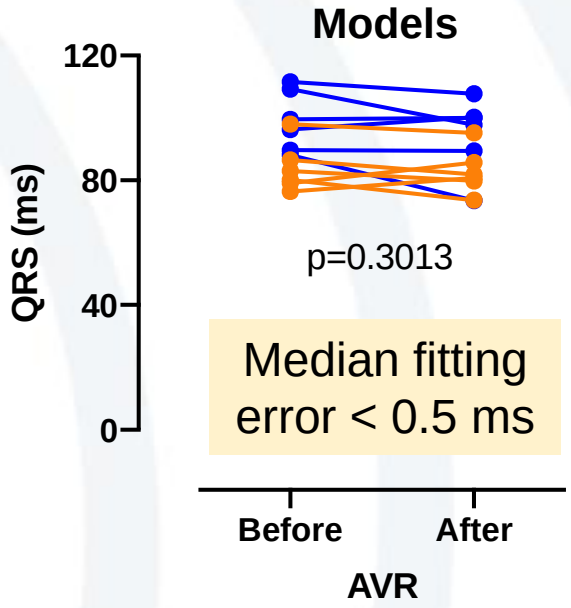




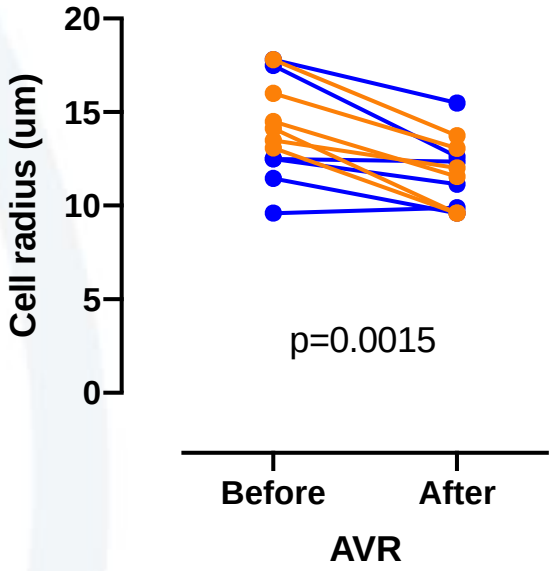


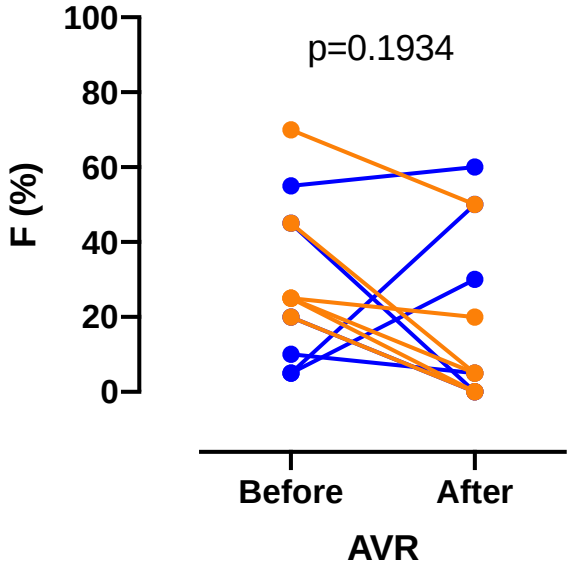
Treibel et al. *JACC* 2018

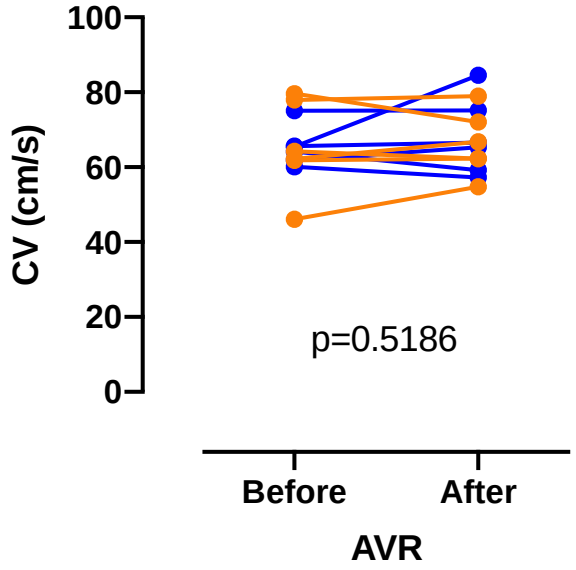
RESULTS - MODEL PARAMETERS

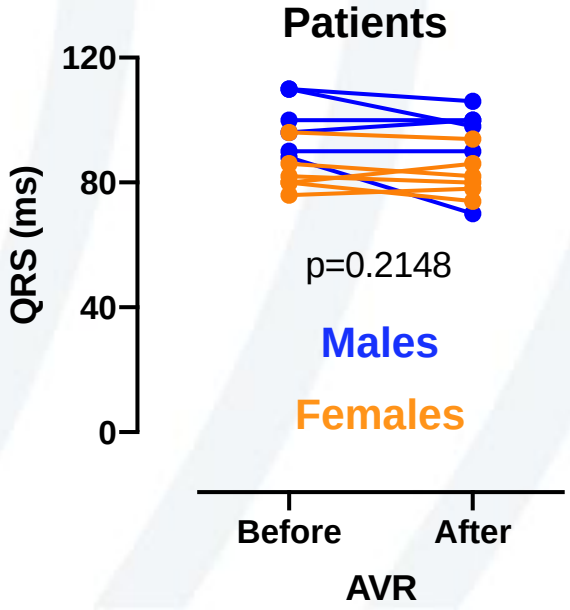


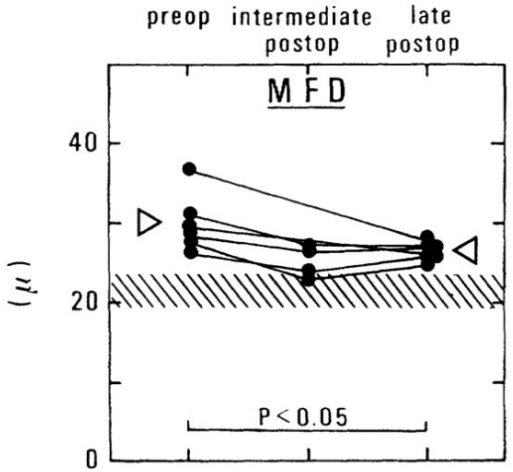
Median fitting error < 0.5 ms



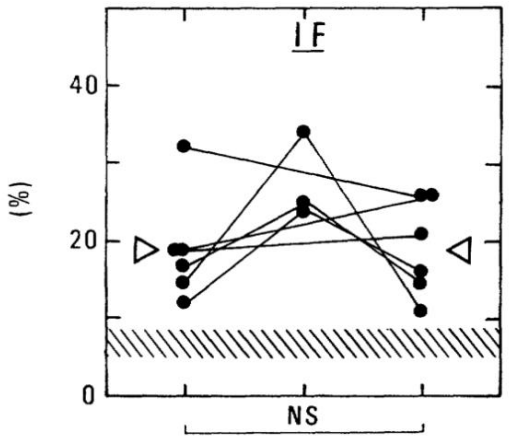








myocyte diameter

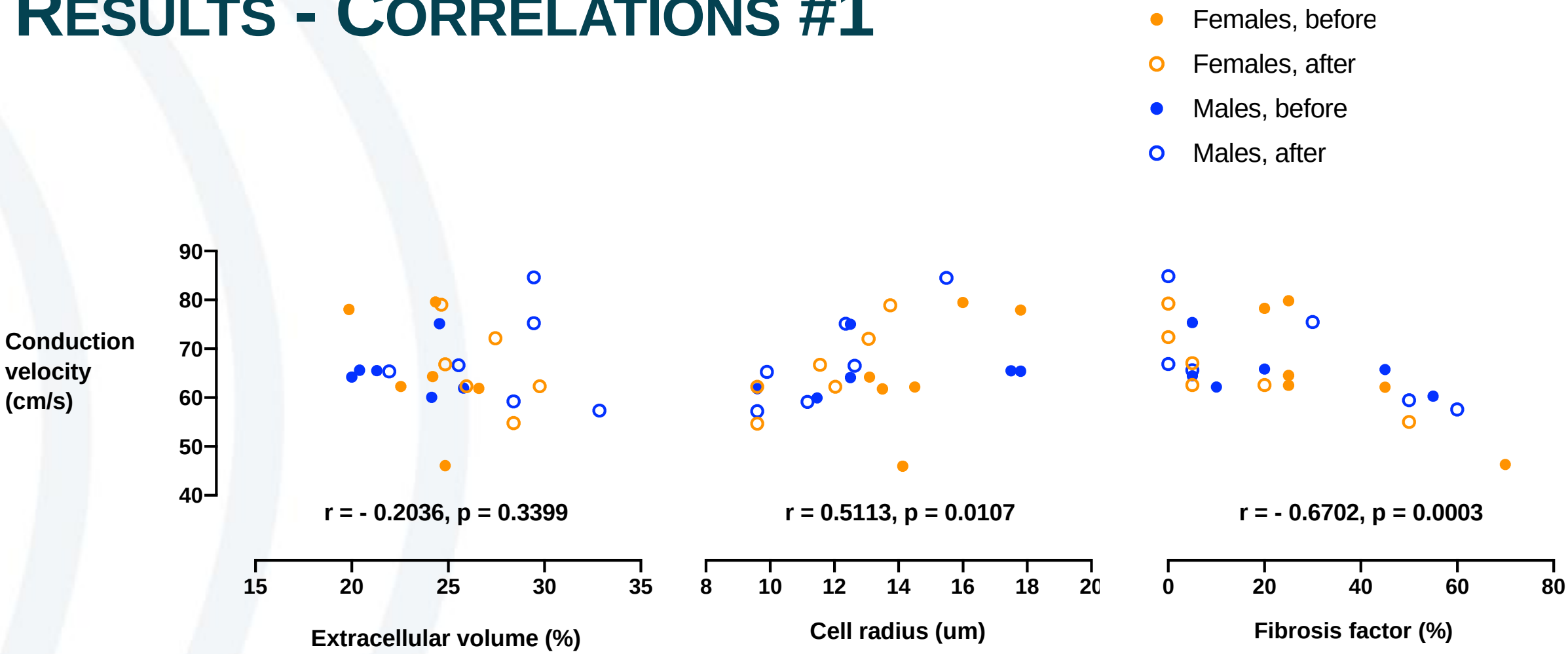


interstitial fibrosis

No change in estimated conduction velocity between the time points!

Krayenbuehl et al. *Circulation* 1989

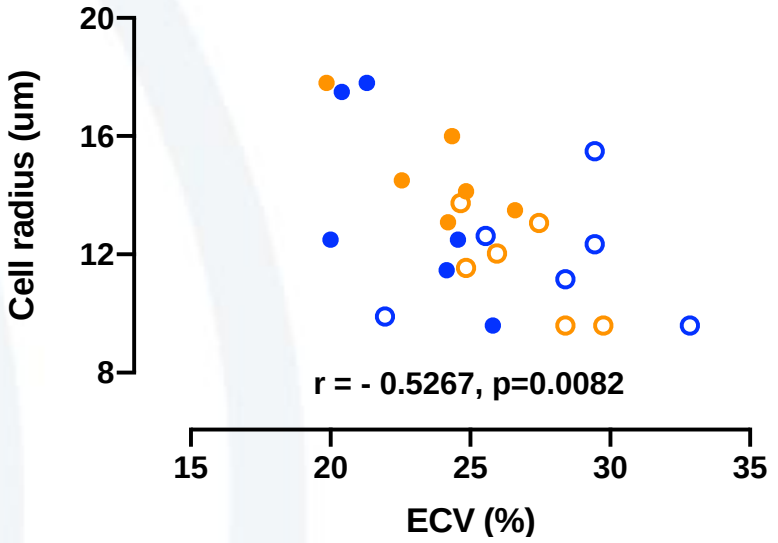
RESULTS - CORRELATIONS #1

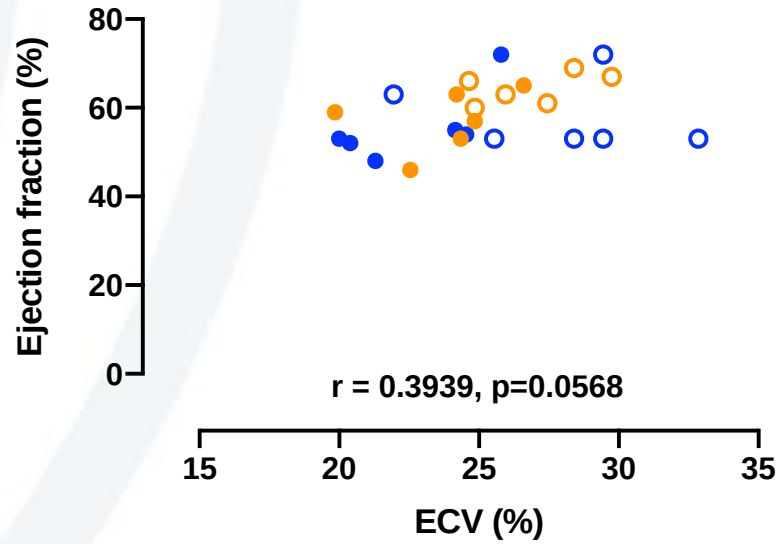


ECV is **not associated** with conduction velocity!

RESULTS - CORRELATIONS #2

- Females, before
- Females, after
- Males, before
- Males, after





ECV is **negatively correlated** with cell radius

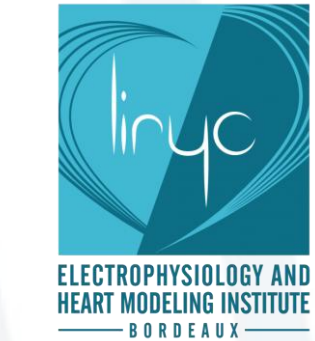
High ECV as a predictor of **positive** outcome?

ECV is **positively correlated** with ejection fraction

CONCLUSIONS

- We developed a new approach for modeling tissue properties in patients with LV hypertrophy
- Reversed ventricular remodeling that follows AVR
  - is associated with an increase in ECV (Treibel et al. 2018)
  - **is not associated with changes in conduction velocity**
- Increased ECV
  - **Before AVR:** is a predictor of mortality (Kwak et al. 2021)
  - **After AVR:** is likely a **footprint of reversed ventricular remodeling** and **does not have to be a predictor of worse outcome**
- Clinical and/or experimental studies should challenge these findings

ACKNOWLEDGEMENTS



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Thank you for your attention!

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Table 1 Patient characteristics

	All patients (n=12)	Before AVR	After AVR	p-value
Age, years	64 [53-74]			
Male sex, n (%)	6 (50)			
Body surface area, m^2	1.9 [1.6-2.0]			
EDV, ml		137 [113-154]	116 [104-124]	0.0171
EDV, indexed, ml/m^2		69 [64-86]	63 [58-70]	0.0425
ESV, ml		61 [43-76]	43 [35-56]	0.0015
ESV, indexed, ml/m^2		31 [25-45]	26 [18-29]	0.0024
Ejection fraction, %		55 [52-62]	62 [53-67]	0.1553
Myocardial mass, g		116 [96-157]	90 [69-127]	0.0005
Myocardial mass, indexed, g/m^2		62 [58-79]	51 [41-60]	0.0005
Extracellular volume (%)		24.2 [20.6-24.8]	28.0 [25.1-29.5]	0.0008
QRS, ms		89 [81-99]	88 [79-100]	0.2148
QTc, ms		421 [404-430]	450 [428-459]	0.0103

Values are presented as median and interquartile range.