Tissue Formation and Remodeling in Tissue Engineered Pulmonary Conduits

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Introduction. Each year, nearly 30,000 children are born in the United States with congenital heart defects. Such defects can manifest in a variety of manners, including tetralogy of Fallot, hypoplastic left heart syndrome, tricuspic atresia, pulmonary stenosis, and pulmonary atresia. Slightly less than half of patients require surgical correction via partial or full reconstruction of the pulmonary artery/right ventricular outflow tract to establish normal anatomy and restore proper blood flow. It is clear that a clinical need exists to develop better conduit therapies for PA/RVOT reconstruction. Yet, there exists a paucity of published research on tissue engineered conduits (TECs). Though some long-term results have been encouraging, most TEC work is empirically based, limited in scope, and has not elucidated time course changes in structure and mechanical behavior necessary to properly evaluate tissue formation and remodeling. The present work elucidates how tissue forms and remodels in TECs in long-term implants.

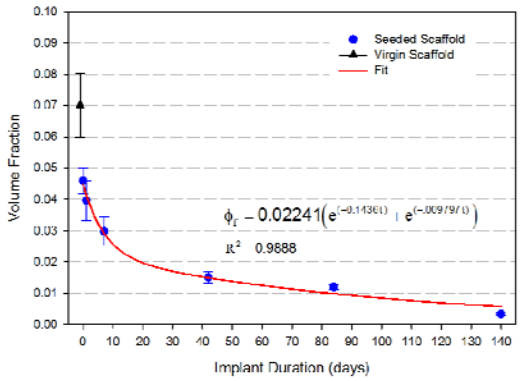

Figure 1 – NNW scaffold fiber geometry and local preferred (PD) and cross-preferred (XD) directions.

Ovine pulmonary artery conduits were created and implanted according to previous published methods (1) and explanted at 1,7,42,84, and 140 days, at which time the animals were exsanguinated, and the heart and lungs were removed after cardiac arrest. The conduit assemblies were explanted; each assembly was cut into three equal-sized radial strips that included portions of the associated conduit, resulting in a total of 63 specimens. Three strips per conduit were stored and frozen in PBS and shipped to our laboratory for further analysis. A total of 17 animals were used.

Summary and Discussion. Using structurally guided large-deformation constitutive models, changes in the tissue phase mechanical properties in in vivo TECs were investigated as a function of implant duration. The strong impact of initially scaffold orientation on "guiding" collagen deposition was observed up to 140 days post implant. Initial tissue-scaffold composite mechanical properties were dominated by the intact scaffold phase with little change in tissue shear modulus between 0 and 7 days implant duration. By 42 days, the scaffold phase was negligible, and dense collagen was observed. Model parameters suggest limited cross linking and crimping of collagen fibers. By 84 and 140 days, however, substantial increases in the effective collagen modulus and substantial shifts in the collagen ensemble recruitment function indicate increased collagen cross linking and collagen crimp. Histology showed evidence of crimping, as well as dense collagen. Importantly, the experimental and modeling results indicate that a substantial amount of remodeling occurs during the 7-42 day implant time. With this work, insights into how TECs remodel and change with implant time are discussed. Further, an important in vivo range of time for the remodeling process is shown, with future work focused on the 7-42 day time period.

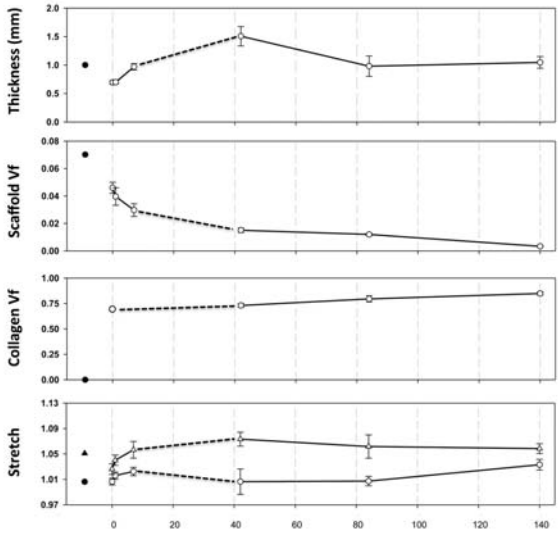

Figure 2 - Summary plots of mechanical and structural changes to TECs with implant duration. White circles indicate TECs; black circles indicate virgin scaffold material. Dotted lines represent possible transition period trend. The implant duration is broken down into virgin scaffold, continuous scaffold, transition period, and discontinuous scaffold phases.

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