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iREVIEW

IMAGING FOR BEST OUTCOMES IN STRUCTURAL HEART INTERVENTIONS SPECIAL ISSUE

3D Printing, Computational Modeling, and Artificial Intelligence for Structural Heart Disease

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ABSTRACT

Structural heart disease (SHD) is a new field within cardiovascular medicine. Traditional imaging modalities fall short in supporting the needs of SHD interventions, as they have been constructed around the concept of disease diagnosis. SHD interventions disrupt traditional concepts of imaging in requiring imaging to plan, simulate, and predict intraprocedural outcomes. In transcatheter SHD interventions, the absence of a gold-standard open cavity surgical field deprives physicians of the opportunity for tactile feedback and visual confirmation of cardiac anatomy. Hence, dependency on imaging in periprocedural guidance has led to evolution of a new generation of procedural skillsets, concept of a visual field, and technologies in the periprocedural planning period to accelerate preclinical device development, physician, and patient education. Adaptation of 3-dimensional (3D) printing in clinical care and procedural planning has demonstrated a reduction in early-operator learning curve for transcatheter interventions. Integration of computation modeling to 3D printing has accelerated research and development understanding of fluid mechanics within device testing. Application of 3D printing, computational modeling, and ultimately incorporation of artificial intelligence is changing the landscape of physician training and delivery of patient-centric care. Transcatheter structural heart interventions are requiring in-depth periprocedural understanding of cardiac pathophysiology and device interactions not afforded by traditional imaging metrics. (J Am Coll Cardiol Img 2021;14:41–60) © 2021 by the American College of Cardiology Foundation.

Transcatheter interventions have redefined the field of structural heart disease (SHD). Cardiac interventions are no longer limited to percutaneous stent implantation but have expanded to percutaneous valvular repair and replacement. However, there is an imaging void within structural heart disease that has yet to be bridged. Unlike surgeons who can palpate the cardiac

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ABBREVIATIONS AND ACRONYMS

3D = 3 dimensional

AI = artificial intelligence

CFD = computational fluid dynamics

CT = computed tomography

FEA = finite element analysis

LAA = left atrial appendage

LVOT = left ventricular outflow tract

CMR = cardiac magnetic resonance

SHD = structural heart disease

TAVR = transcatheter aortic valve replacement

TEE = transesophageal echocardiogram

TMVR = transcatheter mitral valve replacement

chambers to provide patient-centric solutions, transcatheter interventions have developed within the field of cardiology and not cardiac surgery. Within each of these specialties, there are limitations to interpretation of human anatomy given physician-specialty limited access to device-specific training and imaging technologies.

Transcatheter therapies expose the silos that exist within industry device development, physician education, imaging in health care, and need for patient-centric care. Never before has there been as robust a market for research and development investment in transcatheter therapies, with as significant a gap in understanding of 3-dimensional (3D), 4D, and anatomic physiological relationships of the human body (1). To help bridge the dichotomy of real-world in-the-trenches imaging, and futuristic capabilities of computer science and biomedical engineering, there is a role for 3D printing, computational modeling, and artificial intelligence (AI). First and foremost, clinicians must understand the definitions, real-world applications, and nuances of each of these technologies before clinical workflow implementation. In this review, we give an overview of these rapidly evolving domains along with examples that demonstrate real applications of this novel area.

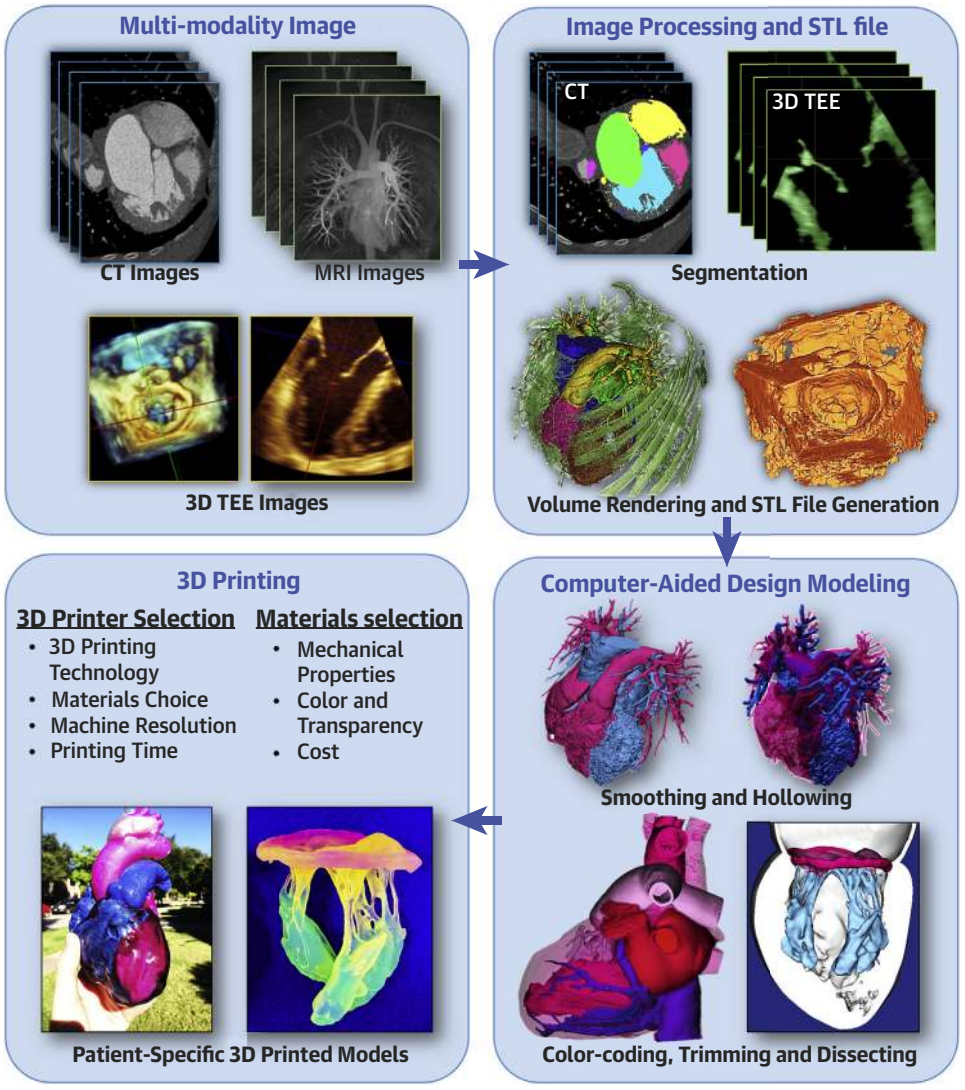
BASICS OF 3D PRINTING, COMPUTATIONAL MODELING, AND AI

WHAT IS "3D PRINTING?". Three-dimensional printing is a manufacturing technique otherwise termed "rapid prototyping or additive manufacturing." This process transforms digital objects into 3D physical replicas by depositing multiple layers of materials over digitally defined geometries. Three-dimensional printed modeling is a multistage process that comprises a series of successive steps (**Figure 1**). The generation of a patient-specific 3D printed model begins with high-quality imaging data acquisition and its conversion into a Digital Imaging and Communication in Medicine (DICOM) format suitable for further image processing. DICOM images are then imported into specialized image processing software to define and build the anatomic body parts of interest in a process called segmentation. Segmentation is followed by 3D volume rendering and digital modeling of patient-specific geometries. Patient-specific 3D digital anatomic models are saved in stereolithography (STL) file formats that contain the surface mesh information of complex geometries suitable for 3D printing, allowing additional refinements through computer-aided design modeling and computational analysis (**Figure 2**).

OVERVIEW OF 3D PRINTING TECHNOLOGIES. Several 3D printing technologies have been applied to cardiovascular medicine (**Table 1**). Stereolithography (SLA) was the first 3D printing technology to be developed back in the 1980s. It uses ultraviolet (UV) laser to cure the base material, which is a photosensitive liquid resin, in a layer-by-layer fashion to produce a 3D part (2). By design, SLA can use only 1 material in a model. In many cases, it needs to print extra supporting structures which must be removed later. SLA is ideal to produce large, highly accurate and transparent models, such as cardiac and vascular models for education, training, and flow testing. Selective laser sintering (SLS) is a technology that uses high-power infrared laser to fuse layers of small particles of thermosensitive materials, such as nylon, metal, and ceramic (3). SLS is mostly used in manufacturing industry, not commonly in cardiovascular applications. Fused deposition modeling (FDM) is a relatively low-cost technology that is suitable for desktop use at home or in office. It melts and extrudes small segments of a thermoplastics filament or metal wire, and deposits them in layers (4). FDM is ideal to produce rigid and strong models at a relatively low budget. The inkjet 3D printing technology works similar to a 2D inkjet printer (5). It deposits tiny droplets of colorful liquid binder to join and solidify layers of powders to form a full-color 3D object. Inkjet can use only a single base material. It is ideal for printing complex cardiovascular structures in color for illustrations. Last, the Polyjet technology developed by Stratasys (Rehovot, Israel), to some extent, is a union of the SLA and inkjet technologies. It deposits UV-curable photopolymers by layers to produce a 3D object (6). By mixing 2 or more base materials, it can print with "digital materials" that have a wide range of color and physical properties. Polyjet has been recently used to print compliant cardiovascular models with rigid parts, such as the aortic root with calcific lesions (7–9).

How the process starts: principles of data acquisition for 3D printing. Volumetric image acquisition plays a critical role in 3D printing. Not only does it determine the geometric accuracy of the 3D model, but also it characterizes tissue properties and directs the choice of the appropriate printing materials. A number of

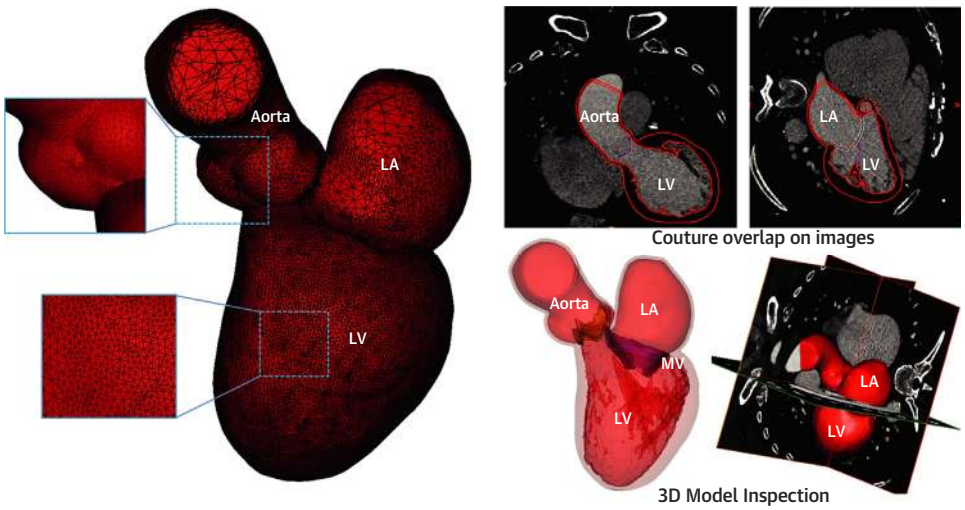
FIGURE 1 **3D Printed Modeling Workflow**



Three-dimensional (3D) printed modeling starts with imaging acquisitions: computed tomography (CT), 3D transesophageal echocardiography (TEE) or cardiac magnetic resonance (CMR) **(top, left)**. Digital Imaging and Communication in Medicine (DICOM) images are then exported for segmentation, volume rendering, and generation of the stereolithography (STL) file **(top, right)**. The STL file is imported into computer-aided design software for further smoothing, hollowing, trimming, color-coding, and dissection **(bottom, right)**. After adjustments, the STL file is exported for 3D printing **(bottom, left)**. 3D printer and 3D print materials are preselected based on the desired quality, mechanical parameters, and costs of the 3D printed replica.

modern cardiovascular imaging techniques have been used to acquire the 3D or 3D+time image data for 3D printing (Table 2). Contrast-enhanced multidetector row computed tomography (CT) with electrocardiographic gating/triggering has been the most commonly used imaging modality for 3D printing (10) because of its fast acquisition, superb spatial resolution, and excellent ability of tissue characterization differentiating metal implants and calcific lesions from soft tissues. The temporal resolution of modern CT varies in the range of 75 to 200 ms, depending on its make and model. Compared with CT, 3D cardiac magnetic resonance (CMR) has a relatively lower spatial resolution and longer acquisition time. However, because of the absence of ionizing radiation, 3D cardiac MRI with free-breathing technique has been

FIGURE 2 Concept of STL or "Standard Tessellation Language" Data



The stereolithography (STL) file represents a collection of triangular faces of different sizes **(left)**. Before sending for 3-dimensional (3D) printing, the interventional team should inspect the accuracy of the model and STL file using the contour overlap technique **(upper right)**. The team should also conduct a thin wall and elements overlapping inspection using transparent visualization **(bottom, right)**, as well as automatic screening. LA = left atrium; LV = left ventricle; MV = mitral valve.

frequently used in modeling the structures of the cardiac chambers and great vessels in pediatric patients and young adults for 3D printing (11,12). On the other hand, because of the wide availability, high temporal resolution, and ease of performing echocardiography at the bedside, echocardiography has been used to acquire images for 3D printing in many studies (13-15). The main limitation of 3D echocardiography is the relatively low signal-to-noise ratio, which makes image post-processing and 3D modeling more challenging. Furthermore, due to the tradeoff between the size of the acoustic window and the spatiotemporal resolution, 3D modeling of the complete heart anatomy using echocardiography remains difficult.

PRINCIPLES OF DATA SEGMENTATION AND IMAGE GENERATION. The process of delineating the boundaries of the interested heart components in medical images is often referred to as image segmentation. It is the first and often the most labor-intensive step in computational modeling of the heart. Specialized 3D segmentation and modeling software have been developed and used to process the volumetric DICOM images acquired in patients with SHD. However, in most cases, manual segmentation/editing is required, as most segmentation tools are based on simple intensity thresholding and region growing, which often fail to delineate the boundaries of complex cardiac structures that share similar intensity profiles. Studies have reported the use of a number of commercial and free tools (16,17), as well as in-house developed tools (18). More recently, more sophisticated image segmentation techniques based on AI have shown promising results (19-21).

The material properties of the cardiac tissues used in computational modeling are mainly derived from in vitro biomechanical tests on animal tissues and/or human cadavers (22,23). However, it is noted that the mechanical property of live human tissues differs from that of animal tissues or cadavers. Moreover, the age, sex, and pathology of the subject play critical roles in determining the tissue property. Even though patient-specific morphologies have been often used in computational modeling of the heart, only a few studies have used the patient-specific material properties (24).

3D PRINTING IN STRUCTURAL HEART DISEASE

3D PRINTING FOR TRANSCATHETER AORTIC VALVE REPLACEMENT. Patient-specific 3D printed models can be instrumental in the pre-procedural planning of transcatheter aortic valve replacement (TAVR) interventions, the sizing of TAVR devices, and the estimation of possible risks for paravalvular leak (8,17,25-27). Three-dimensional printed replicas of

TABLE 1 3D Printing Technologies

Technology	Printing Material	Printing Technique	Pros and Cons	Applications
Stereolithography (SLA)	Photosensitive liquid resin	Ultraviolet laser curing	Pros: capable of printing large, highly accurate, and transparent models with a variety of elasticity. Cons: single material printing; need to print support structure; expensive.	Large and compliant models for illustration, education, and flow testing purposes
Selective laser sintering (SLS)	Thermosensitive particles	High-power infrared laser sintering	Pros: smooth finish and durable model; no need to print support structure. Cons: more expensive and less accessible; single material printing.	Industrial-level applications
Fused deposition modeling (FDM)	Thermoplastic filament or metal wire	Fused deposition	Pros: low-cost; suitable for desktop use; strong model. Cons: rough/stepped surface finish; single material printing.	Rigid and strong models for illustration
Inkjet	Powder material, such as starch and gypsum, and liquid binder	Inkjet and liquid binding	Pros: cost-effective; relatively fast; colorful models. Cons: rough surface finish; needs lengthy post-processing for model reinforcement; single material printing.	Complex colorful models for illustration
Polyjet	Ultraviolet (UV)-curable photopolymers	UV flood lamp curing	Pros: multimaterial printing; digital materials (variant colors and material properties); smooth surface finish. Cons: expensive; must use support material that needs to be removed in post processing.	Complex model with variant elasticity and color; tissue-mimicking models

3D = 3 dimensional.

aortic geometry have proven useful in modeling individual patient hemodynamic conditions and in the in vitro implantation of TAVR devices. Maragiannis et al. (26,28) developed a series of patient-specific, flexible, multimaterial 3D printed models of aortic valve stenosis with calcific structures within the flexible aortic arch. The group 3D printed the aortic leaflets and aortic arch geometry using flexible materials, whereas the calcific structures within the leaflets were fabricated of hard material. The 3D printed aortic models were then subjected to patient-specific hemodynamic conditions, thereby proving the feasibility of replicating in vitro the pressures and flows of specific patients, as well as the echocardiographic parameters found in patients (26,28).

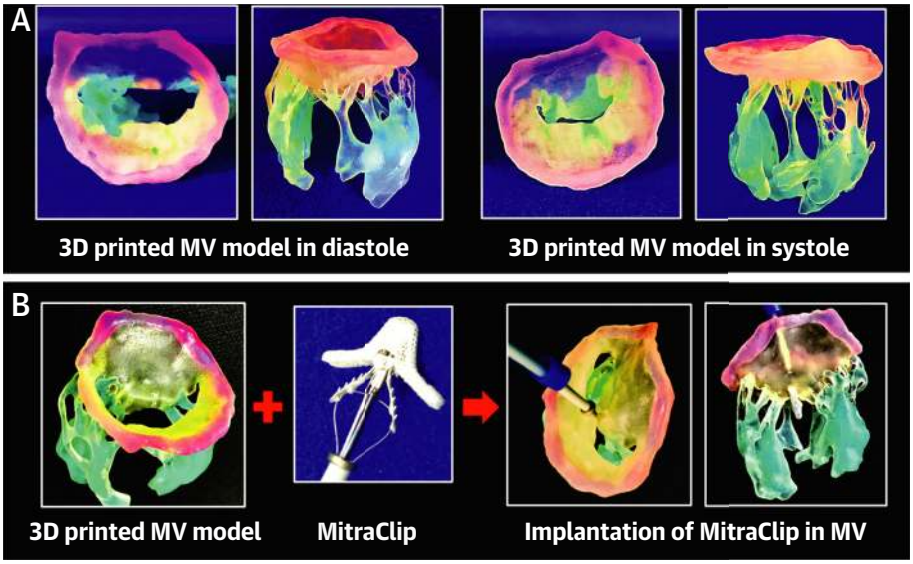
3D PRINTING FOR PERCUTANEOUS MITRAL VALVE REPAIR. Rapid expansion of increasingly complex percutaneous procedures for mitral valve repair has spawned numerous innovations in 3D printing of the mitral valve apparatus. Initial efforts resulted in the generation of the mitral annulus and leaflets for structural anatomic observations of normal and diseased valves (29,30). However, a functional and complete model of the mitral valve apparatus, including the annulus, leaflets, chordae tendineae, and papillary muscles, became necessary to provide a functional benchtop tool to test and simulate devices for patient-centric care. Vukicevic et al. (7,31) developed a multimaterial, 3D printed model of the mitral valve apparatus suitable for the benchtop simulation and planning of percutaneous mitral

TABLE 2 Imaging Techniques for 3D Printing

Imaging Modality	Technology	Pros	Cons	Applications
CT	Contrast-enhanced; ECG triggering	Fast acquisition; superb spatial resolution; excellent ability of imaging calcium; relative ease of image processing and modeling	Use of iodine contrast; mediocre temporal resolution; ionizing radiation; poor differentiation of soft tissues	3D printing of the detailed structures of the heart chambers, great vessels, valves, and coronary arteries and veins
MRI	Stacked 2D cine; free-breathing navigator-gated 3D cine	No need of contrast administration; no ionizing radiation; good spatial and temporal resolutions; good soft tissue characterization	Longer acquisition times; more expensive; lower spatial resolution than CTs	3D printing of the structures of the heart chambers and great vessels in pediatric patients and young adults
Echocardiography	3D TTE/TEE	Wide availability; good temporal resolution; ease of bedside acquisition; excellent ability of imaging valves; low cost	Low SNR; limited acoustic window size; incomplete heart anatomy imaging	3D printing of valves

CT = computed tomography; ECG = electrocardiogram; SNR = signal-to-noise ratio; TEE = transesophageal echocardiography; TTE = transthoracic echocardiogram; 3D = 3-dimensional.

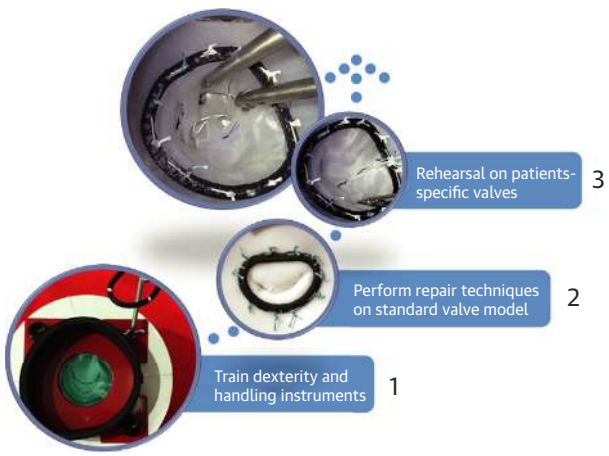
FIGURE 3 Patient-specific, Multimaterial 3D-Printed MV Apparatus



(A) A comprehensive mitral valve (MV) apparatus is extracted from contrast-enhanced computed tomography images. Patient-specific 3D printed models as shown in the diastolic and systolic phases of the cardiac cycle can be printed in different materials and colors to differentiate key cardiac anatomic structures; mitral annulus (pink), leaflets (transparent), chordae (yellow, transparent) and papillary muscles (green). **(B)** This allows for benchtop simulation of MitraClip implantation to facilitate early-operator learning curves.

valve repairs using the MitraClip Device (Figure 3). Within surgical training, high-end 3D printing-based procedural simulation has enabled trainees to obtain more hands-on practice-experience with repair technologies prior to real-world surgical intervention (Figure 4, Supplemental Video 1).

FIGURE 4 3D Print-guided Simulation for Obtaining Levels of Surgical Training

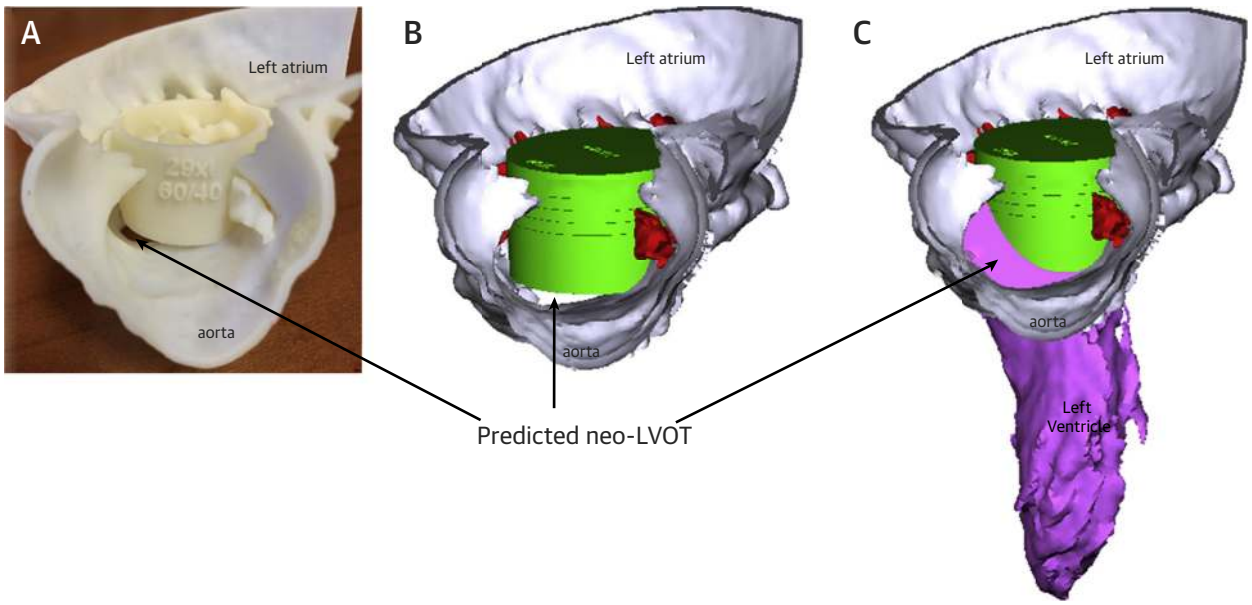


Three-dimensional printing enables high-end simulation of patient-specific valves extracted from medical imaging data suitable for mitral valve repair or cardiac interventions.

3D PRINTING AND VIRTUAL SIMULATION FOR TRANSCATHETER MITRAL VALVE REPLACEMENT. In transcatheter mitral valve replacement (TMVR), comprehension of the "neo"-LVOT (left ventricular outflow tract) first began with benchtop simulation of devices within a patient-specific 3D print of the pertinent LVOT anatomy at risk for outflow obstruction (32). The physical 3D print served as a communication tool and visual test of where the TMVR device landing zone would be in the patient's mitral plane, and a visual assessment of how small the post-TMVR predicted neo-LVOT would be. Once pre- and post-TMVR procedural CTs were obtained on patients, the concept of the neo-LVOT was able to advance from the physical 3D print to virtual 3D print valve implantation and simulation with the transcatheter devices of interest (Figure 5) (33).

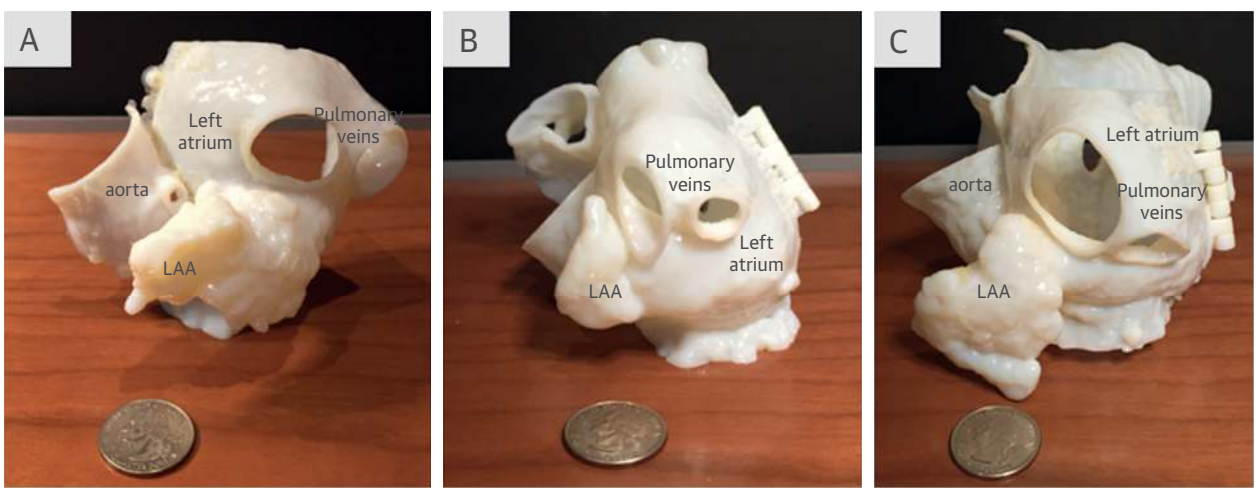
3D PRINTING IN LEFT ATRIAL APPENDAGE CLOSURE. Left atrial appendage (LAA) clinical trials and early feasibility studies did not require the use of 3D printing; however, once the LAA device market became commercial in the United States, it quickly became apparent that there existed an early-operator learning curve to device sizing and device

FIGURE 5 **Benchtop 3D Printing to Virtual 3D Print Simulation**



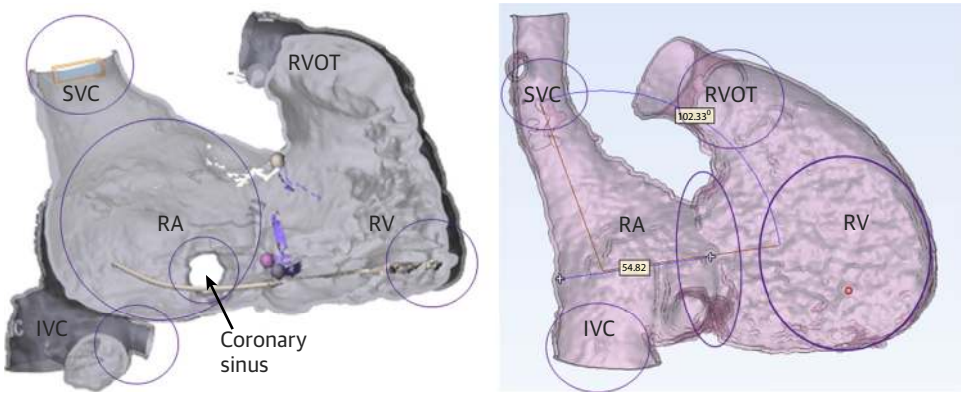
(A) Early experience with transcatheter mitral valve replacement (TMVR) involved physically 3-dimensionally (3D) printing the prosthesis of interest at a predetermined depth of implantation with visual estimation of the neo-LVOT (left ventricular outflow tract). **(B, C)** With understanding of the anatomic landmarks in the mitral landing zone, progression of TMVR planning expanded into virtual valve implant simulation in the mitral landing zone and beyond that of stationary 3D printing.

FIGURE 6 **3D Printing LAA Anatomy**



Early-operator learning curves were significantly reduced with pre-procedural 3-dimensional (3D) printing of the pertinent left atrial appendage (LAA) anatomy. This allowed implanters a thorough understanding of the unique sizing, angulations, landing zone, and geometry of the LAA and its surrounding structures. **(A–C)** Three different LAA 3D prints. Note each LAA has a unique take-off point from the left atrium, and unique angulation away from the left atrium and pulmonary veins.

FIGURE 7 How Many Differences Can You Spot?



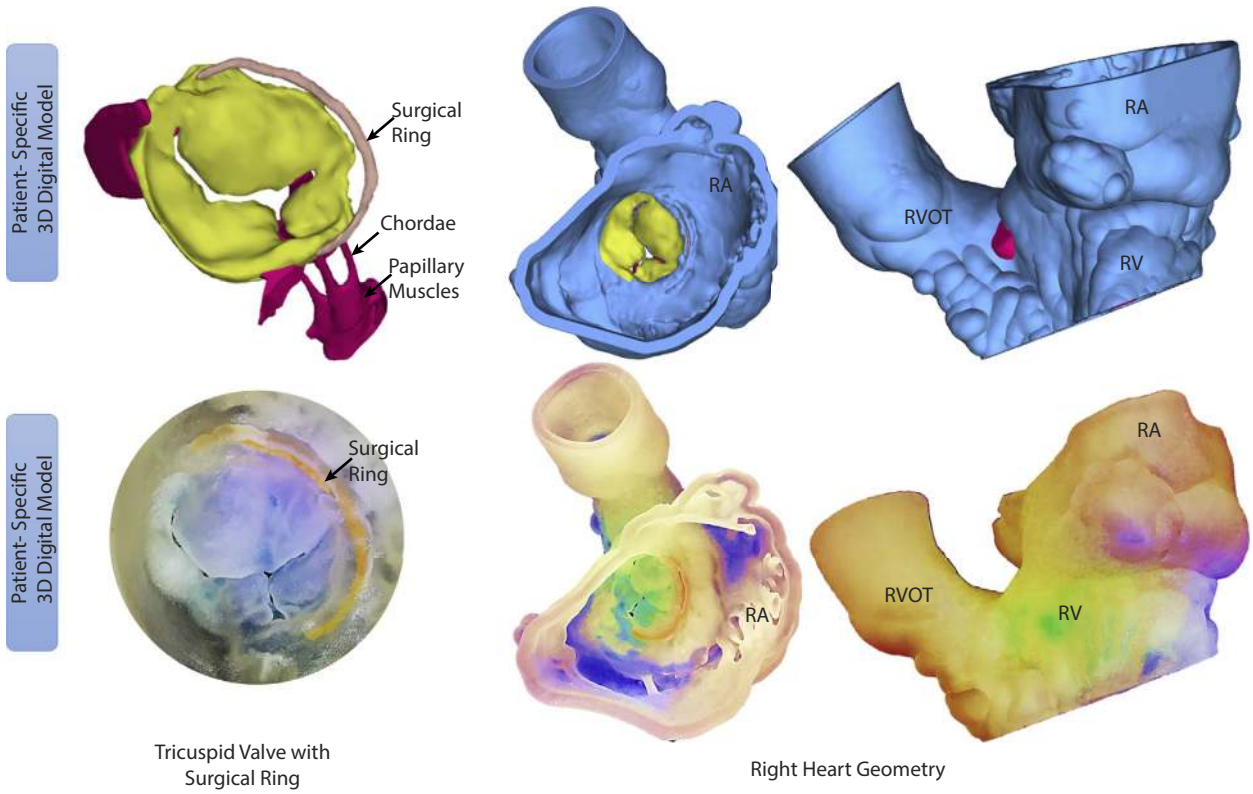
Each circle represents a difference in anatomic structure between 2 patients carrying the exact same diagnosis of tricuspid regurgitation. Circles are illuminating the superior (SVC) and inferior vena cava (IVC), coronary sinus, right atrium (RA) size, right ventricle (RV) size, RV apex location, RV outflow tract (RVOT), and angulation between the different anatomic structures. The differences presented above are only illustrative of the 2Dimensional differences noted from the anterior-posterior (AP) view of the RA and RV chamber. Not accounted for is additional 3Dimensional differences not appreciated from this static AP projection of the heart.

implantation in centers without preexisting exposure to these new technologies (34). Application of 3D printing to LAA periprocedural planning helped pave understanding of the different LAA device-specific landing zones within patients' specific anatomy, and assisted in optimizing device sizing, and catheter and device selection (**Figure 6**) (15,35,36).

3D PRINTING FOR TRANSCATHETER TRICUSPID VALVE REPAIR AND REPLACEMENTS. Percutaneous interventions on the tricuspid valve (TV) have garnered significant attention recently (37,38). Because of the inherent structural complexities of the TV apparatus, including the nonplanar annulus, varying number of leaflets, chordae, location of papillary muscles, and variability of the structures surrounding and within the right atrium and ventricle; traditional imaging modalities are insufficient in evaluating the full complexity of the right heart anatomy (**Figure 7**) and the tricuspid apparatus (**Figure 8**). Several studies have been conducted regarding the extraction of the TV from multimodality images in support of preprocedural planning and anatomic visualizations (39,40). Muraru et al. (39) demonstrated the feasibility of extracting the geometry of normal and abnormal tricuspid leaflets and annuli using 3D transesophageal echocardiogram (TEE) datasets. Their models were 3D printed of solid materials and were suitable for the measurements and quantitative analysis requisite for surgical and interventional planning. In addition, Harb et al. (41) reconstructed a series of right heart models built from multimodality images, including CT images, a combination of 3D TEE and CT data, and hybrid models extracted from MRI and non-contrast-enhanced CT data. They used the 3D printed models for the estimation of tricuspid morphology, with a focus on the interaction of the TV with surrounding elements to enhance the preprocedural planning of percutaneous interventions (41). Cabasa et al. (40) used a 3D printed model of the right heart to plan a transcatheter tricuspid valve-in-ring implantation using a Sapien XT prosthesis (Edward Lifesciences, Irvine, CA). They demonstrated how a 3D printed model reconstructed from CT imaging datasets can be used for the proper sizing and test implantation of the device ultimately selected for the actual procedure.

PATIENT EDUCATION. The value of 3D printing to the Heart Team is not limited to periprocedural case planning. Patient interaction with a physical 3D print during clinical visits has led to enhanced medical discussions around therapeutic options, patient engagement, and patient satisfaction. Traditional informed consent for intraoperative procedures requires patient comprehension of physician's 2D images, and verbal or written descriptions of the procedure they will receive. Early adoption of integration of a physical 3D print in patient education has led to improved understanding and feedback of procedural informed consent.

FIGURE 8 **Digital and 3D Printed Model of the Tricuspid Valve and Right Heart Geometry**



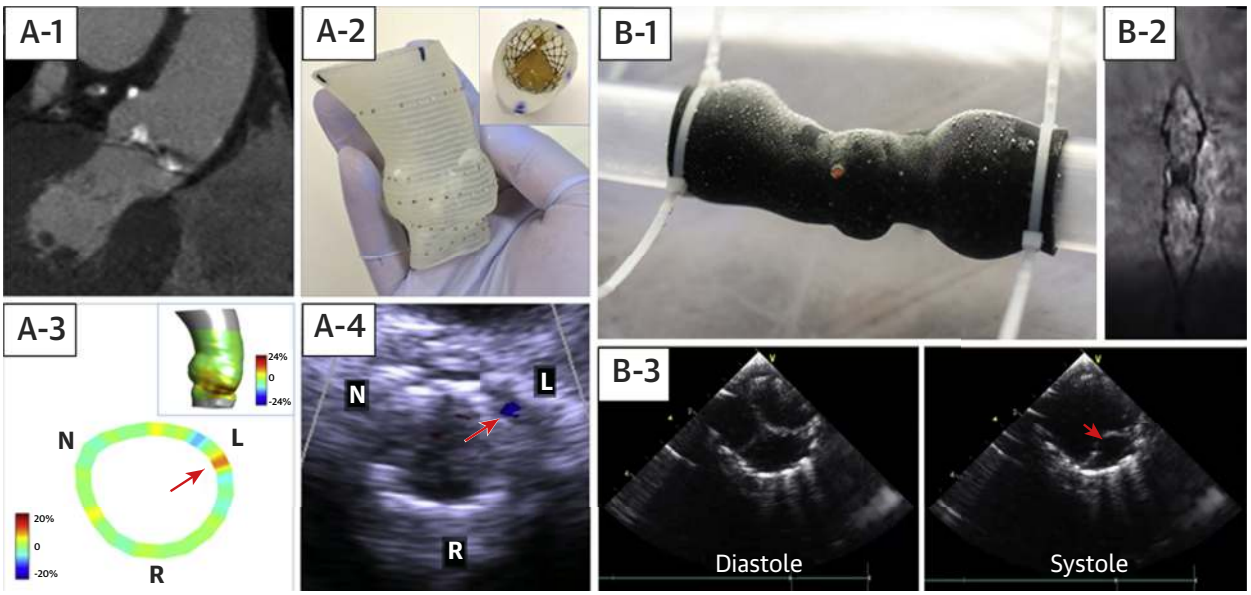
(Top row) Three-dimensional (3D) computer-aided design simulation of the patient's right atrium (RA), right ventricular outflow tract (RVOT), degenerative tricuspid ring, and infra-annular anatomic structures. **(Bottom row)** 3D-printed model of the patient's right heart geometry fabricated from a blend of different materials. RV = right ventricle.

CURRENT LIMITATIONS OF 3D PRINTING. Ideally, a 3D-printed cardiovascular model should mimic both the appearance and the mechanical property of the living organ. For in vitro device test and/or procedural simulation, preferably, the 3D printed model should also imitate the dynamic behavior of the target cardiovascular organ throughout a cardiac cycle; however, it is still challenging to find materials that perfectly match biologic tissues due to the inability of these materials to mimic the nonlinear and anisotopic behaviors of biologic tissues (9).

Recently, 4D printing techniques have been reported to manufacture 3D objects that actively deform (42). However, such technologies are still in their infancy and are not suitable for simulating a fast-beating heart that exerts high-level active force. Moreover, several studies reported that the printing direction and post-processing method significantly affected the printed objects' mechanical behavior (43,44). To produce physiologically and biologically accurate models via 3D printing, further investigation in tissue-mimicking materials is warranted.

BEYOND 3D PRINTING: BASICS OF COMPUTATIONAL MODELING AND AI. Static 3D printed models are one part of the accelerated process research and development teams are currently applying to decrease the turnaround time from new device concept to delivery of percutaneous solutions to the clinical environment. Static prints have evolved to functional 3D printed models under patient-specific pressurized hemodynamic conditions to simulate the ideal testing environment for percutaneous heart valve devices and delivery systems (**Figure 9**). However, 3D prints are not able to emulate the dynamic physical and/or the physiological principles that govern the heart function, such as the definitions of the biomechanical properties of the cardiac tissues and the physical laws of tissue deformation, flow dynamics, and their interactions.

FIGURE 9 Application of 3D Printed Phantoms in Transcatheter Heart Valve Flow-Modeling



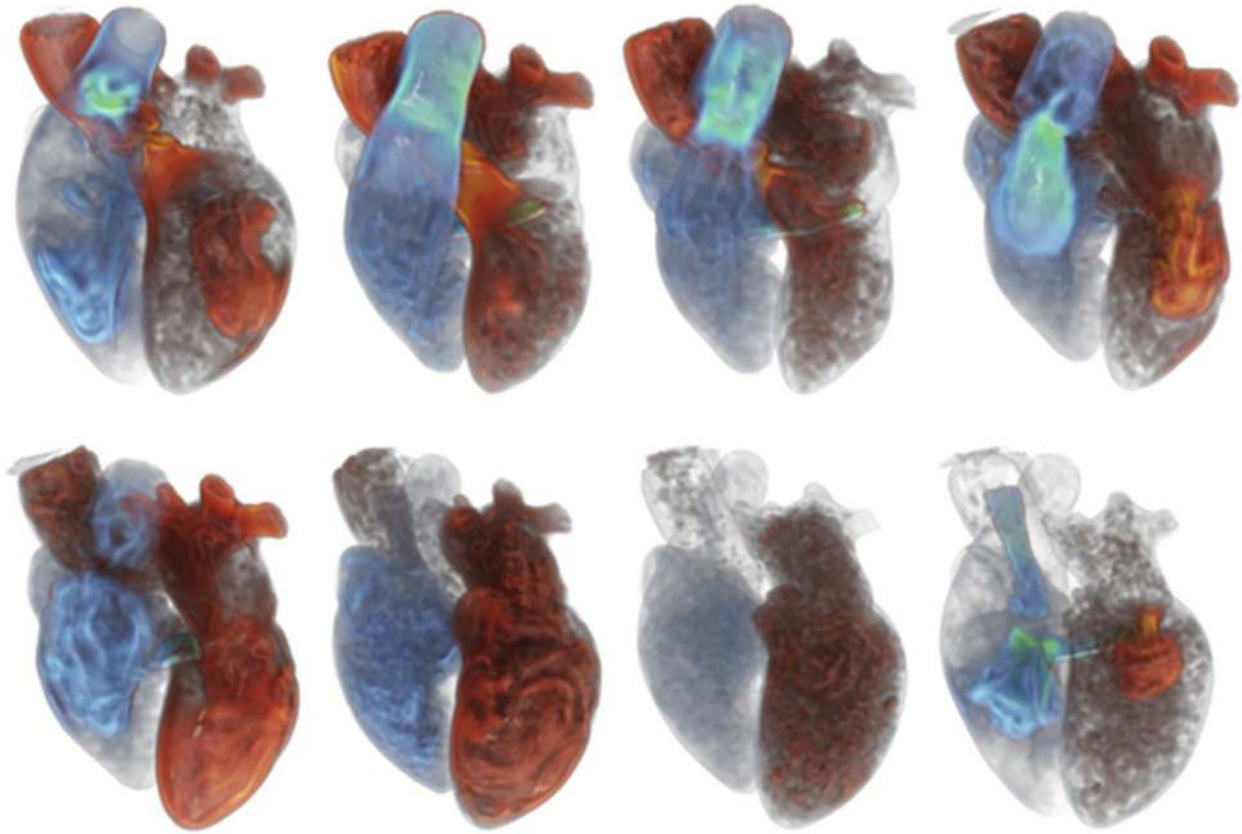
Using computed tomography as the source data **(A-1)**, a 3-dimensional (3D)-printed tissue-mimicking phantom of the aortic root was created for TAVR simulation **(A-2)**. After the in vitro transcatheter aortic valve replacement (TAVR) deployment, the circumferential strain in the aortic root was quantified, and the annular bulge index was calculated **(A-3)**, which predicted post-TAVR PVL **(A-4)**. **(B-1)** The 3D printed phantom was connected to a pulsatile flow loop. **(B-2)** Magnetic resonance and **(B-3)** ultrasound imaging were performed to image the flow and the leaflet motion of the THV. In the ultrasound image, an immobile leaflet was observed during systole **(red arrow)**.

Computational simulation is usually performed using numerical analysis methods such as finite element analysis (FEA) and computational fluid dynamics (CFD) (**Figure 10,** Supplemental Video 2). These techniques have been extensively implemented to quantify the stress and deformation of cardiac tissues (45) and characterize the blood flow pattern in the heart (46). Comprehensive preoperative simulation may take between hours and days depending on complexity of the anatomy and potential interactions between the cardiac tissues and the blood flow to be modeled for a fully coupled fluid-structure interaction (47-49). Hence, the computational cost of FEA and CFD is expensive; especially when large tissue deformation is involved, and fluid-structure interaction is implemented.

One limitation of computational simulation is that it is sensitive to the numerical assumptions that are adopted to simplify the modeling process. For instance, many studies modeled the endocardium of the left ventricle as a smooth surface (50). However, such simplification may produce unrealistic intraventricular flow pattern. As demonstrated by Kulp et al. (51), the highly trabeculated structure of human endocardium can be appreciated in vivo from a time-resolved 3D endocardial surface of the left ventricle on a patient-specific basis, as shown in **Figure 11**, which was further used to drive the CFD simulation of the intraventricular flow. Computational simulation of the blood flow has revealed the critical role of the endocardial trabeculation in facilitating the flow efficiency of the left ventricle in healthy subjects, while causing flow stagnancy in failing hearts. Similarly, CFD simulation has been performed in healthy subjects versus patients with aortic stenosis (52), which demonstrated distinctive patterns of the flow velocity and vorticity in the aortic sinus.

Currently there is a lack of commercial FEA- and CFD-based computational modeling tools for clinical use. The implementation of these techniques requires special programming/engineering skills, and therefore is mostly carried out at research institutions. In clinical practice, as shown in **Figure 12**, overlaying the transcatheter heart valves on the computational model of the heart anatomy has been proposed as a shortcut around. Using this technique, the user can test various valve sizes and anchoring depths. The neo-LVOT area can also be evaluated in pre-TMVR assessment (32,33). LVOT obstruction post-TMVR is not only determined

FIGURE 10 Integrated Model of the Entire Heart Demonstrating Magnitude of Left and Right Heart Blood Flow Vorticity



Blood flow in the heart estimated from a whole heart model derived from 3-dimensional + time cardiac computed tomography. Starting at top left image frame proceeding clockwise **(from top to bottom)**: blood flow in the cardiac cycle is illustrated in early systolic phase of the cardiac cycle, progressing to mid-systole, late systole, followed with early diastole with illustration of pulmonic valve regurgitation, then bottom row **(right to left)** early diastolic filling, mid-diastolic filling, diastasis, and completed with late mitral filling.

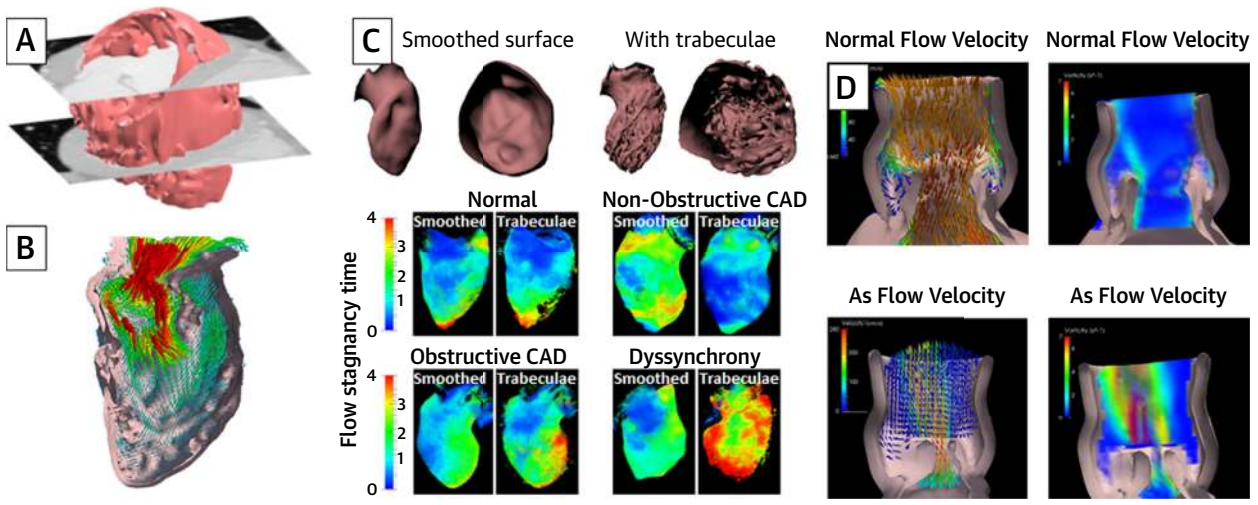
by the neo-LVOT geometry but can also be determined by the hemodynamics in the left ventricle (Figure 13). However, it must be noted that there is no physical interaction modeled in such a setup, and no valve/tissue deformation can be observed.

ROLE FOR AI IN SHD

Health care has significant potential to be influenced by AI. This is being substantiated by a surge of commercial investments in the field for AI solutions that offer to improve health care and enable precision medicine in recent years and large-scale adoption of AI in leading medical companies. As demonstrated in previous sections, SHD is a field that is characterized by an abundance of used, unused, and unmeasured parameters, and suboptimal visualization of 3D structure and "4D" physiology with significant variation between patients, including age, sex, and race. This provides enormous potential for AI solutions that could improve patient care in terms of effectiveness, efficiency, and reducing costs. AI, and more specifically machine learning, is different from classic computer programming, as it is domain agnostic; learning from examples without relying on program-defined rules. As a result, machine-learning models can learn extremely complex associations from large amounts of data without the need for common sense (53,54).

AI-BASED METHODS TO IMPROVE STRUCTURAL HEART INTERVENTIONS. Combining AI with the latest developments in 3D printing has enabled manufacturing of patient-specific anatomic replica, which yields a significant contribution toward precision medicine (55,56). Engelhardt et al. (57) demonstrated realistic minimally invasive surgical training

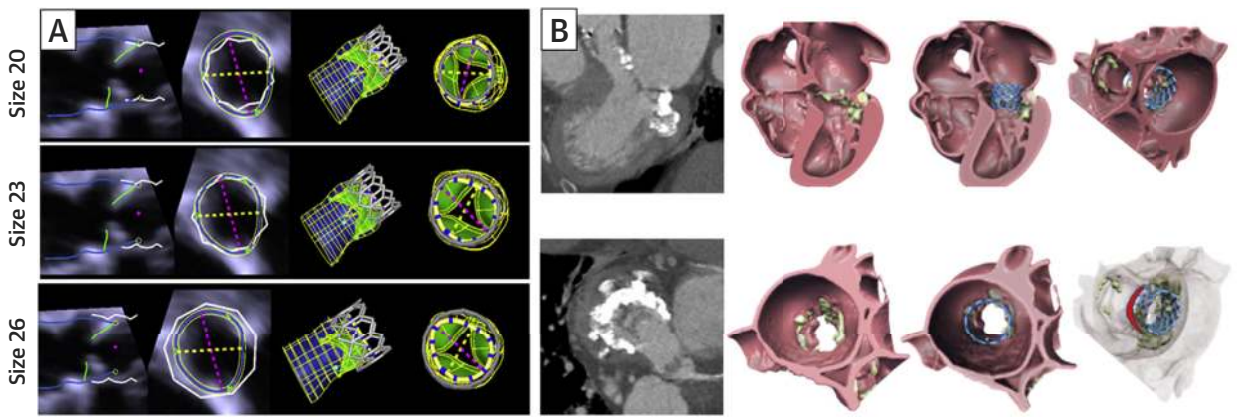
FIGURE 11 CFD Simulation Using Subject-Specific Heart Geometries



(A) The time-resolved 3-dimensional (3D) surface model of the left ventricular endocardium was segmented from the 3D+t computed tomography images. **(B)** Computational flow dynamic (CFD) was performed to simulate the complex flow in the left ventricle. **(C)** A smoothed surface model and a complex surface model with detailed trabeculae were used to simulate flow in a healthy subject, and patients with nonobstructive coronary artery disease (CAD), obstructive CAD, and dyssynchrony. Flow stagnancy time was calculated. **(D)** Flow simulation was performed in the aortic roots of a healthy subject and a patient with severe aortic stenosis (AS).

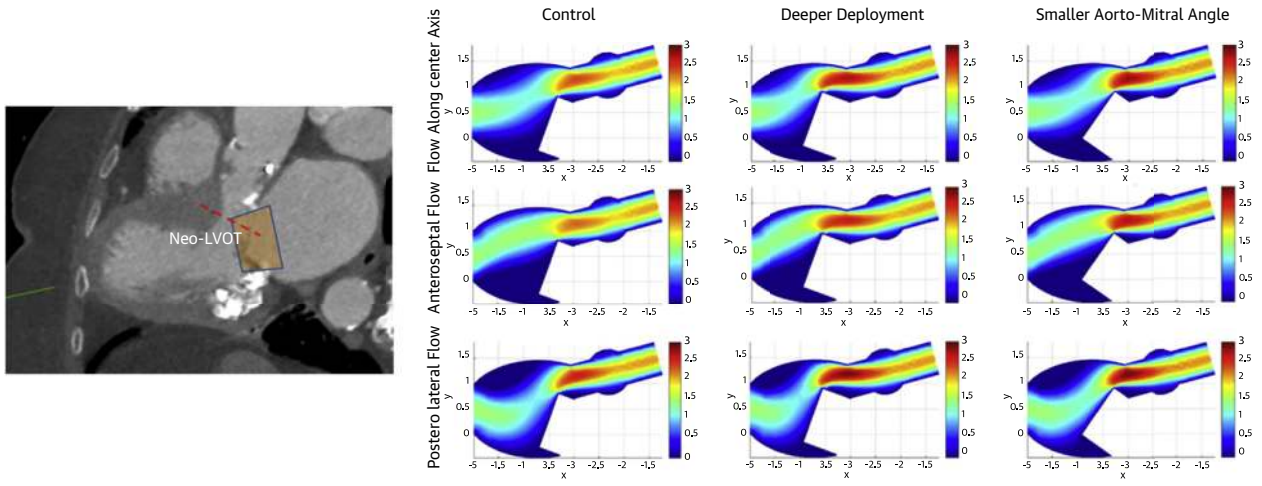
capabilities through the use of a deep neural network that learned key descriptors of the intraoperative scene from endoscopic frames (Figures 14 and 15). The computer network can be taught to learn the key descriptors of the intraoperative scene (i.e., the heterogeneous texture, blood, specularity, instrument, suture application) from many endoscopic examples of mitral valve repair as well as significant features from simulation testing (e.g., silicone surface of the valve replica, instruments, sutures).

FIGURE 12 Computational Simulation of Transcatheter Valve Deployment



Proposed transcatheter heart valves are simulated on patient-specific anatomic models. **(A)** Different-sized transcatheter aortic valve replacement valves are overlaid on a 3-dimensional transesophageal echocardiogram (TEE)-derived patient-specific aortic root model. **(B)** A balloon-expanded transcatheter aortic valve is virtually deployed in the mitral position with severe mitral annular calcification for the assessment of the potential dislodge risk and the neo-left ventricular outflow tract area post transcatheter mitral valve replacement.

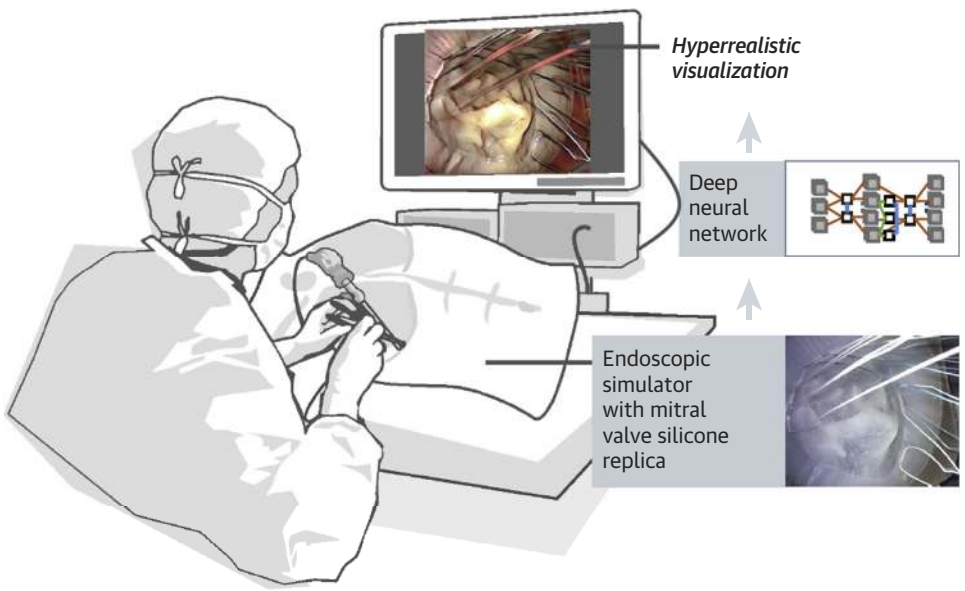
FIGURE 13 LVOT Obstruction Post-TMVR Visualized Using CFD



Computational flow dynamics (CFD) simulation has revealed that the occurrence of left ventricular outflow tract (LVOT) obstruction post transcatheter mitral valve replacement (TMVR) is multifactorial, affected by the valve deployment depth, the valve deployment angle, and the intraventricular flow direction.

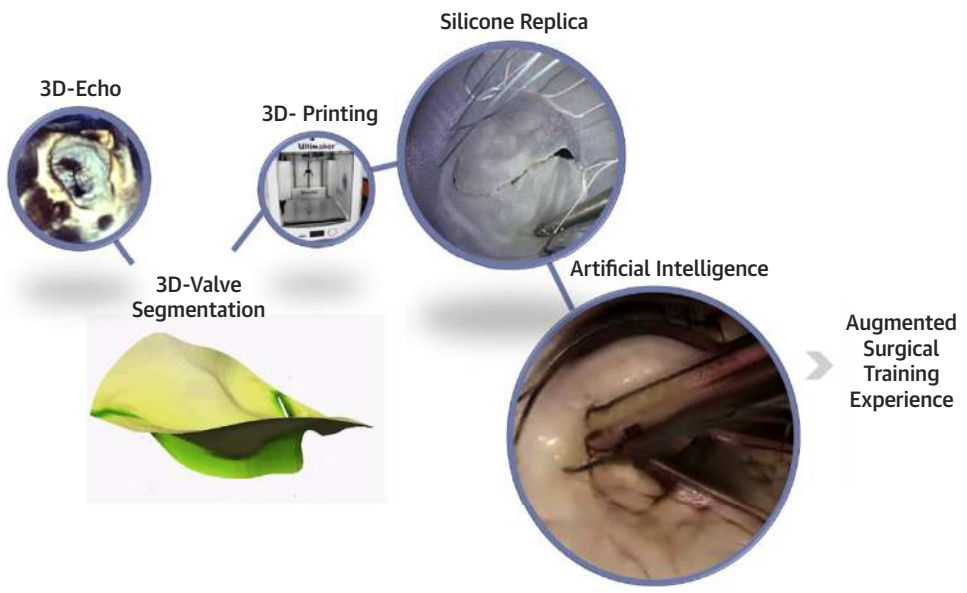
The AI network's training goal is to learn mapping between these 2 domains or simply, how to transform a frame from 1 domain into the other by solely changing the appearance of the objects. This approach, coined *hyperrealism*, a subform of *augmented reality*, is able to generate a simulated reality with details not existing in the original image to enhance the surgical training process with

FIGURE 14 Concept of Hyperrealism



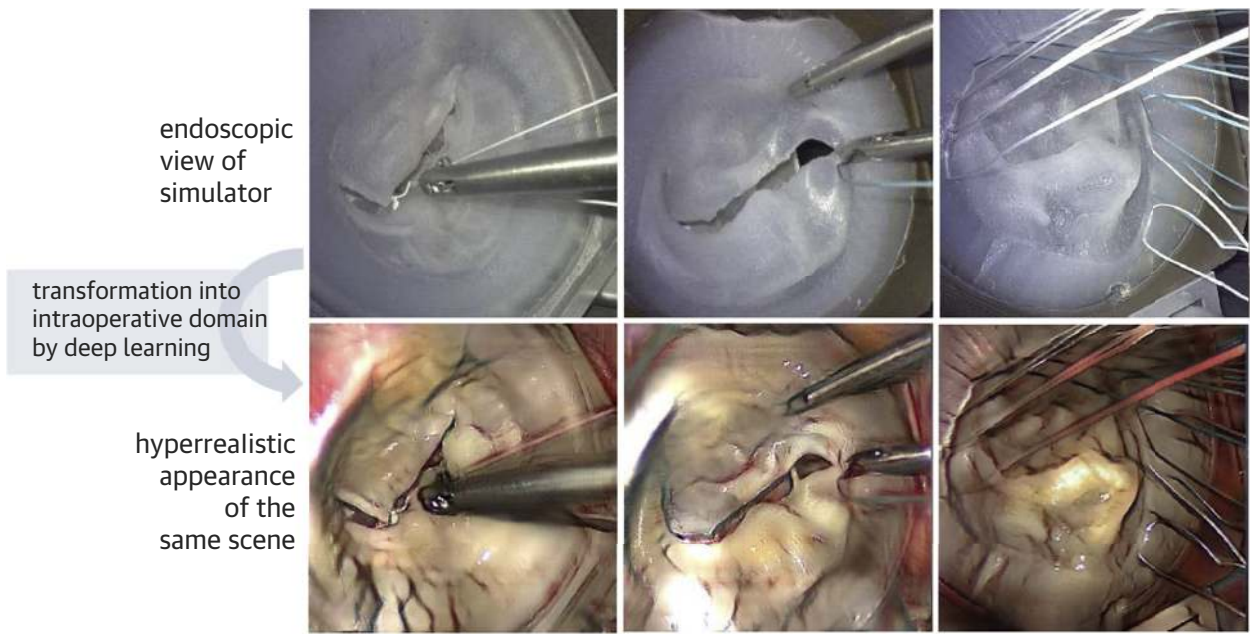
Hyperrealism, a novel subform of augmented reality where real, but artificially looking objects (in this case the silicone valve phantoms) are changed to appear realistically, for example, by including heterogeneous texture and blood. Objects that already look realistic ideally stay the same (in this case the instruments, sutures).

FIGURE 15 Hyperrealism in Surgical Training



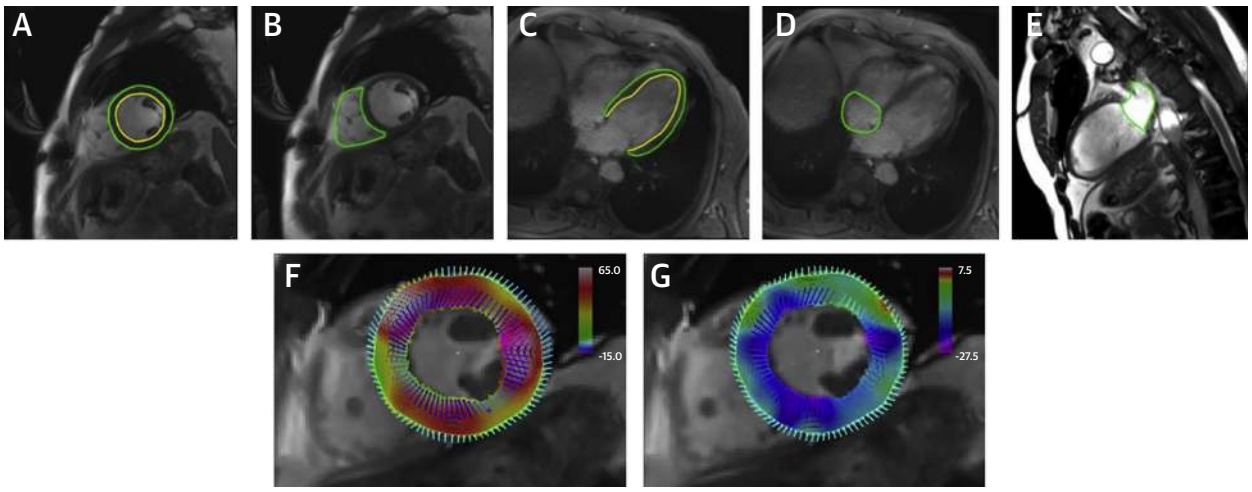
Application of 3-dimensional (3D) image acquisition to virtual image segmentation, to making of a physical 3D print, followed by silicone replica production with incorporation of artificial intelligence in generating an augmented surgical training experience.

FIGURE 16 GANs



Generative adversarial networks (GANs) transform the appearance of a physical phantom into a more intraoperative-like appearance.

FIGURE 17 Deep-Dense Neural Network in Cardiac CMR Segmentation



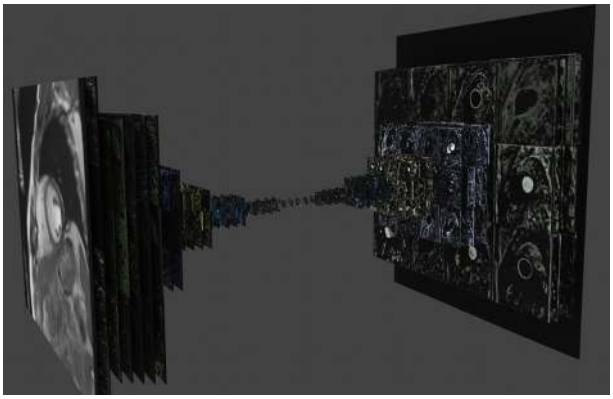
Cardiac cine magnetic resonance analysis: **(A to E)** The Deep-Dense Neural Network estimates the contours of the 4 heart chambers and the contour of the myocardium. **(F, G)** The network also computes the radial and circumferential strain. (Image data courtesy of NYU Langone Health.) CMR = cardiac magnetic resonance.

more realistic renderings from the actual procedure (58). Figure 16 demonstrates the concept of hyperrealism for mitral valve intervention training with a mitral valve silicone phantom.

TRAINING OF INTERVENTIONALISTS AND INTERVENTIONAL IMAGING PHYSICIANS. The potential adaptation of hyperrealism and AI-based simulation in commercial device training will likely form the foundation of future training pathways for new technology development. Integration of full valvular cardiac models in a procedural simulation platform has already demonstrated improved operator confidence of procedural instrument handling and application of surgical techniques intraoperatively (56,59,60). Application of AI in intraprocedural TEE training within the scope of a supervised deep-learning framework allows for computerized objective automatic image quality grading and feedback of acquired TEE images (59). Within the context of physician training for TAVR interventions, automated skill assessment based on motion analysis and surgical tool manipulation patterns has demonstrated reproducible objective metrics such as procedure time, speed, and motion acceleration distinctions between novice and expert-level proceduralists (60). Future integration of real-time 3D TEE datasets with machine learning and AI will allow for enhanced objective scalable modules to be built for the training of interventional imaging physicians and operators.

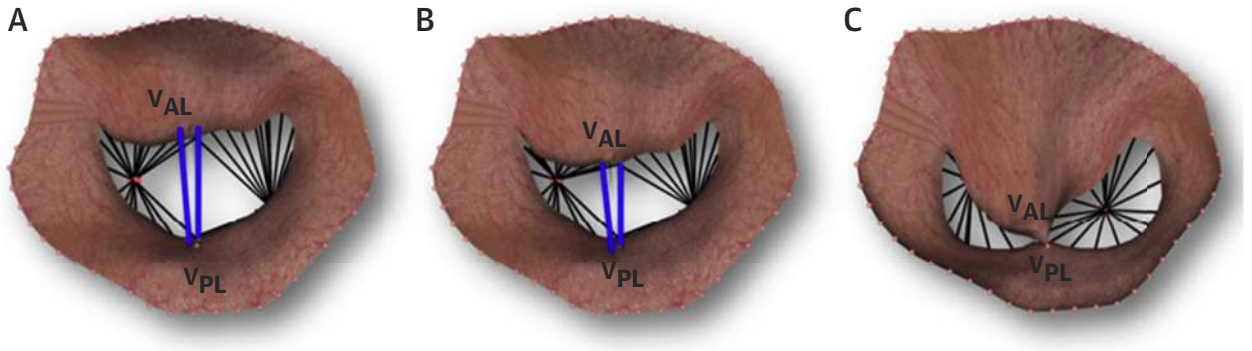
WHERE DEEP LEARNING MAY HELP WITH REAL-WORLD INTEGRATION OF AI. One of the most significant applications of deep learning in medical imaging is in the field of segmentation. Segmentation of cardiac CT and cardiac MRI data into heart chambers provides clinically important information about chamber size, shape, and function (Figure 17) (61).

FIGURE 18 Speed of Deep-Dense Neural Network



The Deep-Dense Neural Network is designed to process cine magnetic resonance data and estimate contours, measurements, and motion of the left and right ventricles and myocardium. The network has an encoder-decoder architecture with 300 layers and 1 million parameters. (Image data courtesy of NYU Langone Health.)

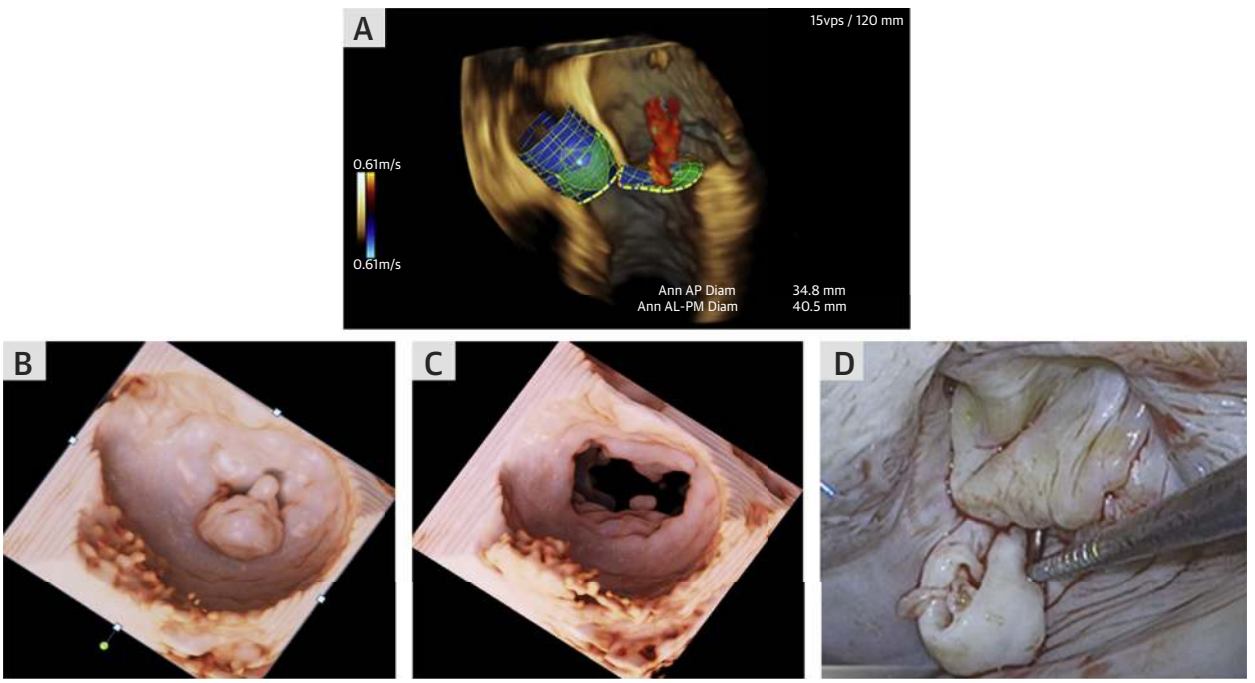
FIGURE 19 User Input Derived Interactive Simulation of Mitraclip Procedure



(A) The user identifies 2 points of grasping for virtual MitraClip implantation (V_{AL} on the anterior mitral leaflet, and V_{PL} on the posterior mitral leaflet). **(B)** A virtual spring is created between the 2 grasping points/vertices (V_{AL} and V_{PL}) that incrementally pulls the zone of coaptation together between V_{AL} and V_{PL} **(blue lines)**. **(C)** Eventually, the zone of coaptation is stitched together by the spring, simulating completion of a virtual MitraClip grasp (64,65).

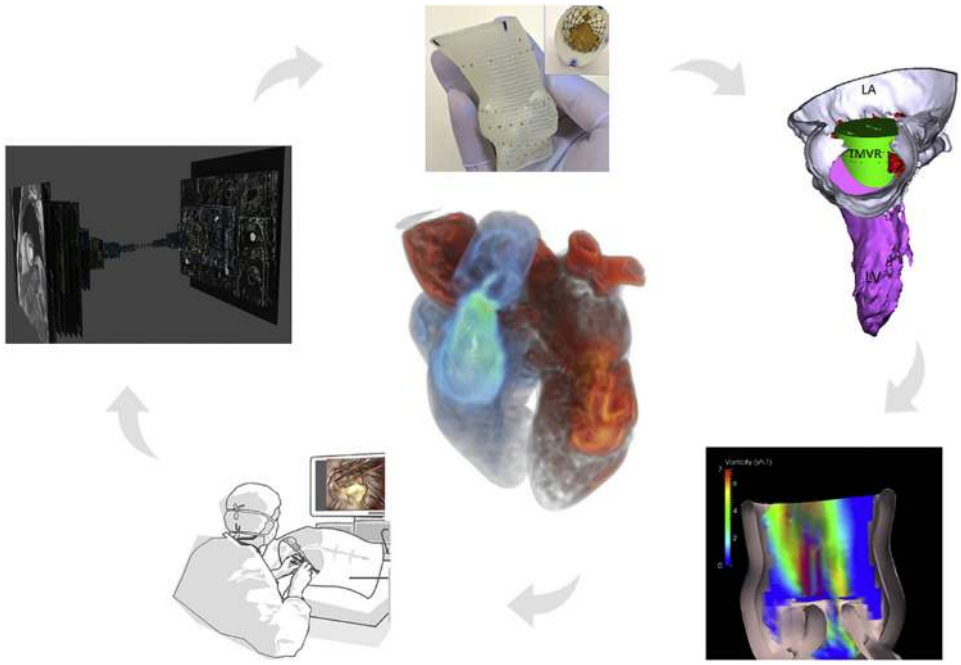
Application of AI may help (1) automate the process and eliminate interoperator and intraoperator variability; and (2) achieve fast and accurate results in a clinically actionable time frame (**Figure 18**). Much of its clinical potential lies in its ability to analyze combinations of structured data originating from heterogeneous sources to generate value in clinical decision support. By integrating complementary information to

FIGURE 20 Real-Time 3D Color to Cinematic Rendering



(A) Application of real-time 3-dimensional (3D) transesophageal echocardiography (TEE) imaging enables full-volume dynamic visualization of cardiac anatomy and color Doppler rendering of blood flow across cardiac structures of interest (66). Machine learning helps to build reproducible models of the valves. 3D TEE acquisition and visualization with cinematic rendering of the surgeon's view of mitral valve apparatus demonstrating ruptured P2 chordae tip with prolapse of body of P2 scallop of the mitral valve in systole **(B)** and diastole **(C)**. **(D)** Surgical view of the same case. (Surgical picture of the mitral valve, courtesy of Dr. Federico Milla, Piedmont Heart Institute)

CENTRAL ILLUSTRATION **Modernizing Medicine**



Wang, D.D. et al. J Am Coll Cardiol Img. 2021;14(1):41–60.

Integration of physical and virtual 3D printing, including procedural simulation, fluid modeling, and artificial intelligence into transcatheter interventions is the next wave of clinical education, device development, and optimization of patient-centric care.

be processed with novel deep-learning methods, previously hidden knowledge in the data could be uncovered, which in turn could foster a more reliable clinical decision support. Each type of data could be analyzed independently or in concert with different types of algorithms to yield innovations. For example, MitraClip procedural simulation could enable users to select the leaflet scallops of interest to clip and evaluate the mitral coaptation zone formation after virtual clip implantation to achieve optimal intraoperative results (**Figure 19**). Intraoperative monitoring of such different types of data could lead to real-time prediction and avoidance of adverse events.

Furthermore, AI could be used to structure, share, and retrieve massive amounts of collected operative video, intraoperative imaging, and electronic medical records across many surgeons and interventionists around the world (62) (**Figure 18**). This would generate a database of practices and techniques against outcomes. The potential benefit of advancing machine learning and AI is the ability to improve on and create more reproducible models of valvular anatomy applied in real-time 3D TEE imaging (**Figure 20**). AI could be then helpful in identification of rare cases of anatomy, integrating data across pre-, intra-, and post-operative phases of care (10) (**Central Illustration**).

TECHNOLOGY CHALLENGES TO ADDRESS AND OVERCOME. The main challenge in real-world application of AI is the presence of vast amounts of unstructured clinical data. Cornerstone of data collection is proper source image formatting, compatibility of file conversions between servers, and ability to directly upload to the learning cloud. Once uploaded data are incorporated into the existing datasets within the cloud, AI algorithms would be activated and improved on as new data are harnessed to compose leaner processes. Similar to the early-operator learning curve appreciated in TAVR (63), the AI algorithm would turn more accurate and efficient as new datasets are added to its training set. However, this application is currently limited in scalability to complex SHD interventions because of the need for more scientific development of adaptive and transfer learning techniques.

Data quality (GIGO: garbage in, garbage out). Implementation of cloud computing and adaptive learning based on the automatically uploaded data is dependent on robust data quality being inputted to existing datasets in the cloud. Low-quality dataset not only deteriorates the efficiency of a functional AI algorithm, but may also reduce the AI's accuracy in determining key procedural steps.

Legal considerations. Once the AI server is established to process inputted data for training sets, there remains a question of ownership of the input/interaction data. Ownership should be clarified to that of the patient whose procedural data are uploaded, the physician who performed the procedure, or another entity supporting the AI application. These legal considerations need to be considered before clinical and global use of AI in medical imaging and particularly for application of AI in the field of SHD interventions.

Privacy and confidentiality. The last but not the least consideration for application of AI to the field of structural heart interventions is the concern for privacy and confidentiality with big data. In the presence of cloud sharing, and server usage; health care data will be at risk for hacking and security breech. Data-sharing risks and medical-legal liability issues must be addressed before large-scale application of AI can be applied to medical imaging and interventions.

CONCLUSION

There is a role for 3D printing, computer simulation modeling, and deep-learning within SHD interventions. Early application of these technologies has potential to diminish the early-operator learning curve witnessed with launch of new device technologies. Future applications of computational modeling and deep-learning will require integration of patient-procedural and patient-data safety into medical records and medical data acquisition and sharing platforms. The future of multimodality cardiovascular imaging will require the integration of the clinical knowledge of cardiac pathophysiology to the technical expertise of biomedical engineers and software development knowledge of computer scientists. It will no longer be just about one clinician's know-how.

HIGHLIGHTS

- Structural heart interventions require in-depth understanding of cardiac pathophysiology.
- 3D printing can decrease the early-operator learning curve for new technology adaptation.
- Computational fluid modeling has potential to emulate dynamic physical and physiological properties of cardiac pathophysiology.
- Application of AI has potential for patient-specific anatomic replica procedural simulation training.

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AUTHOR DISCLOSURES

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REFERENCES

1. Wang DD, Geske J, Choi AD, et al. Navigating a career in structural heart disease interventional imaging. J Am Coll Cardiol Img 2018;11:1928–30.

2. Hull CW. Apparatus for production of three-dimensional objects by stereolithography. In: Uspto, editor. US Patent: UVP Inc; 1986.

3. Deckard CR. Method and apparatus for producing parts by selective sintering. In: Uspto, editor. US Patent: University of Texas System; 1989.

4. Scott Crump S. Apparatus and method for creating three-dimensional objects. In: Uspto, editor. US Patent: Stratasys Inc; 1992.

5. Heonju LEE, Moon M, Jo W, Han S, Lee H, Song I. Ink composition for powder bed and inkjet head 3d printing. In: Uspto, editor. US Patent: Korea Advanced Institute of Science and Technology (KAIST); 2017.

6. Gothait H. Apparatus and method for three dimensional model printing. In: Uspto, editor. US Patent: Object Geometries Ltd; 2001.

7. Vukicevic M, Mosadegh B, Min JK, Little SH. Cardiac 3D printing and its future directions. J Am Coll Cardiol Img 2017;10:171–84.

8. Qian Z, Wang K, Liu S, et al. Quantitative prediction of paravalvular leak in transcatheter aortic valve replacement based on tissue-mimicking 3D printing. J Am Coll Cardiol Img 2017;10:719–31.

9. Wang K, Wu CS, Qian Z, Zhang C, Wang B, Vannan MA. Dual-material 3D printed metamaterials with tunable mechanical properties for patient-specific tissue-mimicking phantoms. Additive Manufacturing 2016;12:31–7.

10. Rengier F, Mehndiratta A, von Tengg-Kobligk H, et al. 3D printing based on imaging data: review of medical applications. Int J Comput Ass Rad 2010;5:335–41.

11. Sodian R, Weber S, Markert M, et al. Pediatric cardiac transplantation: three-dimensional printing of anatomic models for surgical planning of heart transplantation in patients with univentricular heart. J Thorac Cardiovasc Surg 2008;136:1098–9.

12. Costello JP, Olivieri LJ, Krieger A, et al. Utilizing three-dimensional printing technology to assess the feasibility of high-fidelity synthetic ventricular septal defect models for simulation in medical education. World J Pediatr Congenit Heart Surg 2014;5:421–6.

13. Binder TM, Moertl D, Mundigler G, et al. Stereolithographic biomodeling to create tangible hard copies of cardiac structures from echocardiographic data: in vitro and in vivo validation. J Am Coll Cardiol 2000;35:230–7.

14. Mahmood F, Owais K, Taylor C, et al. Three-dimensional printing of mitral valve using echocardiographic data. J Am Coll Cardiol Img 2015;8:227–9.

15. Fan Y, Yang F, Cheung GS, et al. Device sizing guided by echocardiography-based three-dimensional printing is associated with superior outcome after percutaneous left atrial appendage occlusion. J Am Soc Echocardiogr 2019;32:708–19.e1.

16. Faletti R, Gatti M, Cosentino A, et al. 3D printing of the aortic annulus based on cardiovascular computed tomography: preliminary experience in pre-procedural planning for aortic valve sizing. J Cardiovasc Comput Tomogr 2018;12:391–7.

17. Ripley B, Kelil T, Cheezum MK, et al. 3D printing based on cardiac CT assists anatomic visualization prior to transcatheter aortic valve replacement. J Cardiovasc Comput Tomogr 2016;10:28–36.

18. Wang Q, Sun W. Finite element modeling of mitral valve dynamic deformation using patient-specific multi-slices computed tomography scans. Ann Biomed Eng 2013;41:142–53.

19. Liang L, Kong F, Martin C, et al. Machine learning-based 3-D geometry reconstruction and modeling of aortic valve deformation using 3-D computed tomography images. Int L Numer Method Biomed Eng 2017;33:https://doi.org/10.1002/cnm.2827.

20. Zheng Y, Barbu A, Georgescu B, Scheuering M, Comaniciu D. Four-chamber heart modeling and automatic segmentation for 3-D cardiac CT volumes using marginal space learning and steerable features. IEEE Trans Med Imaging 2008;27:1668–81.

21. Ionasec RI, Voigt I, Georgescu B, et al. Patient-specific modeling and quantification of the aortic and mitral valves from 4-D cardiac CT and TEE. IEEE Trans Med Imaging 2010;29:1636–51.

22. Billiar KL, Sacks MS. Biaxial mechanical properties of the natural and glutaraldehyde treated aortic valve cusp—part I: experimental results. J Biomech Eng 2000;122:23.

23. Martin C, Sun W. Biomechanical characterization of aortic valve tissue in humans and common animal models. J Biomed Mater Res A 2012;100a:1591–9.

24. Auricchio F, Conti M, Morganti S, Reali A. Simulation of transcatheter aortic valve implantation: a patient-specific finite element approach. Comput Methods Biomech Biomed Engin 2014;17:1347–57.

25. Hernández-Enríquez M, Brugaletta S, Andreu D, et al. Three-dimensional printing of an aortic model for transcatheter aortic valve implantation: possible clinical applications. Int J Cardiovasc Imaging 2016;33:283–5.

26. Maragiannis D, Jackson MS, Igo SR, Chang SM, Zoghbi WA, Little SH. Functional 3D printed patient-specific modeling of severe aortic stenosis. J Am Coll Cardiol 2014;64:1066–8.

27. Liu K, Lyu B, Ren X, Wang Z, Wu Y, Zheng Z. [Prior transcatheter aortic valve implantation evaluation with 3D printing technology: a case report]. Zhonghua Xin Xue Guan Bing Za Zhi 2015;43:634–5.

28. Maragiannis D, Jackson MS, Igo SR, et al. Replicating patient-specific severe aortic valve stenosis with functional 3D modeling. Circ Cardiovasc Imaging 2015;8:e003626.

29. Mahmood F, Owais K, Montealegre-Gallegos M, et al. Echocardiography derived three-dimensional printing of normal and abnormal mitral annuli. Ann Card Anaesth 2014;17:279–83.

30. Kapur KK, Garg N. Echocardiography derived three-dimensional printing of normal and abnormal mitral annuli. Ann Card Anaesth 2014;17:283–4.

31. Vukicevic M, Vekilov DP, Grande-Allen JK, Little SH. Patient-specific 3D valve modeling for structural intervention. Structural Heart 2017;1:236–48.

32. Wang DD, Eng M, Greenbaum A, et al. Predicting LVOT obstruction after TMVR. J Am Coll Cardiol Img 2016;9:1349–52.

33. Wang DD, Eng MH, Greenbaum AB, et al. Validating a prediction modeling tool for left ventricular outflow tract (LVOT) obstruction after transcatheter mitral valve replacement (TMVR). Catheter Cardiovasc Interv 2018;92:379–87.

34. Wang DD, Eng M, Kupsky D, et al. Application of 3-dimensional computed tomographic image guidance to WATCHMAN implantation and impact on early operator learning curve: single-center experience. J Am Coll Cardiol Intv 2016;9:2329–40.

35. Wang DD, Gheewala N, Shah R, et al. Three-dimensional printing for planning of structural heart interventions. Interventional Cardiology Clinics 2018;7:415–23.

36. Eng MH, Wang DD, Greenbaum AB, et al. Prospective, randomized comparison of 3-dimensional computed tomography guidance versus TEE data for left atrial appendage occlusion (PRO3DLAAO). Catheter Cardiovasc Interv 2018;92:401–7.

37. Avenatti E, Barker CM, Little SH. Tricuspid regurgitation repair with a MitraClip device: the pivotal role of 3D transoesophageal echocardiography. Eur Heart J Cardiovasc Imaging 2017;18:380.

38. Hahn RT, Meduri CU, Davidson CJ, et al. Early feasibility study of a transcatheter tricuspid valve annuloplasty: SCOUT trial 30-day results. J Am Coll Cardiol 2017;69:1795–806.

39. Muraru D, Veronesi F, Maddalozzo A, et al. 3D printing of normal and pathologic tricuspid valves from transthoracic 3D echocardiography data sets. Eur Heart J Cardiovasc Imaging 2016;18:802–8.

40. Cabasa AS, Eleid MF, Rihal CS, Villarraga HR, Foley TA, Suri RM. Tricuspid valve replacement: a percutaneous transfemoral valve-in-ring approach. J Am Coll Cardiol Intv 2015;8:1126–8.

41. Harb SC, Rodriguez LL, Svensson LG, et al. Pitfalls and pearls for 3-dimensional printing of the tricuspid valve in the procedural planning of percutaneous transcatheter therapies. J Am Coll Cardiol Img 2018;11:1531–4.

42. Raviv D, Zhao W, McKnelly C, et al. Active printed materials for complex self-evolving deformations. Sci Rep 2014;4:7422.

43. Sugavaneswaran M, Arumaikkannu G. Modelling for randomly oriented multi material additive manufacturing component and its fabrication. Mater Design 2014;54:779–85.

44. Dizon JRC, Espera AH Jr., Chen Q, Advincula RC. Mechanical characterization of 3D-printed polymers. Additive Manufacturing 2018;20:44–67.

45. Wang Q, Primiano C, McKay R, Kodali S, Sun W. CT image-based engineering analysis of transcatheter aortic valve replacement. J Am Coll Cardiol Img 2014;7:526–8.

46. McQueen DM, Peskin CS. A three-dimensional computer model of the human heart for studying cardiac fluid dynamics. SIGGRAPH Comput Graph 2000;34:56.

47. Kunzelman KS, Einstein DR, Cochran RP. Fluid-structure interaction models of the mitral valve: function in normal and pathological states. Philos Trans R Soc Lond B Bio Sci 2007;362:1393–406.

48. Ma X, Gao H, Griffith BE, Berry C, Luo X. Image-based fluid-structure interaction model of the human mitral valve. Comput Fluids 2013;71:417–25.

49. Mao W, Caballero A, McKay R, Primiano C, Sun W. Fully-coupled fluid-structure interaction simulation of the aortic and mitral valves in a realistic 3D left ventricle model. PLoS One 2017;12:e0184729.

50. Mihalef V, Metaxas D, Sussman M, Hurmusiadis V, Axel L. Atrioventricular blood flow simulation based on patient-specific data. In: Ayache N, Delingette H, Sermesant M, editors. Functional Imaging and Modeling of the Heart. Berlin, Heidelberg: Springer, 2009; p 386–95.

51. Kulp S, Gao M, Zhang S, et al. Using high resolution cardiac CT data to model and visualize patient-specific interactions between trabeculae and blood flow. Med Image Comput Comput Assist Interv 2011;14:468–75.

52. Kulp S, Qian Z, Vannan M, Rinehart S, Metaxas D. Patient-specific aortic valve blood flow simulations. 2014 IEEE 11th International Symposium on Biomedical Imaging (ISBI). IEEE; 2014; p 939–42.

53. Stead WW. Clinical implications and challenges of artificial intelligence and deep learning. JAMA 2018;320:1107–8.

54. Rajkomar A, Dean J, Kohane I. Machine learning in medicine. N Engl J Med 2019;380:1347–58.

55. Engelhardt S, Sauerzapf S, Preim B, Karck M, Wolf I, De Simone R. Flexible and comprehensive patient-specific mitral valve silicone models with chordae tendineae made from 3D-printable molds. Int J Comput Assist Radiol Surg 2019;14:1177–86.

56. Engelhardt S, Sauerzapf S, Brčić A, Karck M, Wolf I, De Simone R. Replicated mitral valve models from real patients offer training opportunities for minimally invasive mitral valve repair. Interact Cardiovasc Thorac Surg 2019;29:43–50.

57. Engelhardt S, Sauerzapf S, Al-Maisary S, et al. Elastic mitral valve silicone replica made from 3D-printable molds offer advanced surgical training. In: Maier A, Deserno T, Handels H, Maier-Hein K, Palm C, Tolxdorff T, editors. Bildverarbeitung für die Medizin 2018. Berlin Heidelberg: Springer, 2018; p 74–9.

58. Engelhardt S, De Simone R, Full PM, Karck M, Wolf I. Improving surgical training phantoms by hyperrealism: deep unpaired image-to-image translation from real surgeries: 21st International Conference, Granada, Spain, September 16–20, 2018, Proceedings, Part I. In: Frangi AF, Schnabel JA, Davatzikos C, Alberola-López C, Fichtinger G, editors. Medical Image Computing and Computer Assisted Intervention – MICCAI 2018. Cham: Springer International Publishing, 2018; p 747–55.

59. Mazomenos EB, Bansal K, Martin B, Smith A, Wright S, Stoyanov D. Automated performance assessment in transoesophageal echocardiography with convolutional neural networks. Medical Image Computing and Computer Assisted Intervention – MICCAI 2018. Springer International Publishing; 2018; p 256–64.

60. Mazomenos EB, Chang P-L, Rippel RA, et al. Catheter manipulation analysis for objective performance and technical skills assessment in transcatheter aortic valve implantation. Int J Comput Assist Radiol Surg 2016;11:1121–31.

61. Bernard O, Lalande A, Zotti C, et al. Deep learning techniques for automatic MRI cardiac multi-structures segmentation and diagnosis: is the problem solved? IEEE Trans Med Imaging 2018;37:2514–25.

62. Hashimoto DA, Rosman G, Rus D, Meireles OR. Artificial intelligence in surgery: promises and perils. Ann Surg 2018;268:70–6.

63. Bavaria JE, Tommaso CL, Brindis RG, et al. 2018 AATS/ACC/SCAI/STS expert consensus systems of care document: operator and institutional recommendations and requirements for transcatheter aortic valve replacement: a joint report of the American Association for Thoracic Surgery, American College of Cardiology, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol 2019;73:340–74.

64. Grbic S, Easley TF, Mansi T, et al. Personalized mitral valve closure computation and uncertainty analysis from 3D echocardiography. Med Image Anal 2017;35:238–49.

65. Zhang F, Kanik J, Mansi T, et al. Towards patient-specific modeling of mitral valve repair: 3D transesophageal echocardiography-derived parameter estimation. Med Image Anal 2017;35:599–609.

66. Comaniciu D, Engel K, Georgescu B, Mansi T. Shaping the future through innovations: from medical imaging to precision medicine. Med Image Anal 2016;33:19–26.

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APPENDIX For supplemental videos, please see the online version of this paper.