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# The Functional Anatomy of Human Cardiac Valves and Unique Visualization of Transcatheter-delivered Valves being Deployed

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***Abstract*—The reanimation of large mammalian hearts, including those of humans, using Visible Heart® methodologies provides a unique perspective of functional cardiac anatomy. This knowledge is critical for design engineers and clinicians who seek less invasive cardiac repair approaches for patients with acquired or congenital structural heart defects.**

## I. Introduction

The evaluation of implantable cardiac devices requires innovative and critical testing in all phases of the design process. Over the past 12 years, my laboratory has developed the *in vitro* isolated heart model known as the "Visible Heart®." These methodologies allow for novel examination of device-tissue interaction as a means to evaluate device placement and performance within functioning hearts. Hence, this research tool provides novel insights for a number of different applications: 1) it gives product designers a rapid method to critically assess device prototypes, thus expediting design decisions; 2) it allows clinicians to directly visualize the deployment of new or problematic clinical systems; and/or 3) it can be used to obtain educational images that are valuable to patients and all types of students. It is clear that the future of cardiac devices will include beating heart procedures (e.g., transcatheter-delivered valves), and such implantations will likely utilize simultaneous multiple imaging modalities. These imaging modes allow for verification of proper device positioning, refinement of device deployment procedures, and eventual evaluation of resultant cardiac function within experimental and clinical settings.

Currently, Visible Heart® methodologies also allow for comparative functional imaging within an isolated working heart. Such visualization and subsequent images have been obtained from large mammalian hearts, including human hearts. As such, our laboratory has investigated the deployment of numerous types of transcatheter-delivered valves under direct visualization with high resolution endoscopes and/or with simultaneous collection of fluoroscopic and echocardiographic images. Such valves have been deployed into the aortic, mitral, or pulmonary positions of both native anatomy and surgically placed bioprostheses to simulate the potential range of beating heart ("off pump") procedures.

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## II. General Features of the Visible Heart® Methodologies

Our laboratory at the University of Minnesota has partnered with Medtronic, Inc. to develop the Visible Heart® methodologies which consist of a large mammalian isolated heart model that functions in either Langendorff [1], right-side working, or four-chamber working modes [2]. This isolated heart model involves the initial step of removing hearts from humans or animals using standard cardioplegia procedures [2,3]; hence, this model is also being used to investigate ways to enhance these procedures. Once isolated, the hearts are reanimated and can eventually function with all four chambers working. Following reanimation, cardiac and systemic pressures and outputs are monitored and preloads and afterloads can be adjusted. Our laboratory routinely utilizes various imaging techniques (both endoscopes and fiberscopes) and has compared them to clinically available methods (e.g., fluoroscopy and echocardiography). This has provided very unique footage of normal and abnormal functional anatomy of both human and animal hearts, not only within a given chamber, but within vessels as well. Shown in Figure 1 is the first frame of a quad-split movie clip demonstrating the deployment of a transcatheter -delivered aortic valve.

The isolated heart apparatus serves multiple roles, e.g., allowing operation in either Langendorff, right-side working, or four-chamber working modes. During the Langendorff mode, the left-side afterload is held constant with a coronary perfusion pressure of approximately 60 mmHg [2]. Thus, the flow through the coronaries is determined by dilation or constriction of the coronary arteries. Right-side working mode combines Langendorff retrograde aortic perfusion with antegrade, or physiologic, flow through the right atrium and right ventricle (adjustable between ~3-5 L/min). During four-chamber working mode, the flow through the heart is normally determined by the intrinsic heart rate and contractility of the heart. The intrinsic heart rate can be modified by altering the temperature of the buffer or adding pharmacological agents. Although no model can perfectly mimic *in vivo* conditions, this apparatus allows for the re-creation of various cardiac states through control of preload and afterload pressures. We can also change the physical

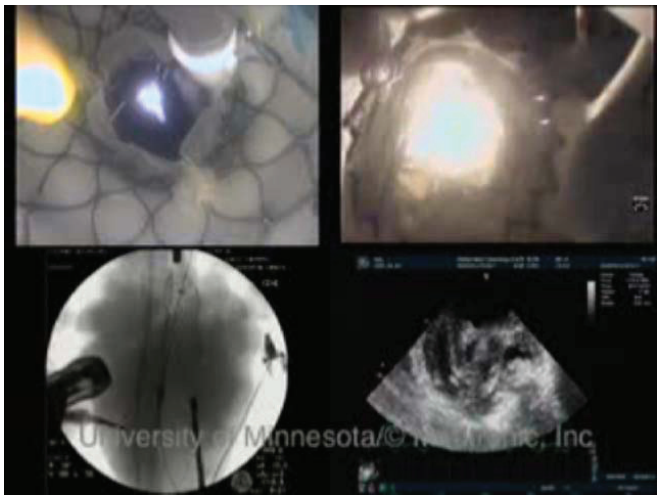

*Figure 1. Deployment of a transcatheter-delivered aortic valve within a reanimated swine heart in vitro, as viewed with muscle imaging modalities including: 1) a videoscope placed within the ascending aorta (upper left panel); 2) a videoscope placed within the left ventricle and viewing the valve from below (upper right panel); 3) fluoroscopy with an anterior-posterior orientation (lower left panel; note that an echo probe and videoscopes can also be identified); and 4) ultrasound (lower right panel).*

orientation of the heart to obtain clinically relevant medical images and/or to simulate the relative heart orientation during a planned clinical procedure.

If one is interested in studying cardiac valves, it is important to understand that, while in four-chamber working mode, the aortic (left side) and pulmonary (right side) valves open during ventricular systole and close during ventricular diastole. Initially, there is a net movement of buffer into the ventricles through the open mitral (left side) and tricuspid (right side) valves during diastole due to the applied preloads. At this same time, the externally applied afterload in the aorta and pulmonary artery is greater than the pressure in the ventricles, effectively closing the aortic and pulmonic valves, respectively. As systole begins, the mitral and tricuspid valves close due to the pressure increase in the ventricles. Once the pressure in the left ventricle exceeds that of the aorta (the applied left heart afterload), the aortic valve opens and the buffer is ejected through the aortic valve. The same is true with the pulmonary valve as it opens when the pressure in the right ventricle exceeds that of the pulmonary artery (the applied right heart afterload). Typically, there are some micro-bubbles observed during ultrasonic imaging within the heart due to imperfect sealing of the preparation and/or inadvertent introduction of air, yet this may actually help one to visualize turbulent flow patterns

## III. EMPLOYING VISIBLE HEART® METHODOLOGIES TO DEVELOP TRANSCATHETER VALVE TECHNOLOGIES

Transcatheter valves have the potential to reduce operative morbidity, expand the indication for valve replacement into non-surgical candidates, and treat patients who have been declined surgery that may be considered high risk due to their current medical status. Several human trials are ongoing, but the development of these devices remains limited by the inability to visualize the interaction of the devices with soft tissues of the heart. Recently, we have aggressively pursued the use of Visible Heart® methodologies as a viable tool for visualizing and evaluating the intracardiac performance of prototype and market released transcatheter valves in the pulmonary, aortic, and mitral positions [4].

In summary, the reanimation of large mammalian hearts, including those of humans, using the Visible Heart® methodologies, has provided a unique perspective of functional cardiac anatomy. By reanimating these hearts using a clear perfusate, we were able to visualize this functional anatomy with endoscopes placed directly within each chamber or large diameter vessel of the heart. We have also created a unique library of such anatomical images and movies that are available in a free access web site, *Atlas of Human Cardiac Anatomy* (http://www.vhlab.umn.edu/atlas). Using this database, one can easily identify the great variability that exists in human cardiac anatomy (both static and functional perspectives). This anatomic knowledge is critical for the design engineer and clinician who will utilize less invasive cardiac repair approaches for patients with acquired or congenital structural heart defects. Furthermore, when direct visualization is simultaneously coupled with standard clinically employed imaging modalities, it provides further critical insights that will be required to more quickly and precisely advance such technologies. Nevertheless, the utilization of Visible Heart® methodologies for device evaluation is considered as complementary to the work by others who utilize *in vivo* or *in vitro* methods to test the reliability, durability, biocompatibility, or other parameters of newly developed valves.

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