31st Annual International Conference of the IEEE EMBS
Minneapolis, Minnesota, USA, September 2-6, 2009

The Development of Transcatheter Heart Valves: Opportunities and Challenges

Tim Laske, Melissa Denton, Carol Eberhardt

Although the heart valve market is relatively mature, many patients currently indicated for valve repair or replacement are either undiagnosed, not referred for surgery, or are too sick/unwilling to undergo the required surgery (Table I). To address this unmet clinical need, the medical device industry has undertaken the development of transcatheter heart valves (TCV). These devices are tissue heart valves that can be delivered without open heart surgery and are intended to complement the portfolio of current and future surgical valve products. Several companies have developed novel product designs. Some transcatheter valves are currently available for the aortic and pulmonic positions via European CE mark, and are in clinical trials throughout the United States.

TABLE I.
U.S. heart valve disease prevalence and current industry surgical valve repair and replacement product volumes [4, 5, 6].

Condition	U.S. Prevalence	Surgically Treated
Severe Aortic Stenosis	125,000	75,000
Moderate/Severe Mitral Regurgitation	2.3 million	48,000
Moderate/Severe Tricuspid Regurgitation	1.6 million	8,000

Transcatheter valves have three primary components: 1) a tissue valve, 2) a supporting frame or stent, and 3) a delivery system (Figure 1). The tissue valve is designed for introduction into the body through a small sheath ($\leq$ 24Fr), for deployment into the targeted location. The frame must accommodate either crimping or compression for introduction into the body, and provide a scaffold to both support the tissue valve and to maintain positional stability in the heart. The delivery system enables remote access to the heart and must be able to navigate the vasculature and the cardiac chambers. Transcatheter valves are delivered either through the vasculature (most commonly the femoral vein or artery), or through a direct puncture into the right or left ventricle [1, 2, 3].

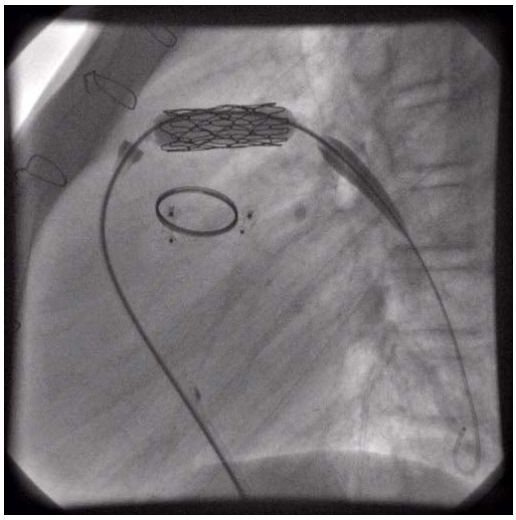


Figure 1. Radiographic image of a transcatheter valve during deployment in the pulmonary artery.

Typically, the tubular tissue valve is attached to a cloth or pericardial tissue skirt in the mid-section of the frame. The pericardial valve's tubular shape can be created by laying one sheet of tissue on a sheet of polyester cloth and sewing a pattern of leaflet commissures and margins of attachment (Figure 2). This stitch line defines valve geometry and leaflet boundaries, which prevents valve leakage.

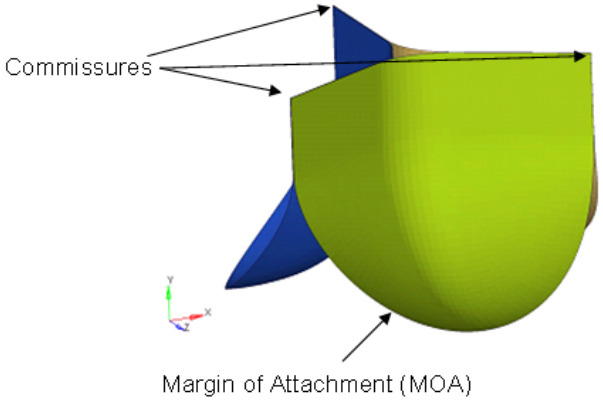


Figure 2. Generic Tissue Valve Model for TCV showing the commissures and margin of attachment (MOA).

Manuscript received April 23, 2009. This work was supported by Medtronic, Incorporated.

Tim Laske is with Medtronic, Inc., Moundsview, MN 55112 USA (phone: 763-514-9782; fax: 763-367-5907; e-mail: tim.g.laske@medtronic.com).

Melissa Denton is with Medtronic, Inc., Santa Ana, CA 92705 USA (e-mail: melissa.denton@medtronic.com).

Carol Eberhardt is with Medtronic, Inc., Santa Ana, CA 92705 USA (e-mail: carol.elsa.eberhardt@medtronic.com).

To meet the design requirements for these unique products, creativity is also required in the application of engineering tools for product design and assessment. Finite element analysis (FEA) can be used in the assessment of the durability of the frame and in the optimization of valve geometries. The commissure response is one of the most important factors when designing the valve since it is usually the area with the highest stress, and is important for durability prediction [7]. Finite element modeling can be used to determine the maximum principal stresses acting on the leaflets to allow the identification of the ideal engineered leaflet geometry [8].

One approach traditionally used is to generate a 3D CAD valve model, build an accurate mesh using software suites like Hyperworks, and in conjunction run the analysis with ABAQUS Standard solver. The modeling can be even more advanced and incorporate the seam and tissue assembly methods by assigning the appropriate thickness (layers) to each of the valve components. The thickness will directly affect the stiffness of each region during the valve opening and closing function. The resulting contour plots (Figure 3) can be used to calculate average stress values and identify the best case valve design conditions, subsequently this then can be used as input for in-vitro testing, which reduces the design cycle time.

With this type of analysis, the valve design can be catered to assembly strengths. One such application is that a leaflet shape could be specifically engineered to have minimal stresses where valve assembly is found to be operator dependant during manufacturing. Another illustration involves minimizing the stresses for areas where the valve maybe susceptible to non-uniform load distribution such as the MOA seams where the valve attachment is reliant on the frame strut locations. Consequently, there are advantageous and disadvantages to adjusting valve features. Reduction in belly stress, often times leads to an increase in free margin stress. Careful balance of valve features must be applied and these analytical tools can help dial in the appropriate design.

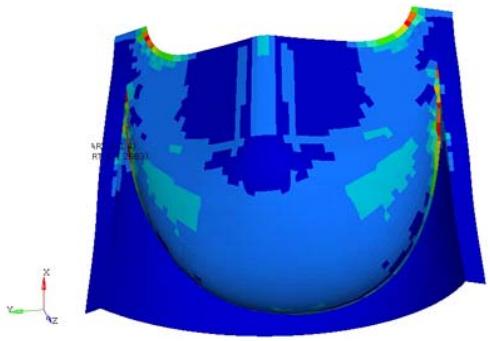


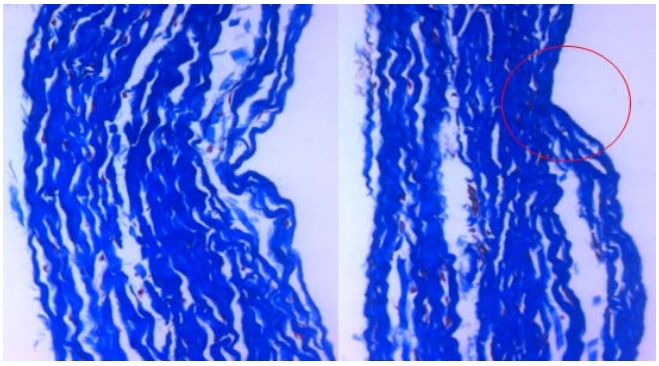
Figure 3. An example FEA Contour plot showing the stress distribution for a generic transcatheter valve.

Another approach to mitigating the high stress that is generally found at the valve commissure locations is to use advanced assembly concepts such as leaflet folding or external support structures. It is important to note that external commissure protection may not be required if commissure protection is built into the frame design and /or specific folding of graft or leaflet material is used to provide adequate reinforcement that allows the valve to maintain the desired performance at anatomical pressures.

From a hydrodynamic performance perspective, transcatheter heart valves must accommodate multiple diameter size ranges and morphological configurations, while still providing adequate regurgitant, leaking, and closing volumes, effective area of orifices, and sufficient leaflet coaptation. Therefore, biaxial and mechanical tissue properties are critical to in-vivo valve performance to ensure consistency of coaptation (minimal leaflet stretching) and high strength for the pericardial tissue. Due to the anisotropic nature of pericardial tissue many manufactures implement a screening that involves tissue selection based on thickness, extensibility, and surface characteristics such as loose fibers discoloration, etc. Besides inspection of the tissue, processing improvements have been developed to acquire the desired tissue behavior. For example researches have demonstrated that application of strain during cross linking may stiffen the tissue and provide nearly isotropic properties [9]. Further testing may demonstrate specific weight class sourcing or directionality of strain application could benefit the mechanical properties.

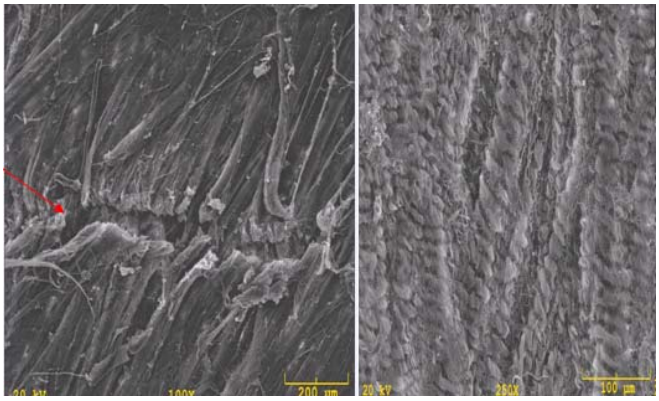
In addition to numerical tools, histological methods and advanced imaging tools can be used in the design and assessment of the valve and frame. In the past histological methods has been used to identify calcification characteristics of biological valves [10], but these methods can also be used to assess the durability of various design concepts. And currently histopathology has been a useful tool to observe any damage at the superficial collagen layers and determine how far it reaches into the inner layers of the tissue (Figure 4). Scanning electron microscopy (SEM) has also been successful to investigate any damage on the tissue surface (Figure 5).

Medical imaging modalities like angiography and computed tomography can be used to predict in vivo loading conditions and anticipated in service deformations. Unique benchtop models such as the Visible Heart Lab at the University of Minnesota (www.visibleheart.com) can also provide unique insight into the deployment and in situ performance of these devices to aid in design decision making. In the future, image guidance may also play a role in enhancing the accuracy of device deployment and the ease of clinical use.



(a) (b)

Figure 4. Histological tissue section of prototype valve leaflets. Slight damage to the collagen is seen in panel (a) and a crease in panel (b). Photos were captured using an optical microscope at 20X.



(a) (b)

Figure 5. SEM images of a damaged leaflet in (a) and a normal leaflet in (b) (200X).

CONCLUSIONS

Although substantial progress has been made, the biomedical engineering community can provide tremendous value to both patients and clinicians through continued innovation in product design, development of new tools for product testing, and through novel means of improving the ease and accuracy of device deployment. In addition, smaller crimp profiles may be feasible as technology and design advancements are made. A smaller TCV could then target a larger patient population, and allow easier delivery during procedures for patients with tortuous and severely diseased anatomies.

ACKNOWLEDGEMENTS

The authors would like to thank Maria Botrous and Christopher Webster for their design and testing contribution to this work as part of the Medtronic Heart Valve product development team (Santa Ana, CA) and Steve Ford of Altair engineering who contributed extensively to the FEA analyses referenced.

REFERENCES

[1] Grube, E., Schueler, G., Buellesfeld, L., et al., 2001, "Percutaneous Aortic Valve Replacement for Severe Aortic Stenosis in High Risk Patients using the Second and Current Third Generation Selfexpanding CoreValve Prosthesis : Device Success and 30-day Clinical Outcome," J Am Coll. Cardiol, 50 :69-76.

[2] Walther, T., Falk, V., Borger, M.A., et al., 2007 "Minimally Invasive Transapical Beating Heart Aortic Valve Implantation-Proof of Concept," Eur J Cardiothorac Surg, 31: 9-15.

[3] Beyersdorf, F., 2007, "Transapical Transcather Aortic Valve Implantation," European Journal of Cardio-Thoracic Surgery 31: 7-8

[4] Health Research International Report. Report no. 057-1-US-0705-221, ES-5.

[5] Stewart BF, Siscovick D, Lind BK, et al. Clinical factors associated with calcific aortic valve disease. J Am Coll Cardiol. 1977;29:630-4.

[6] Iivanainen AM, Lindroos M, Tilvis R, et al. Natural history of aortic valve stenosis of varying severity in the elderly. Am J Cardiol. 1996; 78:97-101.

[7] Thubrikar, M., 1990, The Aortic Valve, CRC Press, Inc, pp. 119-126.

[8] Denton, M., Ford, S., January 2009, " Tapping into Digital Design Tools," Journal of Medical Device and Diagnostic, pp. 92-101.

[9] Langdon, S., Chernecky, R., Pereira, C., Abdulla, D., Lee, M., 1999, " Biaxial Mechanical /Structural Effects of Equibiaxial Strain during Crosslinking of Bovine Pericardial Xenograft Materials," Journal of Biomaterials 20: 137-153.

[10] Attmann, T., Quaden, R., Freistedt, A., et al., 2007, « Percutaneous Heart Valve Replacement : Histology and Calcification Characteristics of Biological Valved Stents in Juvenile Sheep, » Cardovascular Pathology 16 : 165-170.