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Effects of organ-level mechanical pre-conditioning in the development of tissue engineered heart valves

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Objectives:
For long term viability necessary for human implantation, enhanced durability of TEHVs is required, which may be possible through mechanical pre-conditioning [2]. In this study, we demonstrate improved methods of mechanical conditioning at the organ scale using functional tri-leaflet TEHVs with bone-marrow derived mesenchymal stem cells (BMSC).

Method:
Ovine BMSCs were isolated as previously reported in [1]. Non-woven 50:50 blend, mesh of PGA-PLLA were cut into three leaflets that were subsequently sewn onto a stent. Seeding was performed by immersing TEHVs into culture media contained within hybridization tubes. The tubes were rotated in a rotisserie for 3 weeks with a seeding density of $6x10^6$ cells per cm^2 of outer scaffold area. After this period, some of the valves continued in this manner for an additional 3 weeks while others were exposed to dynamic culturing conditions.

Results:
Evidence of both endothelial and fibroblast-like phenotypes was demonstrated at 6 weeks similar to our previous studies using scaffold strips undergoing combined flexural and flow driven mechanical stimulation [2]. Further we analyzed the leaflet surface imaging results to correlate histological results to local leaflet deformations. Implications of these studies will be discussed.

Conclusions:

This study reinforces the role of mechanical forces in a physiologically simulated environment in guiding in-vitro TEHV growth and guiding cell differentiation at the scale of an organ valve.

References:
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