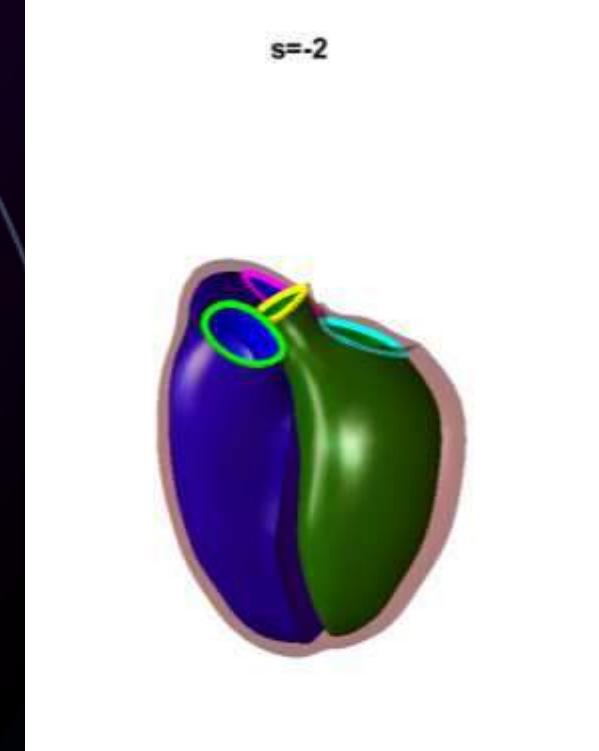
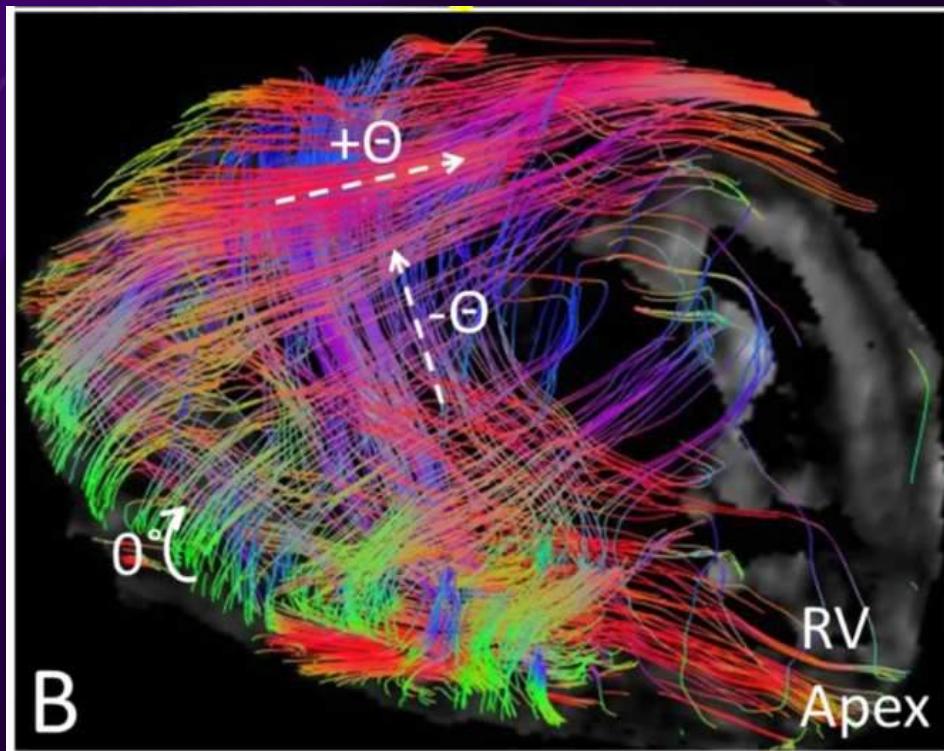
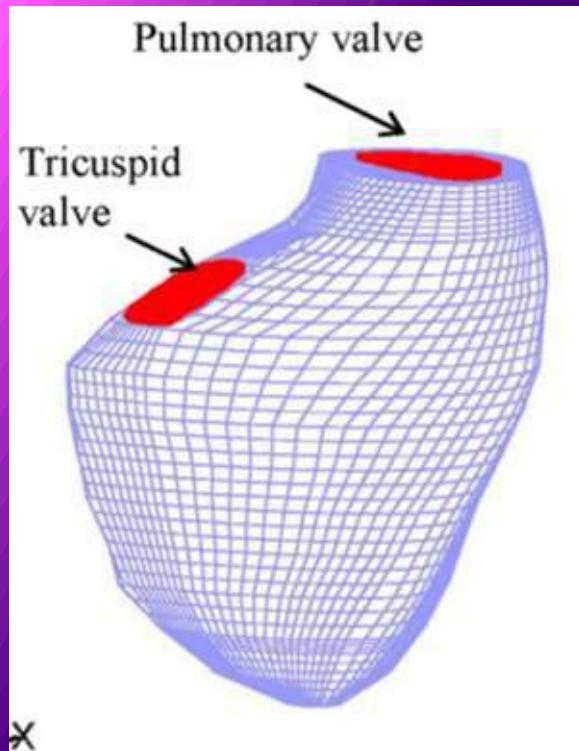


# MODELING THE RV



**Mark A Fogel, MD FACC, FAHA, MSCMR, FNASCI, FAAP**

Professor of Pediatrics (Cardiology) and Radiology

Director of Cardiac MR

# DISCLOSURES

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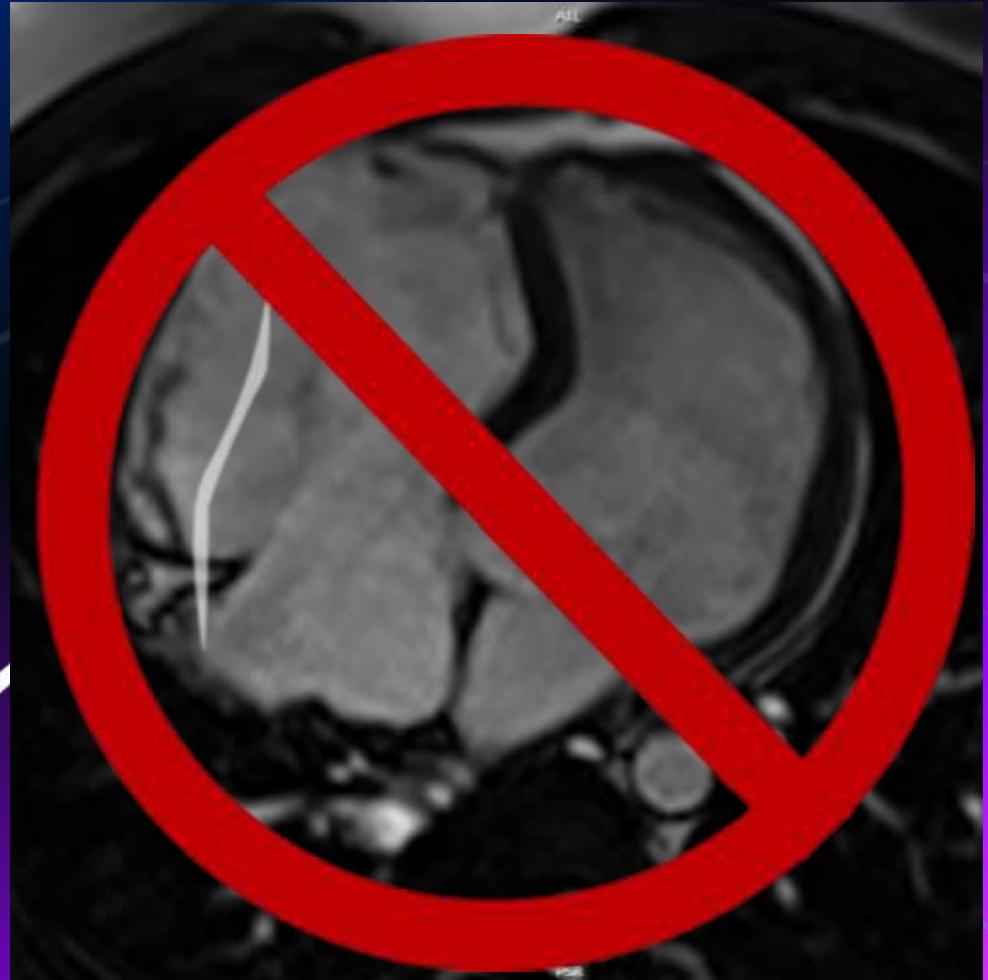
- NIH RO1
- Additional Ventures Grant
- CMP Pharma – grant of drug
- Rocket Pharma – Core Lab



# AGENDA

---

- What is modeling?
- Why bother modeling?
- What is modeling dependent on?
- Types of modeling with examples
- In depth and understand SSM



# DEFINING MODELING

The use of computational or mathematical techniques to simulate and analyze the heart and cardiovascular system

Structure



Function



Behavior

Respond to  
changing  
environment

# WHY BOTHER WITH MODELING?

Study complex processes in a controlled environment

Understand how changes (eg HR or BP) affect the various components of the system

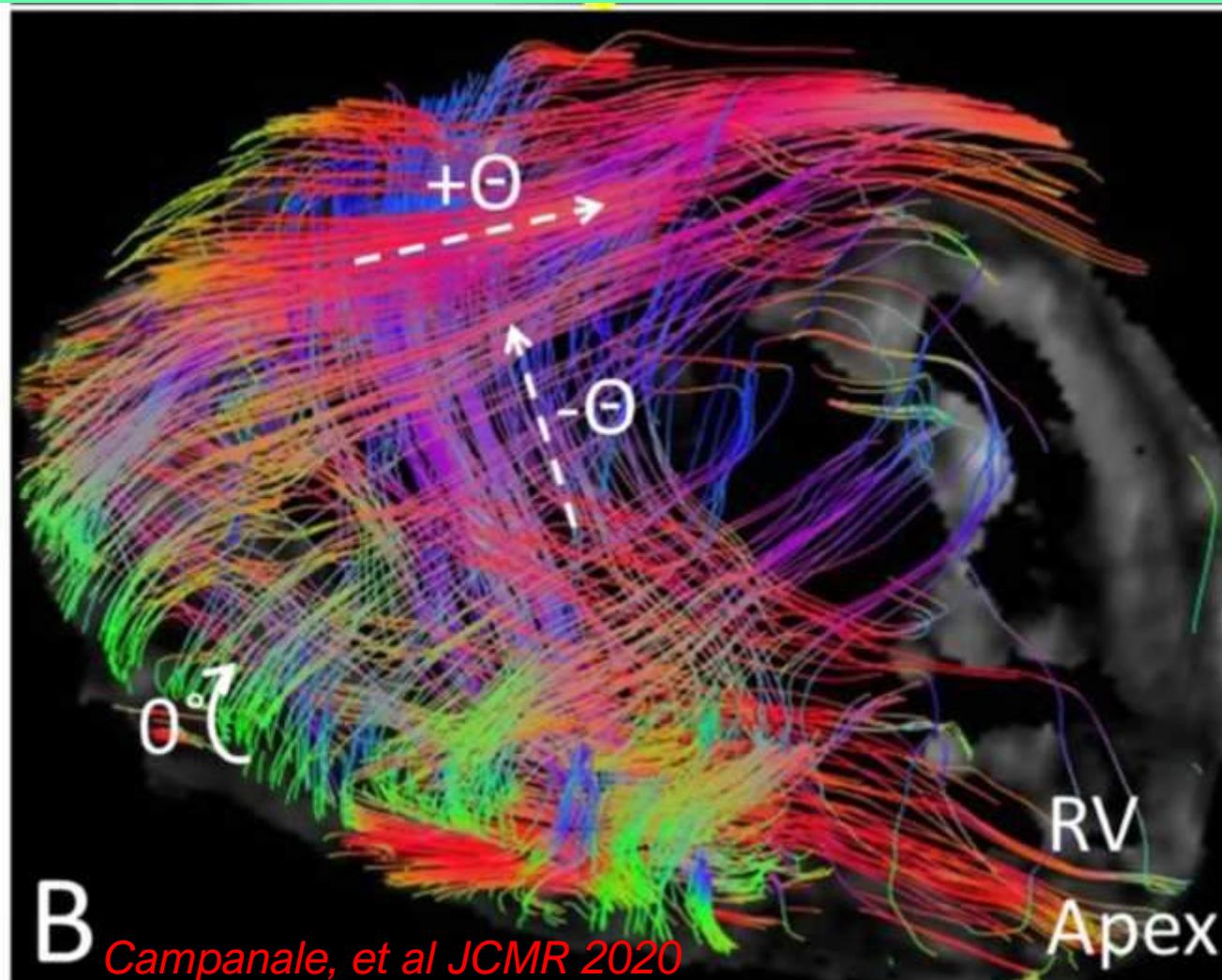
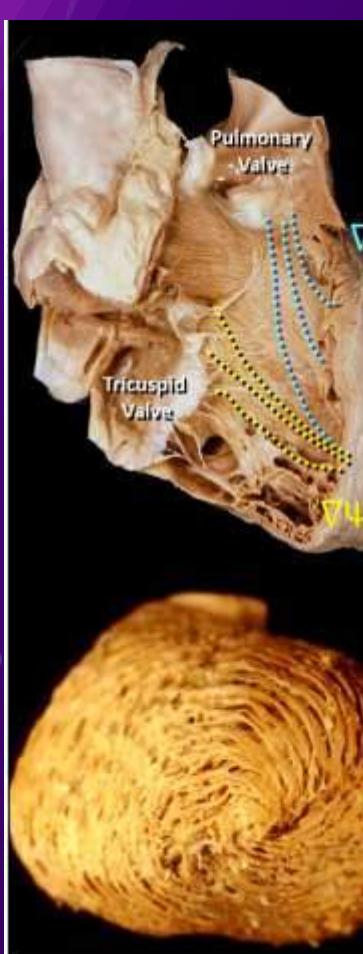
Gain insights into underlying mechanisms of the healthy and diseased heart

Test different treatment strategies without patient risk

Device design

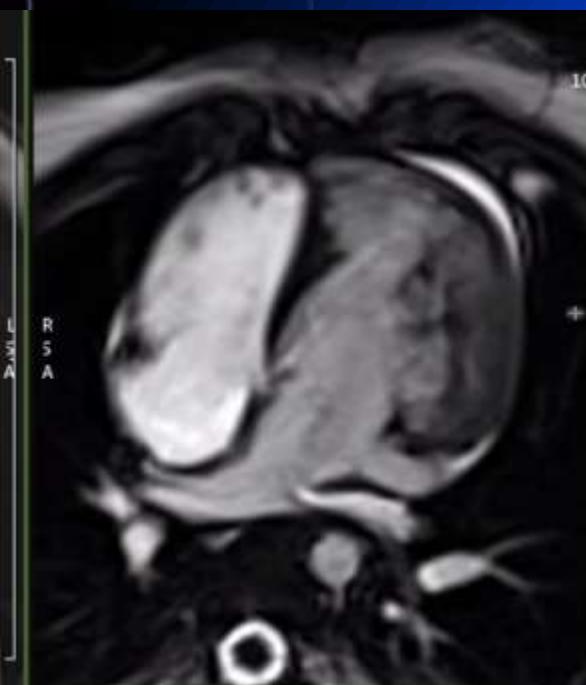
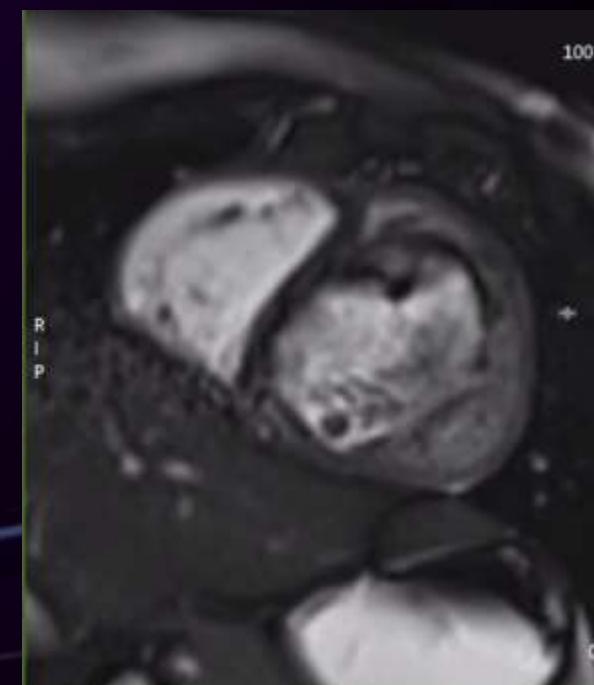
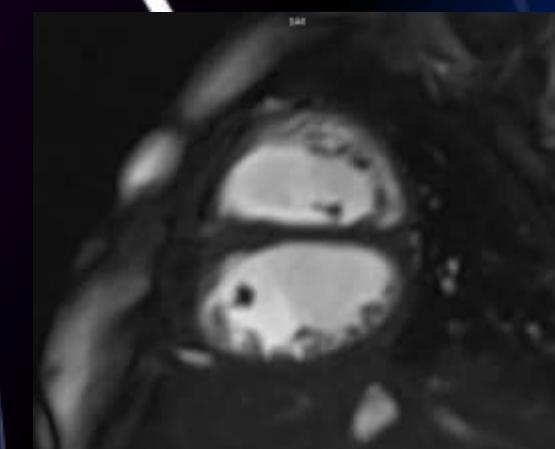
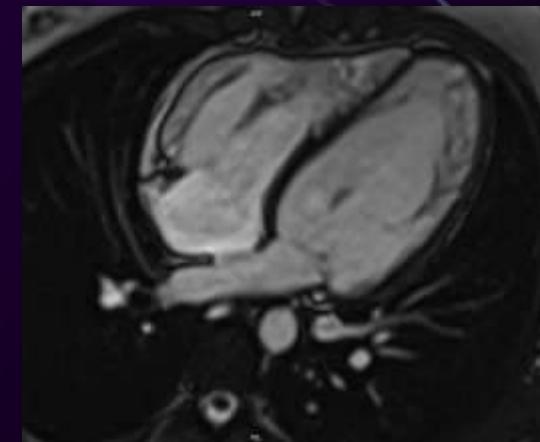
# MODELING DEPENDENT UPON

RV and LV fiber orientation



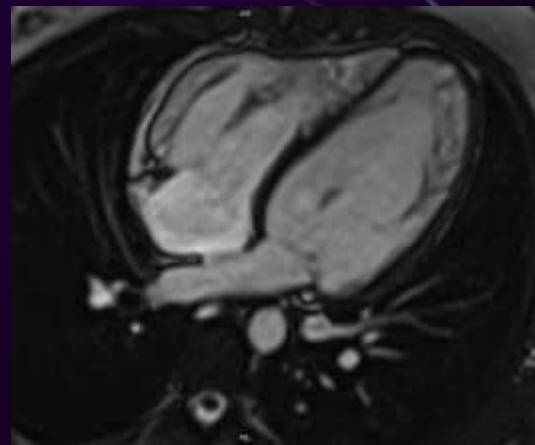
# MODELING DEPENDENT UPON

Shape

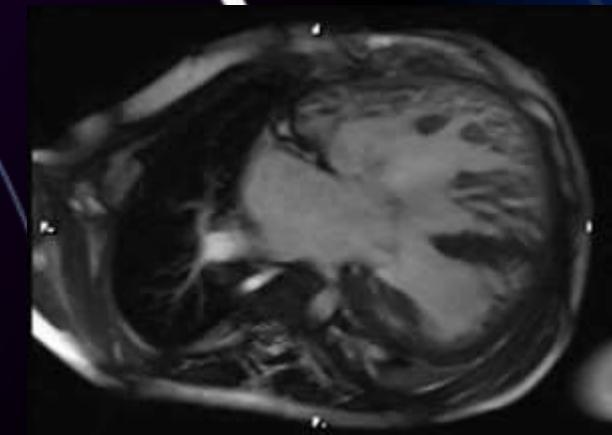


# MODELING DEPENDENT UPON

Shape

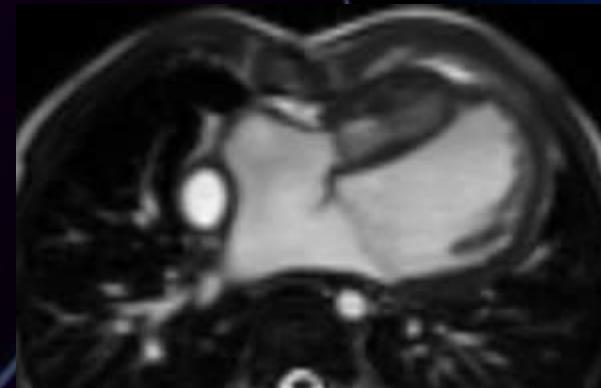


Size



Mechanical properties

Compliance



V-V interaction

Wall motion

Boundary Conditions

RV inflow

RV outflow

Extrinsic

# MODELING DEPENDENT UPON

Shape

Size

Mechanical properties

Boundary Conditions

Compliance

V-V interaction

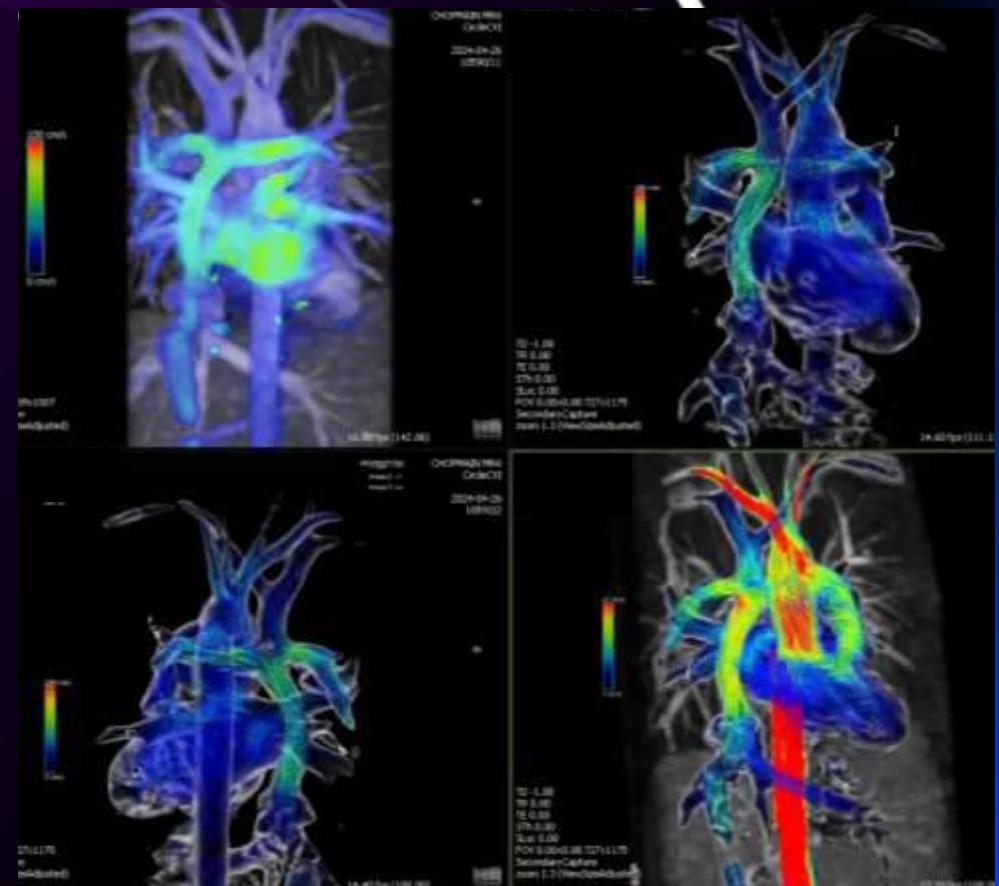
Wall motion

RV inflow

RV outflow

Extrinsic

Intraventricular Flows



# MODELING DEPENDENT UPON

## Left Ventricular Pressure Effects on Right Ventricular Pressure and Volume Outflow

Catheterization and Cardiovascular Diagnosis 19:269–278 (1990)

Ralph J. Damiano, Jr., MD, James L. Cox, MD, James E. Lowe, MD, and William P. Santamore, PhD

## Contribution of each wall to biventricular function

Cardiovascular Research 1993;27:792-800

Kun S Li and William P Santamore

V-V interaction

## Significant left ventricular contribution to right ventricular systolic function

Am. J. Physiol. 261 (Heart Circ. Physiol. 30): H1514– H1524, 1991

RALPH J. DAMIANO, JR., PAUL LA FOLLETTE, JR., JAMES L. COX, JAMES E. LOWE, AND WILLIAM P. SANTAMORE

- Targeted ischemia of each wall of each ventricle
- Electrically isolating each wall
- Gluteraldehyde of walls
- Ripping the RV free wall off (and it still generated pressure)

Up to 63% of RV ejection, depending on how you measure, is due to the LV!

## A Study in Ventricular–Ventricular Interaction

Single Right Ventricles Compared With Systemic Right Ventricles in a Dual-Chamber Circulation

Mark A. Fogel, Paul M. Weinberg, Kenneth E. Fellows, and Eric A. Hoffman

Circulation

Volume 92, Issue 2, 15 July 1995; Pages 219-230

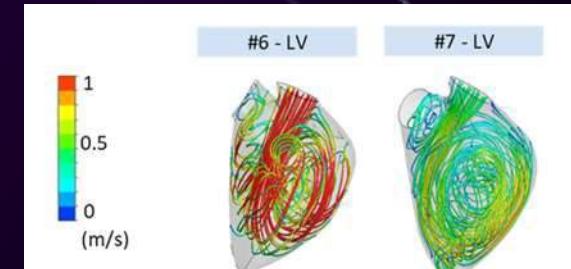
## Imaging Right-Left Ventricular Interactions

Mark K. Friedberg, MD

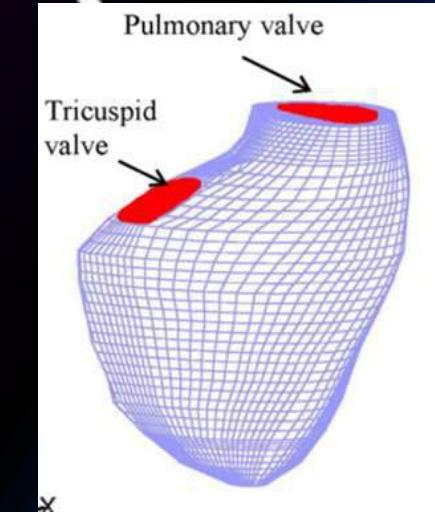
(J Am Coll Cardiol Img 2018;11:755-71)

# TYPES OF RV MODELING

Intraventricular flow with CFD

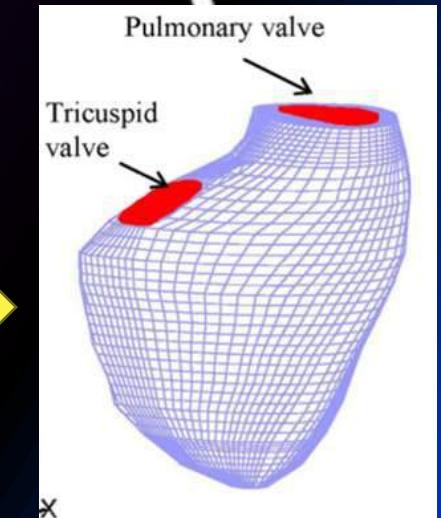
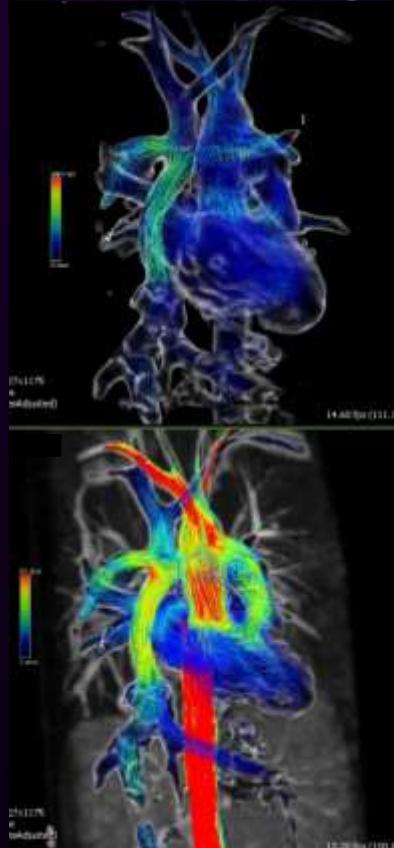


Finite Element Analysis (FE)



# TYPES OF RV MODELING

Intraventricular flow with CFD



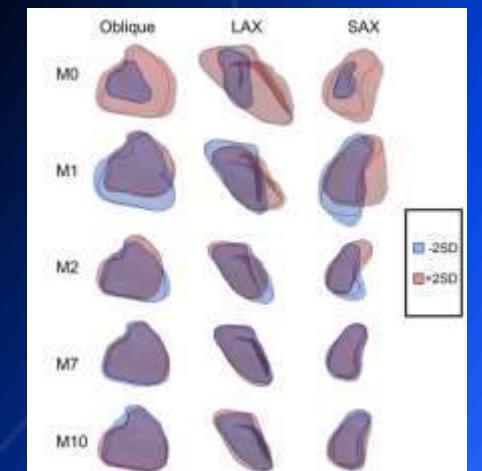
Finite Element Analysis (FE)



Fluid Structure Interaction (FSI)

Statistical Shape Modeling (SSM)

Electrophysiological and electro-mechanical modeling



# RV INTRAVENTRICULAR FLOW

## Intraventricular Flow Simulations in Singular Right Ventricles Reveal Deteriorated Washout and Low Vortex Formation

*Cardiovascular Engineering and Technology*, Vol. 13, No. 3, June 2022 (© 2021) pp. 495–503

ANNA GRÜNWALD,<sup>1</sup> JANA KORTE,<sup>1</sup> NADJA WILMANNS,<sup>3</sup> CHRISTIAN WINKLER,<sup>2</sup> KATHARINA LINDEN,<sup>2</sup> ULRIKE HERBERG,<sup>2</sup> SASCHA GROß-HARDT,<sup>1</sup> ULRICH STEINSEIFER,<sup>1</sup> and MICHAEL NEIDLIN <sup>1</sup>

<sup>1</sup>Department of Cardiovascular Engineering, Institute of Applied Medical Engineering, Medical Faculty, RWTH Aachen University, Aachen, Germany; <sup>2</sup>Department of Pediatric Cardiology, University Hospital of Bonn, Bonn, Germany; and

<sup>3</sup>Institute of General Mechanics, RWTH Aachen University, Aachen, Germany

Applied CFD to echocardiographic data to simulate flows in 5 single RV vs 2 normal LVs

# RV INTRAVENTRICULAR FLOW

## Intraventricular Flow Simulations in Singular Right Ventricles Reveal Deteriorated Washout and Low Vortex Formation

*Cardiovascular Engineering and Technology*, Vol. 13, No. 3, June 2022 (© 2021) pp. 495–503

ANNA GRÜNWALD,<sup>1</sup> JANA KORTE,<sup>1</sup> NADJA WILMANNS,<sup>3</sup> CHRISTIAN WINKLER,<sup>2</sup> KATHARINA LINDEN,<sup>2</sup> ULRIKE HERBERG,<sup>2</sup> SASCHA GROß-HARDT,<sup>1</sup> ULRICH STEINSEIFER,<sup>1</sup> and MICHAEL NEIDLIN <sup>1</sup>

<sup>1</sup>Department of Cardiovascular Engineering, Institute of Applied Medical Engineering, Medical Faculty, RWTH Aachen University, Aachen, Germany; <sup>2</sup>Department of Pediatric Cardiology, University Hospital of Bonn, Bonn, Germany; and

<sup>3</sup>Institute of General Mechanics, RWTH Aachen University, Aachen, Germany

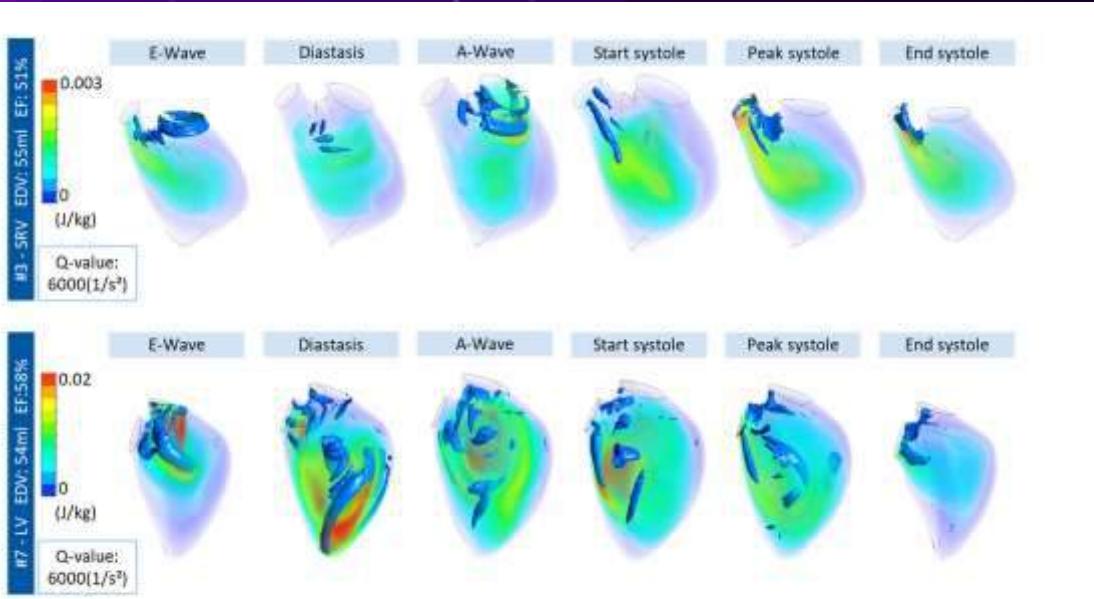


FIGURE 1. Representative turbulent kinetic energy (J/kg) and vortex structure formation with Q-value (1/s) for subject #3 (SRV) and subject #7 (LV). TKE represented by different scales, subject #3 max 0.003 J/kg, subject #8 max 0.02 J/kg.

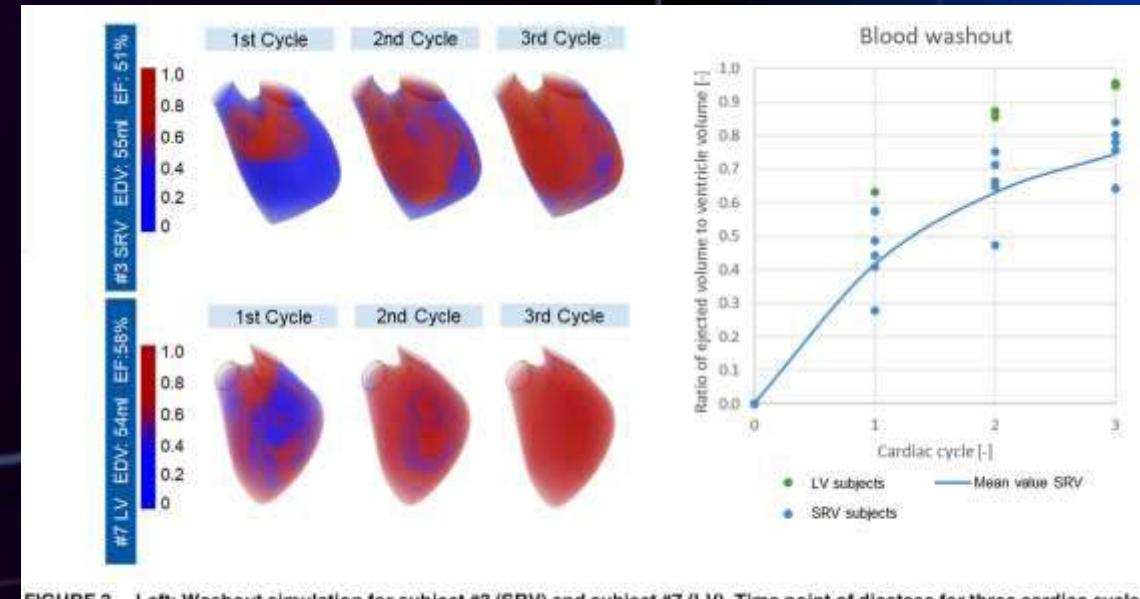
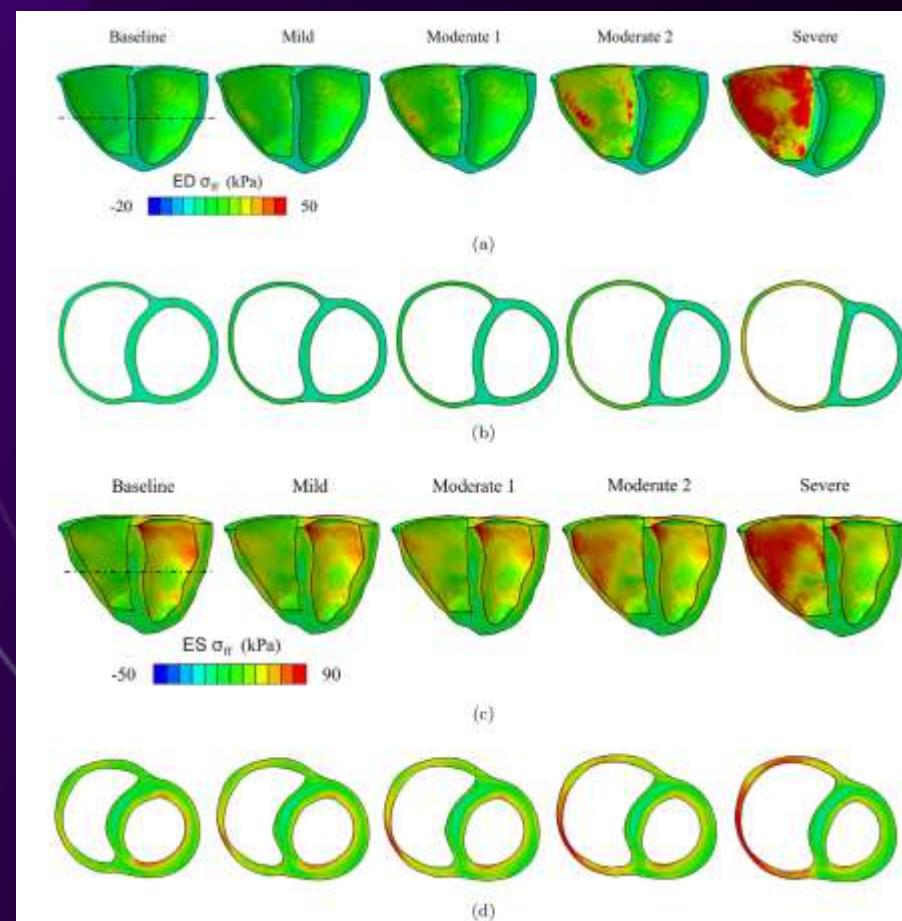


FIGURE 3. Left: Washout simulation for subject #3 (SRV) and subject #7 (LV). Time point of diastase for three cardiac cycles. Blue old blood, red new blood. Right: Volume percentage distribution of ejected volume to the total ventricle volume for SRV subjects and LV subjects (green).

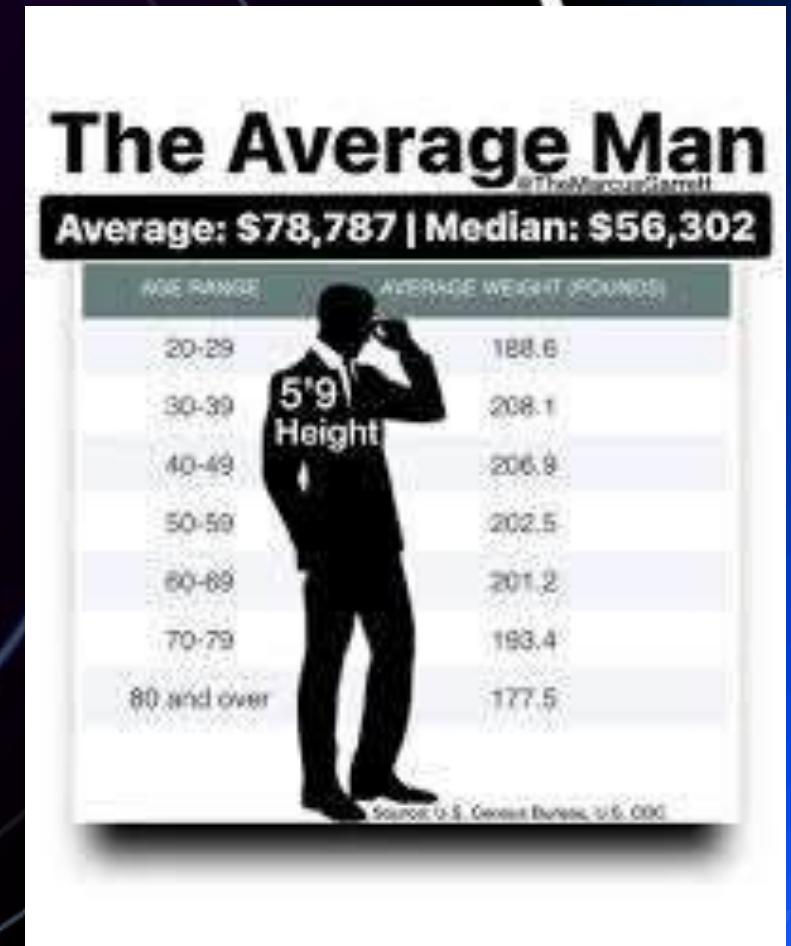
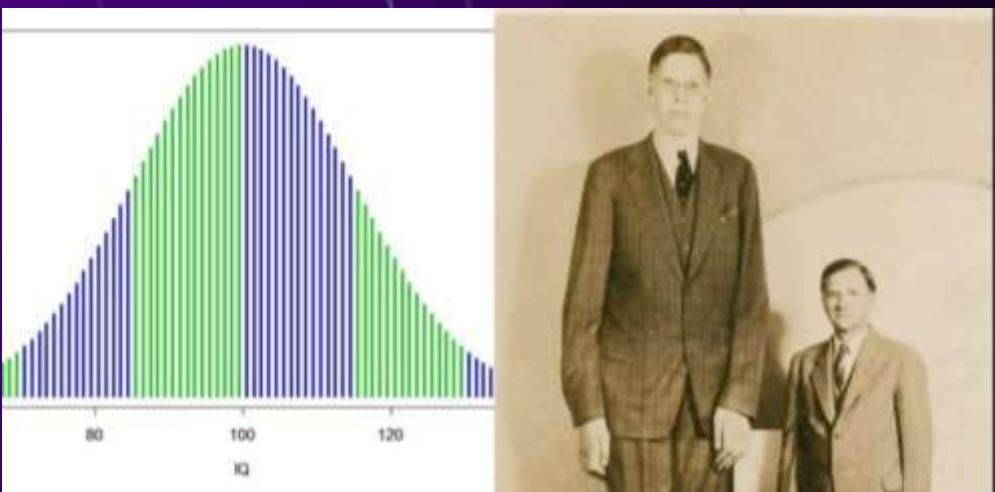
# RV FINITE ELEMENT ANALYSIS (FE)

Effect of pulmonary regurgitation on cardiac functions based on a human bi-ventricle model

Xueqing Yin<sup>a</sup>, Yingjie Wang<sup>a,\*</sup> Computer Methods and Programs in Biomedicine 238 (2023) 107600



# STATISTICAL SHAPE MODELING (SSM)



# STATISTICAL SHAPE MODELING (SSM)

MODE 2

Height

$$40/180=22\%$$

$$\frac{22\%}{22\%+57\%} = 28\%$$

$$\frac{57\%}{22\%+57\%} = 72\%$$

MODE 1

Weight

$$40/70=57\%$$



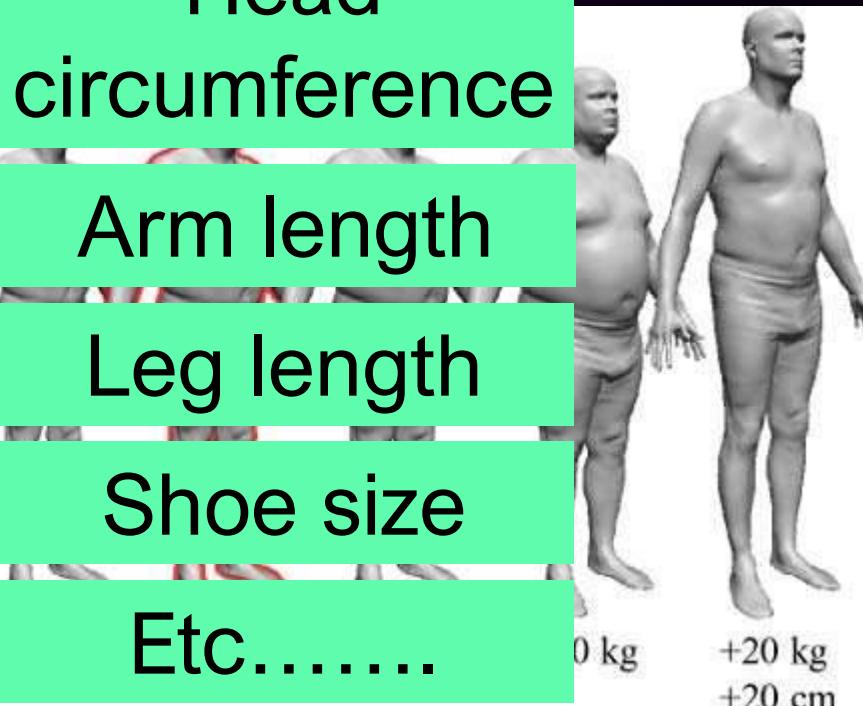
Head circumference

Arm length

Leg length

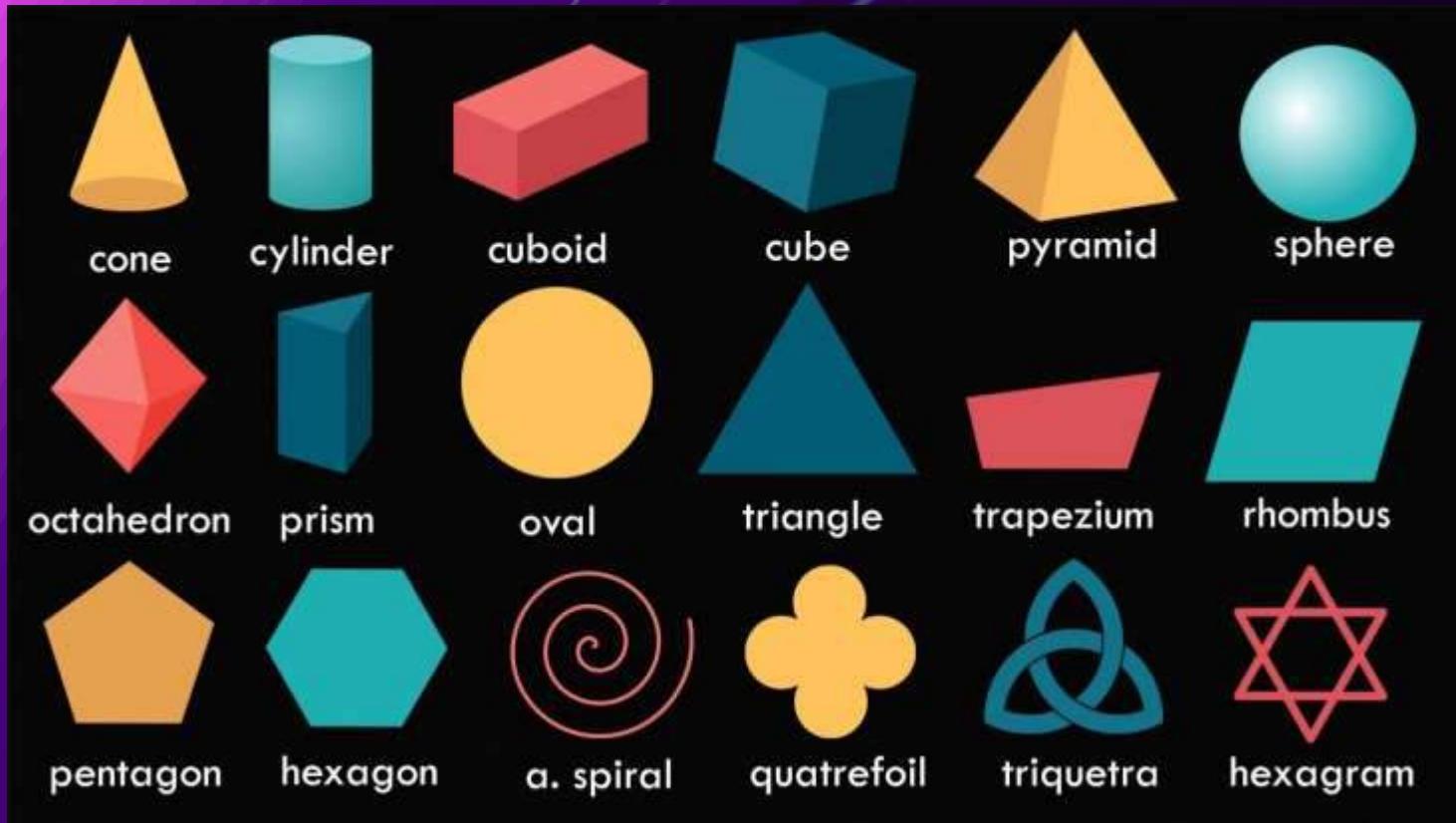
Shoe size

Etc.....



Principle Component Analysis (PCA)

# STATISTICAL SHAPE MODELING (SSM)



Number of sides

Diameter

Color

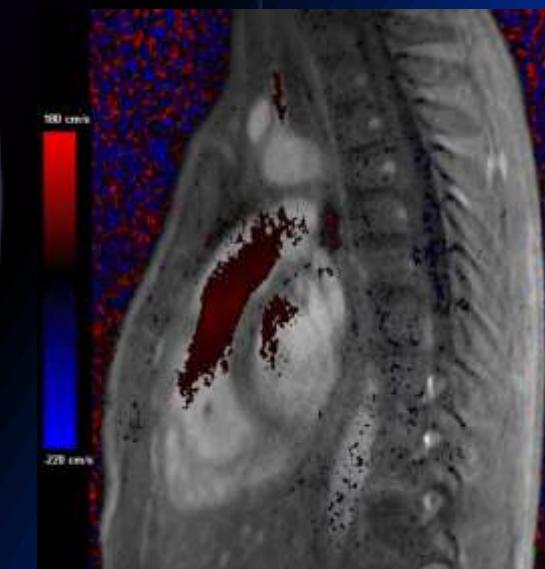
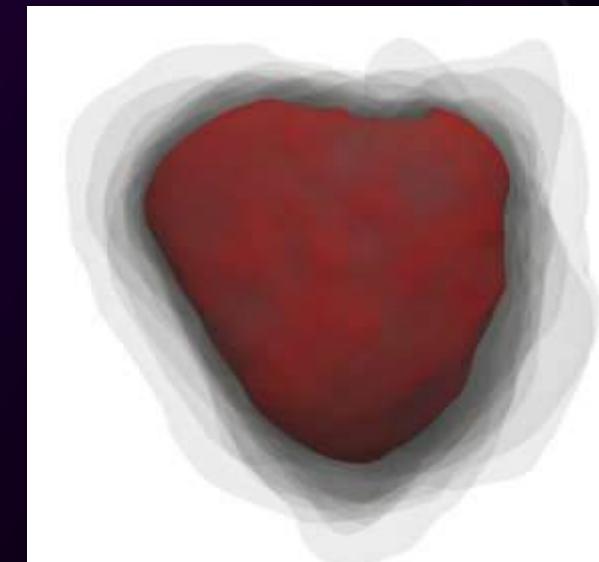
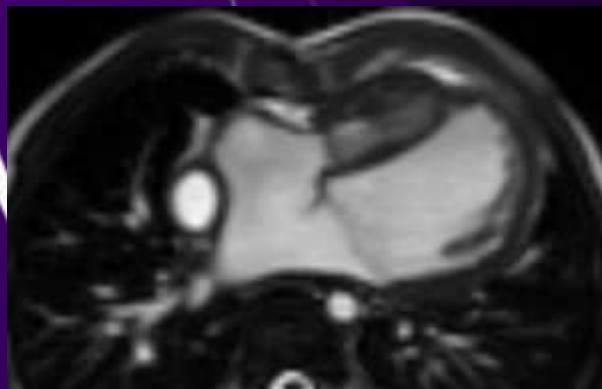
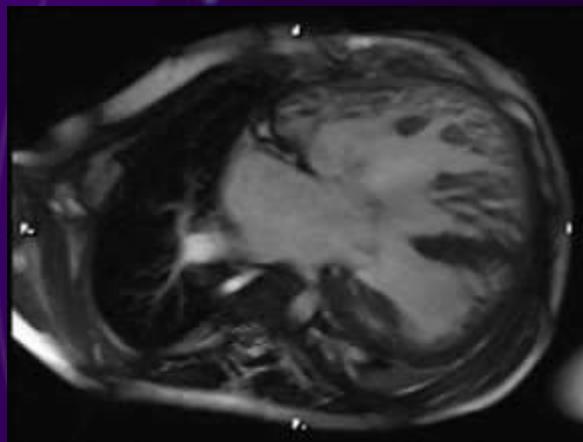
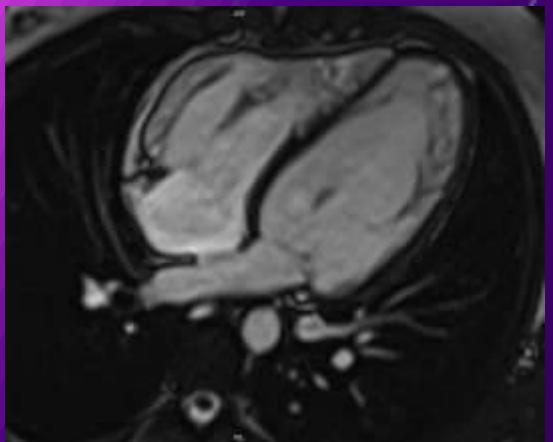
Area

Circumference

Etc.....

# MODELING DEPENDENT UPON

Shape of the RV



# SSM OF THE RV

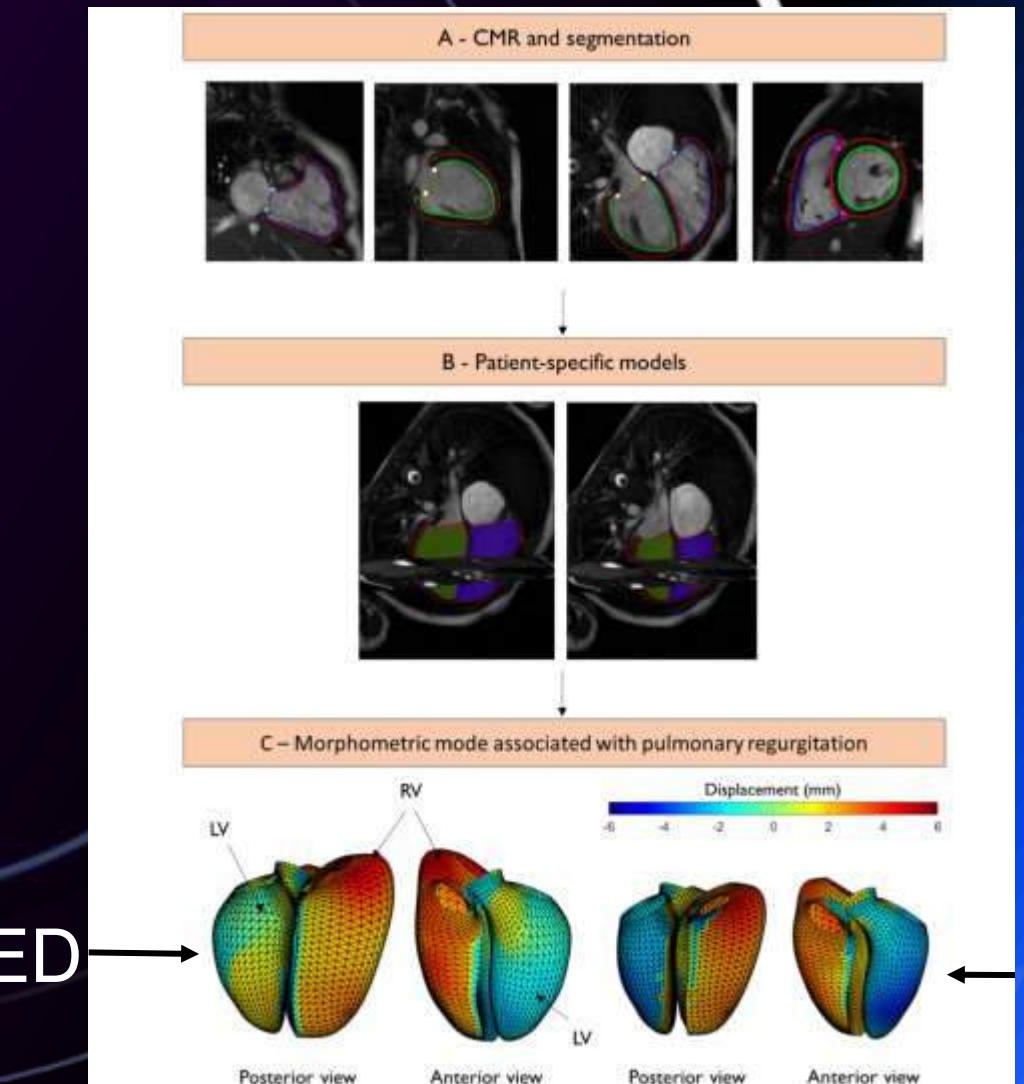
## Right-left ventricular shape variations in tetralogy of Fallot: associations with pulmonary regurgitation

Charlène A. Mauger<sup>1,2†</sup>, Sachin Govil<sup>3†</sup>, Radomir Chabiniok<sup>4,5,6,7</sup>, Kathleen Gilbert<sup>2</sup>, Sanjeet Hegde<sup>3,8</sup>, Tarique Hussain<sup>4</sup>, Andrew D. McCulloch<sup>3</sup>, Christopher J. Occleshaw<sup>9</sup>, Jeffrey Omens<sup>3</sup>, James C. Perry<sup>3,8</sup>, Kuberan Pushparajah<sup>10</sup>, Avan Suinesiaputra<sup>11</sup>, Liang Zhong<sup>12,13</sup> and Alistair A. Young<sup>1,10\*</sup>

*J Cardiovasc Magn Reson*

(2021) 23:105

- N = 88 TOF patients
- Mean age = 16 yrs
- RV and LV volumes
- Pulmonary regurgitation



# SSM OF THE RV

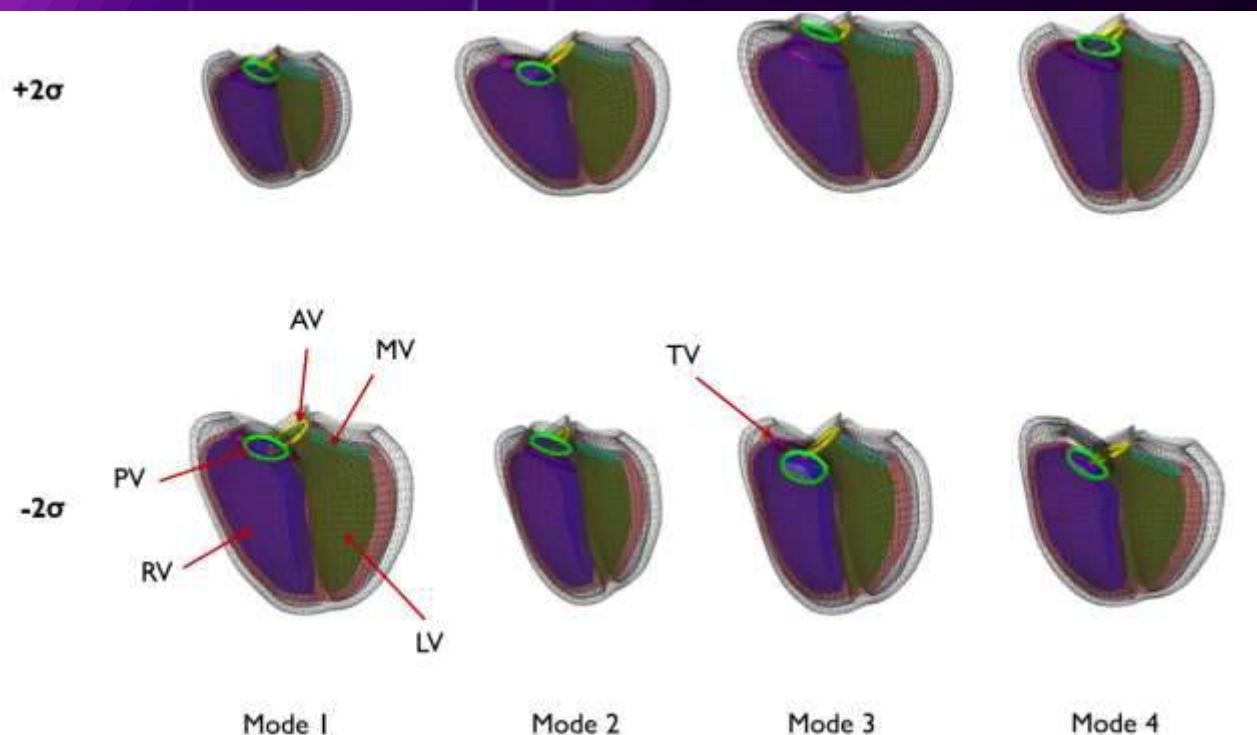
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*J Cardiovasc Magn Reson*

(2021) 23:105

Four PCA modes accounted for 59% of overall variation



### Mode

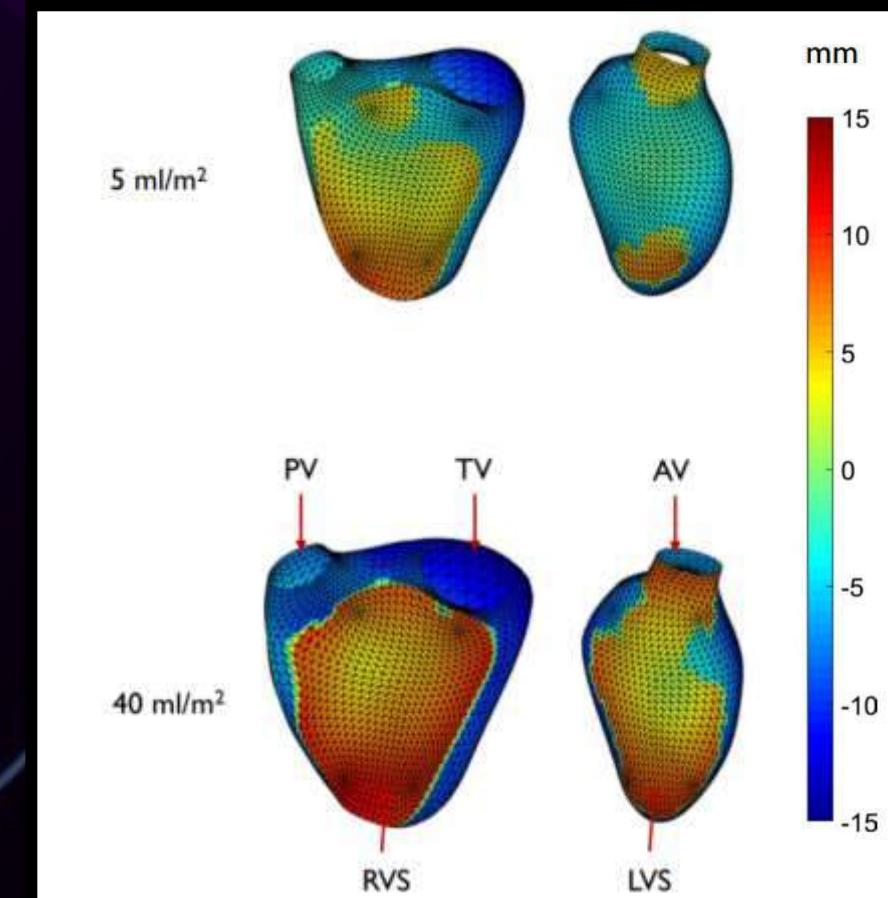
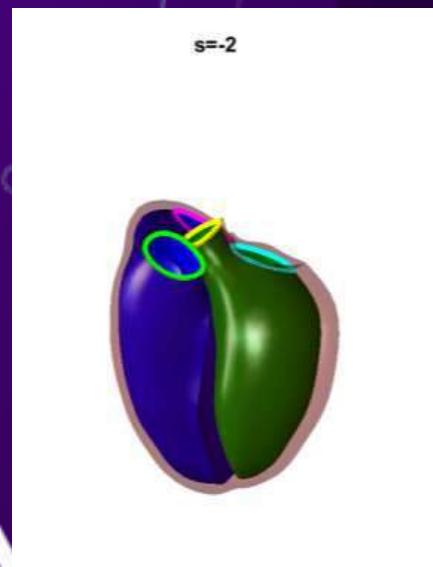
- 1 = overall RV size
- 2 = Septal-free wall dimension
- 3 = basal vs apical bulging (basal away from septum)
- 4 = Systolic septal bulging towards LV

# SSM OF THE RV

## Right-left ventricular shape variations in tetralogy of Fallot: associations with pulmonary regurgitation

Charlène A. Mauger<sup>1,2†</sup>, Sachin Govil<sup>3†</sup>, Radomir Chabiniok<sup>4,5,6,7</sup>, Kathleen Gilbert<sup>2</sup>, Sanjeet Hegde<sup>3,8</sup>, Tarique Hussain<sup>4</sup>, Andrew D. McCulloch<sup>3</sup>, Christopher J. Occleshaw<sup>9</sup>, Jeffrey Omens<sup>3</sup>, James C. Perry<sup>3,8</sup>, Kuberan Pushparajah<sup>10</sup>, Avan Suinesiaputra<sup>11</sup>, Liang Zhong<sup>12,13</sup> and Alistair A. Young<sup>1,10\*</sup>

*J Cardiovasc Magn Reson* (2021) 23:105



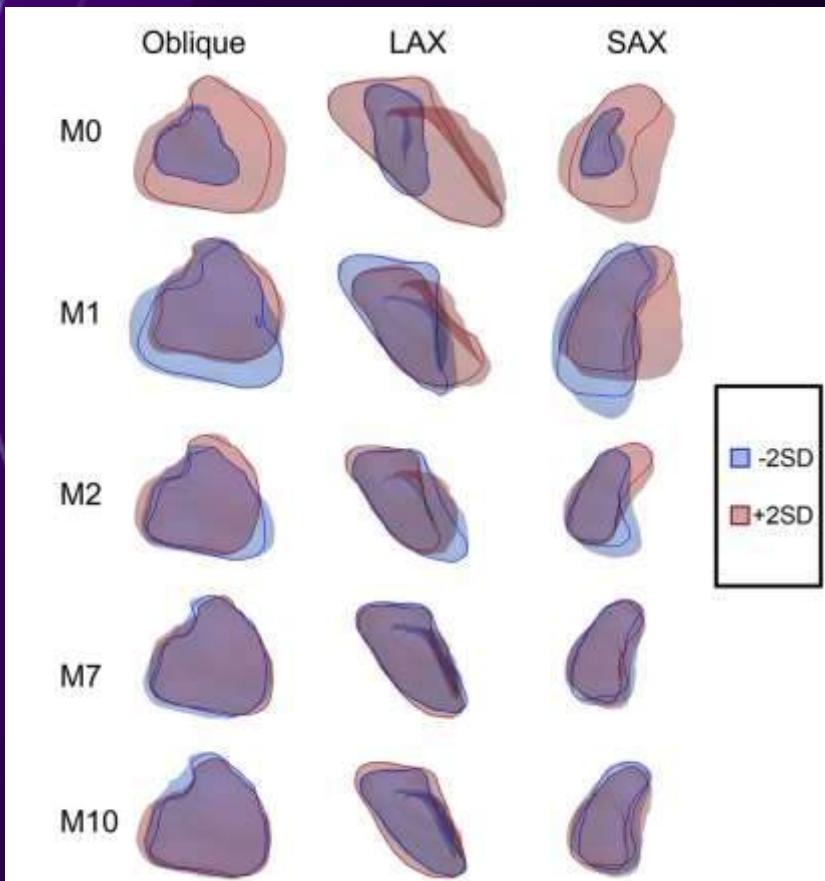
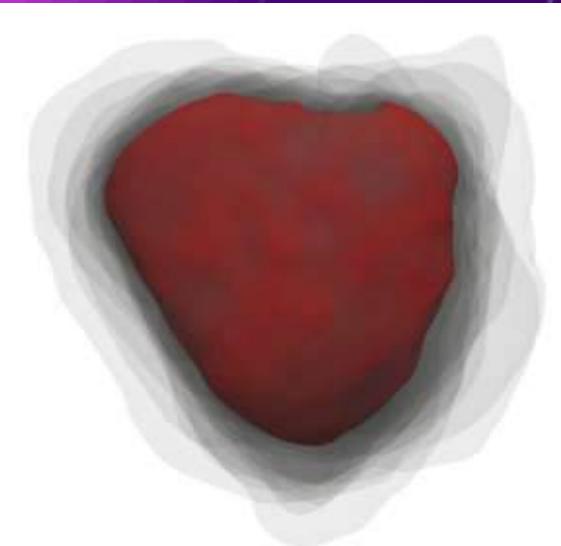
Using SSM, increasing PR: a) RV dilation, b) decreased LV septal-lateral dimension (LV flattening), c) paradoxical septal motion & d) RV basal bulging

# SSM OF THE RV

Statistical shape modeling reveals the link between right ventricular shape, hemodynamic force, and myocardial function in patients with repaired tetralogy of Fallot

Am J Physiol Heart Circ Physiol 323: H449–H460, 2022.

• Sarah Kollar,<sup>1</sup> Elias Balaras,<sup>2</sup> Laura J. Olivieri,<sup>3</sup> Yue-Hin Loke,<sup>1\*</sup> and Francesco Capuano<sup>4\*</sup>



## Mode

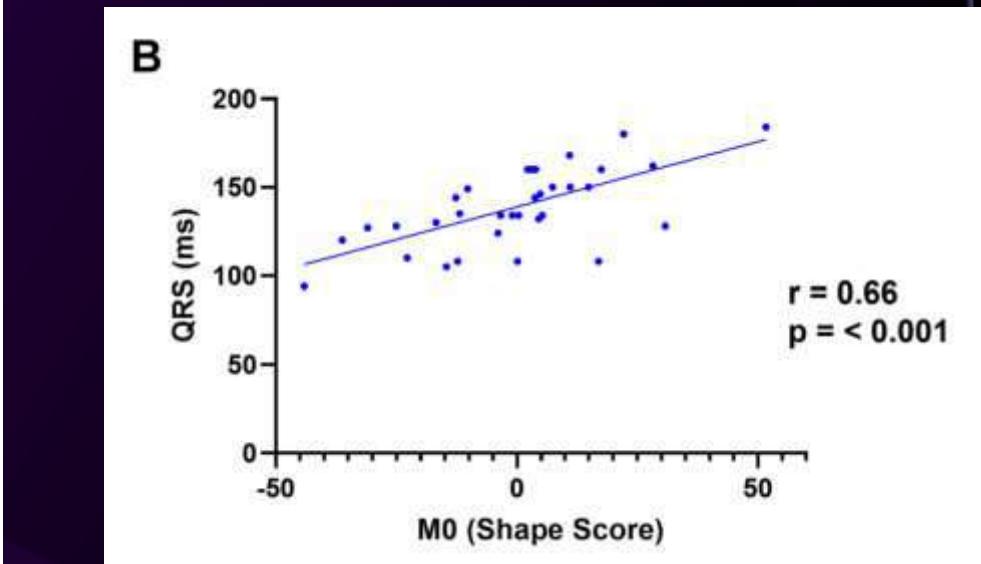
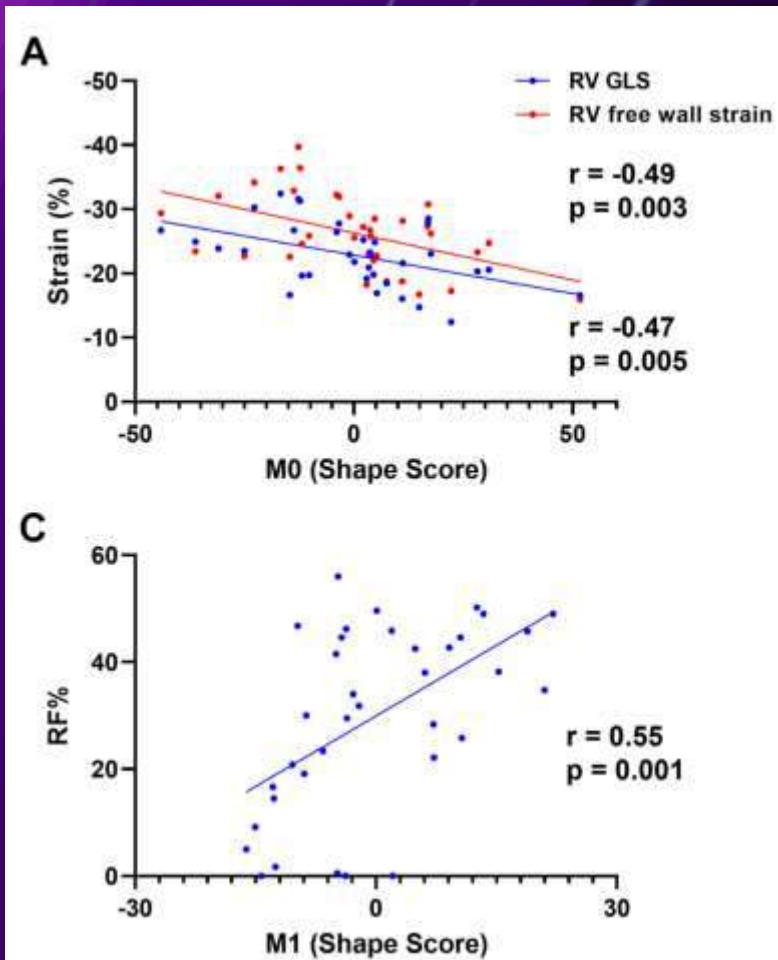
- 0 = overall RV size
- 1 = Apical bulge & RVOT diameter
- 2 = Longitudinal shortening,  $\triangle$  of RV inflow-outflow, globular RV
- 7 =  $\triangle$  of RV inflow-outflow, RV apical bulge
- 10 = Apical bulge, length from base to apex, circumference of the RV inflow portion and RVOT size

# SSM OF THE RV

Statistical shape modeling reveals the link between right ventricular shape, hemodynamic force, and myocardial function in patients with repaired tetralogy of Fallot

Am J Physiol Heart Circ Physiol 323: H449–H460, 2022.

• Sarah Kollar,<sup>1</sup> Elias Balaras,<sup>2</sup> Laura J. Olivieri,<sup>3</sup> Yue-Hin Loke,<sup>1\*</sup> and Francesco Capuano<sup>4\*</sup>



## Mode

- 0 = overall RV size
- 1 = Apical bulge & RVOT diameter

# SSM OF THE RV

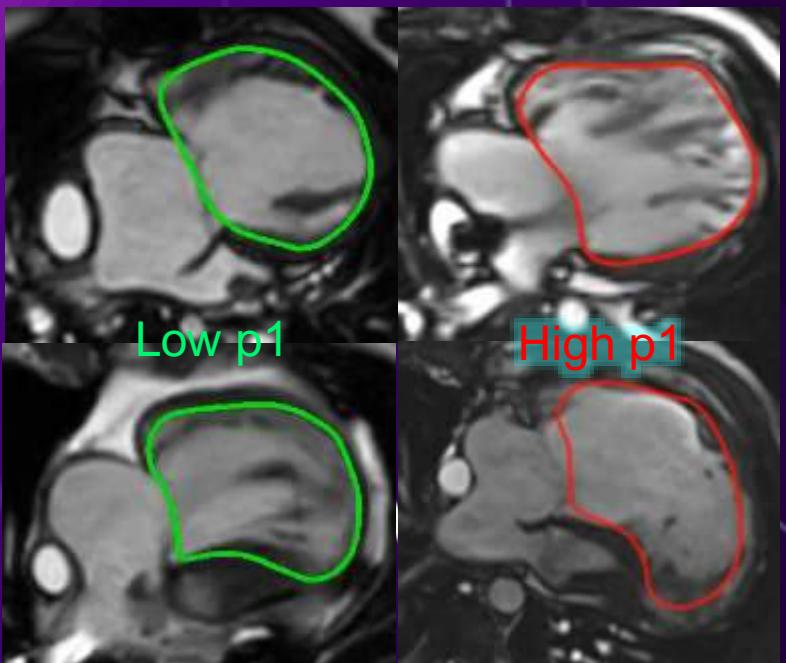
## ABSTRACT

| Originally Published 11 November 2024 | 

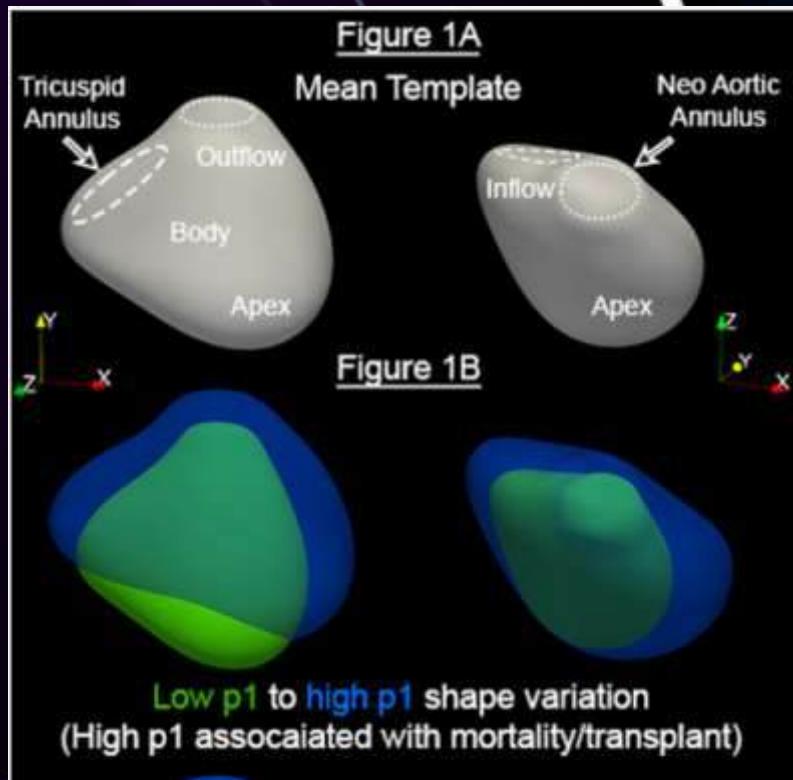
**Abstract 4114497: Shape Variations in Right Ventricular 3D Geometry are associated with adverse outcomes in Hypoplastic Left Heart Syndrome Patients: A Fontan Outcomes Registry using CMR Examination (FORCE) Study**

Yue-Hin Loke, MD, Ryan O'Hara, BS, Jacqueline Contento, BSE, Nicole Marella, MD, Lekha Anantuni, MD, Susana Gaviria, MD, Sarah Kollar, DO

[SHOW ALL](#) and Francesco Capuano, PhD [AUTHOR INFO & AFFILIATIONS](#)



N=388 HLHS Fontan Patients



Multivariable Analysis	Odds Ratio (Death or heart transplantation)	(95% CI) 2.5 % 97.5 %	p-value
Shape Mode p1*	2.67	1.44, 10.67	<0.01
RV Mass <sub>i</sub> (gm/m <sup>2</sup> )	1.025	1.005, 1.041	0.01

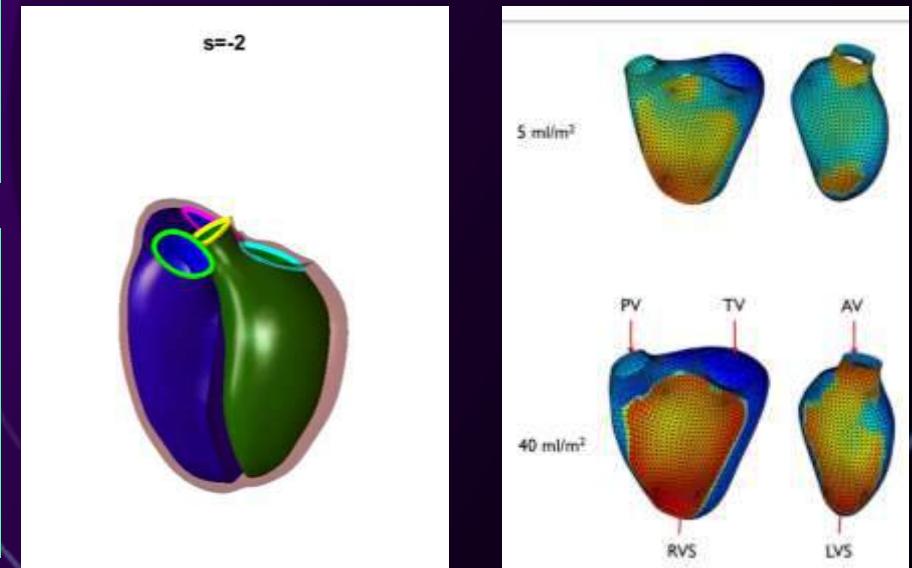
# SUMMARY

Modeling – math and computational methods for structure, fxn, behavior

- Understanding mechanics
- Test different Tx strategies
- Design device

Various types of modeling

Up to 63% of RV ejection is due to the LV!



Fellow/junior attending:  
Modeling in Ebstein's is wide open

## SSM

- Variations from the “average”
- Insights into pathophysiology
- ? Predictor of events

THANK YOU

# THANK YOU AND CREDITS

## CHOP CMR Team



### Cardiac Anesthesia

Adreas Lopke, Susan Nicolson

### CMR Nursing

Denise Virden, Traci Sullivan

### CHOP Administration

Joe Rossano, Kasa Darge, Larry Barnes

Ana Spraycar, Jim Zheng, Trish Mecca

### CT Surgery

Jonathan Chen, Stephanie Fuller, Bill Gaynor

Kats Maeda, Mo Nuri, Constantine Mavroudis

### Cardiac Cath

Jack Rome, Matt Gillespie, Jessica Tang,

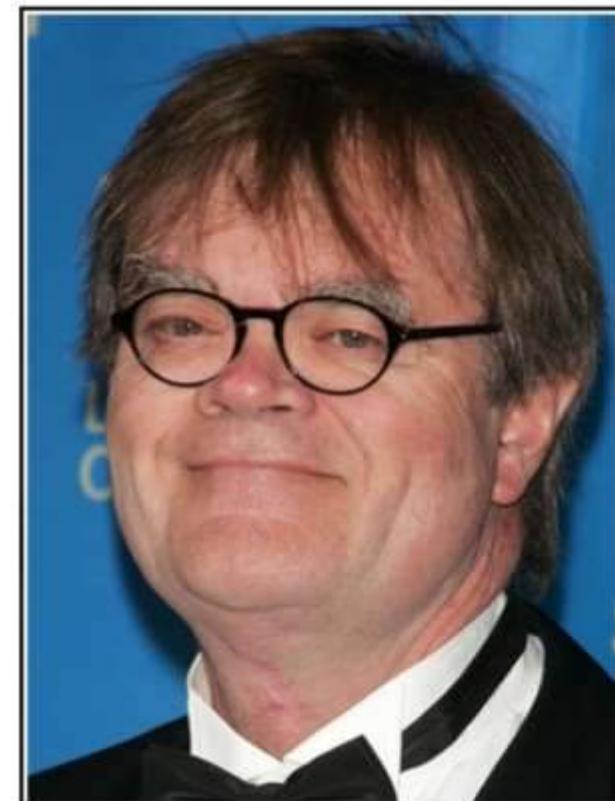
Mike Obyrne, Yoav Dori

### Cardiac Scheduling

Heather Meldrum

### 3D Post-processing Lab

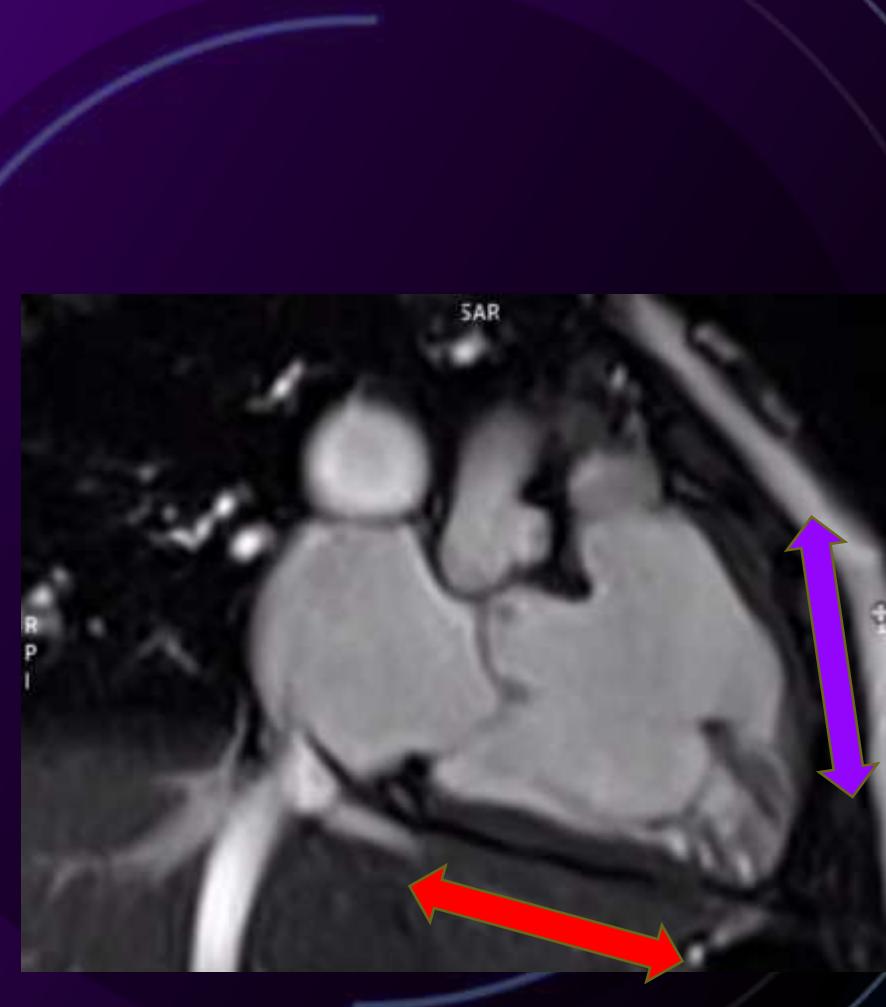
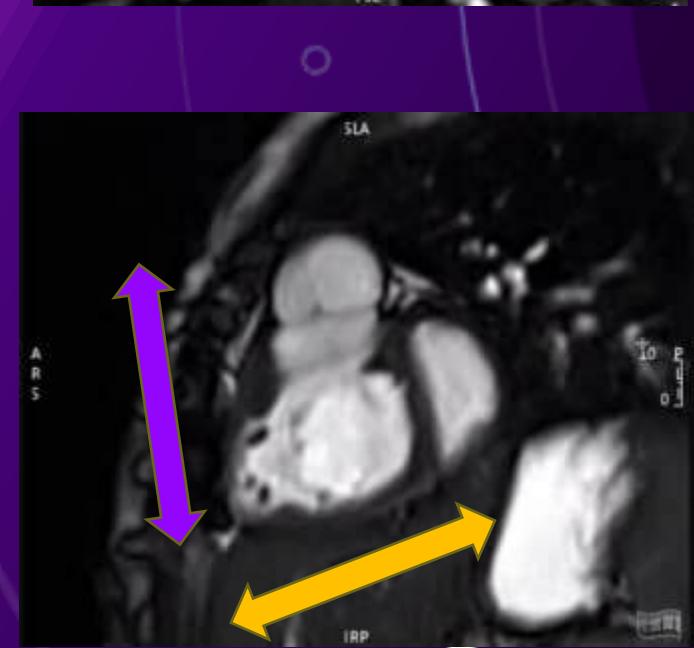
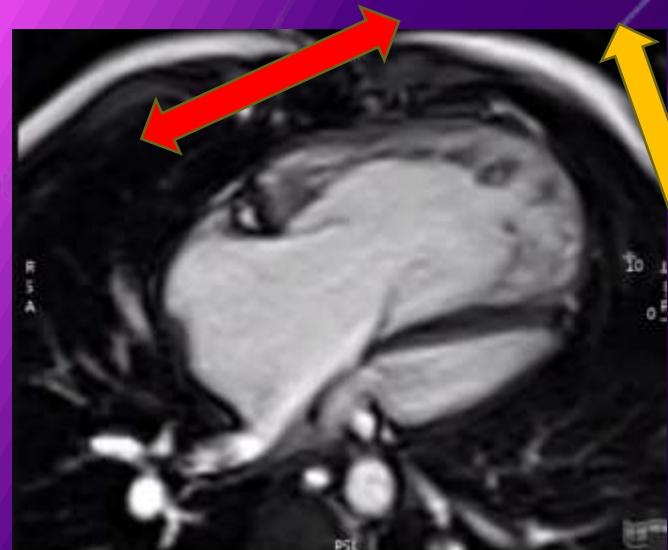
# IT MAY BE DISHEARTENING TO THINK OF AN “AVERAGE” PERSON AND SOME OF US BELOW IT BUT...



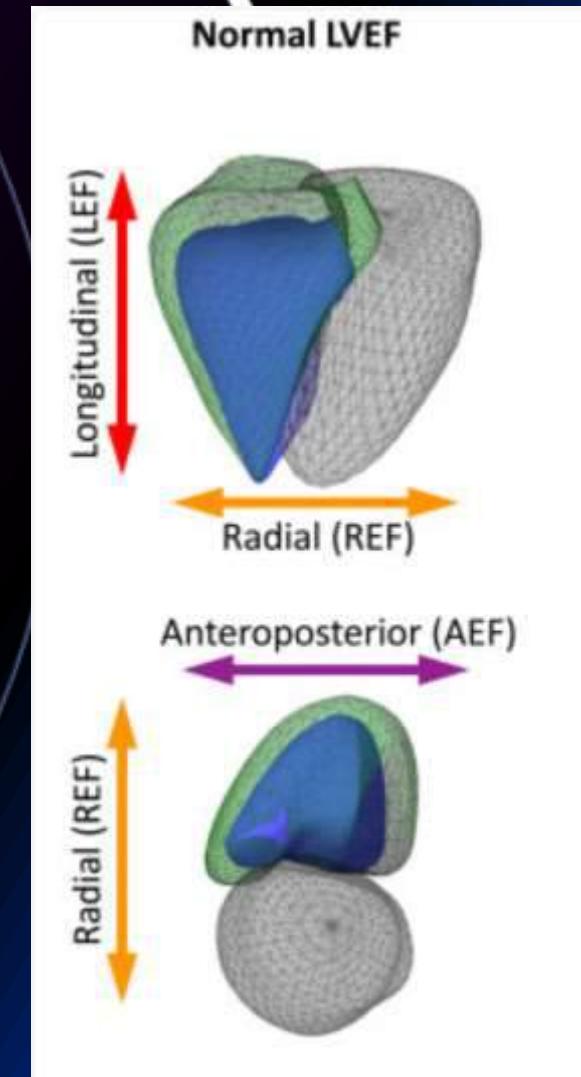
Welcome to Lake Wobegon, where  
all the women are strong, all the  
men are good-looking, and all the  
children are above average.

— Garrison Keillor —

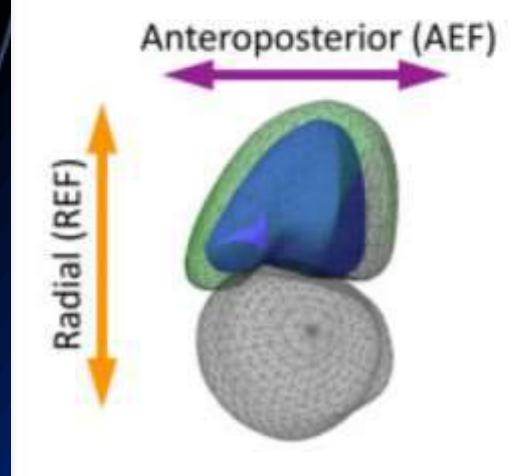
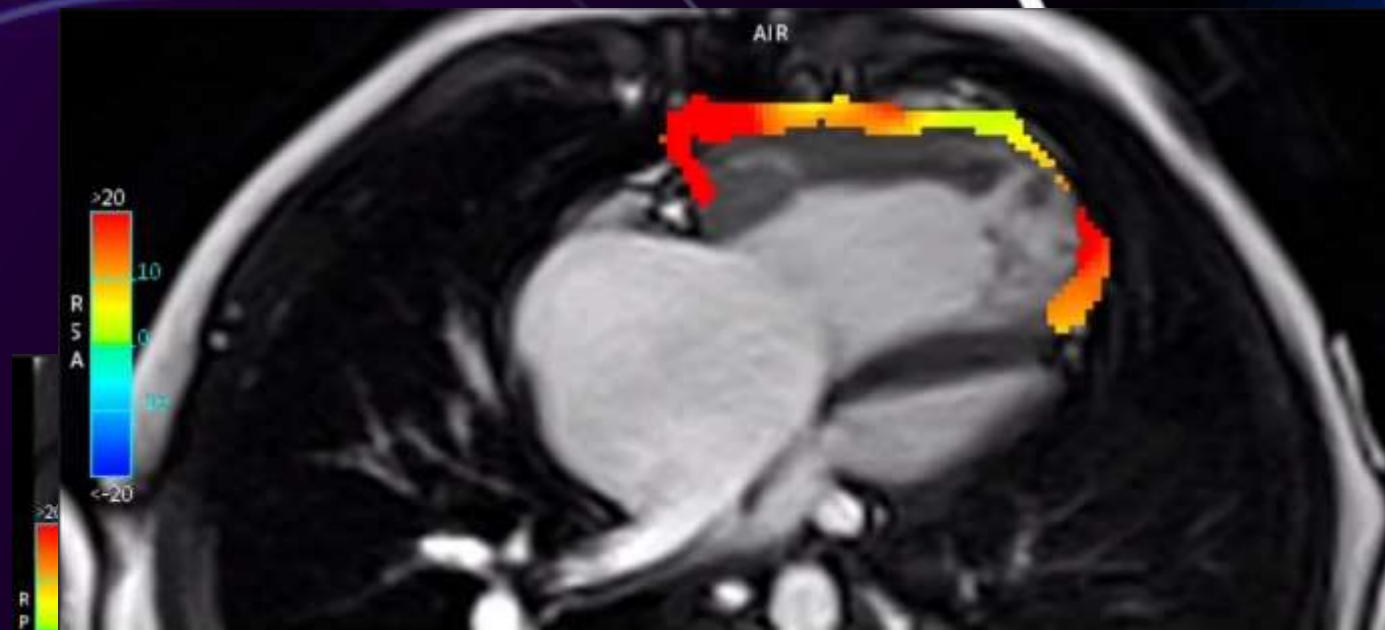
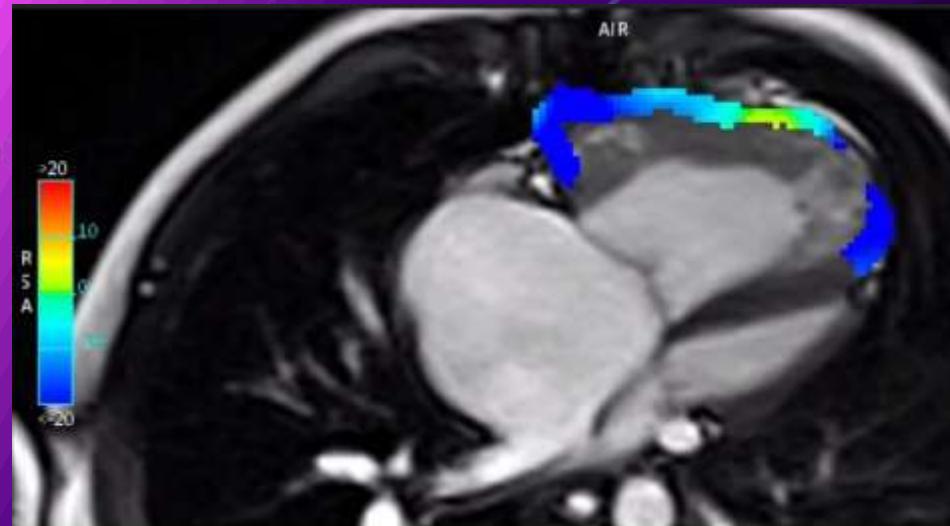
# MODELING THE RV - MOTION



Using REALIZE software



# MODELING THE RV



# RV FINITE ELEMENT ANALYSIS (FE)

Can RV pre-PVR stress and strain predict RV performance after PVR?

RV pre-PVR stress and strain

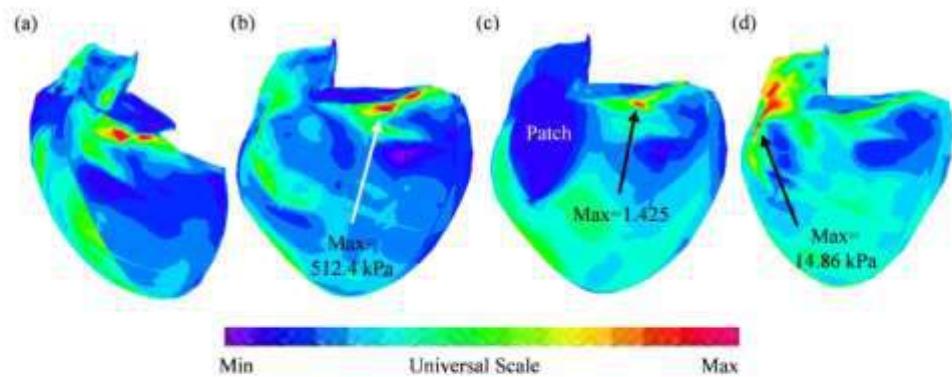


Figure 4 (online).

Selected cut-surface, maximum principal stress (Stress- $P_1$ ) and strain (Strain- $P_1$ ) corresponding to end-of-diastole and end-of-systole pressure conditions. (a) Position of the cut surface; (b) Stress- $P_1$ , end-of-diastole; (c) Strain- $P_1$ , end-of-diastole; (d) Stress- $P_1$ , end-of-systole.

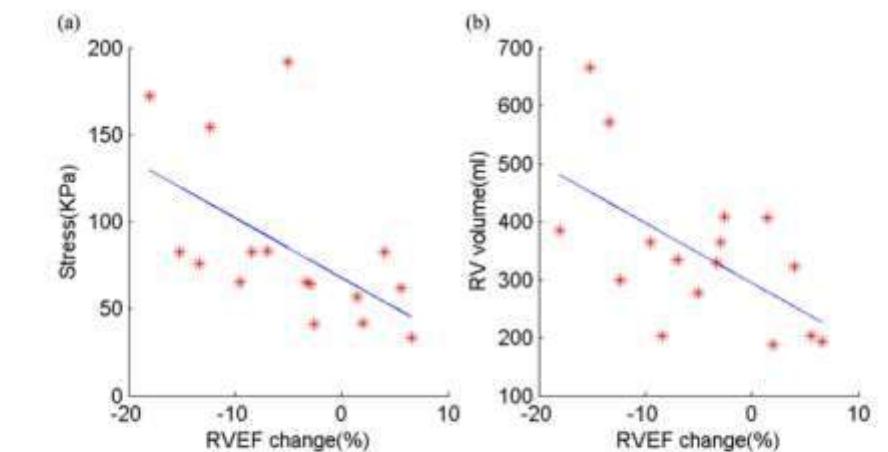


Figure 5 (online).

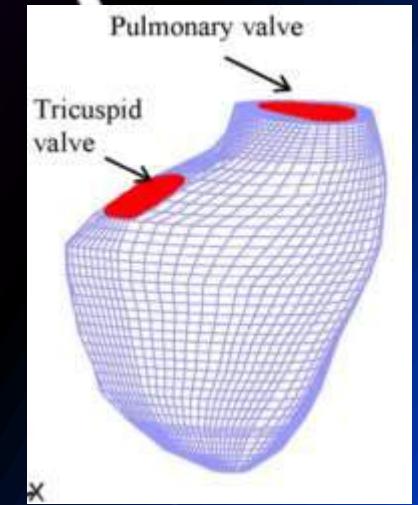
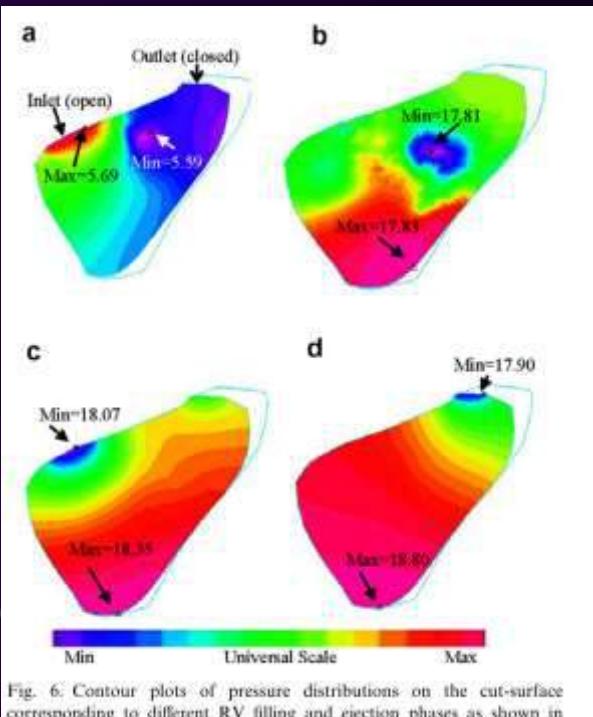
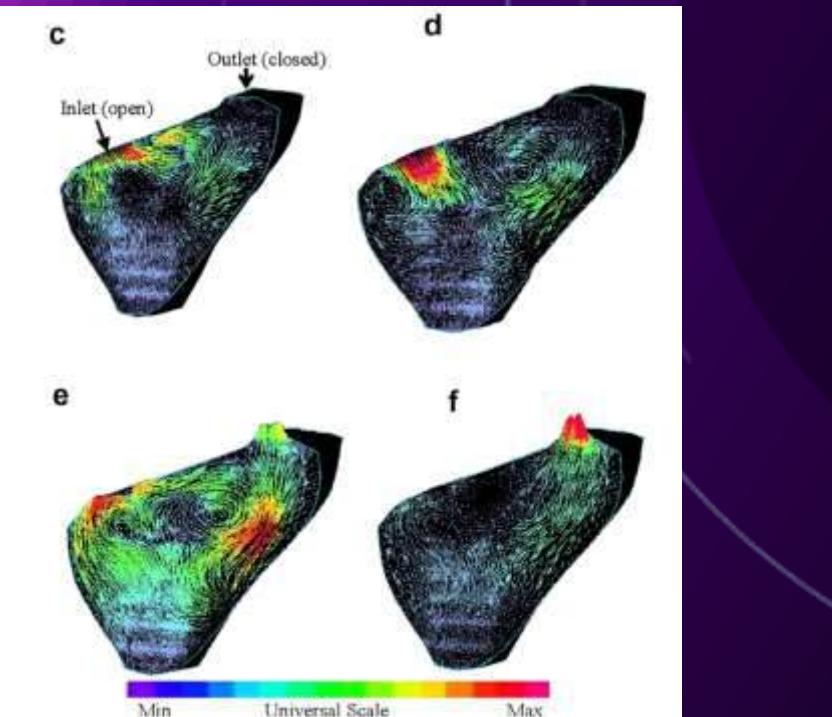
RVEF change correlated negatively with stress ( $r = -0.56$ ,  $p = 0.025$ ) and with pre-PVR RV volume ( $r = -0.60$ ,  $p = 0.015$ ). (a) Stress vs. EF change; (b) pre-PVR RV volume vs. EF change.

# RV FLUID STRUCTURE INTERACTION (FSI)

*In vivo* MRI-based 3D FSI RV/LV models for human right ventricle and patch design for potential computer-aided surgery optimization

Chun Yang <sup>a</sup>, Dalin Tang <sup>b,\*</sup>, Idith Haber <sup>c</sup>, Tal Geva <sup>d</sup>, Pedro J. del Nido <sup>c</sup>

Computers and Structures 85 (2007) 988–997



Combination of flow and  
stress strain associated with  
RV morphology, material  
properties and BP

# RV INTRAVENTRICULAR FLOW

## Intraventricular Flow Simulations in Singular Right Ventricles Reveal Deteriorated Washout and Low Vortex Formation

*Cardiovascular Engineering and Technology*, Vol. 13, No. 3, June 2022, pp. 495–503

ANNA GRÜNWALD,<sup>1</sup> JANA KORTE,<sup>1</sup> NADJA WILMANNS,<sup>3</sup> CHRISTIAN HERBERG,<sup>2</sup> SASCHA GROß-HARDT,<sup>1</sup> ULRICH LINDEN,<sup>2</sup> and ULRICH LINDEN<sup>1</sup>

<sup>1</sup>Department of Cardiovascular Engineering, Institute of Biomedicine and Biotechnology, University, Aachen, Germany; <sup>2</sup>Department of Pathophysiology, University of Bonn, Bonn, Germany; and <sup>3</sup>Institute of General Medicine, University, Aachen, Germany

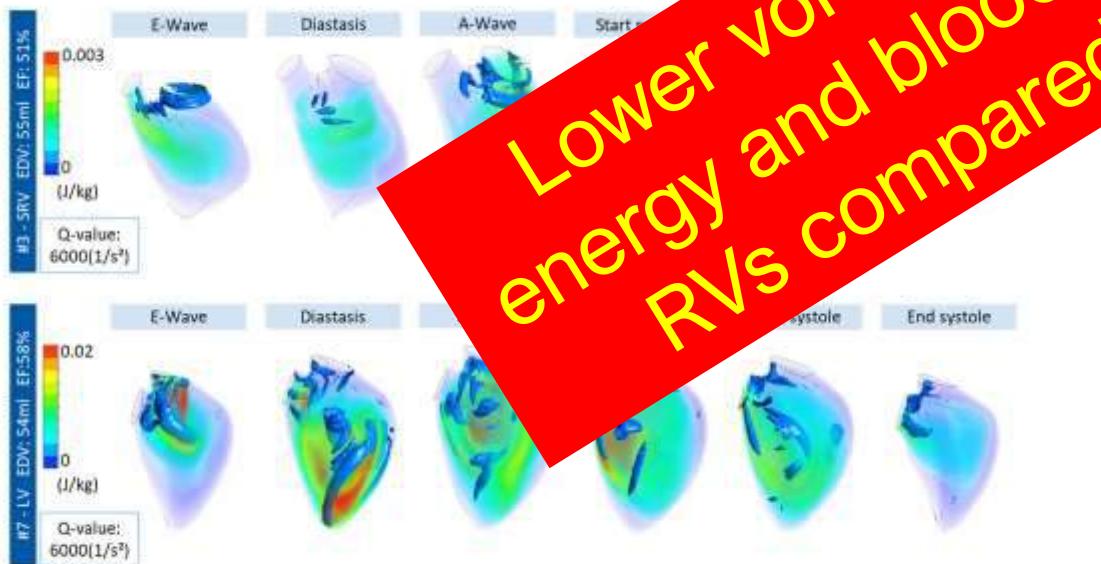


FIGURE 1. Representative turbulent kinetic energy (J/kg) and vortex structure formation with Q-value (1/s) for subject #3 (SRV) and subject #7 (LV). TKE represented by different scales, subject #3 max 0.003 J/kg, subject #8 max 0.02 J/kg.

Lower vortex formation, kinetic energy and blood washout in single RVs compared to normal LVs

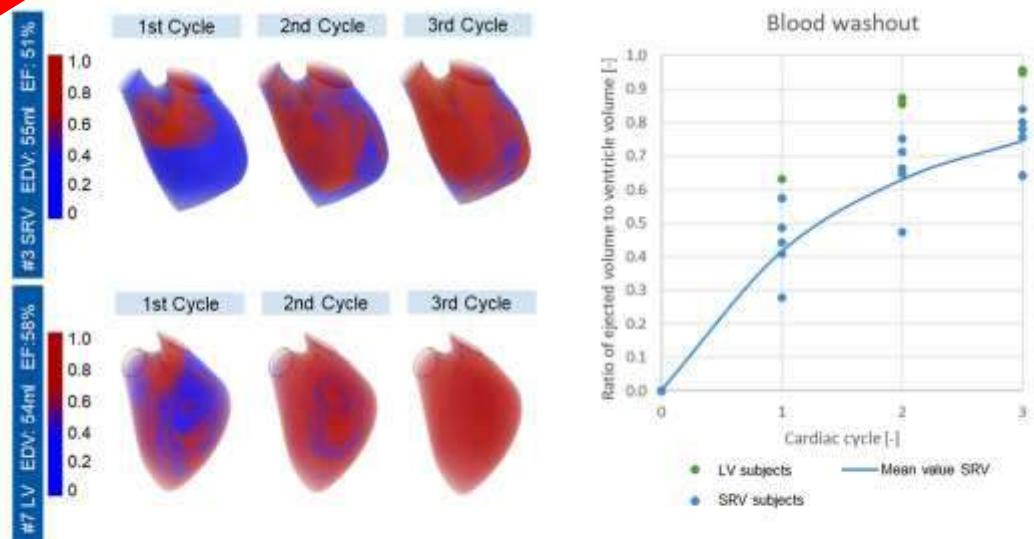


FIGURE 3. Left: Washout simulation for subject #3 (SRV) and subject #7 (LV). Time point of diastole for three cardiac cycles. Blue old blood, red new blood. Right: Volume percentage distribution of ejected volume to the total ventricle volume for SRV subjects and LV subjects.

# RV INTRAVENTRICULAR FLOW

## Intraventricular Flow Simulations in Singular Right Ventricles Reveal Deteriorated Washout and Low Vortex Formation

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ANNA GRÜNWALD,<sup>1</sup> JANA KORTE,<sup>1</sup> NADJA WILMANNS,<sup>3</sup> CHRISTIAN WINKLER,<sup>2</sup> KATHARINA LINDEN,<sup>2</sup> ULRIKE HERBERG,<sup>2</sup> SASCHA GROß-HARDT,<sup>1</sup> ULRICH STEINSEIFER,<sup>1</sup> and MICHAEL NEIDLIN <sup>1</sup>

<sup>1</sup>Department of Cardiovascular Engineering, Institute of Applied Medical Engineering, Medical Faculty, RWTH Aachen University, Aachen, Germany; <sup>2</sup>Department of Pediatric Cardiology, University Hospital of Bonn, Bonn, Germany; and

<sup>3</sup>Institute of General Mechanics, RWTH Aachen University, Aachen, Germany

Applied CFD to echocardiographic data to simulate flows in 5 single RV vs 2 normal LVs

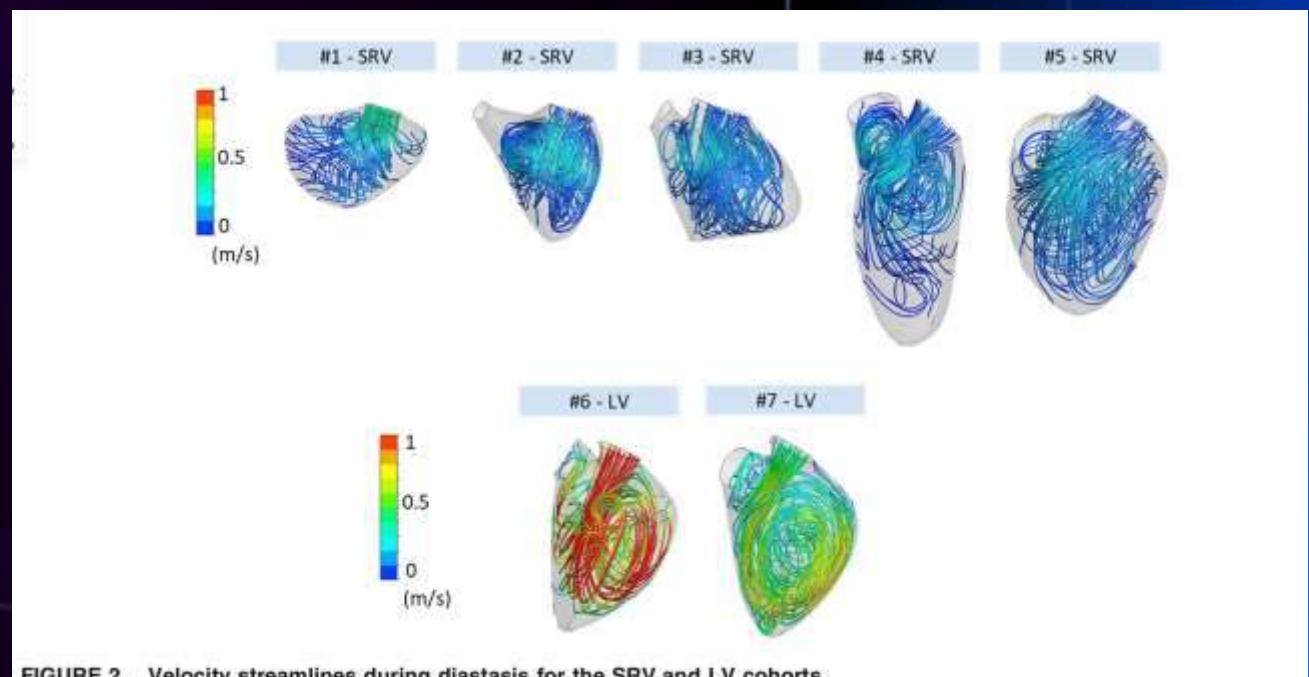
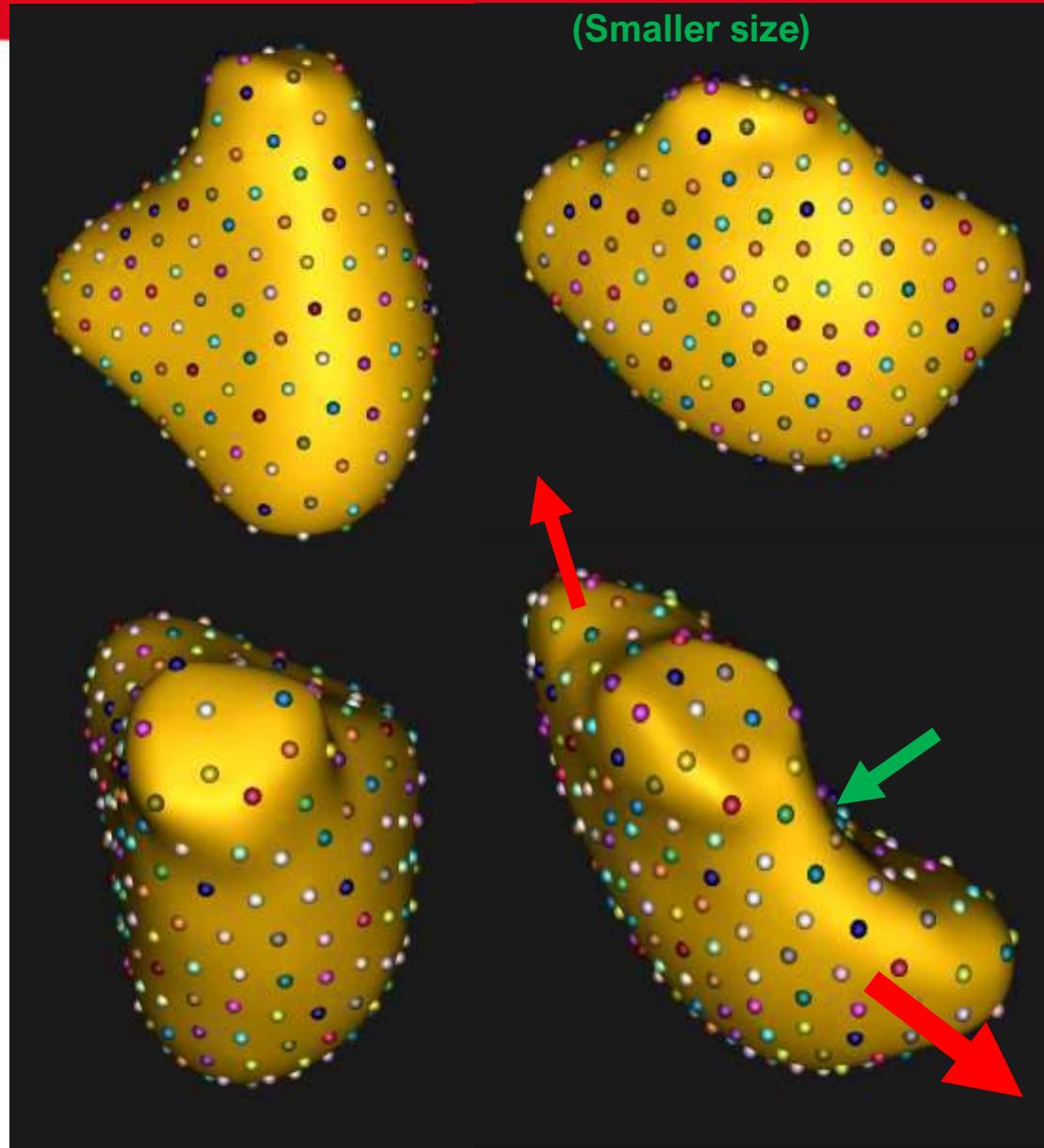


FIGURE 2. Velocity streamlines during diastasis for the SRV and LV cohorts.

## Statistical Shape Modeling of HLHS (FORCE)

- Shapeworks Studio (NIH/NIGMS CIBC) to derive mean template from 329 HLHS patients
- Quantified shape variations (shape mode) representing deviation from the mean.
- Relationships between RV shape and adverse outcomes (mortality/transplant, heart failure, plastic bronchitis, protein losing enteropathy) assessed

Loke et al. Shape Variations in Right Ventricular 3D Geometry are associated with adverse outcomes in Hypoplastic Left Heart Syndrome Patients: A Fontan Outcomes Registry using CMR Examination (FORCE) Study. AHA Scientific Sessions 2024 Circulation Volume 150, Number Suppl\_1 [https://doi.org/10.1161/circ.150.suppl\\_1.4114497](https://doi.org/10.1161/circ.150.suppl_1.4114497)



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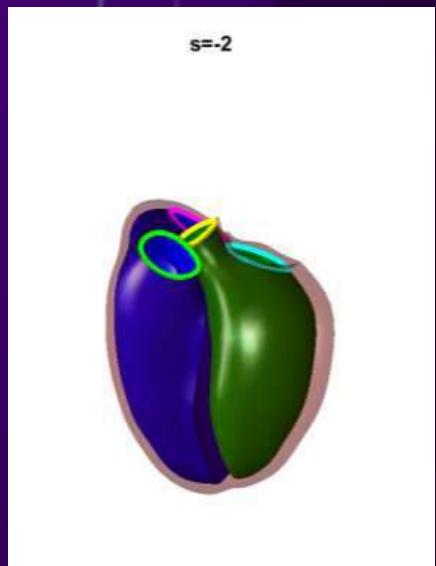
Shape Mode	Score for SV_25
p0	-141.724
p1	64.0497
p2	22.1053
p3	-59.9196
p4	-19.135
p5	26.0906

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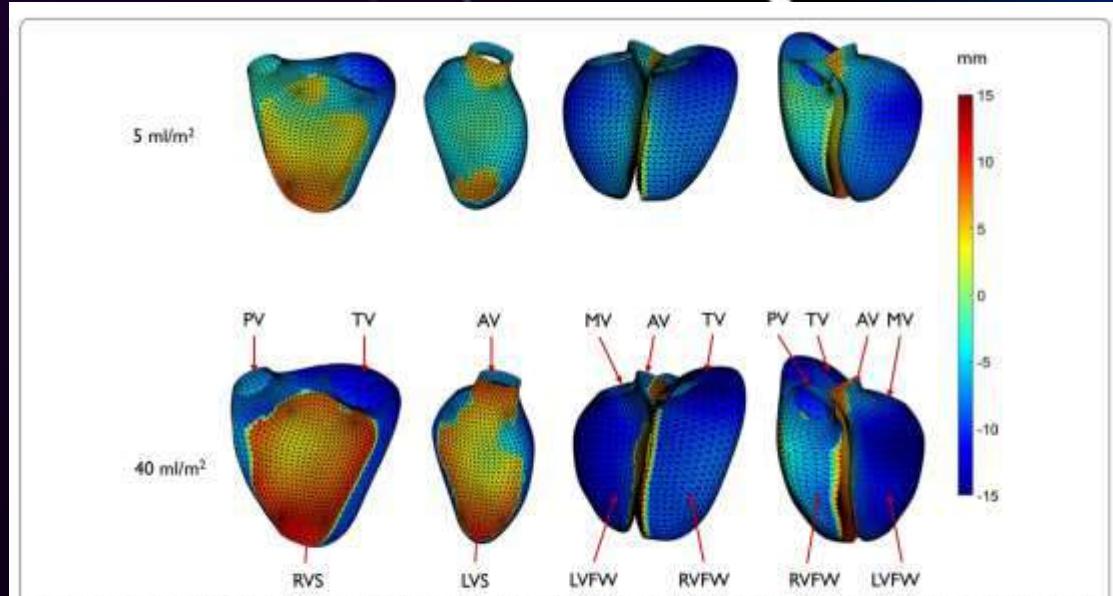
# SSM OF THE RV

## Right-left ventricular shape variations in tetralogy of Fallot: associations with pulmonary regurgitation

Charlène A. Mauger<sup>1,2†</sup>, Sachin Govil<sup>3†</sup>, Radomir Chabiniok<sup>4,5,6,7</sup>, Kathleen Gilbert<sup>2</sup>, Sanjeet Hegde<sup>3,8</sup>, Tarique Hussain<sup>4</sup>, Andrew D. McCulloch<sup>3</sup>, Christopher J. Occleshaw<sup>9</sup>, Jeffrey Omens<sup>3</sup>, James C. Perry<sup>3,8</sup>, Kuberan Pushparajah<sup>10</sup>, Avan Suinesiaputra<sup>11</sup>, Liang Zhong<sup>12,13</sup> and Alistair A. Young<sup>1,10\*</sup>



*J Cardiovasc Magn Reson* (2021) 23:105



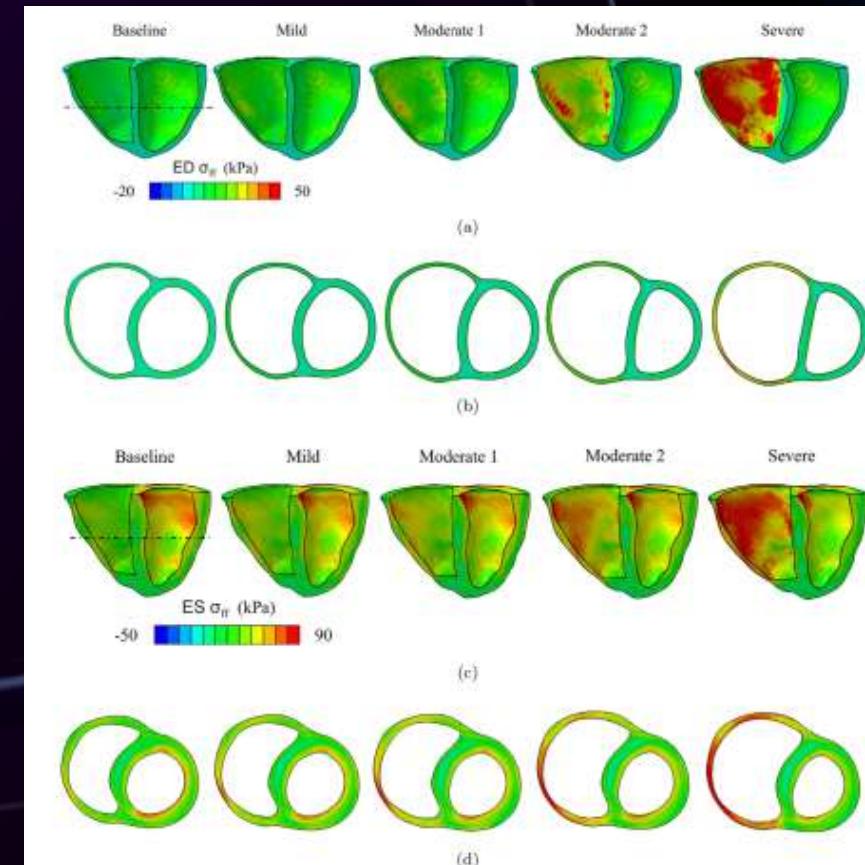
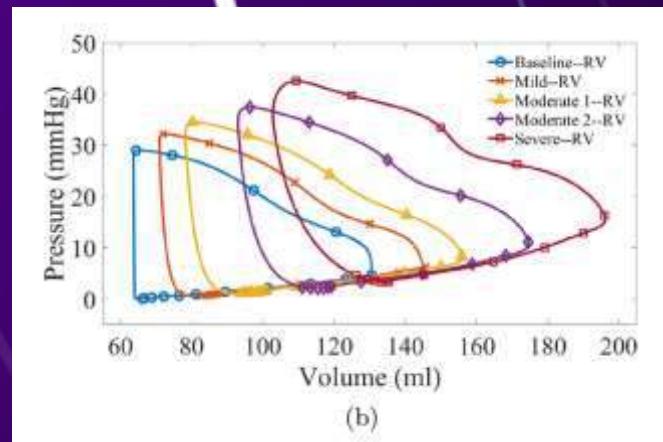
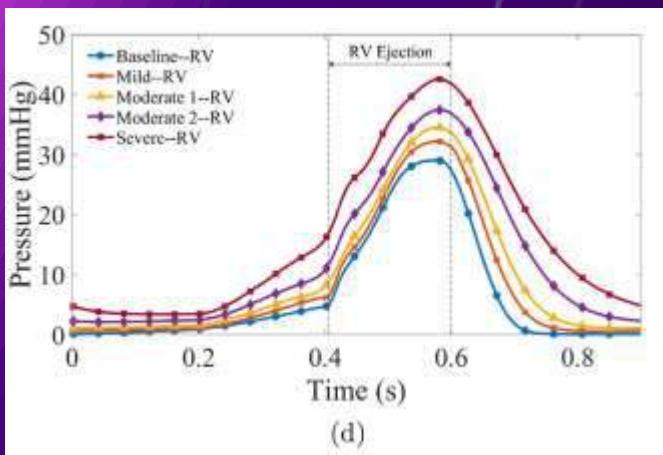
**Fig. 5** Changes in contraction patterns associated with increasing pulmonary regurgitation. Paradoxical septal motion is observed as regurgitation increases, as shown by an outward displacement of the septum toward the RV. AV aortic valve, PV pulmonary valve, TV tricuspid valve, MV mitral valve, RVFW right ventricular free wall, LVFW left ventricular free wall, RVS right ventricular septum, LVS left ventricular septum

Using SSM, increasing PR: a) RV dilation b) RV basal bulging, c) decreased LV septal-lateral dimension (LV flattening) and d) paradoxical septal motion

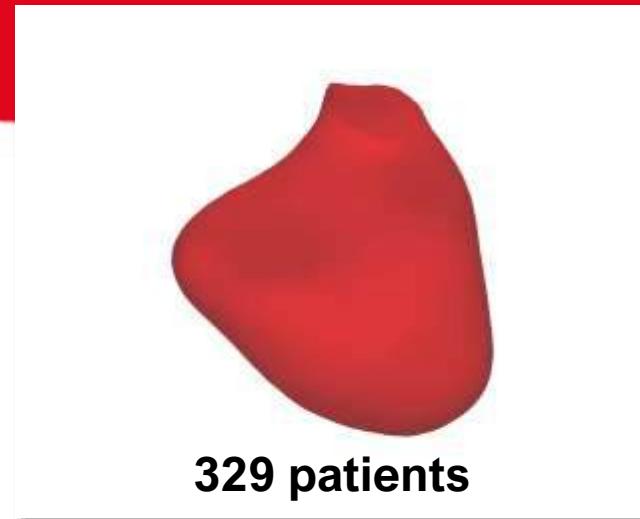
# RV FINITE ELEMENT ANALYSIS (FE)

Effect of pulmonary regurgitation on cardiac functions based on a human bi-ventricle model

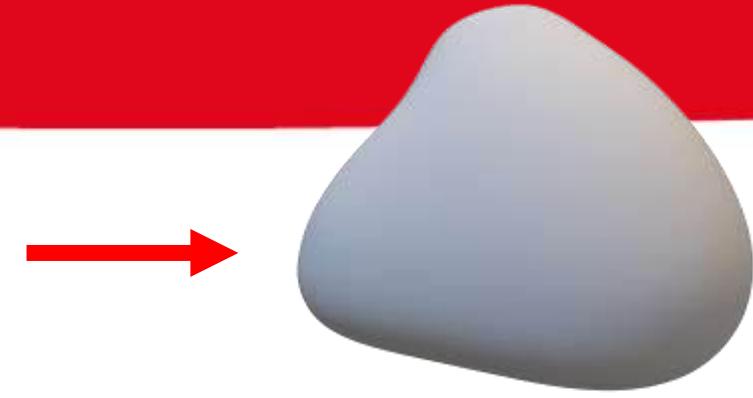
Xueqing Yin<sup>a</sup>, Yingjie Wang<sup>a,\*</sup> Computer Methods and Programs in Biomedicine 238 (2023) 107600



- Circumferentially dilated RV with loss of concavity in septal wall.
- p1 – apical bulge variant
- p3/p5 –crescent-shaped RV body to a spherical RV body

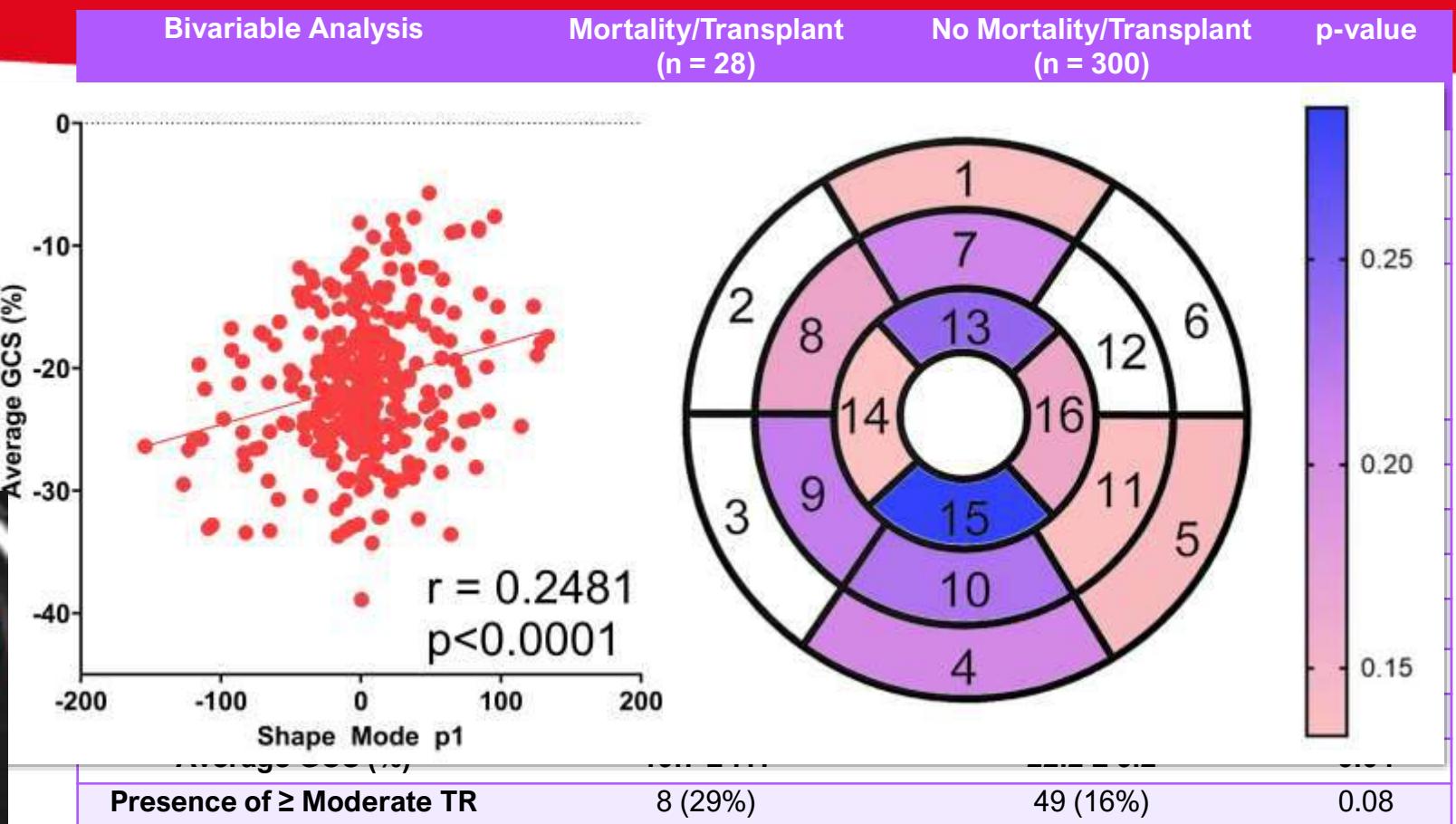
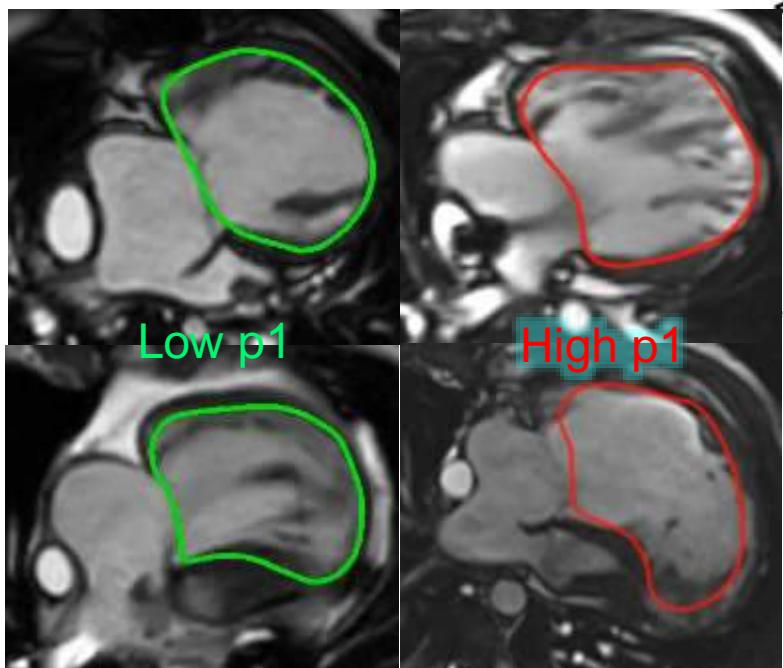


329 patients

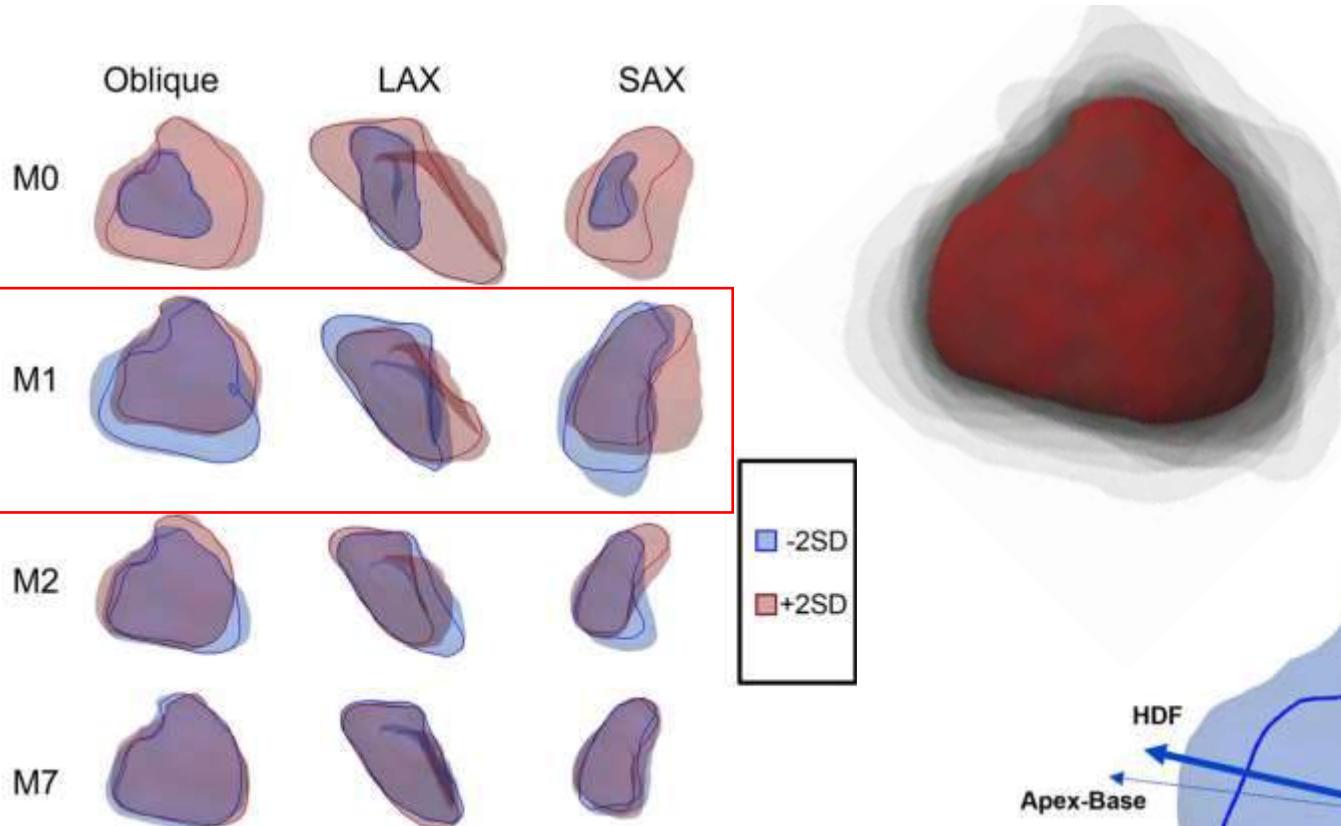


Mean Shape Template

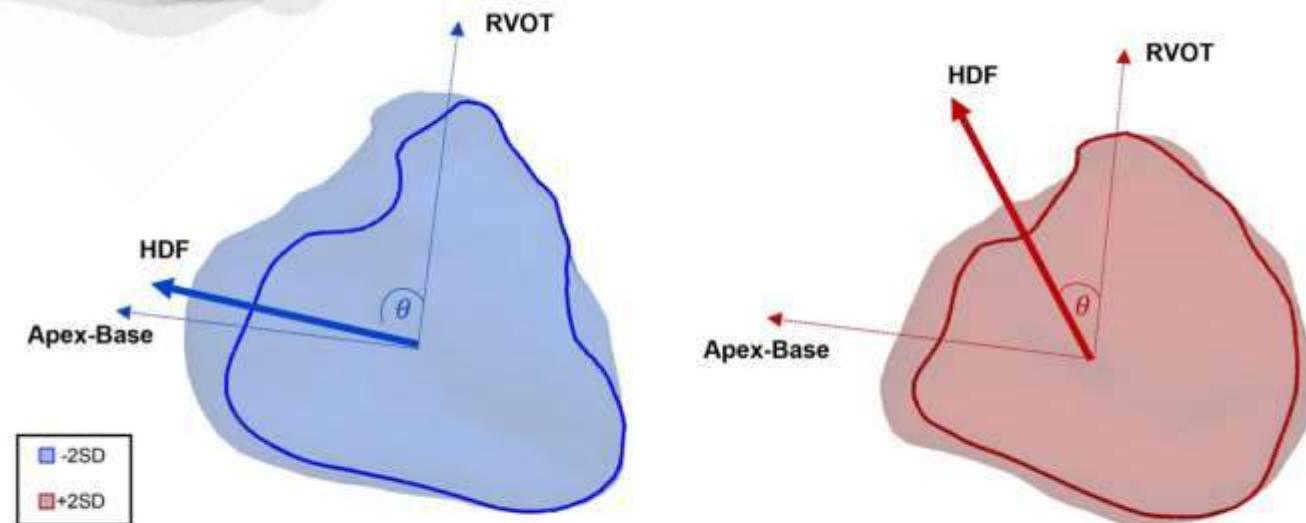
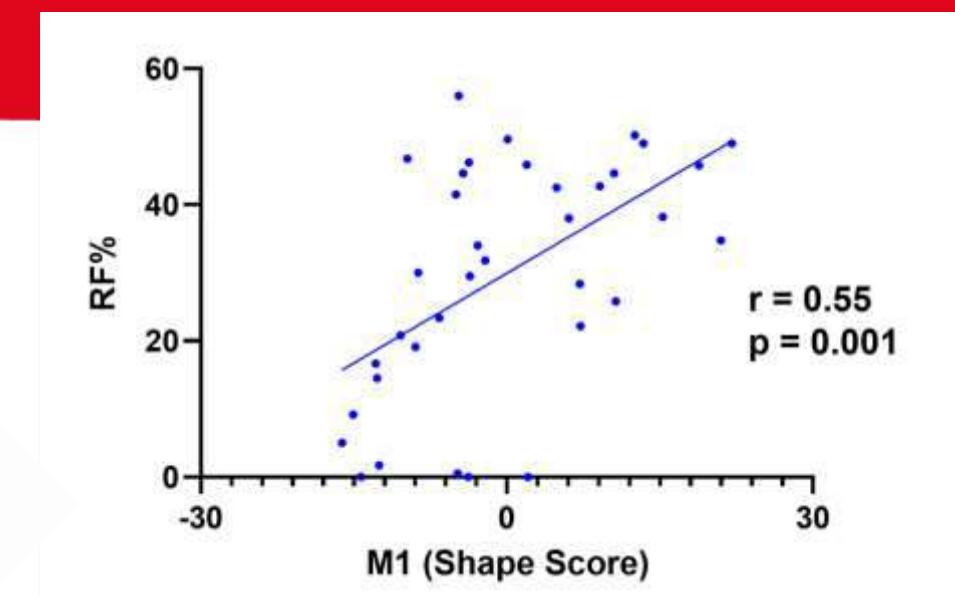
- Twenty-eight patients (8.5%) with mortality/heart transplant at  $2.5 \pm 2.4$  years after CMR.
- p1 associated with mortality/heart transplant
- Independent of size/mass; corresponded to reduced GCS (inferior and apical segments).



Multivariable Analysis	Odds Ratio	(95% CI) 2.5 %    97.5 %	p-value
Shape Mode p1*	2.67	1.44, 10.67	<0.01
RV Mass <sub>i</sub> (gm/m <sup>2</sup> )	1.025	1.005, 1.041	0.01

Statistical Shape Modeling Reveals the link  
between RV shape, hemodynamic force, and  
myocardial function in patients with rTOF

Shape mode M1 – related to PI  
and alterations in intraventricular  
forces; apical bulge and  
enlargement of RVOT diameter

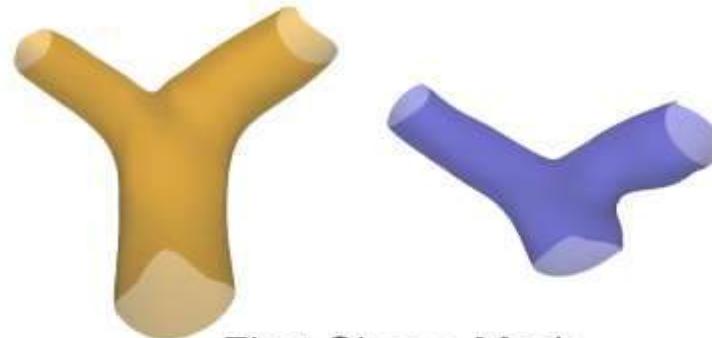


**Figure 8.** Outline of right ventricle (RV) in the oblique/frontal view. Blue outline denotes  $-2SD$  from the template shape and red outline denotes  $+2SD$  toward the shape variation of interest. An increased propensity toward M1 (red) is associated with a more acute angle between the direction of the total force vector (hemodynamic force, HDF) and the right ventricular outflow tract (RVOT) axis. There is increased contribution of the RVOT force to the overall HDF as the two vectors become more parallel to each other (red).

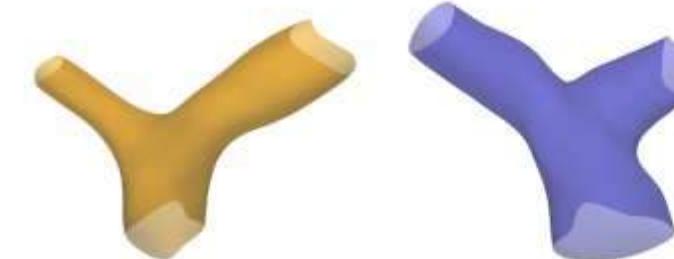
## Pulmonary artery shape variations in repaired Tetralogy of Fallot



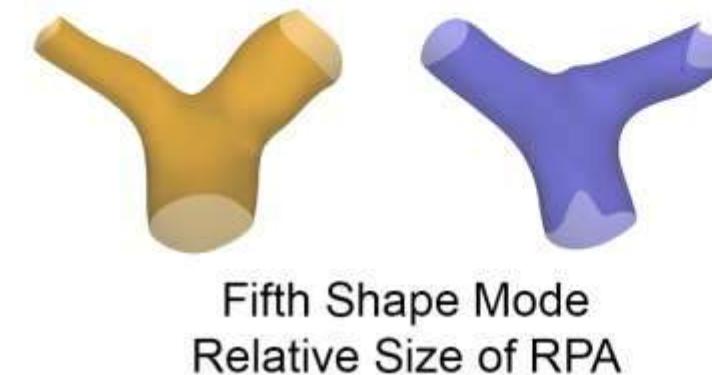
Mean template of pulmonary arteries (n = 103)



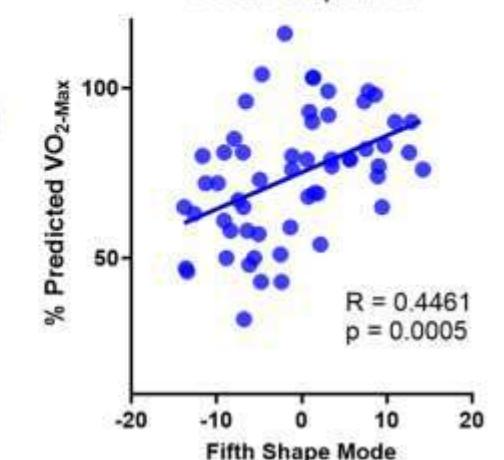
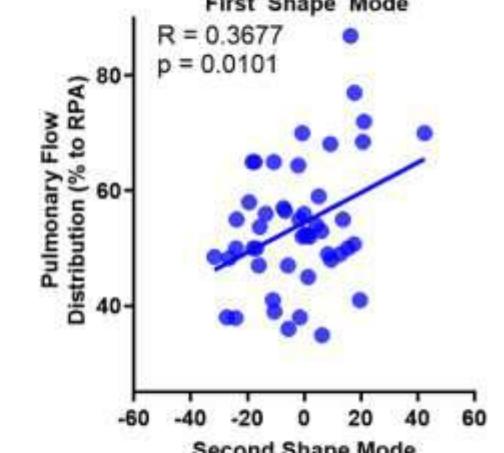
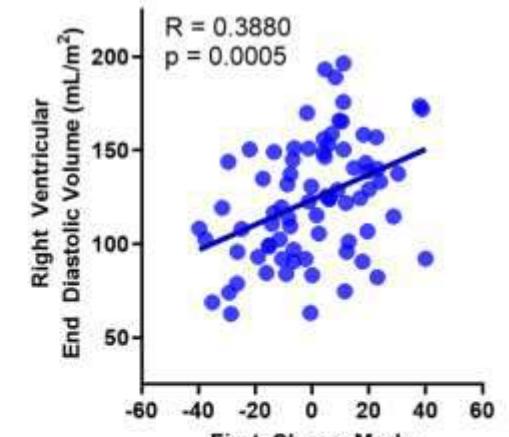
First Shape Mode  
LPA Kinking



Second Shape Mode  
Relative Size of RPA



Fifth Shape Mode  
Relative Size of RPA



# STATISTICAL SHAPE MODELING (SSM)



Figure 1: the shape variation represented by the first principal component of the hand model, where the hand on the left shows a deformation with  $\hat{\alpha}_1 = -3$ , the middle hand shows the mean deformation ( $\hat{\alpha}_1 = 0$ ) and the hand on the right the deformation with  $\hat{\alpha}_1 = 3$ .