Computational Modeling of Cardiovascular Flows: from Fundamental Research to Clinical Applications

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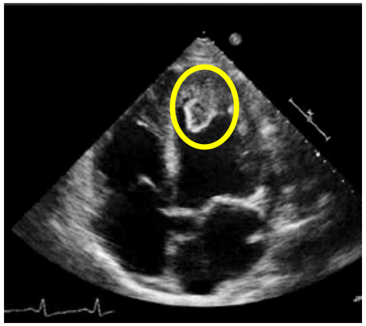
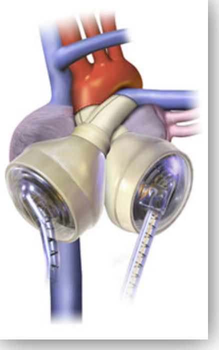
Outline of Seminar Series

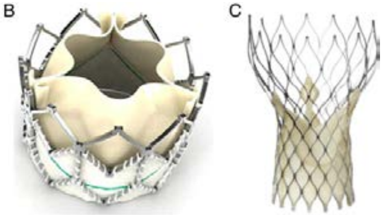
- **July 5**
  I. Computational Modeling of Cardiac Flows: Opportunities and Challenges
  II. Immersed Boundary Method and Investigation of Some Fundamental Questions Regarding the "Design" of the Heart



- **July 6**
  III. Flow Effects on Thrombogenesis: Insights from Computational Models
  IV. Computational Modeling and Analysis of Heart Murmurs



- **July 7**
  V. Hemodynamic Considerations in the Design of Heart-Assist Devices
  VI. Leaflet Dynamics and Thrombogenesis in Transcatheter Heart Valves



I

Computational Modeling of Cardiac Flows: Opportunities and Challenges

Rajat Mittal, Jung Hee Seo, Kourosh Shoele Vijay Vedula

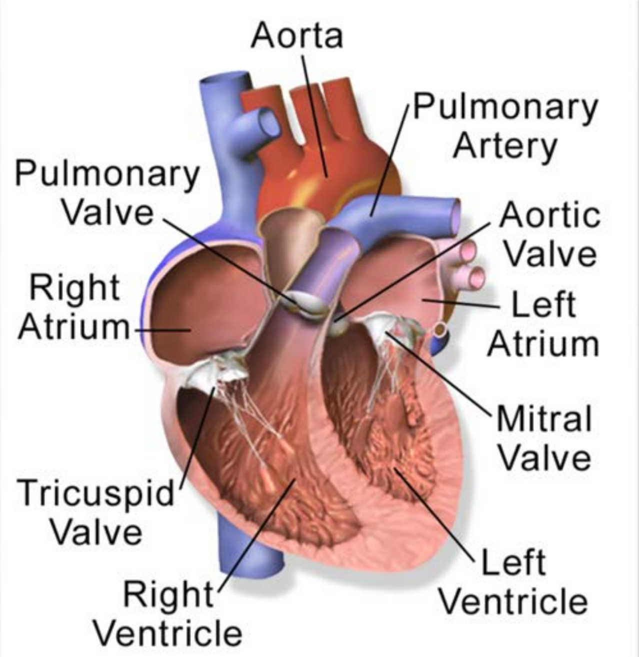
Mechanical Engineering

Theodore Abraham, and Richard T. George

Cardiology

The Human Heart

- Pulsatile, positive displacement pump.
- Transports oxygenated, nutrient-rich blood to the body (systemic circulation)
- Transports blood to and from lungs (pulmonary circuit).



Anatomy of the Heart

- 1 Hz rate
- 100,000 beats/day
- 5 liters/minute
- Mean aortic pressure ~ 100 mm Hg.
- Resting Output ~1W
- Efficiency ~ 25%
- Increases (5X) cardiac output on demand.
- Ejection fraction (EF) ~ 55%

- Does not fail easily
- Does not damage blood
- Does not generate clots

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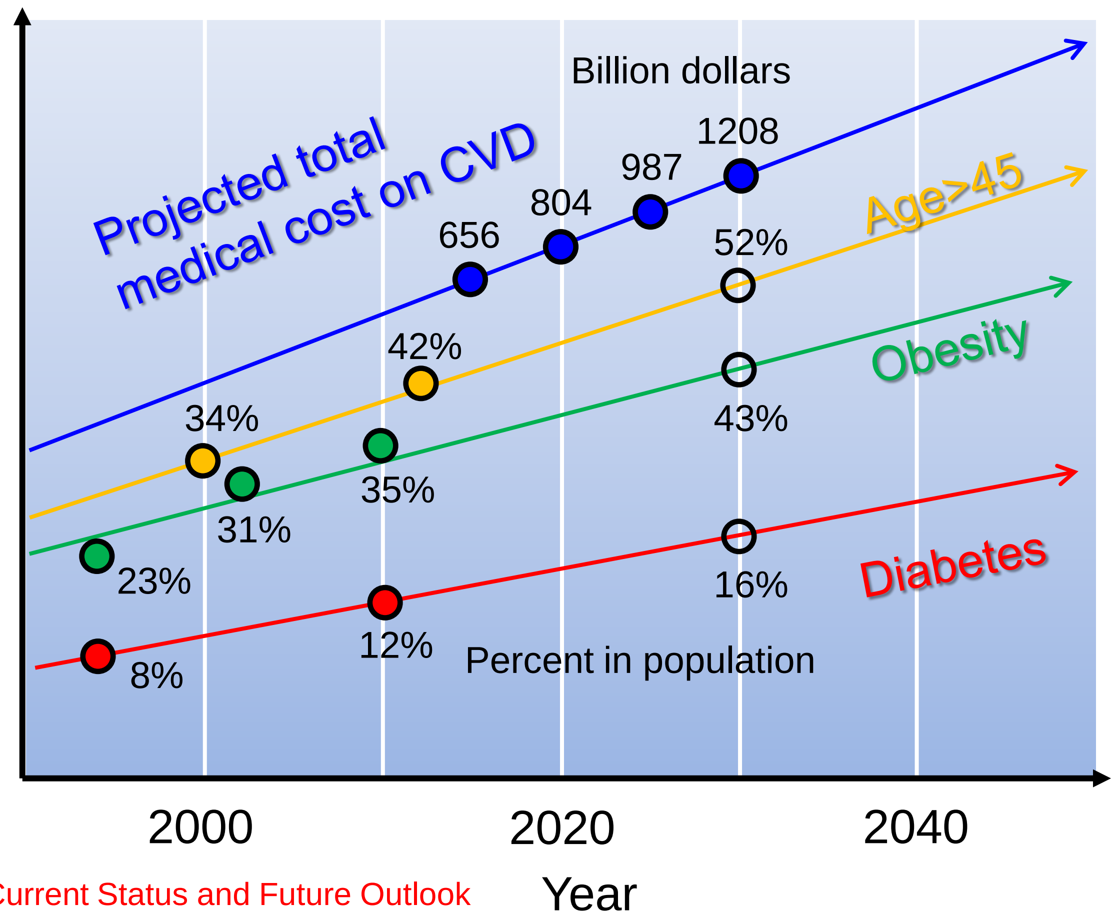
Trends in Heart Disease

- Cardiovascular Disease (CVD) is the leading cause of death in US
- Strong correlation with diabetes, obesity, and age.
- Cost of treatment ↑

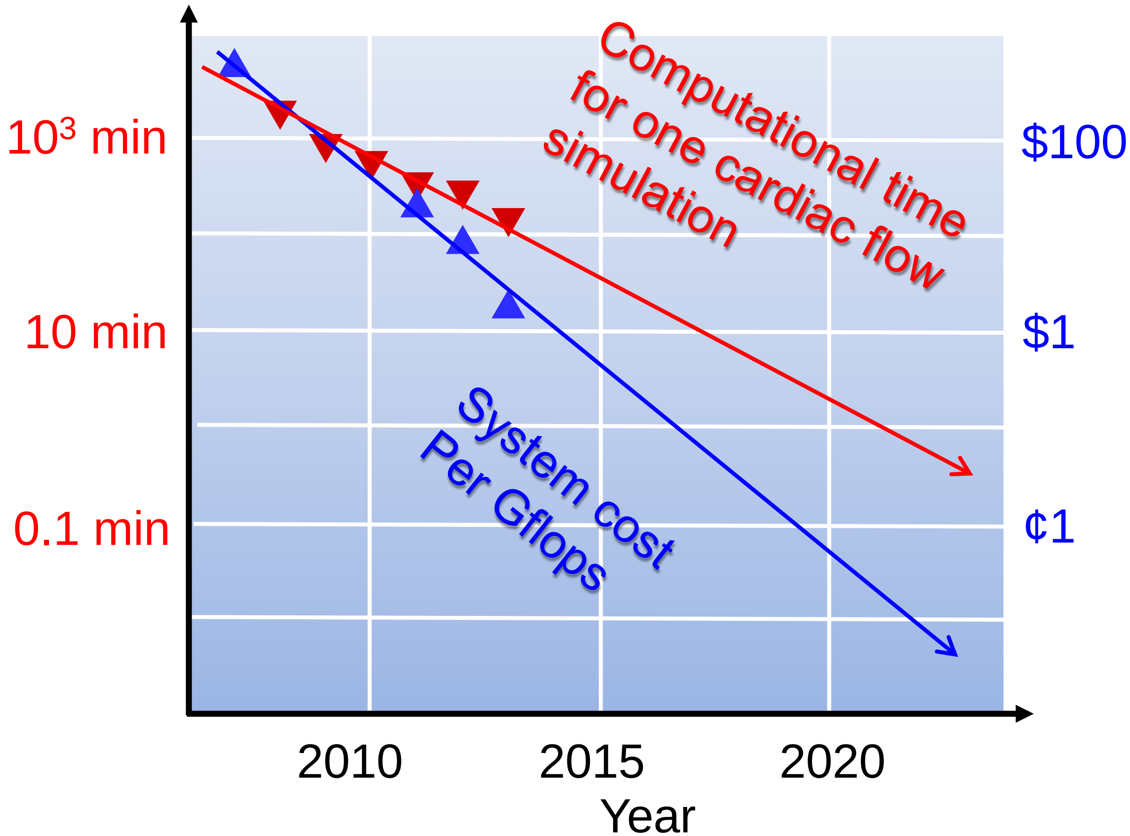
Needs to counteract these unfavorable trends with trends that are favorable



Computational modeling of Cardiac Hemodynamics:Current Status and Future Outlook
Journal of Computational Physics, Mittal et al. 2016

Favorable Trend: Moore's Law

- *Moore's Law: Performance of computer doubles in ~2 yr years*
- Cost of computing decreases with a similar rate



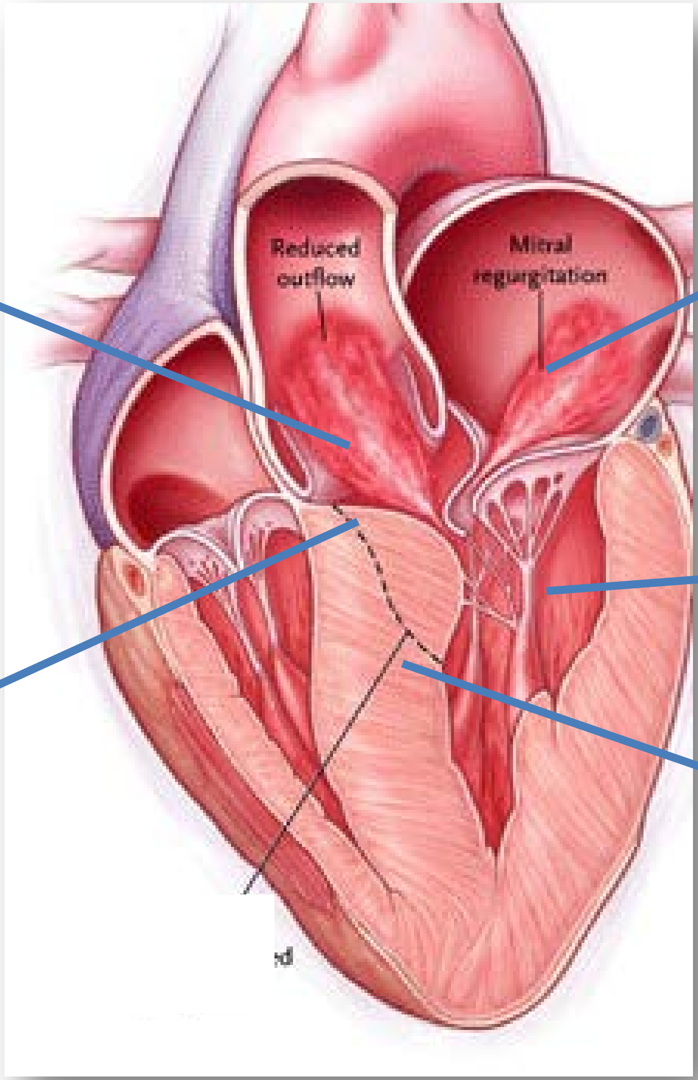
New therapies and diagnostic protocols that exploit computational modeling and simulation could lead to more effective treatments.

Computational modeling of Cardiac Hemodynamics: Current Status and Future Outlook *Journal of Computational Physics*, Mittal et al. 2016

Possible Contributions of Computational Modeling

Understanding the "Design" of the Heart

What can be included/excluded in computational models?



Improved diagnostic procedures

Design of prosthetic Devices (LVAD, valves etc)

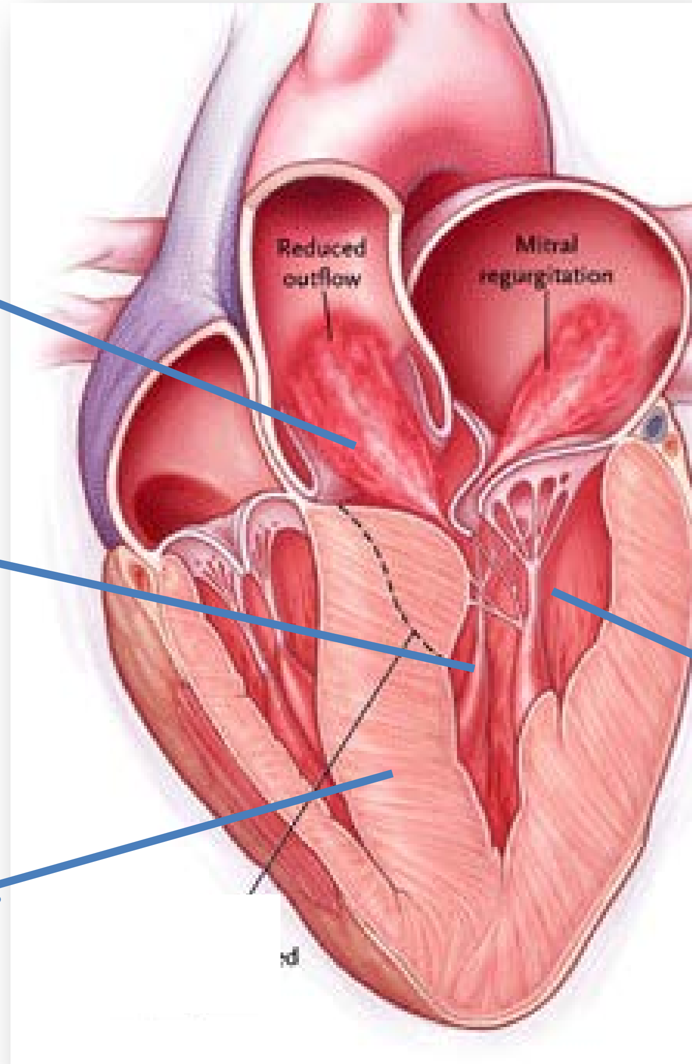
Improved Therapy & surgical planning

Cardiac Flows – Rich Substrate for Multiphysics Computational Modeling

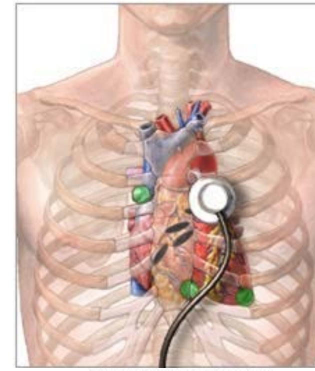
Fluid-Structure Interaction
Valve Dynamics

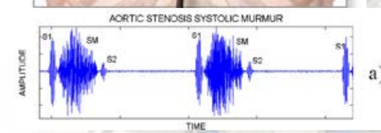
Transitional Flow
(Re~4000)

Electro-mechanics
Active Muscle Contraction
Wall deformation



Acoustics
Heart Sounds

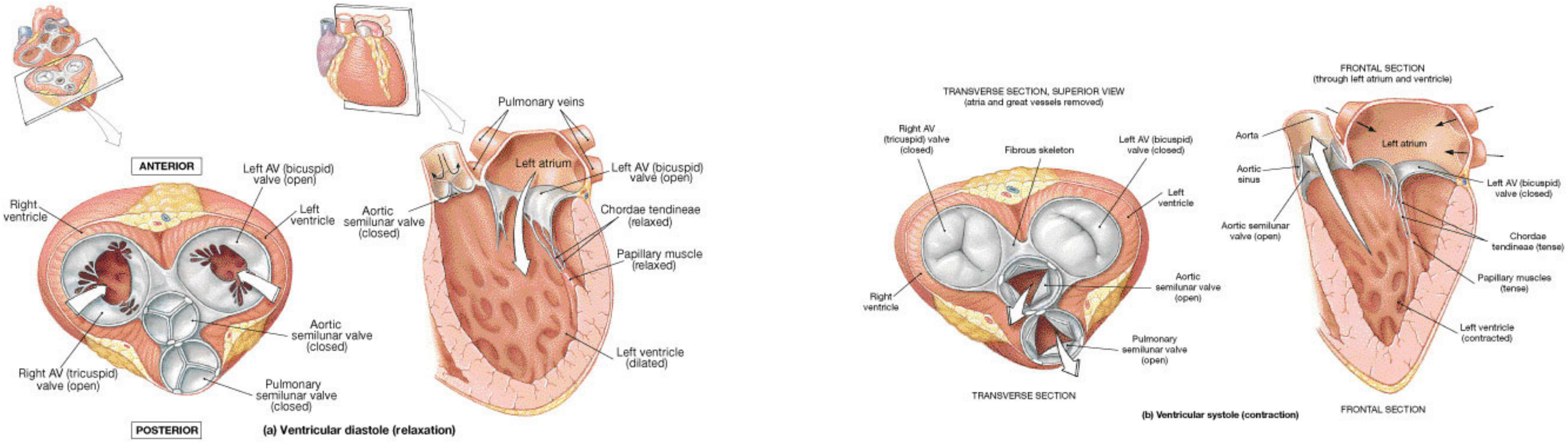




Biochemistry
Coagulation & Thrombogenesis

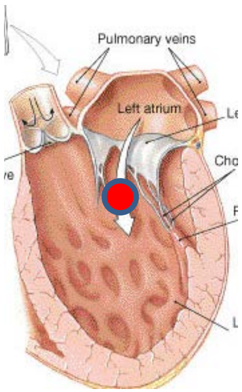
Fundamental Questions about the “Design” and Modeling of the Heart

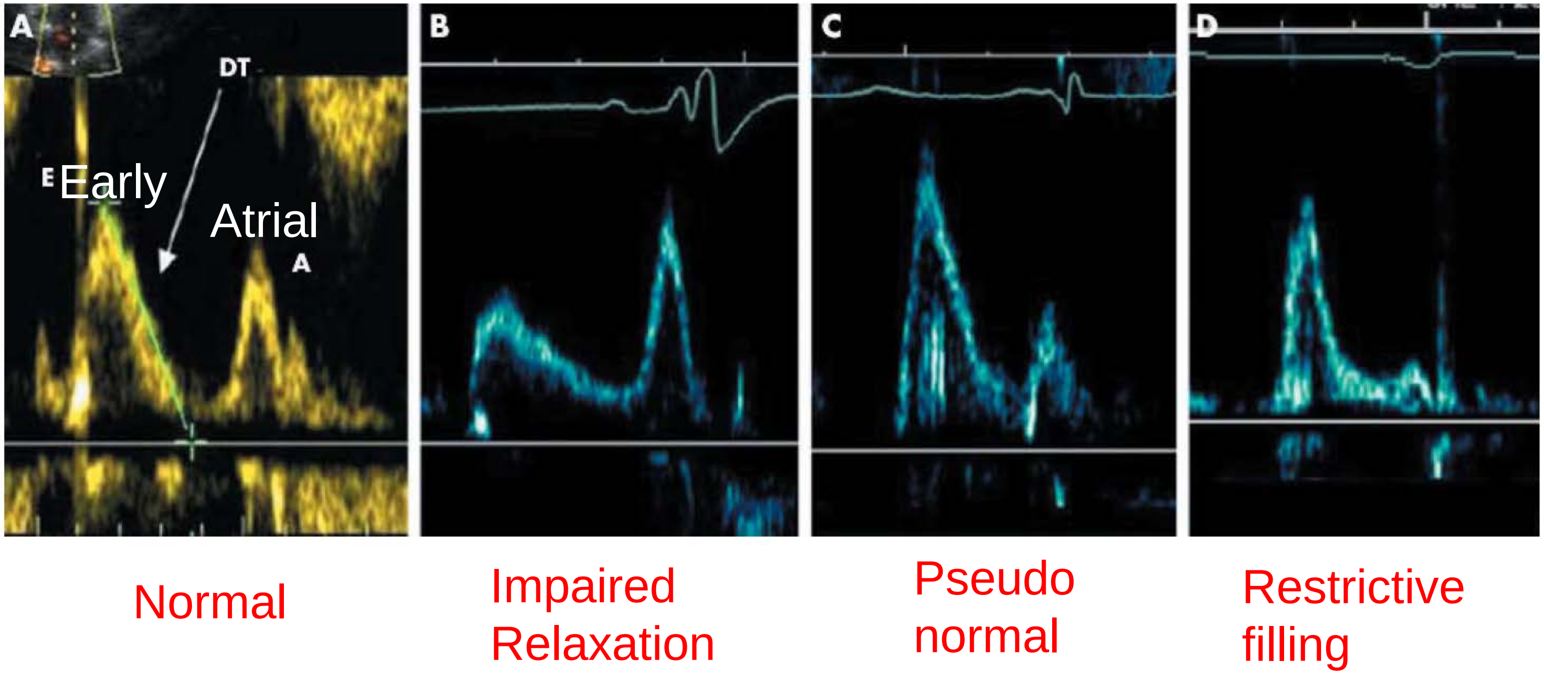
- Focus on the left side of the heart.



- What are the implications of the construction and operation (frequency, stroke volume, ejection fraction) of the heart on the hemodynamic function?
  - Hydrodynamic efficiency?
  - Mixing, shear stress, residence time?
- Are flow patterns merely driven by the heart or do flow patterns modify the function of the heart??
- How best to model the hemodynamics
  - What to include/exclude from the computational model?

Hemodynamic Implications of Bi-Phasic Diastole

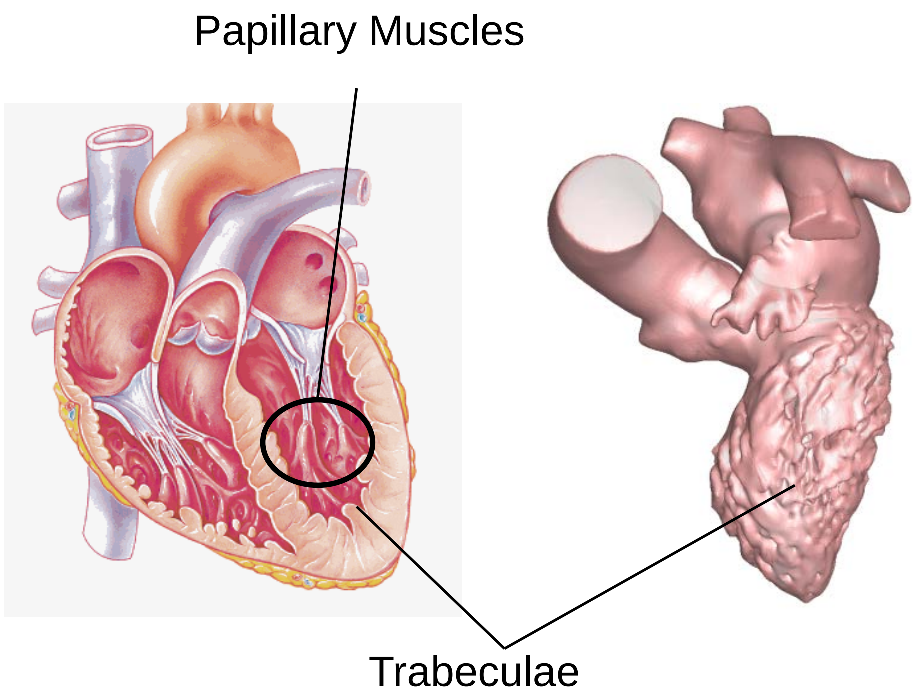




- Normal E/A ratio ~ 1.2 – 1.8
- Why bi-phasic? Reduces peak Reynolds number and turbulence!
- Does this E/A ratio have particular hemodynamic significance.

Why is the LV trabeculated?

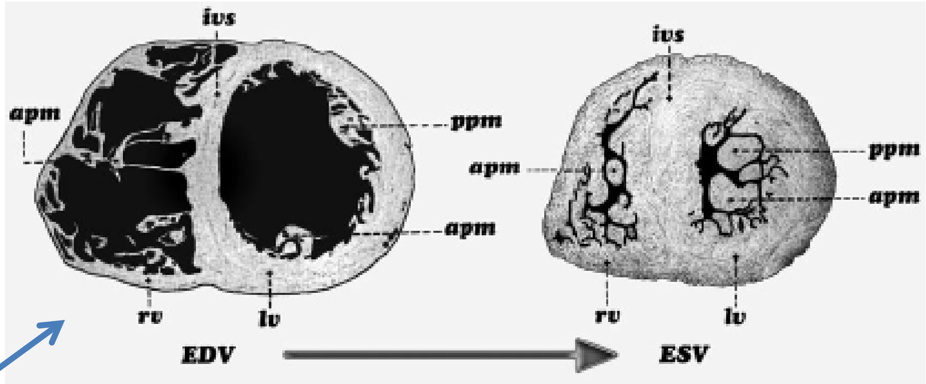
- Left ventricular endocardium is not smooth.
- Every other blood transporting vessel is smooth!!
- Surface trabeculae and papillary muscles protrude deep into ventricular cavity.
- Trabeculae
  - Helically spread on ventricular free wall
  - Account for 12-17% of LV by mass.
- Papillary muscles
  - Two large muscular bundles on endocardium
  - Connected to mitral valve via chordae tendinae
  - Ensure complete valve closure



Boyd et al., *JACC,* 1987, vol. 9(2)
Madu & D'Cruz, 1997, vol. 20(2)
Papavassiliu et al., *Radiol.*, 2005, vol.236 (1)
Jacqueir et al., *EHJ*, 2010, vol. 31

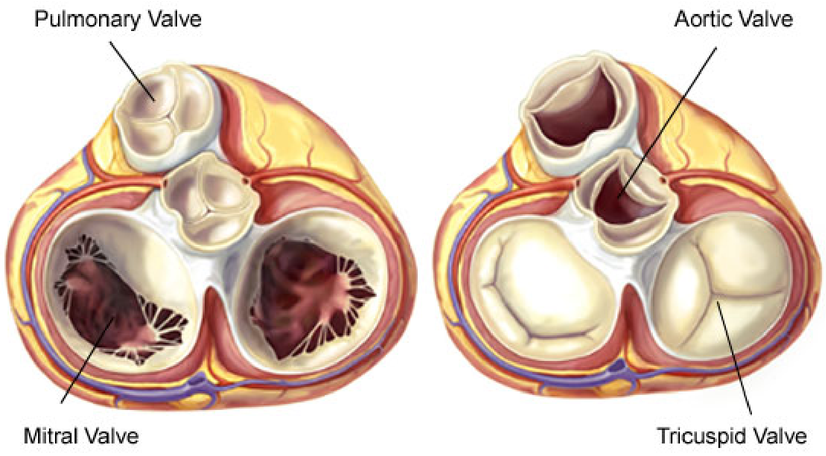
Implications

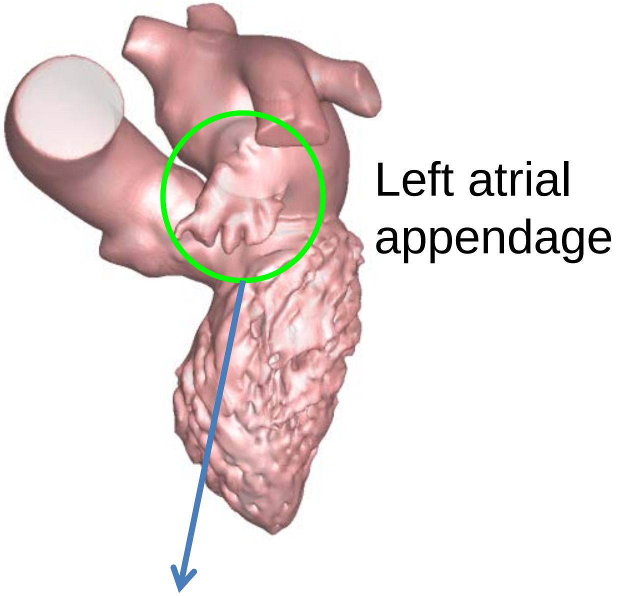
- Hemodynamic implications of trabeculae? Not fully understood!
- ‘Roughness’ promotes transition to turbulence and possibly increase pressure losses
- Interstitial spaces seem to increase the possibility of local flow stagnation.
- Pasipoularides (2010): trabeculae enhance the ability of LV to “squeeze” flow from apical region during systole

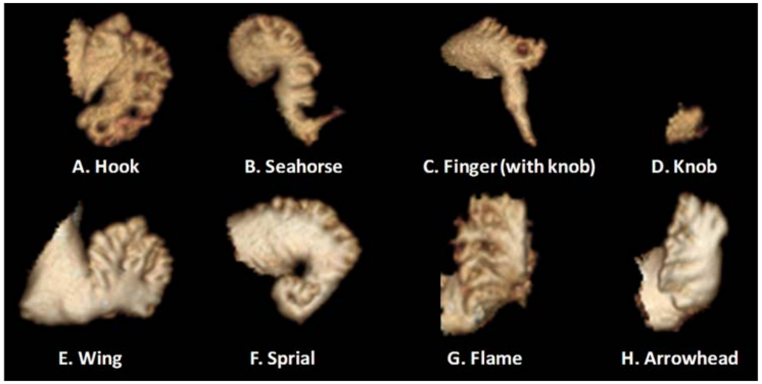


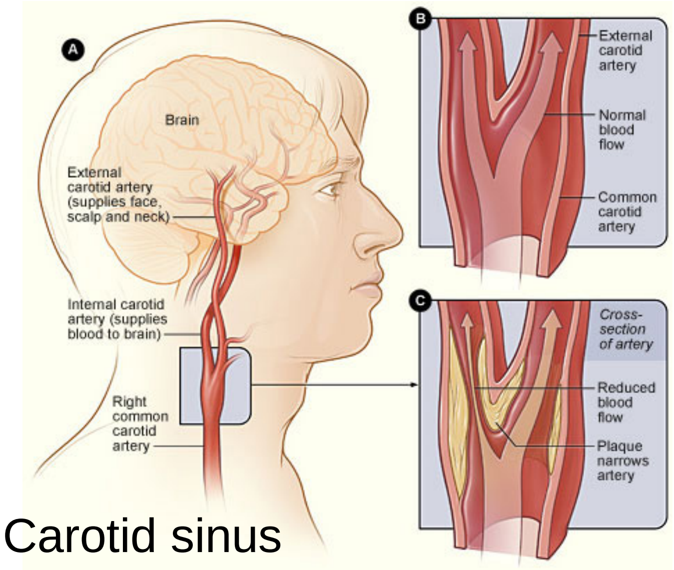
Heart’s Vortex, Pasipoularides, PMBH, Connecticut

Other Fundamental Questions……









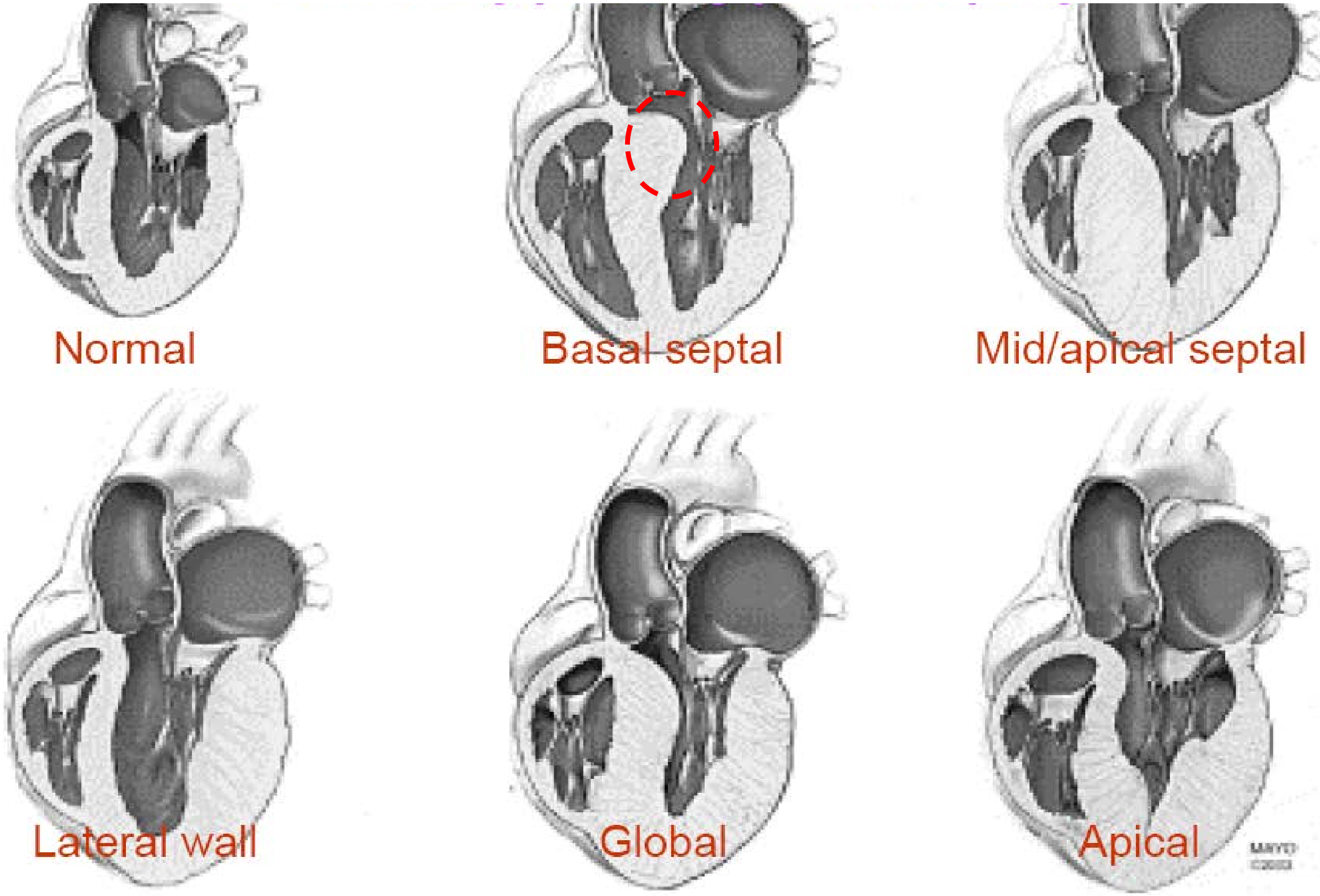
Opportunities for Modeling in Clinical Cardiology

- Modeling could enhance existing modalities.
  - Vast amount of data generated through imaging is not used.
  - Image-based modeling could add "value" to these modalities.

Modality	Spatial Resolution	Temporal Resolution	Risk	Expense
Echo	Low	High	Low	Low
CMR	High/Low	Low	Low	High
Cardiac CT	High	Low	Moderate	High

- Improved therapy
  - Improved analysis of disease condition could enable optimization of drug therapy.
  - Patient-specific modeling could help optimize surgical interventions.

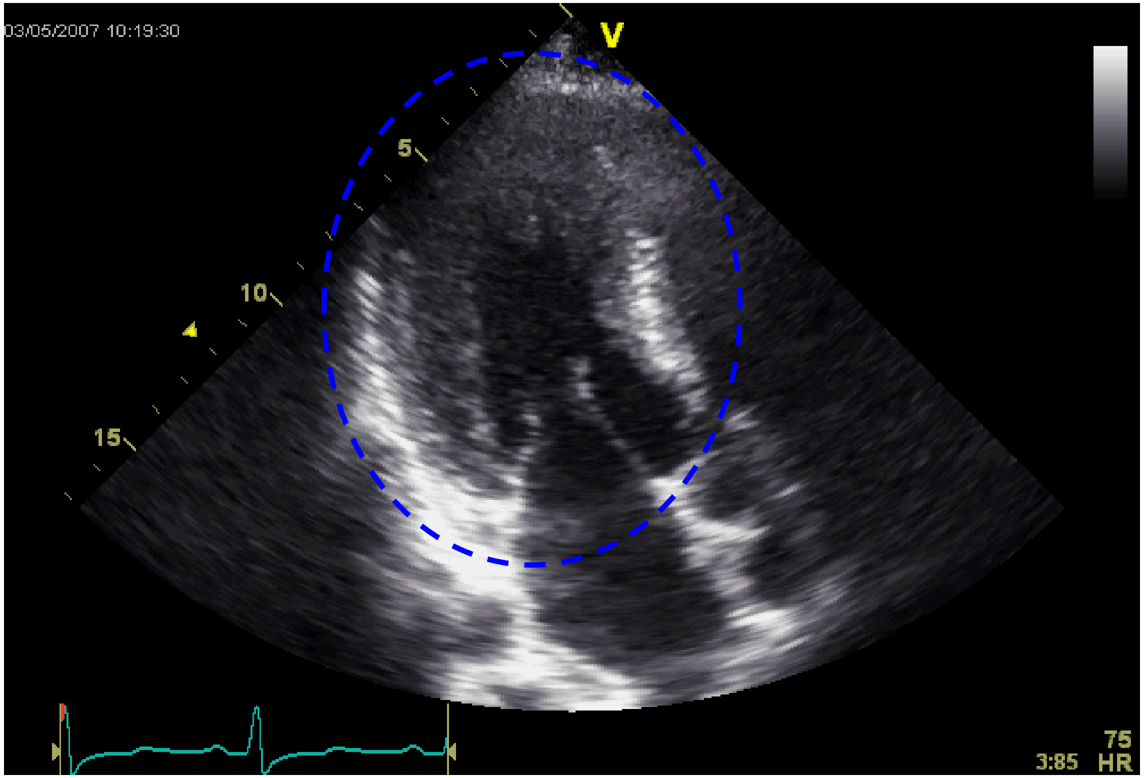
Hypertrophic Cardiomyopathy (HCM)

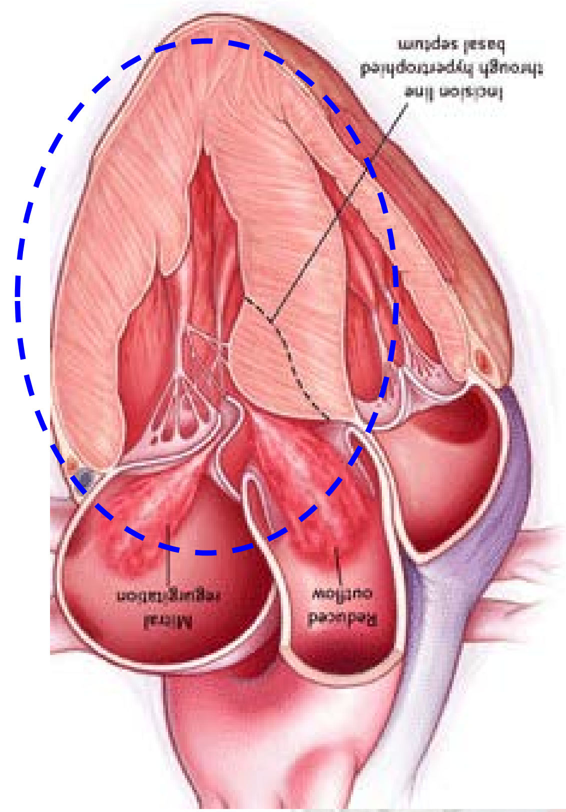


- **Most common inherited CVD (1:500 worldwide)**
- **Hopkins is a major center for HCM treatment**
- **200+ new patients each year.**

Source: Mayo Clinic

Hypertrophic Cardiomyopathy (HCM)





- Most common inherited CVD (1:500 worldwide)
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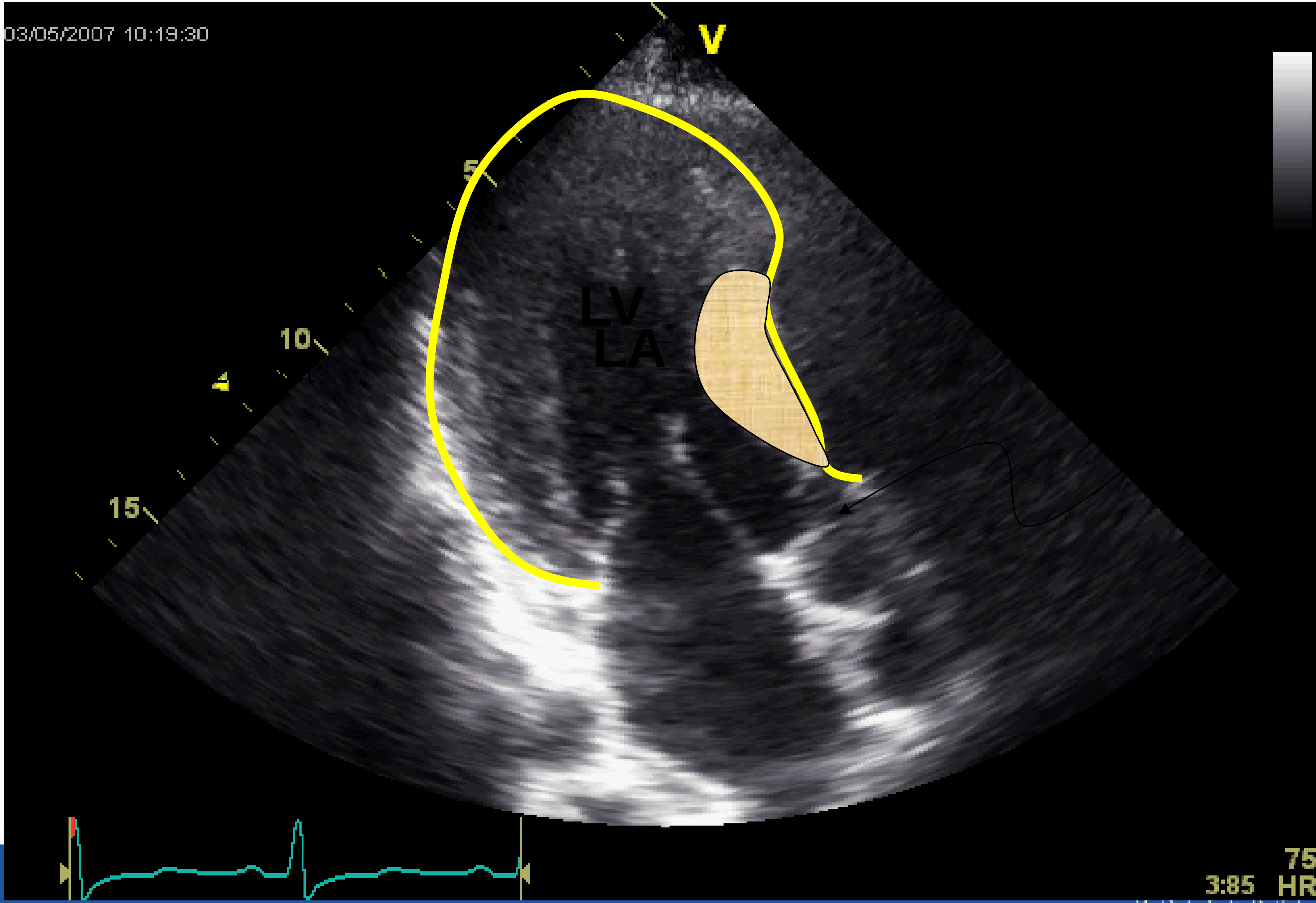
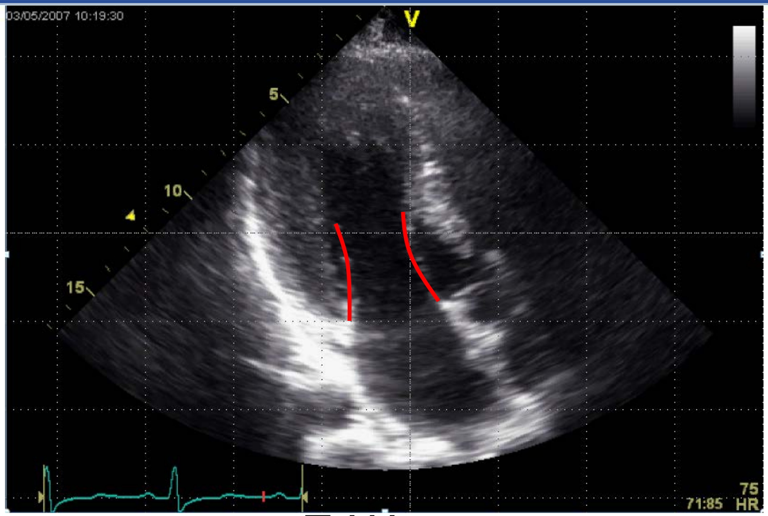
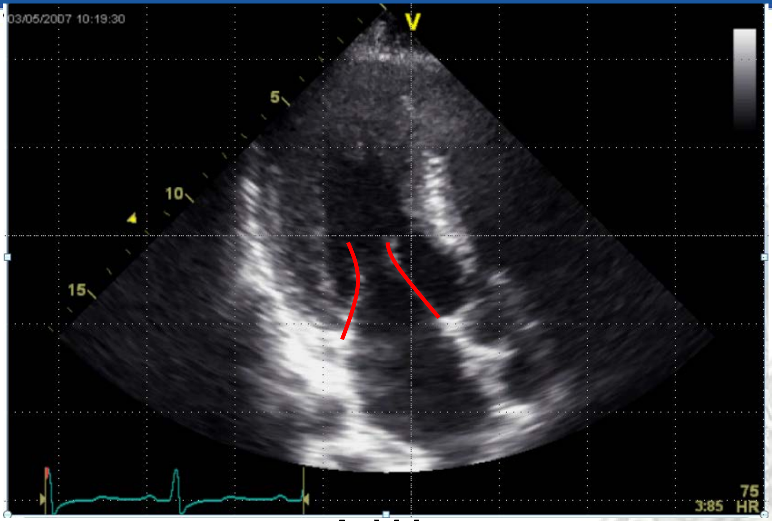
Cardiac Dynamics: Left Ventricle with HCM



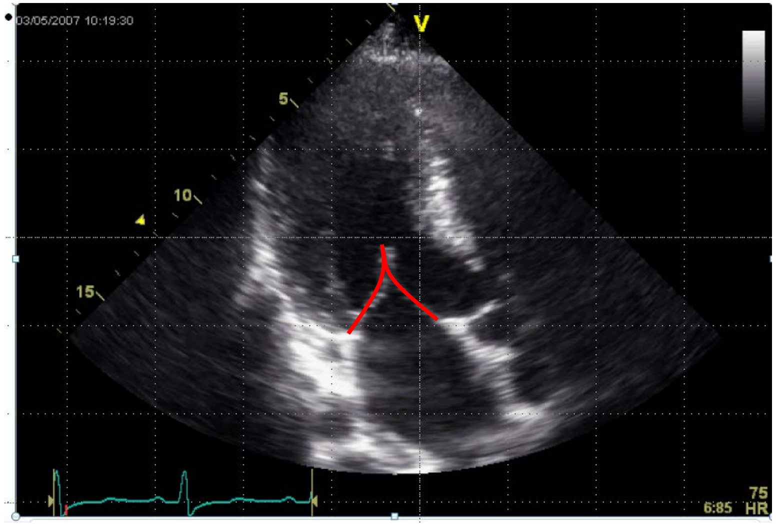
Systolic Anterior Motion (SAM) of Mitral Valve



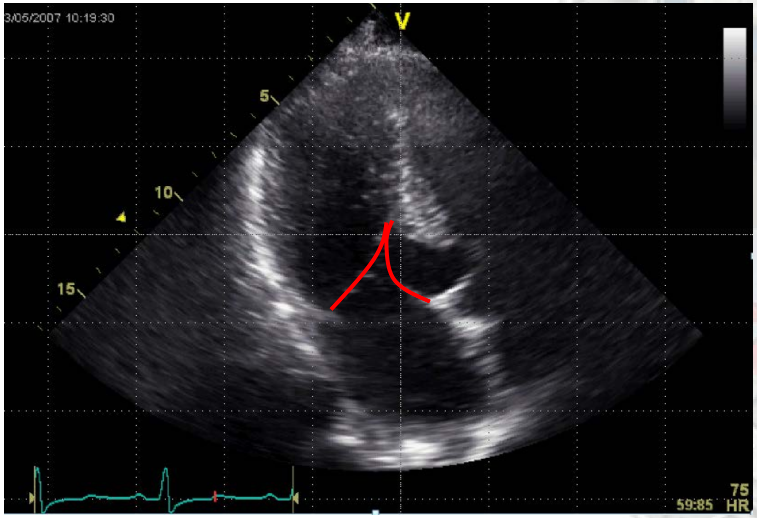
E-Wave



A-Wave



End Diastole



Mid Systole

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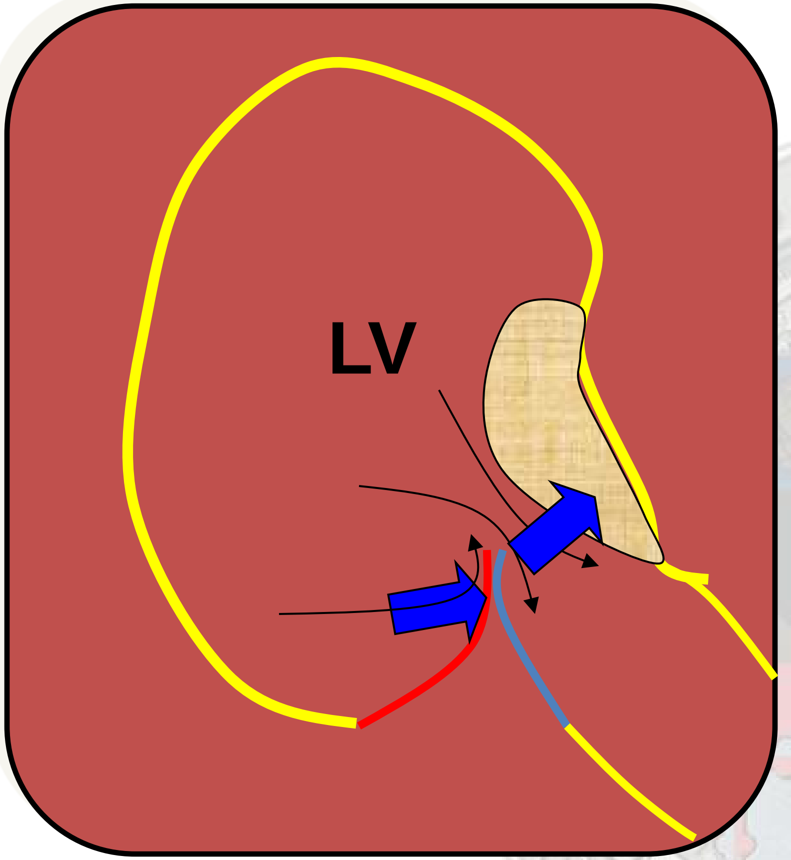
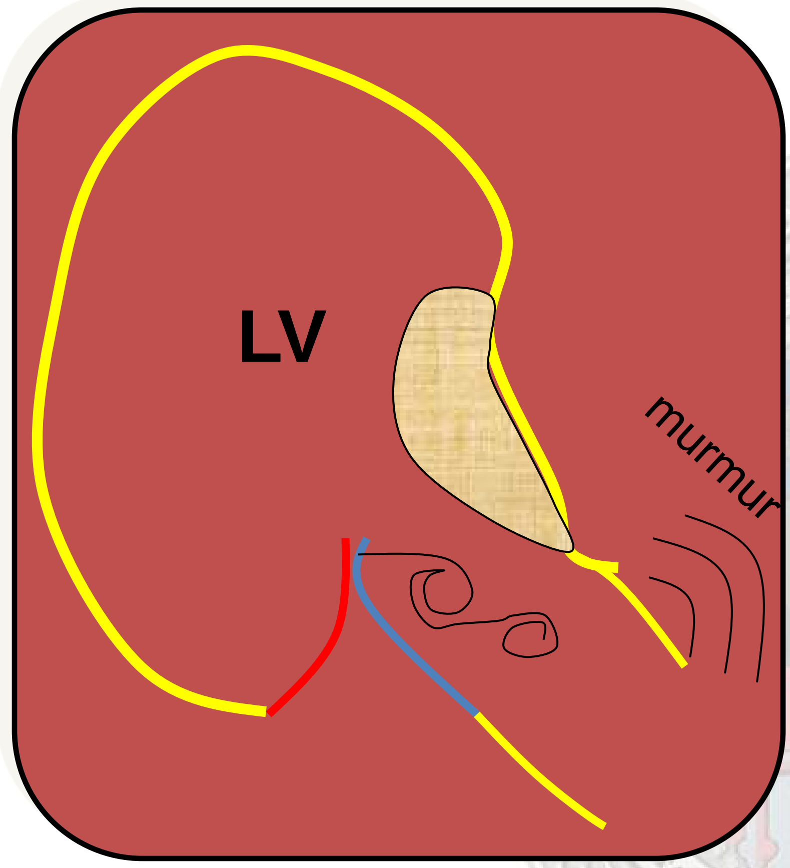
HCM: Implications & dynamics

- Obstructive HCM implicated in sudden cardiac death
  - Most common cause of death in young athletes
  - Hang Gathers, Reggie Lewis,…
- Pull or Push??
  - Venturi effect pulls the mitral leaflets towards aortic entrance?
  - "Drag" pushes the leaflet?



HCM: Diagnosis?

- Typically undetected until severe symptoms manifest
- Easily observed in a echo-cardiogram
- However echo-cardio is not part of routine checkup.
- Only chance of detecting HOCM in a routine exam is through auscultation
  - Causes a characteristic murmur
  - May be confused with aortic stenosis



Hemodynamics and Heart Sounds

- Auscultation -- 3000 year history for diagnosis of heart disease.
- Phonocardiography
  - Electronic stethoscope
  - Computer-based acoustic analysis
  - Variable specificity !
- Computational modeling of heart murmurs could provide clear link between cause-and-effect

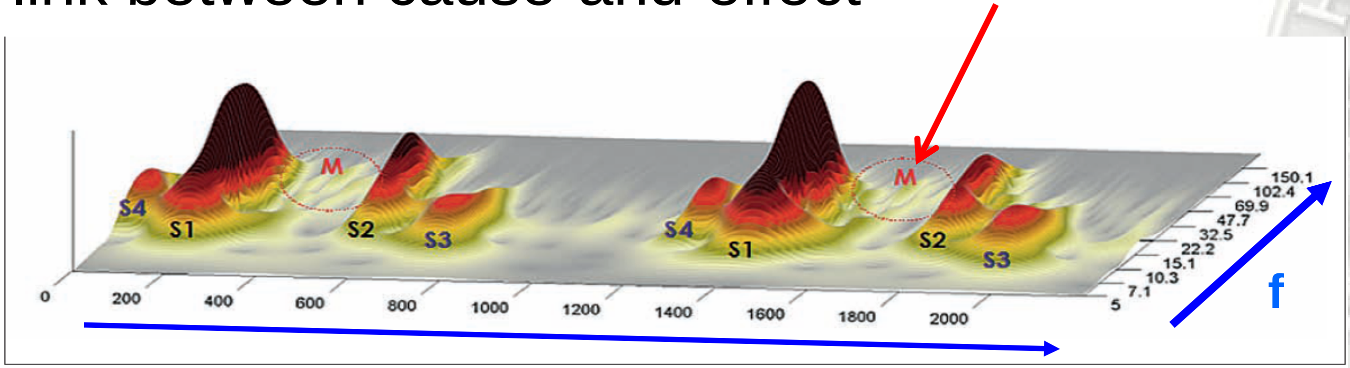
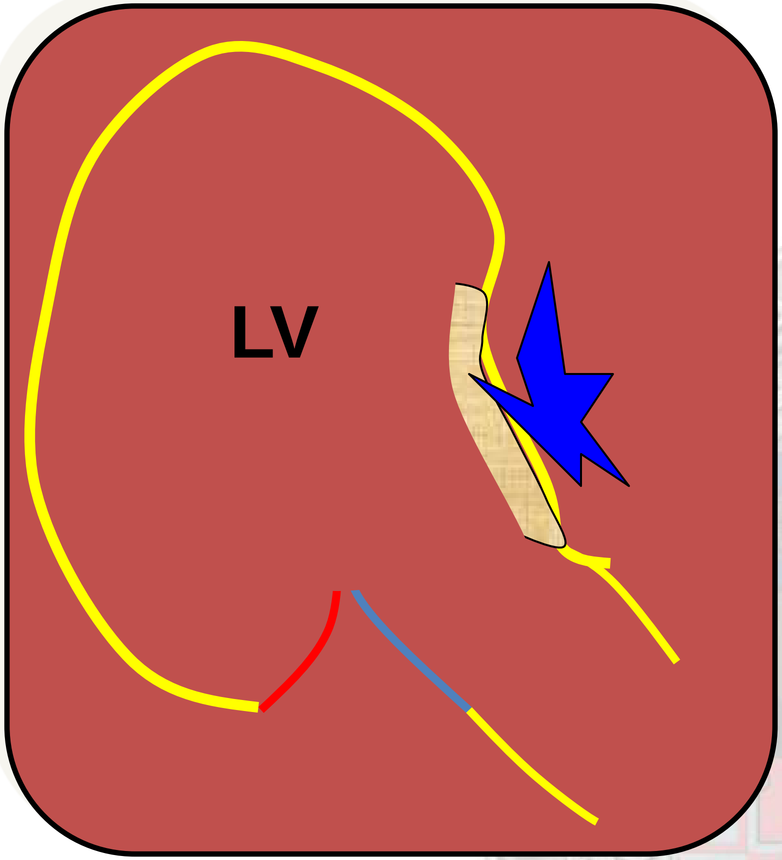


Figure 6

Acoustic cardiography report and time-frequency analysis of heart sounds for a subject with a systolic murmur.
The upper panel (a) shows an acoustic cardiography report for a subject with a systolic murmur and the panels below (b) illustrate the 2D and 3D scalogram views for a few beats from the acoustic cardiography rhythm strip shown above. Since murmurs have higher frequency components than diastolic heart sounds, they do not have to be high in intensity to be detected by the human ear. Thus in this case, it will be easier for the human ear to detect the murmur than the low frequency third and fourth heart sound.

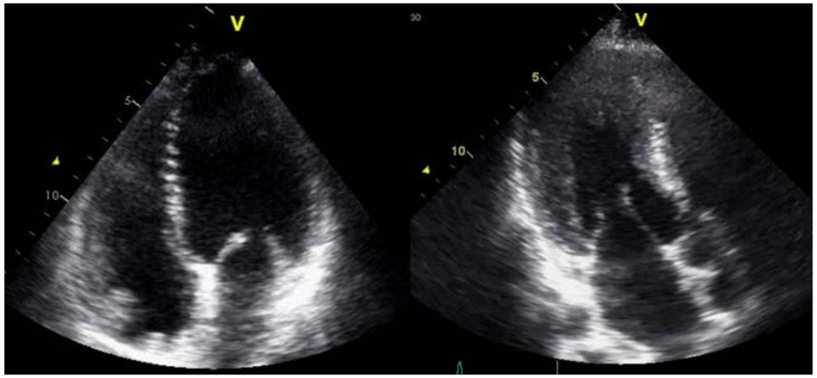
HCM: Surgical Management?

- Surgical septal myectomy
- Alcohol septal ablation
  - Induced a controlled heart attack to cause infarction hypertrophic region.
- Leaflet Plication
  - Reduce the mitral leaflet length
- Each of these approaches have risks & uncertainties
  - Too much or too little?
- Could computational modeling be used for surgical planning?

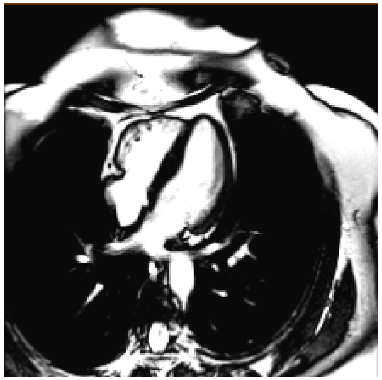


Patient Specific Modeling

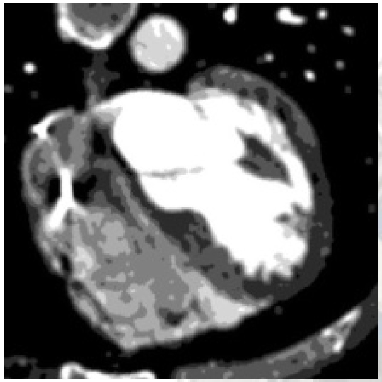
- Tremendous challenge for computational modeling
- Full electro-mechano-fluidic models require information about the organ that is not usually available for patients.



(a) Echo



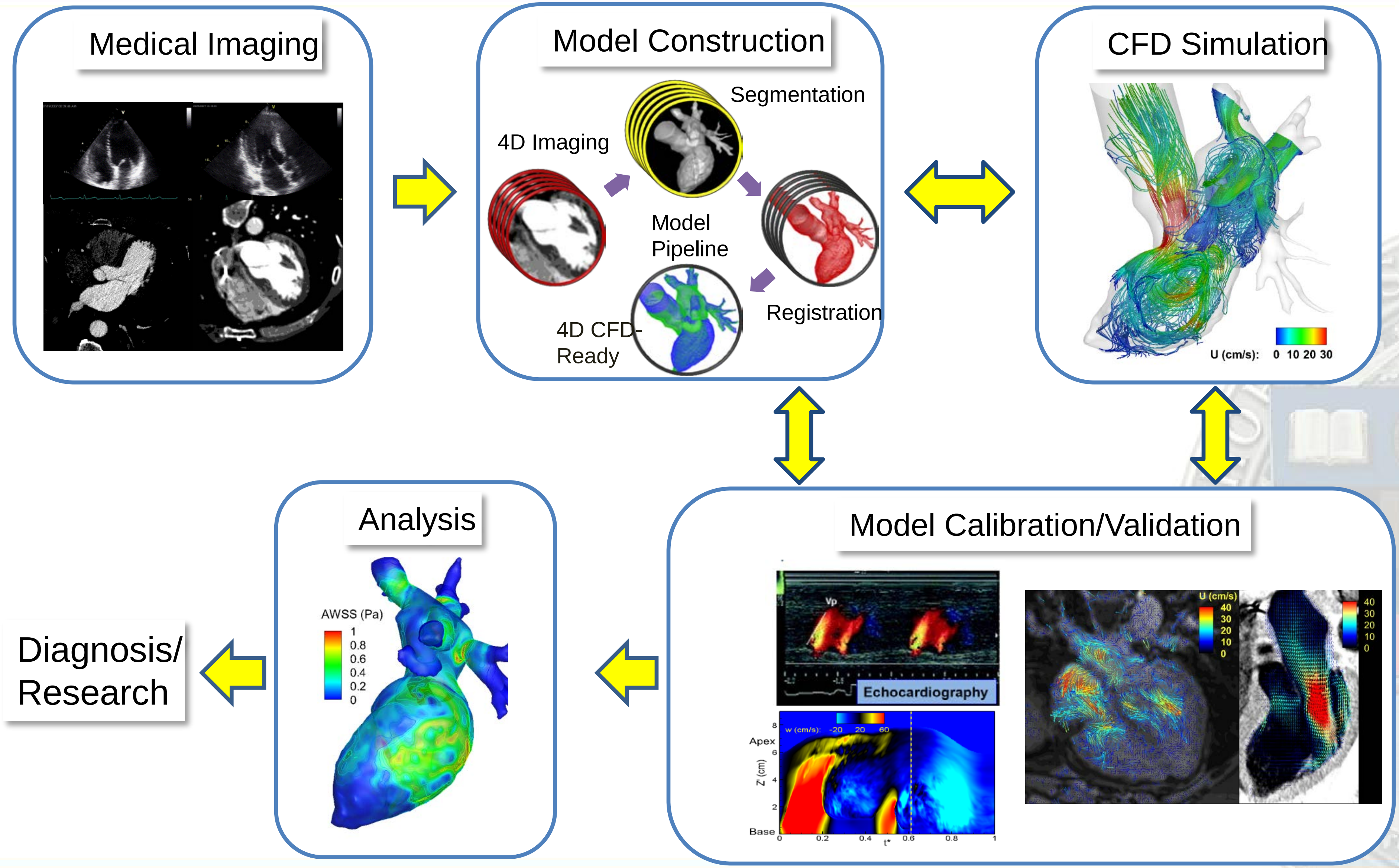
(b) 4D MR



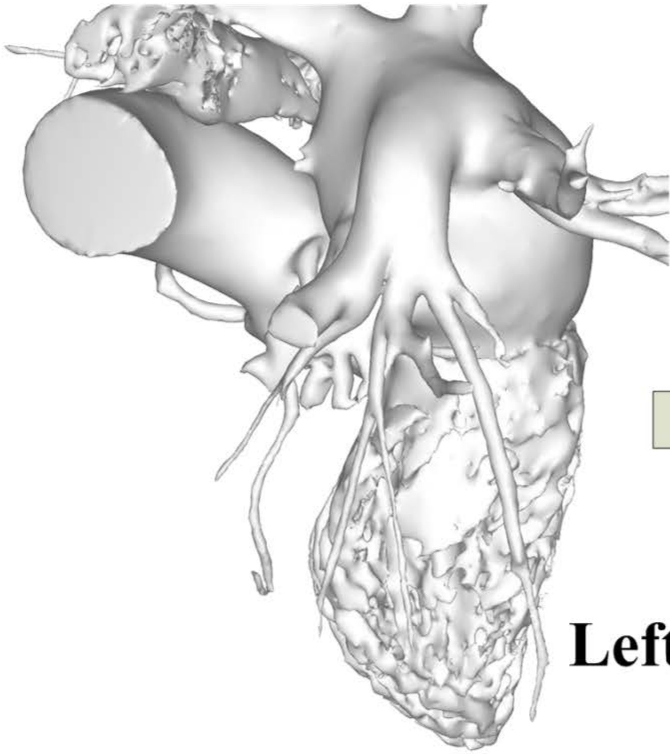
(c) 4D CT

- Resolution limits of Imaging (Echo, CMR, CT) result in “gappy” incomplete data that requires tremendous human effort to segment.
  - 20-100 hrs of human effort per model is not unreasonable.
- Boundary conditions might not be available.

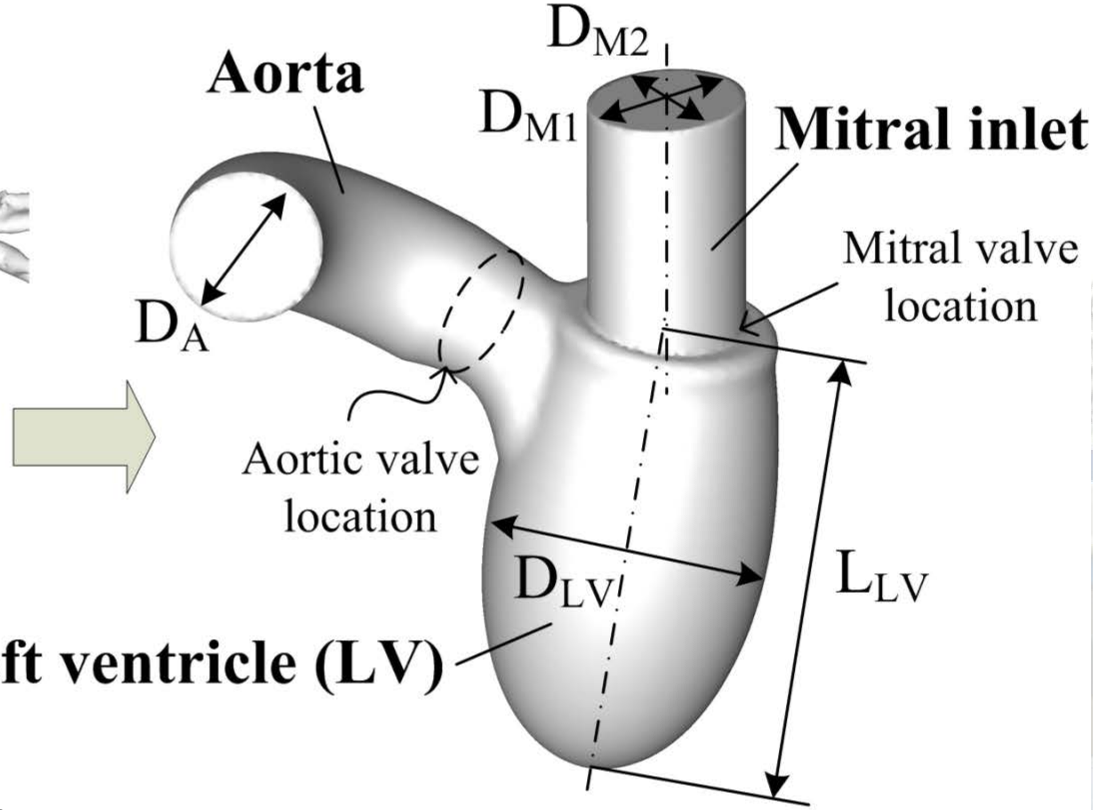
Computational Framework



What to Include/Exclude?

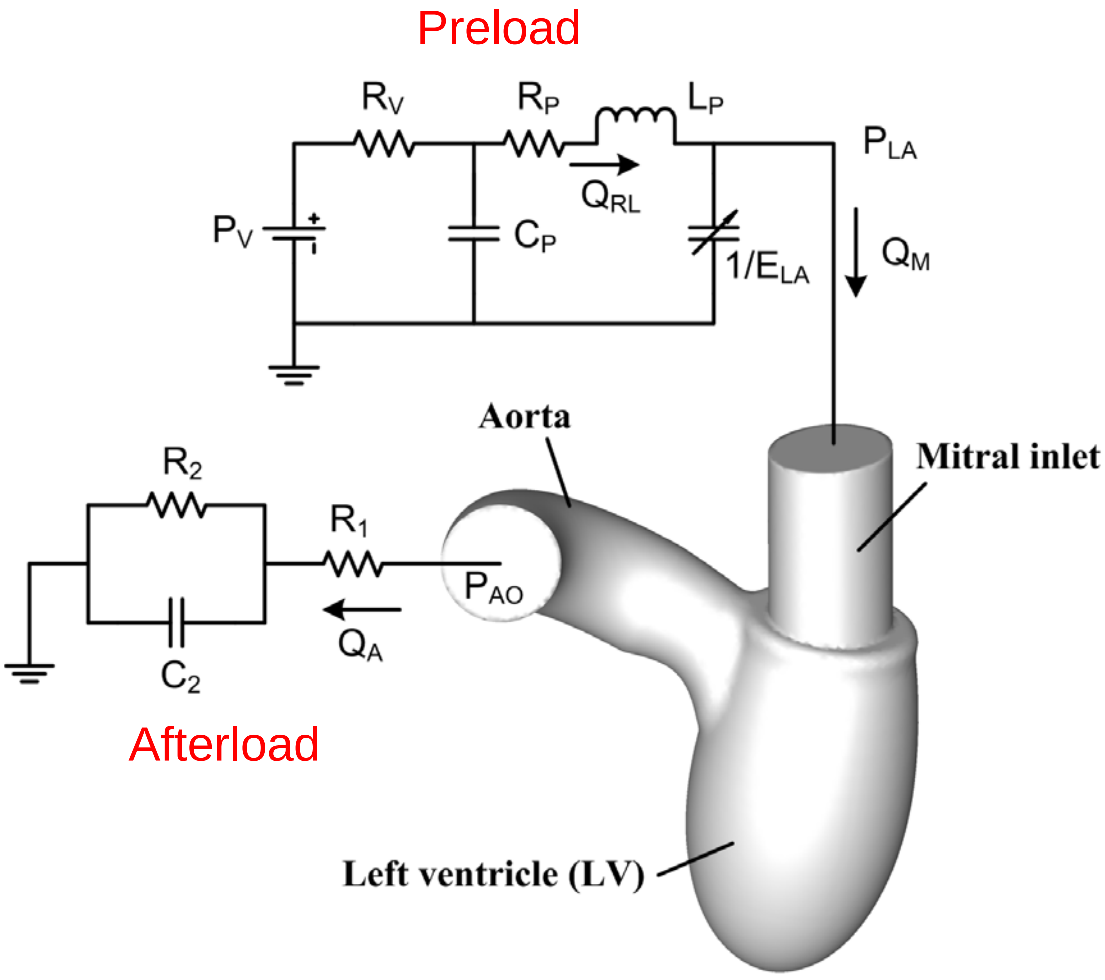


3D model constructed from the contrast CT-scan data



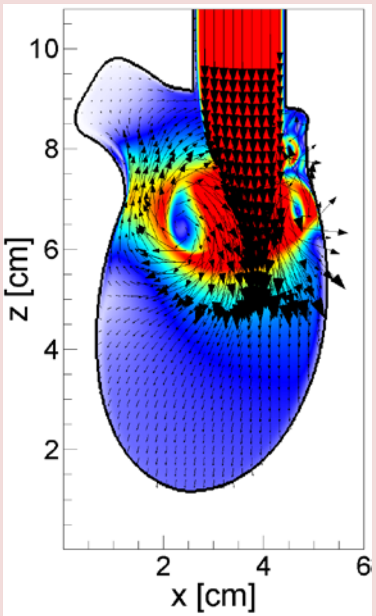
Simplified model for the computational analysis

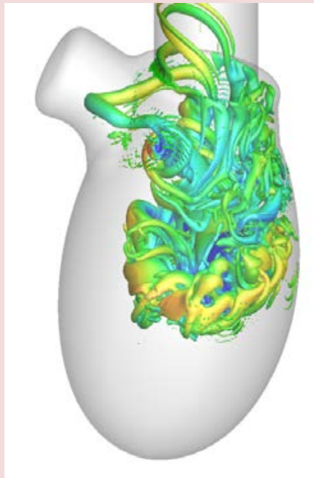
Boundary Conditions?

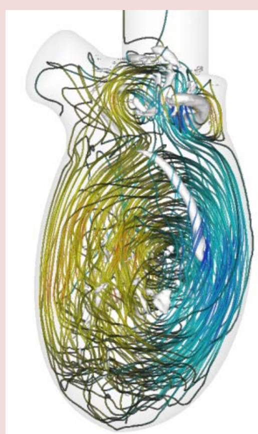


Validation against Clinical Data?

Engineering Data







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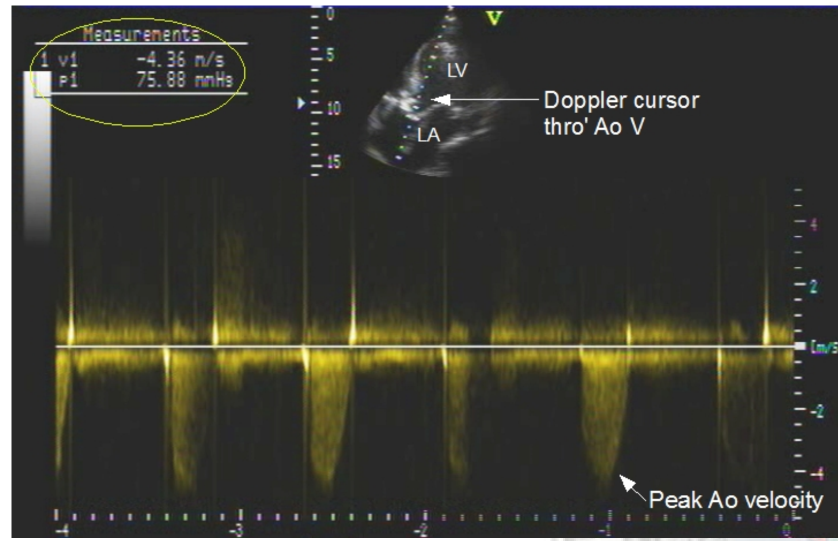
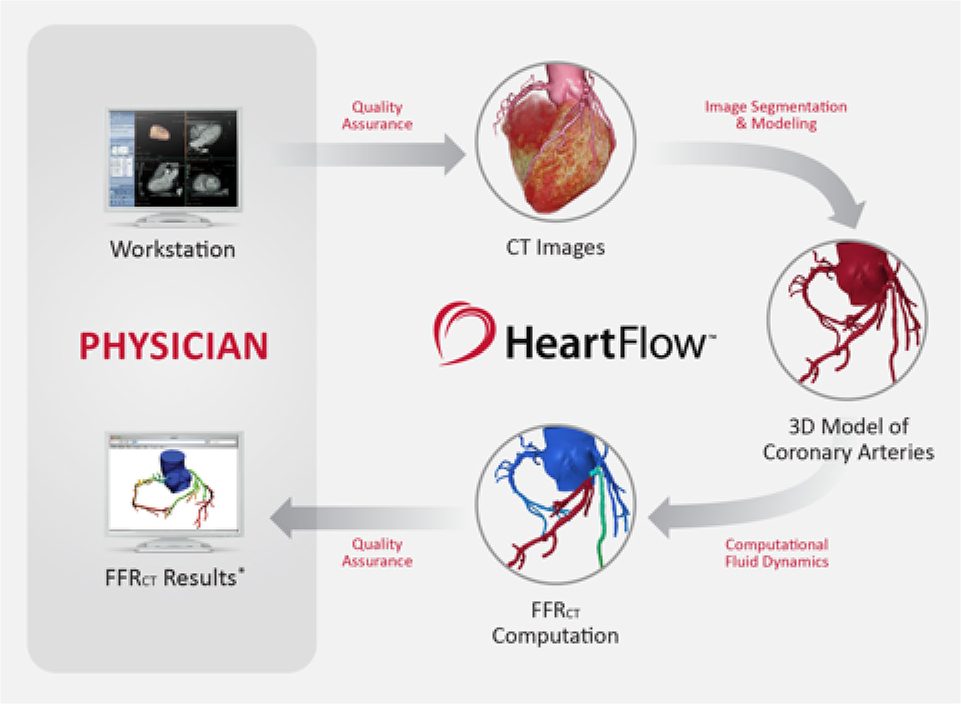
Clinical Data

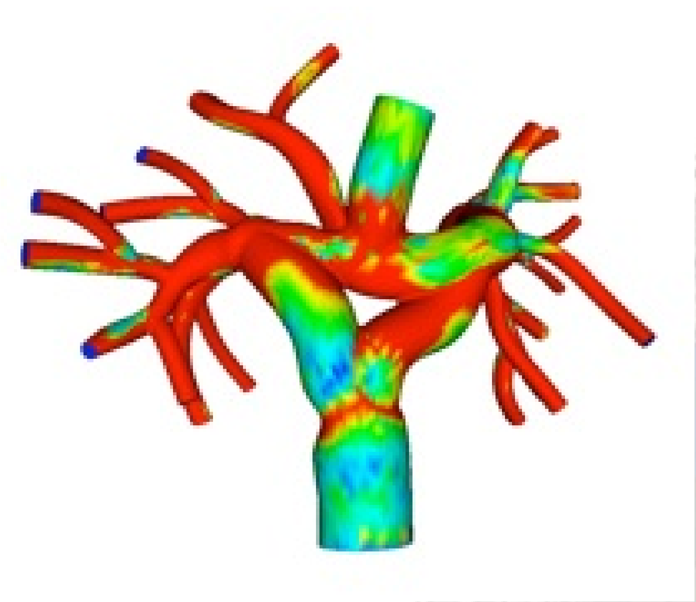


Doppler Echocardiography

CFD Success Stories in Cardiology



CFD Based Assessment of CAD
CFD Based Planning of PCI
Multicenter trial recently concluded
>$150 million in venture capital
HeartFlow Inc.



Optimization of Novel
Y-Graft for Fontan
Clinical Trial is Underway
Alison Marsden, UCSD
Jeffrey Feinstein, Stanford

Computational Speed → Applications

Clinical Application

Research Tool in Cardiology and Cardiac Surgery

Surgical Planning: Valve Repair, Prosthetic Valve Implantation, HOCM, CRT, Congenial Heart Disease, etc.

Rapid Intervention: Myocardial Infarction, Heart Failure, Pediatric Heart Disease, etc.

Computational Speed

1 TFLOPS

10 TFLOPS

100 TFLOPS

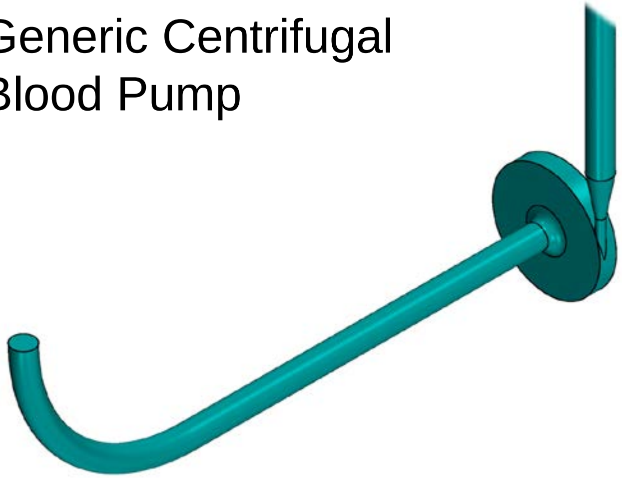
Current Status

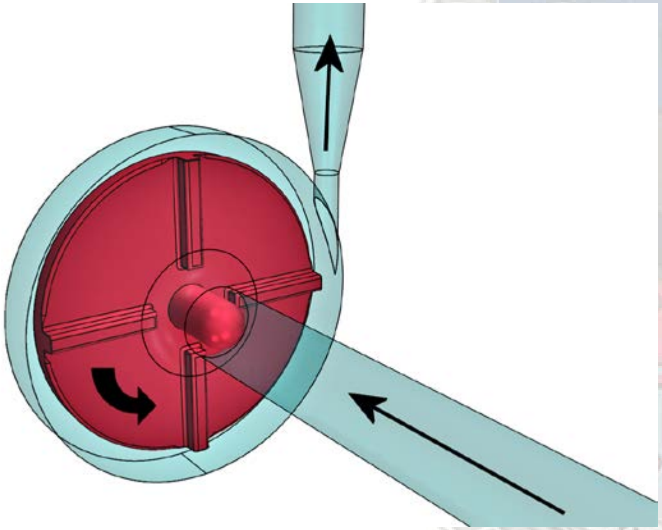
US FDA CFD Challenge

GOALS

- Accelerate the safety assessment of medical devices in the preclinical stage,
- Particular attention paid to blood damage, and
- Standardize CFD techniques for such use.

Generic Centrifugal Blood Pump





OUTPUTS FOR COMPARISON

- pump performance data (e.g., HQ curves, pump efficiencies)
- Velocities, pressures, shear stresses, and eddy viscosities along planes and surfaces
- Compare hemolysis indices
- Inlet and outlet pressures, shaft torque,

Conclusion from recent workshop: CFD is unreliable!!

Cited Paper - Relevant Papers

- Rajat Mittal, Jung Hee Seo, Vijay Vedula, Young J. Choi, Hang Liu, H. Howie Huang, Saurabh Jain, Laurent Younes, Theodore Abraham, and Richard T. George. "Computational modeling of cardiac hemodynamics: Current status and future outlook." *Journal of Computational Physics*, Volume 305, 2016.

- FDA CFD Validation Challenge-- https://fdacfd.nci.nih.gov/