A Novel Mitral Valvuloplasty Model for Heterograft Biomaterial In-vivo Assessment

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Statement of Purpose: Our overall hypothesis is that triglycidyl amide (TGA) crosslinking, a novel epoxy-based method (1) and related reactions, including those with bisphosphonates, enhance biocompatibility, improve biomechanics, and inhibit bioprosthetic heart valve degeneration due to major modifications of the structural proteins of the extracellular matrix (ECM), and cellular interactions with the TGA crosslinked ECM that lead to subsequent changes in gene expression associated with inhibition of calcification. However, development of bioprosthetic heterograft biomaterials is often confounded by the bioprosthetic design itself. To overcome this limitation, we have developed a novel technique to evaluate heterograft biomaterials in a blood contacting environment subjected to levels of stress and strain comparable to those in functional bioprostheses.

Methods: 5 10 mm x 10 mm tissue patches made from TGA treated bovine pericardium were implanted into the ovine MV anterior leaflet, with the original leaflet tissue removed of the same size removed prior to implant (Fig. 1). An array of four sonomicrometry transducers were implanted on the implant corners and were used to compute the complete in-surface strain tensor over the cardiac cycle (Fig. 1). The chest was closed and a baseline reading taken. 4 weeks later, another reading was obtained. From the strain tensor, we computed the major eigenvalue (EG1 or radial) and minor (EG2 or circumferential) principal stretches, as well as the areal stretch = EG1*EG2.

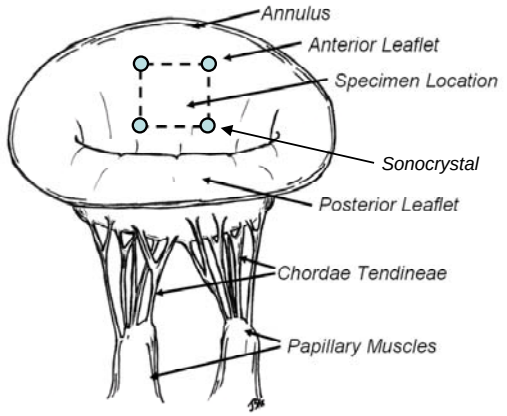

Figure 1 – Anatomical schematic of the mitral valve annuloplasty animal model.

Results / Discussion: Typical of sonocrystal-derived strain data, the resulting strain data was very smooth with time (Fig. 2). We noted also the valvuloplasty implant was subjected to large anisotropic stretches comparable to those of the native mitral valve anterior leaflet (2,3) (Fig. 2). In particular, we noted large ratial stretches and contractile circumferential stretches (Fig. 2). Results were also consistent between animals (Fig. 3). After 4 weeks, only small changes in radial stretches were observed, suggesting the TGA treated valvuloplasty implant remained mechanically stable (Fig. 3).

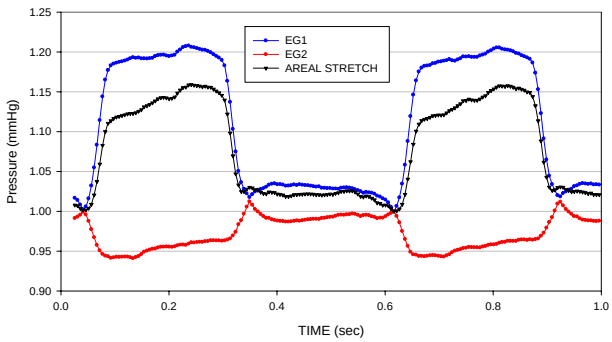

Figure 2 – Representative principal stretch-time data, showing large anisotropic stretches over 2 cardiac cycles.

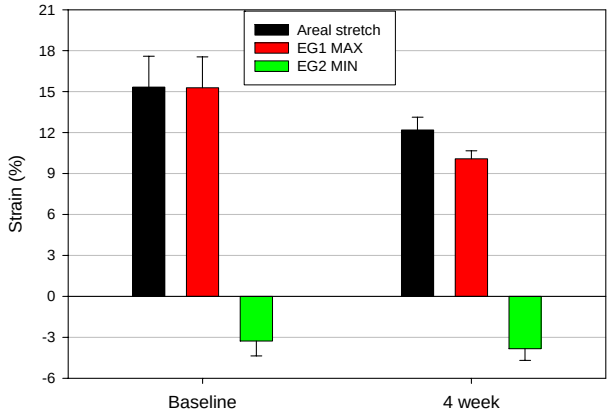

Figure 3 – Mean (error bar=1sem) results from baseline and 4 week implant, revealing minimal changes.

Conclusions: We were able to quantify changes in implant deformation during the cardiac cycle in an in-vivo prep exposed to valve-level stresses. This may be particularly of interest if calcification occurs, which would stiffen the tissue. Moreover, we can quantify dimensional changes of the implant with time, which would be a good indication of creep and/or shrinkage.

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References

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