Proceedings of the 28th IEEE
EMBS Annual International Conference
New York City, USA, Aug 30-Sept 3, 2006

BIOMECHANICS OF ENGINEERED HEART VALVE TISSUES

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On the most basic functional level, the aortic heart valve is essentially a check-valve that serves to prevent retrograde blood flow from the aorta back into the left ventricle (Fig. 1-a). This seemingly simple function belies the structural complexity, elegant solid-fluid mechanical interaction, and durability necessary for normal aortic valve function [1]. For example, the aortic valve is capable of withstanding 30-40 million cycles per year, resulting in a total of ~3 billion cycles in single lifetime [2]. No valve made from non-living materials has been able to demonstrate comparable functional performance and durability.

However, this staggering level of performance can be cut short by aortic valve disease, the most common form being stenosis resulting from calcification. Currently, the treatment of aortic valve disease is usually complete valve replacement. First performed successfully in 1960, surgical replacement of diseased human heart valves by valve prostheses is now commonplace and enhances survival and quality of life for many patients. The vast majority of prosthetic valve designs are either mechanical prosthesis and bioprosthetic heart valves (BHV). Mechanical prostheses are fabricated from synthetic materials, mainly pyrolytic carbon leaflets mounted in a titanium frame. BHV are fabricated from either porcine aortic valve or bovine pericardium, chemically treated with glutaraldehyde to reduce immunogenecity and improve durability, and usually mounted onto a flexible metal frame (stent) which is covered with Dacron to facilitate surgical implementation.

Of these two major prosthesis designs, BHV are now used in approximately 40% of the estimated 75,000 US and 275,000 worldwide valve replacements done annually [3]. BHV aortic valve the advantage of low rates of thromboembolic complications without chronic anticoagulation therapy (and its associated morbidity and mortality risks) required for mechanical prostheses. However, they suffer high rates of late structural dysfunction owing to tissue degradation [4, 5]. The principal processes that account for BHV tissue degradation in vivo are widely considered to be 1) cuspal mineralization, causing cuspal stiffening with or without tearing, and 2) non-calcific cuspal damage, including mechanical fatigue and possibly proteolytic degradation of the collagenous extracellular matrix, causing cuspal tears and perforations [4, 5]. Approximately 90% of all BHV fabricated from porcine aortic valves fail with tearing, and some fail with little or no calcification [5-7].

While much effort in currently underway in both ours and other laboratories to improve current BHV [8-16], in the long-term new technologies will aortic valve to be developed. This is especially the case in pediatric applications, where growth of the replacement valve is essential to eliminate the need for re-operations. Further, repairs of congenital deformities require very small valve sizes that are simply not commercially available.

Tissue engineering (TE) offers the potential to create cardiac replacement structures containing living cells, which has the potential for growth and remodeling, overcoming the limitations of current pediatric heart valve devices [17-23]. Using autologous cells and biodegradable polymers, TE heart valves (TEHV) have been fabricated and have functioned in the pulmonary circulation of growing lambs for up to five months, with the beginnings of a specialized layered structure [18]. Despite these promising results, significant questions remain. For example, the role of initial scaffold structure and mechanical properties to guide the development of optimal extra-cellular matrix (ECM) structure and strength are largely unexplored. While detailed biomechanical investigations of the in-vitro incubation process could shed much light on optimizing TEHV designs, little work has been conducted to date.

Perhaps the current biomechanical challenges with TEHV are best exemplified by the principals of Functional Tissue Engineering, as recently stated by Butler et al. [24]. While a long-term goal is duplication of the native valve, interim TE prostheses do not necessarily have to achieve this goal to be successful. *There is thus a need to establish minimal functional parameters necessary to produce a functional valve replacement.* Further, there is a need for models of long-term remodeling and implant survival to minimize costly animal trials, particularly since conventional durability testing techniques are inapplicable. The purpose of this paper is to present a review of the structure-strength relationships for native and engineered heart valve tissues.

ACKNOWLEDGMENTS

This work was supported by from NIH grant HL-068816.

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