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Implications of Paravalvular Leakage (PVL) in Aortic Transcatheter Valve Implants (TAVI)

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Senior Research Project Proposal

I. Title: Implications of Paravalvular Leakage (PVL) in Aortic Transcatheter Valve Implants (TAVI).

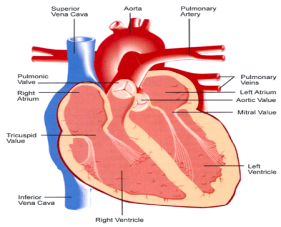
II. Statement of Purpose:

The project's objective is to construct an accurate artificial representation of the aortic valve. The model of the aortic endocardium will serve as simulated test environment to locate and diagnose instances of Paravalvular Leakage. The scope of the test environment won't expand past a moderately stenotic aortic valve.

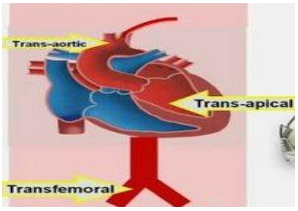
III. Background:

Growing up, other than the isolated melodramatic experiences of getting a flu shot, I had no understanding of the vastness of the medical field. My first exposure to any of the subject matter was when my grandfather was diagnosed with lung cancer. During his final years, I would visit him and sit at the foot of his bed staring glassy eyed at both the oxygen concentrator and heart monitor. These experiences ignited my desire to achieve a higher understanding of the medical field. In my grandfather's final weeks I observed physicians and nurses give him a sense of sanctity and comfort in the face of death. Seeing individuals with the power to help someone in such a substantial way is what drove me towards the medical field. Since then, I've been pursuing the medical field of Cardiology, hoping to one day cure and calm my patients in need.

IV. Prior Research:

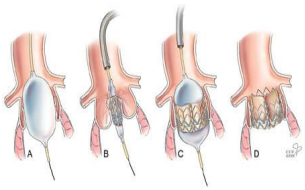


The heart is composed of four chambers and four valves: the right atrium, right ventricle, left atrium, and left ventricle, the tricuspid valve, the pulmonary valve, the mitral valve, and the aortic valve respectively (Figure 1). The scope of this research expands no further than the aortic valve. Diseases of the aortic valve are typically related to anomalies or malformations of the structure of the valve. However, a diseased aortic valve will always show signs of stenosis, incompetence or both (Figure 2). Stenosis of a valve is when there is an obstruction of blood flow through the valve. Usually, this is the result of the orifice narrowing in. The degree of stenosis can be measured by the analysis of pressure differences across the valve or the pressure differences in the area of the orifice. An incompetent valve, typically results in a smaller net-forward blood flow. This is due to blood flowing back into the left ventricle due to regurgitant or leakage. Valve incompetence can be tested by inserting radiopaque dye into the aortic root and analyzing the amount of backflow into the left ventricle through X-rays. Once the severity of disease in the aortic valve is assessed, several treatments can remedy symptoms.



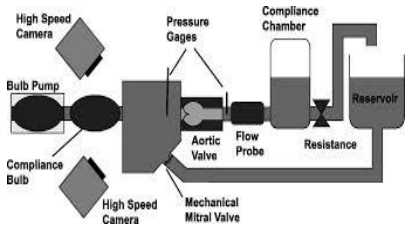
For example, Aortic Valve Replacement (AVR) surgery has been in clinical application since the early 1960s. Due to AVR's invasive nature, alternative means of valve repair have risen. Transcatheter Aortic Valve Implants (TAVI or TAVR) were first used twelve years ago and over 30,000 more TAVI cases have been performed since then. Essentially, this is a procedure where the aortic valve is accessed through a catheter entering from an external blood vessel, whether that's transaortic, transapical, or transfemoral (Figure 3).

Simply stated, the valve is implanted in four steps (Figure 4): To temporarily increase the diameter of the orifice, a catheter with an angioplastic balloon is positioned within the the stenotic valve and is inflated. Next, the valve implant



is positioned inside of the aortic root and the sheath covering the valve is removed. Then an additional angioplastic balloon is inflated to expand the frame of the artificial valve implant and fix it into place. And finally, the catheter is then extracted.

TAVI procedures have been proven to increase the life expectancy of patients, who were otherwise deemed inoperable, by at least 2 years. A complication that arises with this valve implant is paravalvular leakage. This is when the circumference line of the valve is compromised and leakage or backflow occurs.



When a Transcatheter Aortic Valve Implant undergoes research and development it is commonly placed within a left heart generator (Figure 5) to observe its functionality *in vitro* ("within the glass" or in a simulated environment) as opposed to *in vivo* ("within the living" or inside a biological entity.) Factors such as the viscosity of blood, diastolic/ systolic chamber pressure and the sequencing of a heart contraction are mimicked inside a left heart generator.

V. Significance:

Currently, no standardized test method for paravalvular leakage exists in the biomedical community. If successful, this test method can be replicated as a verification method in research and development of TAVI design. The successful execution of this test method could lead to further research in the development of treatment of paravalvular leakage and the extension of TAVI patient's life expectancy.

VI. Methods and Design:

After the initial step of understanding the geometry of a stenotic aortic root, a basic model needs to be constructed. As a preliminary representation of what will be constructed, I will simply mold several models out of clay that reflect the geometry of a stenotic aortic root. We will use this representation to develop a three-dimensional model with computer aided design (CAD) software. The CAD model will be used as a blueprint for a three-dimensional printer. The printer will be used to construct the endocardium out of silicon or a material that is compatible with the left heart simulator. We will then deploy a TAVI device into the printed model (it will look similar to stage D in figure 4). In order to simulate an environment that is analogous to the heart the entire model will be placed inside the Vivitro pulse duplicator (a left heart simulator). We will then use echocardiography to pinpoint and quantify the amount of leakage that is occurring around the circumference of the valve. Additionally, as a control to compare to, we will deploy and test for leaks in a TAVI device inside a perfectly round cylinder. The amount of leakage will be measured by using an echocardiographic transducer (this is essentially a smaller scale version of doppler radar). Conveniently,, echocardiography is used to measure the degree of leakage in clinical studies on patients who have been implanted with a TAVI device. The significance of this is, the results from the test model that we constructed can be compared to clinical data. The goal is to prove that we can replicate the clinical environment of a device implanted inside a patient with aortic stenosis inside a laboratory.

VII. Problems:

The biggest possible problem my project could face is the comparison of results between clinical data and my data because it solely relies on the echocardiographic machine functioning properly. Problems with echocardiography stem from many places, including the transducer. If the orientation of the transducer is skewed or dysfunctional, the sound waves it emits change based on the new orientation, altering the data needed to complete the project and even compare the results to clinical data.

Additionally, the prosthetic endocardium of the aortic root must fit the into the left heart generator flawlessly. The chamber has specific dimensions and if the prosthesis has dimensions below those of the

chamber, more leaks will occur. These are all possible problems in the project, but most can be quickly solved with careful calculations and precise methods used prior to data collection.

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