An Experimental Setup for Studying Hemodynamics Through Tissue Engineered Aortic Heart Valves

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Calcific aortic valve disease (CAVD) is the most common valvular disorder, affecting approximately 25% of the population aged over 65 years. The formation of calcific nodules on the aortic surface of the leaflets contributes to a progressive obstruction of the left ventricular outflow and leads ultimately to heart failure (Stewart et al., 1997). While CAVD has been described historically as a passive degenerative process, it has now emerged as a highly regulated pathology presumably triggered by a combination of conventional cardiovascular risk factors, mechanical and hemodynamic cues. As an important hemodynamic force, fluid shear stress (FSS) is the frictional force acting in the direction of blood flow on the leaflet endothelium. FSS is experienced by the ventricularis when blood flows past the leaflets during systole and on the fibrosa when blood pools into the sinuses during diastole. Previous studies showed that FSS affect the molecular mechanisms that eventually lead to formation of calcific nodules for CAVD. (Sun, Rajamannan, & Sucosky, 2013). A severely calcified aortic valve needs to be replaced with an artificial valve. Mechanical or prosthetic valves are durable but come with the lifelong anticoagulant treatment. An alternative approach is tissue engineered valves within which aortic valve cells can grow, enhancing the biocompatibility of the valve (Bezuidenhout, Williams, & Zilla, 2015). No matter the artificial valve is mechanical, prosthetic or tissue engineered, when placed into the patient, it should interact with blood flow with minimal disturbance in order for not causing additional complications. Therefore, these valves need to be tested experimentally for the hemodynamic performance. In this study, we have developed an experimental system to investigate hemodynamics for artificial aortic heart valves. The system is composed of Aptus pulsed duplicator system and GE Vivid-q ultrasonic medical imaging system. Aptus pulsed duplicator generates the flow environment for left ventricular outflow tract. Artificial aortic valves can be placed inside the system and these valves are exposed to natural blood flow environment (i.e. natural pressure, heart rate, ejection fraction). GE Vivid-q system enables us to visualize how valve leaflets open and close in each pulse via b-mode ultrasound imaging. M-mode enables us to measure valve orifice size at peak
ejection. Doppler mode on the other hand enables us to measure flow velocities through valves, which then are used to estimate FSS levels. Pressure measurement probes inside the pulse duplicator gives simultaneous pressure readings which are then used to calculate pressure difference across the valve which is another parameter to define valve function. Aptus bioreactor platform is equipped with a holder system that enables testing virtually any material (including woven and knitted fabrics) as a scaffold for heart valve leaflet. The holder is build out of transparent PDMS to enhance optical visibility. The valve geometries that will be tested can be chosen at different wall thicknesses and other dimensions. For example, geometry of the sinuses and leaflets can be freely chosen/designe. This enables comparison of different prototypes for the optimized tissue engineered scaffolds. We will compare the performance of the scaffolds that are designed in our lab with commercially available prosthetic valves. In conclusion, we were able to develop an ultrasound based experimental flow system that will enable us to evaluate the tissue engineered heart valve scaffolds in natural heart environment.

References
