Biomechanical and Functional Comparisons of Bioprosthetic Heart Valve Tissue Anti-Calcification Treatments

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Purpose: The purpose of the present work was to compare the biomechanical and functional characteristics of tissue and bioprosthetic heart valves made from tissue that had been subjected to different anti-calcification treatments. The effectiveness of the anti-calcification treatment has been demonstrated using small and large animal tests [1]. However, it is important to verify that the basic hydrodynamic performance of the valve has not been adversely affected by the tissue treatment. Therefore, a comprehensive battery of sensitive biomechanical tests as well as functional whole valve performance evaluations have been carried out to demonstrate that the anti-calcification treatment can be implemented confidently.

Methods: Two different chemical treatment processes were evaluated: the standard anti-calcification treatment used at Edwards Lifesciences for bioprosthetic tissue, XenoLogiX (XLX, Edwards Lifesciences) and a new process that adds a heat treatment step, ThermaFix (TFX, Edwards Lifesciences).

Given that the tissue treatments were only applied to the tissue, a variety of tissue biomechanical tests were deemed appropriate to compare the effects of the two treatments. All tissue tests were performed at room temperature either in saline, or maintained moist throughout the test. *Uniaxial tensile testing* was carried out on strip specimens to determine the yield stress and yield strain at failure. *Equibiaxial tensile testing* was performed using square specimens to determine the stress/strain characteristics up to a representative physiological load of 1 MPa. *Flexure testing* was performed on strip specimens as an extremely sensitive test to evaluate any potential subtle changes in bending characteristics. Finally, *leaflet deflection testing*, an empirical test that determines the overall stretch of actual leaflet specimens under a given load, was performed.

In addition to biomechanical tests on leaflets or specimens cut from leaflets, *whole valve testing* was also performed. Real time, physiologically relevant testing was performed in pulse duplicators using whole bioprosthetic valves made from leaflets subjected to both treatments. *Steady forward flow and steady backflow* tests were performed in accordance with the FDA's 1994 Draft Heart Valve Guidance. Finally, *accelerated valve durability tests* (AWT) were performed out to 200 million cycles (5 equivalent years).

Results / Discussion: Overall, the tests showed no significant differences in biomechanical properties or in whole valve behavior.

Uniaxial tension test results showed a yield stress of 9.42 MPa +/- 1.34 MPa for the XLX yield stress, compared to a 10.5 MPa +/- 1.48 MPa for the TFX. Statisical analysis (one-way ANOVA) demonstrated no statistically significant difference in the yield stress ($p=0.063$).

Equibiaxial tension test results up to 1 MPa showed no statistically significant differences (one way ANOVA analysis) in the stretch properties between the XLX and TFX test groups (Figure 1) in either direction.

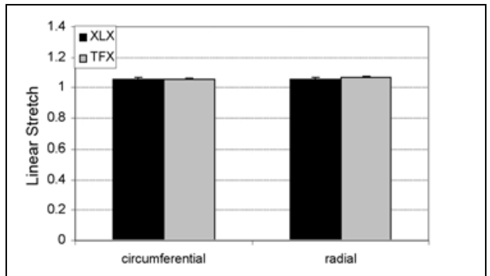

Figure 1. Biaxial test results.

Flexure test results showed an instantaneous effective modulus of 1.31 MPa +/- 0.133 MPa for XLX, compared to a 1.21 MPa +/- 0.093 MPa for TFX, with no directional differences evident. Statisical analysis (one-way ANOVA) demonstrated no statistically significant difference.

Leaflet deflection test results showed deflection value of 0.170 inch +/- 0.033 inch for the XLX leaflets, compared to a 0.184 inch +/- 0.030 inch for the TFX leaflets. Statisical analysis (t-test) demonstrated no statistically significant difference in the leaflet deflection ($p=0.88$).

Functional testing results showed generally comparable behavior between valve types. Pressure drops increased with smaller valves and higher cardiac outputs, as expected, in valves with leaflets treated with both processes. Steady forward and backflow tests showed no appreciable differences. Finally, valve durability, as measured in the AWT, showed no appreciable differences between the two tissue treatment methods: all valves remained competent past 200 million cycles, or the equivalent of five years.

Conclusions: The biomechanical properties of the TFX treated tissue are not statistically different from the XLX treated tissue. The overall functional tests of valves made with XLX and TFX treated leaflets show comparable behavior. Valves treated with either anti-calcification process appear functionally normal and durable.

References:

[1] J. Dove, J. Olin, M. Thubrikar, J. Davidson, "An Improved Dual-Action Anti-Calcification Processing Method for Bioprosthetic Heart Valve Tissue", European Journal of Cardiothoracic Surgery, (2005, in press); presented at EACTS, Barcelona, September 2005.