# **NSF Progress Report**

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

> Cardiovascular Hemodynamics Imaging Laboratory 09/08/2014





	Study time-dependent FSI problem in flow chamber giving rise to Coanda effect.		
YEAR 1	Obtain Bifurcation Diagram for physiologically relevant pressure data.		
	Produce compliant orifice plates giving rise to Coanda effect.		
YEAR 2	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 1<sup>st</sup> 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.



- <u>Little</u> 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)
- <u>Maragiannis</u> presented research related to this NSF proposal at conferences including: American Society of Echocardiography (Portland, June 2014), American Heart Association (Dallas, December 2013)



- 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 <u>Topics Workshop at MBI</u> 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



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.\*

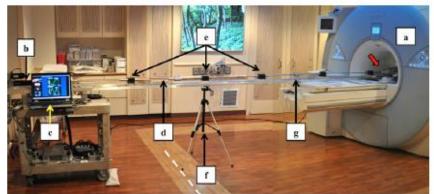
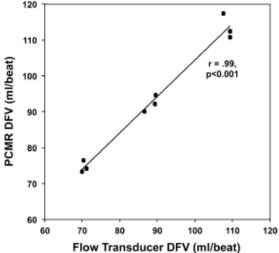


FIGURE 1. MRI-compatible system: all ferromagnetic elements, the linear actuator, servo, and control laptop are positioned outside the 5 gauss line (dashed line) of the MR magnet (a); where the magnetic field is negligible. Components of the system include a linear actuator (b); heartbeat simulator control 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.

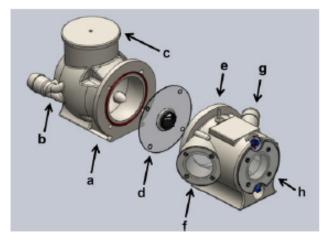


FIGURE 3. Mitral valve imaging chamber: an exploded view of a CAD model of the imaging chamber shows the layout of the three main components; The atrial chamber (a) is shown with one of the two dual inflow tubes (b) representing the pulmonary veins and the compliance tower (c) visible; Between the ventricle 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.

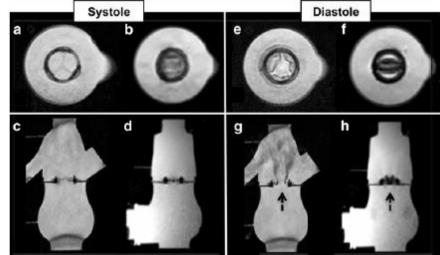
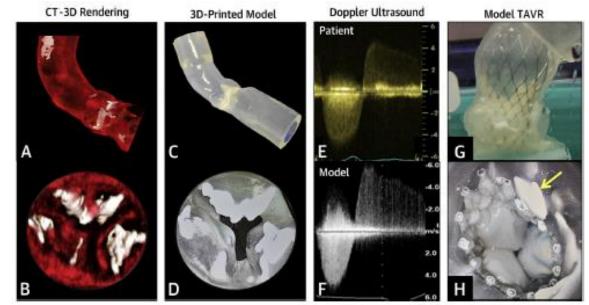


FIGURE 8. CMR imaging of mitral valve prostheses: a 31 mm Hancock II bioprosthetic and a 31 mm Medtronic Open Pivot<sup>®</sup> Mechanical MV prosthesis are shown. During systole the bioprosthetic and the mechanical valve are closed as can be seen in short axis views (a, b, respectively) and orthogonal 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 (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



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)

Cards-usador Region-ring and Technology (10 2014) DOI: 10.1007(s).10234-014-01777	BUNKES STATES	ADDRIAL OF DOL AND ATTACK THE LASE OF CARDINALOUF YOU. 4.5, 4.5 IF ON A THE ADDREAM OF LASE OF CARDINAL OF FOUNDATION IN A DTEM INVESTIGATE OF IN A MARK INC.
Development of a Multi-modality	y Compatible Flow Loop System	
for the Functional Assessmen	t of Mitral Valve Prostheses	
		Letters
MATTHEW S. JACKEON, <sup>1</sup> STEPHEN R. IGO, <sup>1</sup> THO KAREN E. CHEN, <sup>1</sup> KYLE AUTEY, <sup>1</sup> ROBERT SCHU WILLIAM B. KLENE, <sup>2</sup> an	UTT III, <sup>1</sup> DIPAN J. SHAH, <sup>1</sup> PIETRO VALSECCHI, <sup>2</sup>	
<sup>1</sup> Houston Methodist DeBakey Heart and Vascular Center,		Functional 3D Printed  assessed transvalvular stroke volume flow. A flow condition for the model was chosen t
Company, Hoa	stor, TX, USA	Patient-Specific Modeling of the stroke volume recorded during the
(Received 28 July 2003; a	corpied 12 January 2014)	of Severe Aortic Stenosis cal educardiogram. A multifrequency trans
Associate Editor Ait F. Yoganatha		transducer and nonimaging probe (F23, Healthcare, Andover, Massachusetts) were u
And the factor April 1 togethere		Committed tomography (CT) provides high resolution functional imaging of the 3D model. Acritic val
		images of the aortic valve with clear localization of (AVA) (in cm <sup>2</sup> ) was calculated by the Dopple
		calcium deposition. Three-dimensional (jD) stereo- nuity method such that AVA <sub>loopter</sub> = stroke v lithographic printing can be used to convert these time velocity integral (TVI), where TVI was a
Abstract—We sought to build a robust pulsatile flow model permitting comparison of 3D Color Doppler and phase	MRI-compatible flow loop system for comparison of multim- edulity imaging techniques to assess prosthetic valve function.	data into a physical model (1,2). We hypothesized that by continuous wave Doppler across the printe
contrast magnetic resonance (PCMR) flow and orifice area		patient-specific, multimaterial, 3D printed models construct.
measurements of prosthetic valve function that would provide an in vitro gold standard for evaluation of the	KeywordsProsthetic heart valves, Canliac MRI, PC-MRI, Echocanlicementy, Flow loop.	could be created from dinical CT imaging data, and In total, we created 3D printed AS mod
accuracy of new imaging techniques. A multi-modality compatible, pulsatile linear actuation system, control soft-	Echocardiography, Plow toop.	these models would accurately replicate both the 4 different patients and performed fur anatomic and functional characteristics of severe testing of each model under 7 different fic
ware, and mock circulation loop was designed and created		anatomic and functional characteristics of severe testing or each model demonstrated accurate aortic valve stenois (45).
using non-ferromagnetic components, NI Labview, and ranid prototoping. The developed watern's ability to create	INTRODUCTION	We retrospectively selected imaging data from a duction of the caldific deposits within the
pulsatile, controlled flow was assessed by cuamining peak	In the U.S., it is estimated that 30,0000 people are	pool of patients (N - 250) who had undergone both a orfic cusps, and aortic root. In addition, th
distolic flow, distolic period, and distolic flow volume (DFV) of 12 consecutive cardiac cycles at 3 different DFVs.	living with prosthetic heart valves.3 Since the first	CT and Doppler echocardiographic studies before of the orifice area at the cusp tips was quali transcatheter aortic valve replacement. Electrocar- very similar in comparison to the correspondence of
Reproducibility of flow was tested by examining the systems ability to generate the same target DFV after draining and	prosthetic mitral valve (MV) implant almost 50 years ago, the non-invasive assessment of prosthetic MV	diogram (6CG)-gate mid-systelic CT DICOM (Digital clinical CT. Ultrasound imaging properties
re-configuring the flow loop components. Furthermore, the	function has remained a significant challenge. Current	Imaging and Communications in Medicine) images functional construct were similar in quality
system was evaluated by CMR and echocardiography to examine image quality. DFV quantification, and an initial	guidelines recommend use of Doppler echocardiogra-	were imported into anatomic modeling software clinical study. Spectral Doppler evaluation re (Mimics X64 15.0, Materialise, Leuven, Relgium) with similar signal quality and replication of d
functional assessment of prosthetic mitral valve (MV) orfice	phy (echo) as the initial method to assess prosthetic valve function. <sup>2</sup> However, the accurate assessment of	(at mic A to 4.5.6, Automatics, Leaven, negating with standard quarky and represented to a which the antomic regions of interest (left ventics - meaningful hemodynamic values. Mean 1
area by four different imaging methods. The system was able to reproducibly create prescribed flow volumes across 31 mm	prosthetic valve function can be limited by a patient's	ular outflow tract (LVOT), aortic valve, and proximal AVA was 0.65 ± 0.15 cm <sup>2</sup> (range 0.41 to 0.1
bioprosthetic and mechanical MV's under a range of flow conditions. In vitro image quality for the identification of MV	body habitus, available imaging windows, and the	ascending aorta) were isolated and calcified regions and mean Doppler gradient was $36.1 \pm 14.7$
sewing ring, struts and leaflets was similar to clinical imaging	Doppler imaging angle relative to the axis of flow. As such, there is increasing interest in the use of other	identified. By combining the caldified and non- (range 12.6 to 61.3 mm Hg), and correlate calcified image datasets, we then created 3D fused- with catheter-derived AVA and mean g
quality for both echocardiographic and MRI methods. For the quantification of DFV, the PCMR method demonstrated	modalities such as magnetic resonance imaging (MRI),	material physical models of this patient-specific (r = 0.975 and r = 0.976, $p < 0.001$ , respec
an error range of 1.4-9.2% and a mean difference of	which does not share these potential limitations. In	anatomy. Calcified anatomic regions were printed For each patient model, the AVAGeopter dif
4 ± 2 mL/heat compared to the flowmeter reference stan- dard. Across the three flow conditions the hioprosthetic	particular, the feasibility of cardiac MRI (CMR) to determine the effective valve area of aortic and MV	using a rigid material (VeroWhitePlus RGD835, Stra- between the model and dinical echocardic tarys, Rehovot, Israel), and all soft tissue structures study was small (range 0% to 17% diffe
MV disatolic flow area was statistically similar by MRI planimetry, phase contrast MRI planimetry, and 3D color	bioprostheses has already been demonstrated for	(ancel, active), states, and an soft assoc statuties staty was small (large 0% to 1/% dim (noncalified case) segments, LVOT, and according with some of that variation being attribut
Doppler planimetry methods (mean area 3.2 ± 0.5 cm <sup>2</sup> ,	valves with normal and abnormal function. <sup>11,13,19-20</sup>	aorta) were printed using a rubber-like material limitations of the LWOT Doppler method in d
ANOVA, $p = NS$ ), but the effective orifice area by 2D spectral Doppler (continuity) method was smaller (mean	For a direct measure of prosthetic valve function, cardiac MRI can be used to assess the peak trans-	(Objet Tango Hus FLX930, Stratays). the true LV stroke volume. These data sugg
area $2.0 \pm 0.3$ cm <sup>2</sup> , ANOVA, $p < 0.001$ . We describe	valvular velocity using phase contrast (PC) techniques.	For the functional assessment of these patient. the geometric value area of the model v specific AS models, we then coupled each model to accurate replication of the patients' value an
the development and initial functional testing of a novel	Like Doppler methods, PC CMR derives a measure of	our pulsatile flow imaging circuit, which has been that the ultrasound properties of the
	flow volume as the product of the integration of the peak velocity and the flow area. However PC-CMR	previously described (3). In brief, the circuit in- were sufficient to permit diagnostic quality I
Address correspondence to Stephen H. Little, Houston Meth- odist Dellakey Heart and Vacular Center, Houston, TX, USA	techniques provide significantly lower temporal reso-	corporates a pulsatile pump, arterial compliance/ imaging (Figure 1).
Electronic mail: shittle@imba.org	lution compared to spectral Doppler methods and are	resistance elements, a fill reservoir, and a water bath Previous studies have created models of to facilitate ultrasound imaging. Pressures proximal valves, aortic root, and various congenital str
		and distal to the aortic valve construct were defects from clinical echocardiographic or (
	C 204 Novelind Represent Society	measured using high-fidelity pressure catheters (1,4,5). However, these anatomic models w
Published online: 23 January 2014		(Millar, Houston, Texas). In-line ultrasonic flow created to be functional constructs or to transducers (Transonic Systems, Ithaca, New York) replication of pathological hemodynamic con
		transoucers (transourd: Systems, imaca, New York) reparation or pathological nemotynamic con-

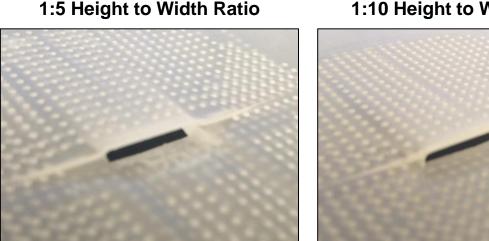
# 3D CAD Models of Coanda Effect Test Plates Research Highlights



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

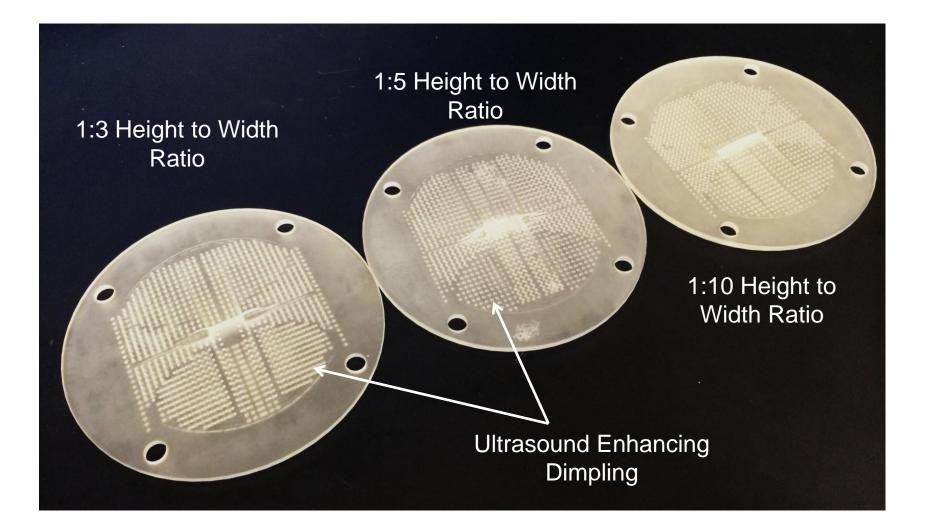


1:10 Height to Width Ratio

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



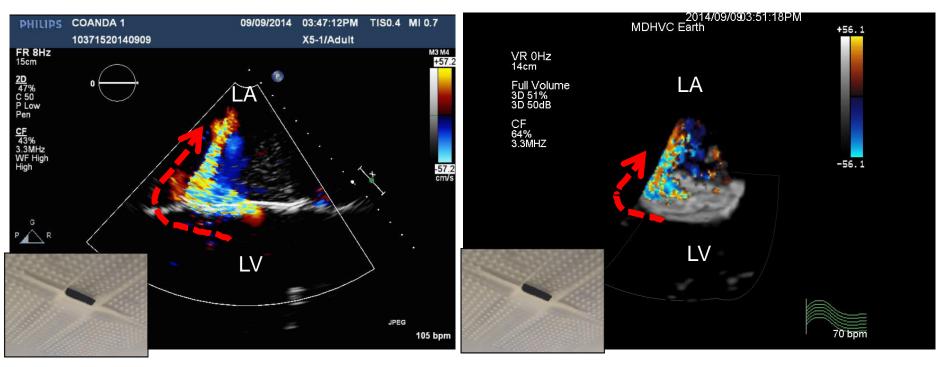


# 3D Color Doppler Analysis of Coanda Effect Plates Research Highlights



3D color Doppler

# 2D 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).



- 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.



