NSF Progress Report

Collaborative Research: Advancing the Diagnosis and Quantification of Mitral Valve Regurgitation with Mathematical Modeling

Cardiovascular Hemodynamics Imaging Laboratory

09/08/2014

HOUSTON Methodist DEBAKEY HEART & VASCULAR CENTER

Summary of Proposed Milestones

Cardiovascular Hemodynamics Imaging Laboratory

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YEAR 1	Study time-dependent FSI problem in flow chamber giving rise to Coanda effect. Obtain Bifurcation Diagram for physiologically relevant pressure data.
YEAR 2	Produce compliant orifice plates giving rise to Coanda effect. Compare *in vitro* and *in silico* Coanda flows. Compare Coanda flows in mock prolapsed and in mock planar regurgitant valves.
YEAR 3	Classification of color Doppler presentations of regurgitant jets. Study improvements in color Doppler quantification of MR jets.

TABLE 1: Timeline for the proposed work.

Actions taken towards goals

- Designed and fabricated physiologic imaging chambers and Coanda effect test plates for in vitro study of Coanda Flows.
- Evaluated one Coanda effect test plate within the *in vitro* flow system using 3D color Doppler to obtain preliminary data and assess the efficacy of the model.
- Created STL files for meshing of imaging chambers and test plates to use in numberical simulations.
- Created an MRI compatible flow loop that can allow for further validation of numerical simulations by utilizing velocity field measurements taken from 4D PC-CMR.

Graduate & Undergraduate Students

Research and education activities

- One biomedical engineering undergraduate student from Texas A&M University (Rock Rickel) was involved in the project in 2014. Rock participated in concept development and CAD design of experimental mitral valve prolapse constructs as an summer intern within the Houston Methodist DeBakey Heart & Vascular Center. Rock was mentored by Matthew Jackson and Stephen Little throughout the internship.
- One cardiology post-doctoral fellow (Dimitrios Maragiannis) was involved in the concept development and clinical imaging conducted over the last year. He has been mentored by Stephen Little through out his time at Methodist. He is in the process of completing a PhD in Cardiology at the 1st Department of Cardiology, National and KA Podistrian University of Athens, Hipokration General Hospital in Greece.
- Dr. Little provided a guest lecture for Dr. Canic's applied mathematics graduate course: *Cardiovascular Hemodynamics*, and invited Dr. Canic and her entire class (10 graduate students) to tour his lab and watch a live cardiac surgery procedure.

Presentations

Research and education activities

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- Little presented research related to this NSF proposal at conferences including: Annual scientific sessions of the American College of Cardiology, and of the American Society of Echocardiography.
- Jackson presented research related to this NSF proposal at conferences including: MBI Special Topics Workshop "Mathematics Guide Bioartificial Heart Valve Design" (Colombus, October 2013), Biomedical Engineering Society (Seattle, September 2013)
- Maragiannis presented research related to this NSF proposal at conferences including: American Society of Echocardiography (Portland, June 2014), American Heart Association (Dallas, December 2013)

Miscellaneous

Research and education activities

- **Collaboration with Mathematicians:** Collaboration with Prof. Suncica Canic and Annalisa Quaini of University of Houston with the member of the Houston Methodist research team has been further established in design of experiments and test constructs to most effectively test mathematic hypotheses.
- **Organization of Symposia and Workshops:** The PIs organized a Special Topics Workshop at MBI in October 2013. The title of the Workshop was " Mathematics Guiding Bioartificial Heart Valve Design". Invited speakers included: Prof. Arash Kheradvar of UC Irvine, Prof. Boyce Griffith of NYU Medical Center, Dr. Gerald Lawrie of Methodist Hospital, Prof. Alessandro Veneziani of Emory University, and the PIs. Dr. Little organized a heart valve summit in March 2014 (Bastrop, TX) and a workshop focused on clinical use of multimodality imaging in cardiovascular disease in September 2014 (Houston, TX).
- **Special Courses:** Little---add courses if any

MRI Compatible Pulse Duplicator

Research Findings

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Moving forward from the previously described echocardiography and Doppler ultrasound compatible cardiovascular flow simulator the team at the Methodist Hospital focused their efforts on development of an MRI compatible mock circulation flow loop. The development and validation of the accuracy of this simulator within the MRI scanner for assessing valve function and transvalvular flow was published this year.*

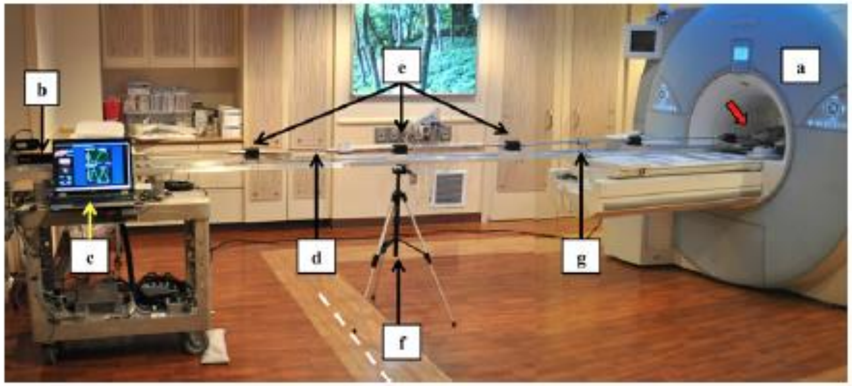
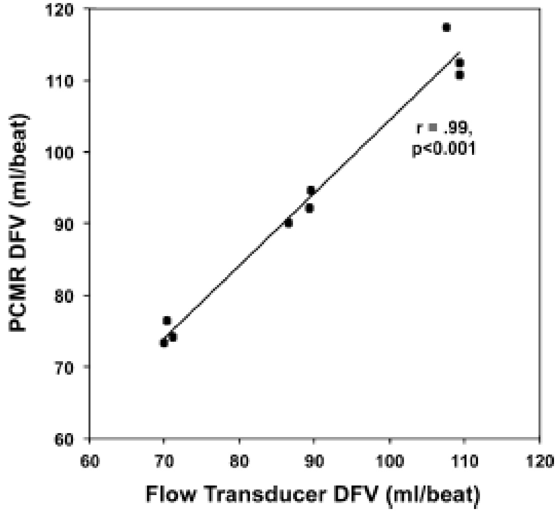


FIGURE 1. MRI-compatible system: all ferromagnetic elements, the linear actuator, servo, and control laptop are positioned outside the 5 gauss line (dashed line) of the MR magnet (a); where the magnetic field is negligible. Components of the system include a linear actuator (b); heartbeat simulator control software (c); extended drive shaft (d); linear motion bearings (e); weight bearing support tripod (f); and linear couplings (g). The flow loop is positioned within the bore of the magnet (red arrow).



MRI compatibility will allow for quantification of the volumetric velocity field utilizing 4D-flow phase contrast cardiac magnetic resonance (PC-CMR). This will provide a unique data set by which to validate numerical simulation findings.

*Jackson MS, Igo SR, Lindsey TE, Maragiannis D, Chin KE, Autry K , Shah DJ, Valsecchi P, Kline WB, **Little SH**. Development of a Multi-Modality Compatible Flow Loop System for the Functional Assessment of Mitral Valve Prostheses. *Cardiovascular Engineering and Technology* 2014, 5(1), 13-44.

3D Printed, Physiologic Mimicking Cardiac Imaging Chamber

Research Highlights

The group at Methodist has also developed a new mitral valve imaging chamber that incorporates four pulmonary artery inflow tubes, atrial compliance, a prolate ellipsoidal ventricular shape along with a accurately positioned left ventricular outflow tract. This chamber incorporates the same physiologically accurate echocardiography windows as previous imaging chambers as well as uses only non-ferromagnetic materials to allow for further MRI compatibility.

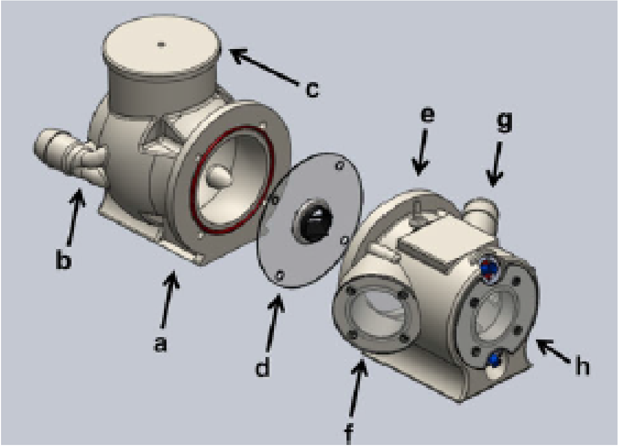


FIGURE 3. Mitral valve imaging chamber: an exploded view of a CAD model of the imaging chamber shows the layout of the three main components; The atrial chamber (a) is shown with one of the two dual inflow tubes (b) representing the pulmonary veins and the compliance tower (c) visible; Between the ventricle and atrial components a valve-mounting plate (d) is shown with a mechanical mitral valve mounted in its center; The ventricle chamber (e) is shown with the left ventricular outflow (g), parasternal imaging window (f), and apical imaging window (h) identified.

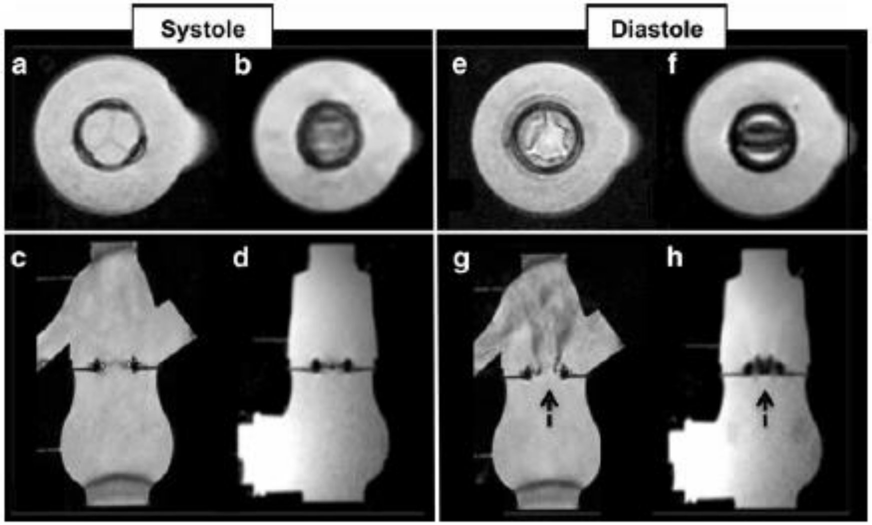


FIGURE 8. CMR imaging of mitral valve prostheses: a 31 mm Hancock II bioprosthetic and a 31 mm Medtronic Open Pivot® Mechanical MV prosthesis are shown. During systole the bioprosthetic and the mechanical valve are closed as can be seen in short axis views (a, b, respectively) and orthogonal long axis views (c, d, respectively); During diastole the bioprosthetic and the mechanical valve are open in short axis views (e, f, respectively) and orthogonal long axis views (g, h, respectively). Note that two different but orthogonal long axis views were used to visualize the leaflet motion of the mechanical and bioprosthetic valves, hence the apparent difference in imaging chamber geometry. Dashed arrow indicts flow direction.

3D Printed Patient Specific Models of Aortic Stenosis

Research Highlights

To act as a bridge between simulations within in vitro stylized geometric models towards patient specific data sets, Methodist Collaborators have begun developing a technique of creating 3D printed patient specific models of valvular disease conditions, by which in the future computational models can be validated across more complex conditions that would be encountered within the human anatomy while still under controlled, measureable flow conditions. (Maragiannis et al, JACC 2014)

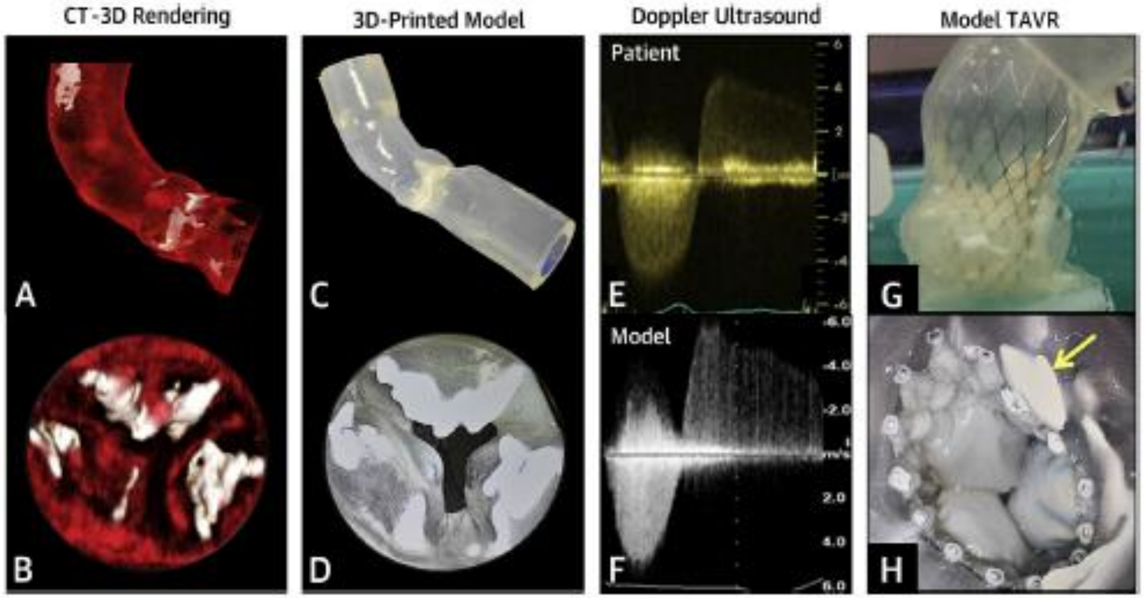


Figure 1. Computed tomography (CT) data from a patient with severe aortic stenosis
Long axis (A) and short axis (B) views were segmented into soft-tissue structures (red) and calcific nodules (white). These DICOM data were manipulated in engineering software to create 3D printed fused-material patient specific models, long axis (C) and short axis (D) views. Functional aortic stenosis was demonstrated with matched Doppler characteristics between the clinical patient study (E) and the patient-specific model (F). Deployment of a transcatheter aortic valve within a model is demonstrated (G) with regional "calcific" resistance (yellow arrow) to a self-expanding nitinol stent frame as viewed from the left ventricle (H).

Publications Related to NSF Research

Research Highlights

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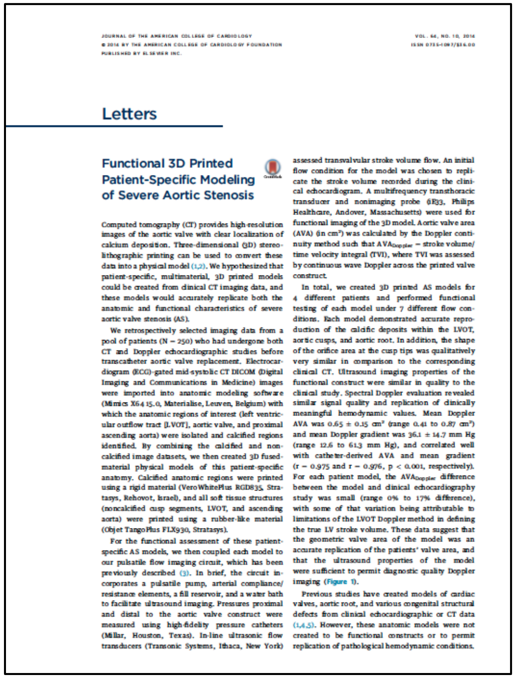
1. Maragiannis D, Jackson MS, Igo SR, Chang SM, Zoghbi WA, Little SH. *Functional 3D Printed Patient-Specific Modeling of Severe Aortic Valve Stenosis.* JACC Vol.64, No. 10, 2014. ISSN 0735-1097. September

2. Jackson MS, Igo SR, Lindsay TE, Maragiannis D, Chin KE, Autry K, Schutt III R, Shah DJ, Valsecchi P, Kline WB, Little SH. *Development of a Multi-modality Compatible Flow Loop System for the Functional Assessment of Mitral Valve Prosthesis*. Cardiovascular Engineering and Technology.2014 March 5(1)

Development of a Multi-modality Compatible Flow Loop System for the Functional Assessment of Mitral Valve Prostheses

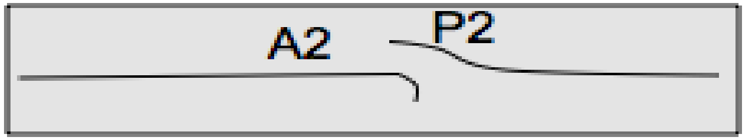


Letters

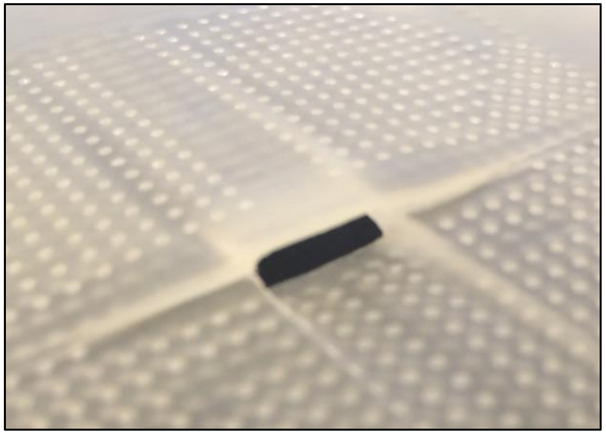
Functional 3D Printed Patient-Specific Modeling of Severe Aortic Stenosis

3D CAD Models of Coanda Effect Test Plates
Research Highlights

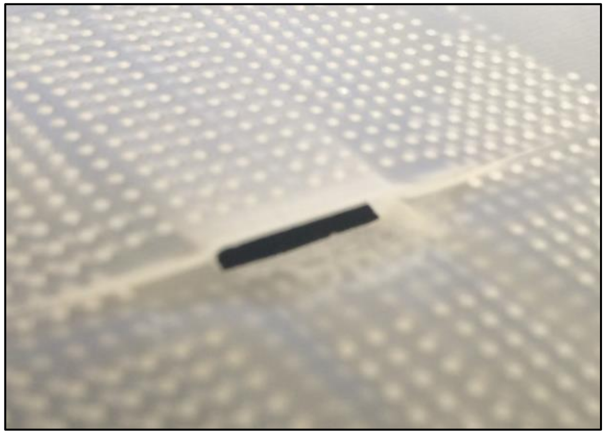
Collaborators have designed and fabricated 3 Coanda test plates of different scales (height to width orifice ratios of 1:3, 1:5, & 1:10) with ultrasound noise reduction dimples, and physiologic MV geometry for use to test the Coanda effect mathematics.



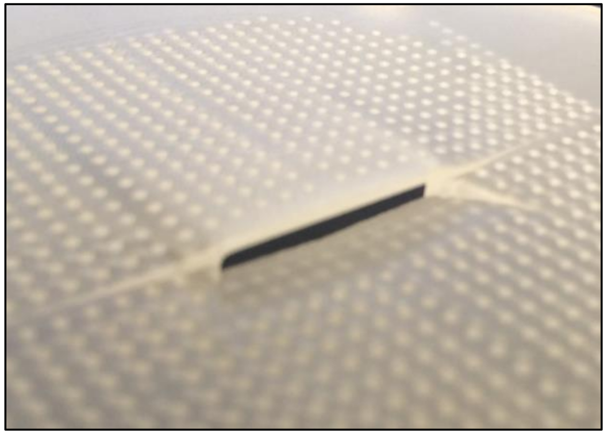
1:3 Height to Width Ratio



1:5 Height to Width Ratio



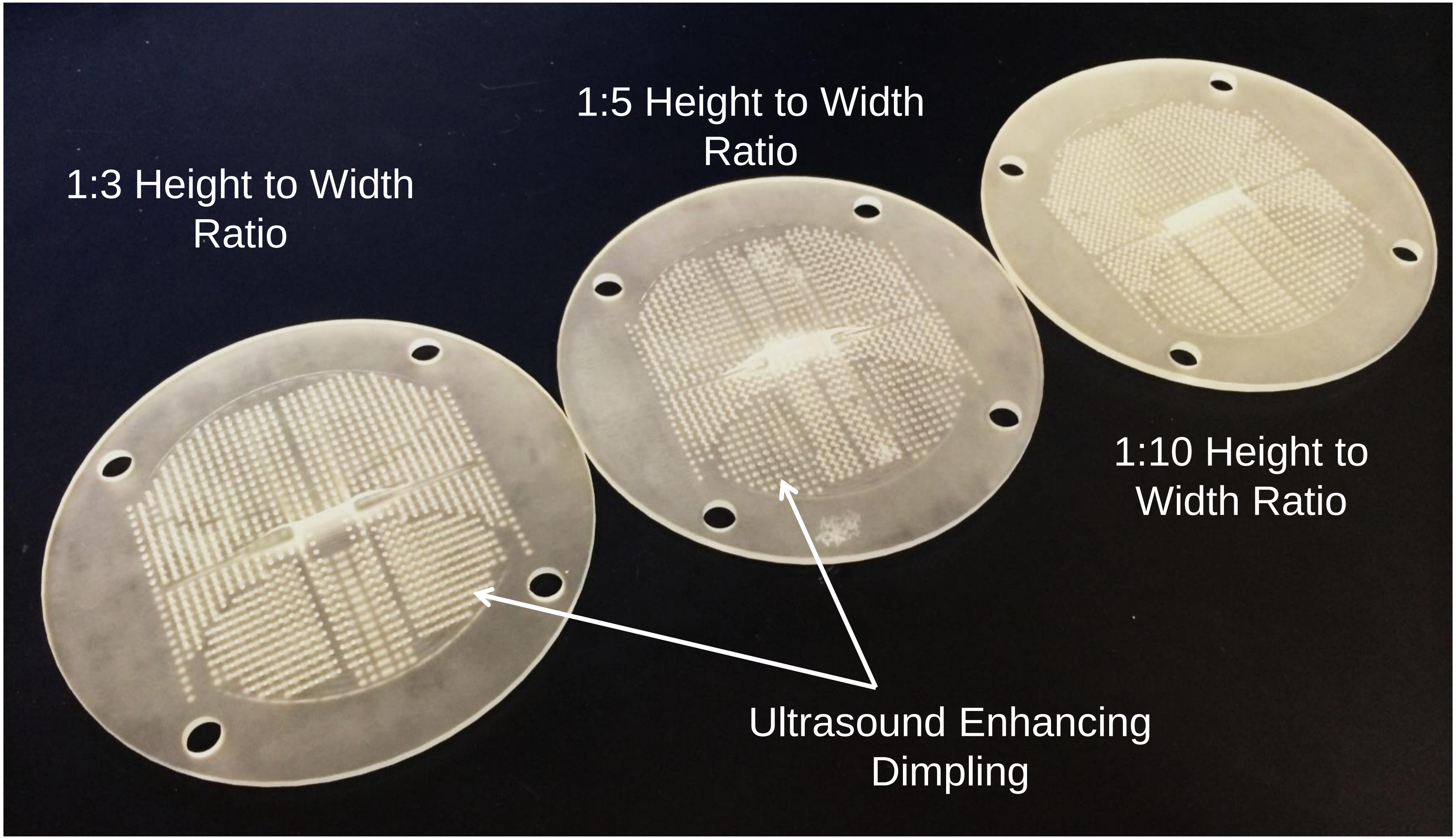
1:10 Height to Width Ratio



All plates are created using a high resolution 3D printer (Projet, 3D Systems) that allows for high accuracy translation of computer rendered geometries in the form of an STL file into physical models made of plastic. This same STL file can be ultimately meshed and used for numerical simulations.

3D Printed Models of Coanda Effect Test Plates

Research Highlights



3D Color Doppler Analysis of Coanda Effect Plates

Research Highlights

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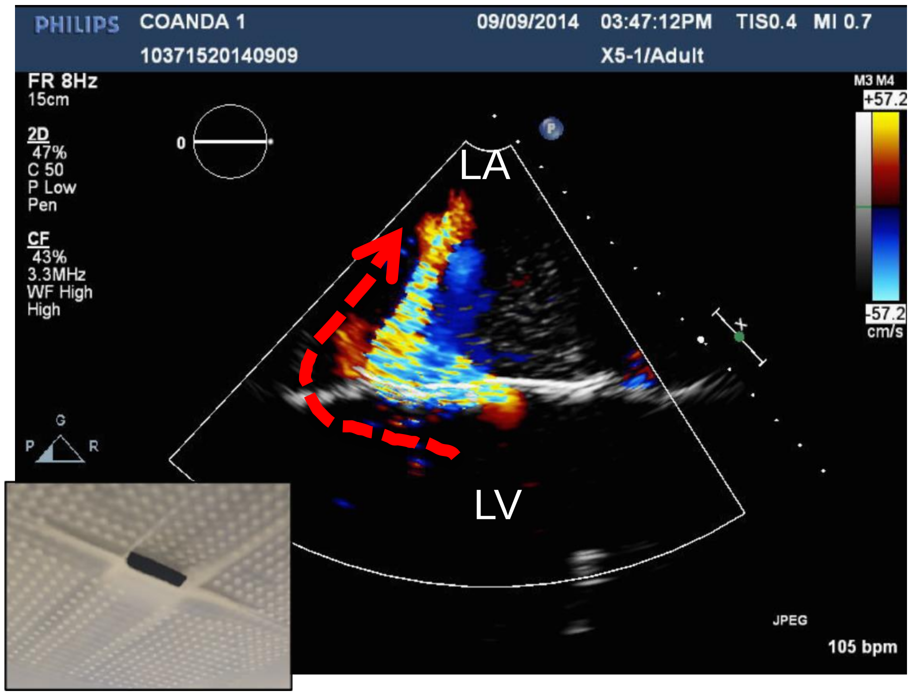
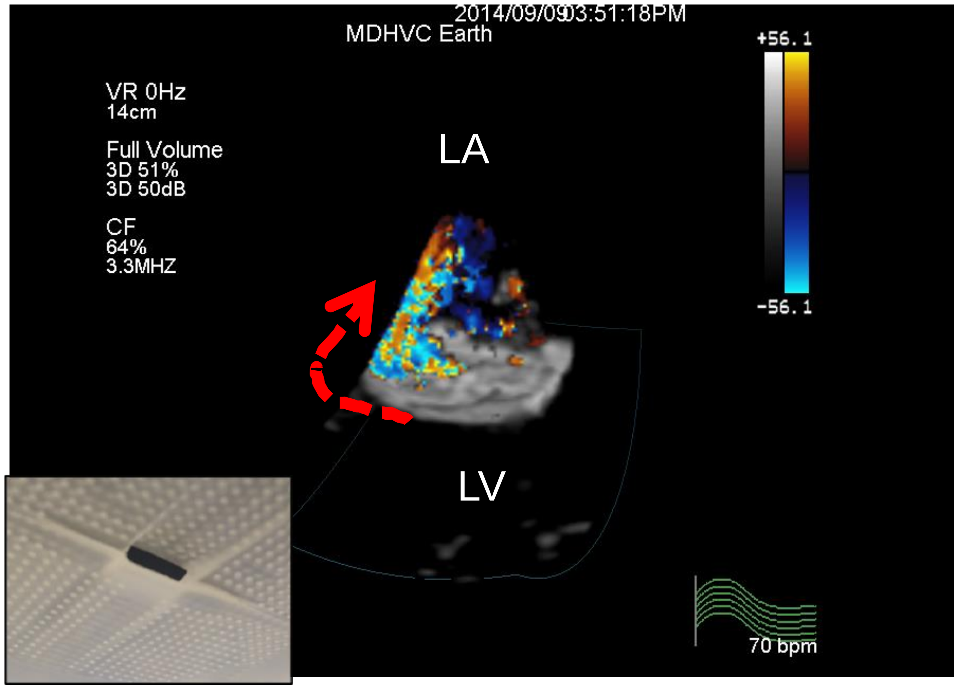
2D color Doppler



3D color Doppler



Wall hugging (coanda) effect is clearly demonstrated while pulsing flow through a 3D printed plate designed to replicate mitral valve prolapse. Both 2D and 3D color Doppler echocardiography demonstrate the eccentric MR jet (red arrow) as it flows from left ventricle (LV) to left atrium (LA).

Continued Research
Research Highlights

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- Evaluate all Coanda test plates in the controlled flow loop over multiple flow conditions utilizing echocardiography & PC-MRI for measurement of velocity, transvalvular gradient, and flow volume.
- Compare in vitro and simulated results.

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