

## **Image-Based Computational Modeling for Cardiovascular Diseases with Potential Clinical Applications**

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### **Summary**

Image-based computational models for blood flow in the heart and diseased arteries have been developed for disease assessment and potential clinical applications. Models with fluid-structure interactions for human right ventricle (RV) remodeling surgery design, carotid and coronary atherosclerotic plaques and abdominal aortic aneurysm (AAA) were presented. Organ morphology, material properties, governing equations, proper initial and boundary conditions, controlling factors and research focuses for each model were discussed.

### **Introduction**

Advanced computational modeling techniques have been developed to model blood flow in the heart and arteries leading to many important findings in recent years [1-3]. Imaging technologies (MRI, CT, ultrasound, etc.) have been used to obtain organ morphologies and some flow quantities *in vivo* non-invasively with reasonable resolutions. Image-based patient-specific modeling aiming to provide information and guidance for surgery and clinical applications is emerging, subject to many limitations from availability of data and computational power [3-4]. Aided with more quantitative analysis and disease state assessment, better surgical procedures, preventive and medical treatment of cardiovascular diseases are possible. In this short paper, we try to provide some of our current model developments related to cardiovascular diseases assessment, key elements and limitations in the modeling process, and future efforts.

### **Models and key controlling factors for cardiovascular diseases**

Image-based patient-specific modeling process consists of the following major steps: data acquisition – modeling – validation – clinical trials – production. Earlier models are mostly rigid-walled flow models quantifying some flow characteristics related to disease initiation and progression. However, biological organs such as the heart and arteries are compliant and their models really should consist of three basic parts: fluid model, solid model, and proper fluid-solid coupling and initial boundary conditions. The importance of introducing compliant models with fluid-structure

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interactions (FSI) has been gradually recognized in recent years [1,3-4]. Patient data needed for FSI models can be classified into three groups which are also the key controlling factors of solution behaviors: organ morphology, tissue material properties, and flow velocity and pressure boundary conditions. When models are solved, careful analysis needs to be performed to identify critical indicators and biological markers which can be used for diagnosis, disease assessment and optimal medical treatment.

### Image-Based FSI model for human right ventricle remodeling surgery

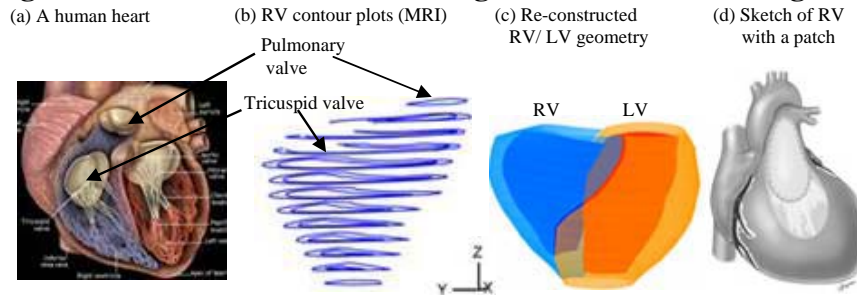


Figure 1: Model construction for human right ventricle remodeling surgery design.

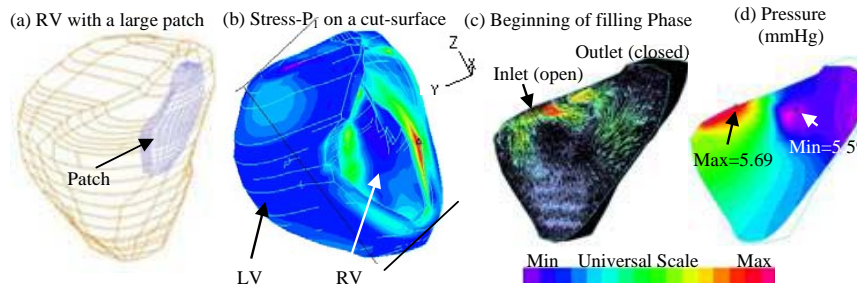


Figure 2: The RV patch model, maximum principal stress (Stress- $P_1$ ), flow velocity and pressure.

Computational simulations could be used to simulate blood flow and evaluate ventricle cardiac functions. This can replace empirical and often risky clinical experimentation to examine the efficiency and suitability of various reconstructive procedures in diseased hearts so that optimal surgical procedure could be found. Patient-specific RV/LV morphologies were acquired using cardiac MRI (see Fig. 1). The ventricle tissue was assumed to be hyperelastic, isotropic, nearly-incompressible and homogeneous. The left ventricle (LV) was included in the RV/LV combination model so that the RV structure could be set in a more realistic supporting environment. Various patch designs were put on the RV to assess their effects on RV cardiac functions based on computational simulations. The non-linear modified Mooney-Rivlin model was used to describe the material properties

of the muscle with parameters chosen to match experimental data available in the literature [1,3]. Blood flow was assumed to be laminar, Newtonian, viscous and incompressible. The Navier-Stokes equations with ALE formulation were used as the governing equations. Pressure conditions were prescribed at the inlet (tricuspid valve) and outlet (pulmonary valve). No-slip boundary conditions and natural force boundary conditions were specified at all interfaces. The structure-only (LV) and FSI (RV) models were solved using a commercial finite element package ADINA (ADINA R & D, Watertown, MA, USA). Fig. 2 gives an illustration of results obtained from our model.

One key issue to make computational modeling useful is to choose proper indices which can be used for clinical application purpose. The main function of the heart is to provide blood to the body. Two measures of RV functions are RV stroke volume (SV= RV end diastolic volume - RV end systolic volume) and ejection fractions (EF =SV/ RV end diastolic volume). Simulations were conducted for 5 cases: (1), the baseline model without patch; (2), RV with scar tissue and old patch as shown by Fig. 1(d) (illustrative); (3), RV with a new patch (Fig. 2(a)); (4), RV with a smaller patch; (5), RV with a softer patch. Ejection fractions and EF recovery rates are compared in Table 1 which shows the predicting power and potential of our approach.

Table 1: RV ejection fraction and recovery comparisons for 5 cases simulated.

Cases considered:	Case 1	Case 2	Case 3	Case 4	Case 5
	Normal Tissue	Scar+old Patch	New Patch	Small Patch	Soft Patch
Ejection Fraction (%)	52.7	44.9	47.7	48.6	50.5
<b>EF Recovery</b>	<b>100%</b>	<b>0%</b>	<b>35%</b>	<b>49%</b>	<b>72%</b>
Stroke volume (ml)	39.7	28.5	32.2	33.5	36.4
<b>SV Recovery</b>	<b>100%</b>	<b>0%</b>	<b>31%</b>	<b>45%</b>	<b>71%</b>

### MRI-based models for carotid plaque progression and rupture

Cardiovascular diseases (CVD) are often related to atherosclerotic plaques which may rupture without warning and leading to serious clinical events such as stroke and heart attack. *In vivo* MRI images of human carotid atherosclerotic plaques were provided by Dr. Yuan and his group with informed consent obtained (Fig.3). 3D geometry reconstruction and mesh generation were done using ADINA. The *in vivo* geometry obtained from MRI data was shrunk by 10% to get the zero-stress geometry for our model so that the actual *in vivo* shape could be recovered when initial axial pre-stretch (10%) and pressurization were applied. The 10% shrink rate was determined numerically so that the lumen geometry from the FSI model would have a best match with MRI lumen dimensions. The modeling process, FSI model, and solution procedures can be found in [3-5] with material parameter values chosen to match experimental data for arteries. Figures 3-4 illustrate the modeling process and some solution features.

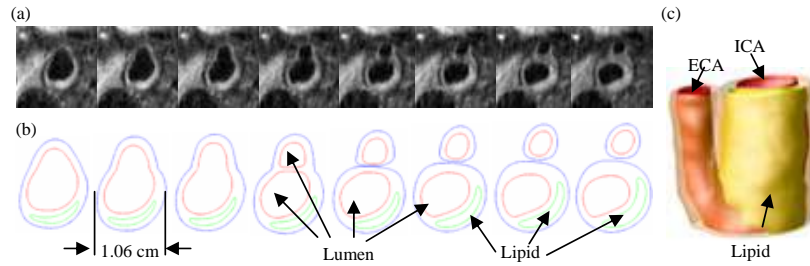


Figure 3: *In vivo* MRI images of a human carotid plaque (8 out of a 24-slice 3D set), contour plots and re-constructed 3D geometry.

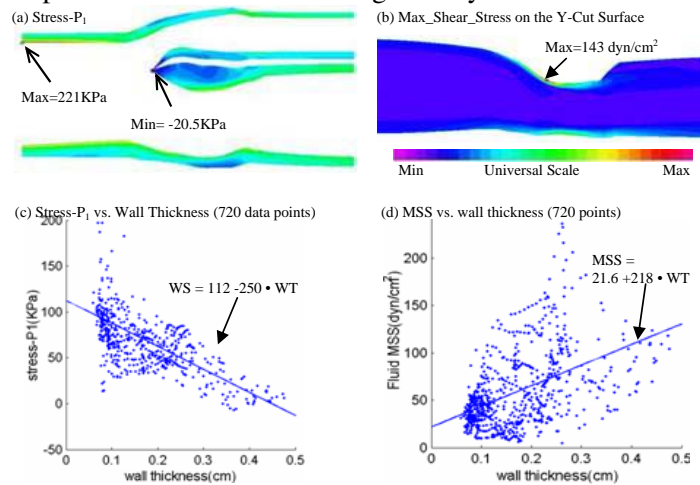


Figure 4: Results from *in vivo* MRI-based FSI models show that plaque wall thickness correlates positively with flow maximum shear stress, and negatively with structure wall stress.

Compared to a popular belief that plaque vulnerability may be related to maximum stress in the plaque, we have shown that local maximum principal stress at selected critical sites have much closer correlation with plaque vulnerability defined by histopathological analysis [5]. The computational plaque vulnerability index (CPVI) defined by our stress analysis has 89% agreement rate with histopathological classifications using 34 2D samples [5]. Another well-accepted hypothesis is that atherosclerosis initiation and progression correlate positively with low and oscillating flow shear stresses. As popular as it is, this shear stress mechanism cannot explain why advanced plaques continue to grow under elevated flow shear stress conditions (Fig. 4). Our results indicate that there is a highly statistically significant negative correlation between Stress- $P_1$  and wall thickness and positive correlation between flow maximum shear stress and wall thickness (Fig. 4). These results suggest that low structure stress may play an important role in plaque progression,

especially for advanced plaques. More investigations are needed to quantify the relationship between plaque stress/strain conditions and plaque changes which can serve as the basis to simulate and predict further plaque progressions.

### MRI-based FSI models for coronary plaques with cyclic bending

One major factor affecting coronary stress/strain distributions is cyclic bending caused by heart motion and the associated curvature variations. Cyclic bending was introduced into our FSI model by specifying displacement at the lower edge of the tube. FSI models based on *in vitro* experimental and *ex vivo* MRI data was constructed and Fig. 5 shows that cyclic bending caused 400% higher stress variations and must be included for accurate predictions.

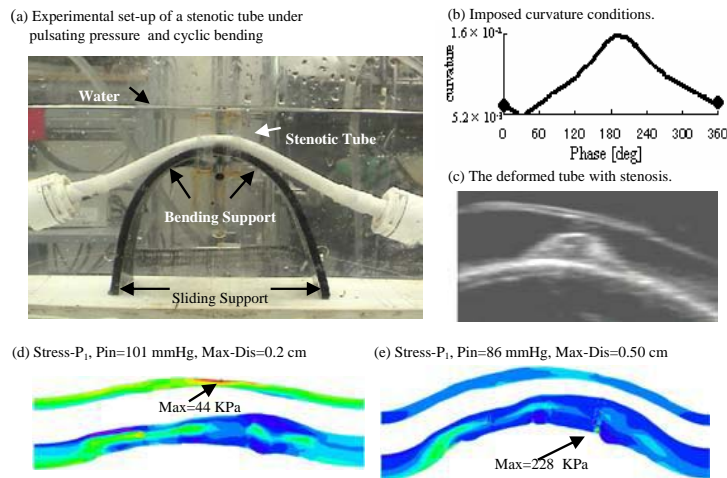


Figure 5: *In vitro* experimental set-up for coronary plaques under pulsating pressure and cyclic bending. Cyclic bending causes significant stress variations in the plaque ( $\sim 400\%$ ).

### CT-based FSI models for human abdominal aortic aneurysm

Several groups have published papers introducing FSI models for human abdominal aortic aneurysm (AAA) with the hypothesis that mechanical analysis of AAA may lead to more accurate assessment of AAA vulnerability. Fig. 6 presents some results from a CT-based human AAA FSI model showing that wall thickness and curvature have considerable effect on stress behaviors.

### Limitations, discussions, and conclusions

Image resolution remains to be a major limitation. Obtaining initial stress/strain conditions is difficult because we do not have the means to get the zero-stress state of living organs. Patient-specific tissue material properties are hard to get non-invasively. Selecting proper model simplifications, identifying verifiable biological indices and end points, and designing proper validation tools are the key items for

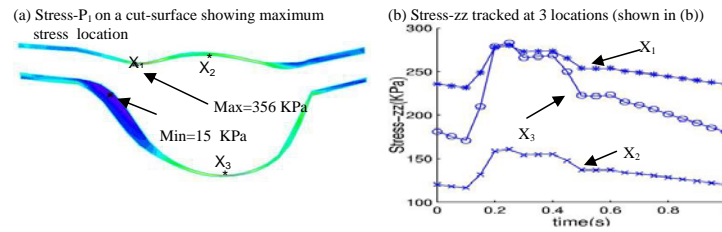


Figure 6: Maximum principal stress on a cut-surface and selected sites from an AAA model.

achieving realistic and accurate models and reliable predictions.

### Acknowledgement

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