Tissue-to-cellular level deformation coupling in cell micro-integrated elastomeric scaffolds

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Background

- Approximately 75,000 prosthetic heart valves are implanted annually in the US
  - Still no ideal solution ie. pediatrics
- Tissue engineering aims to replicate the structure, composition, and mechanical function of native tissue
- Lacking knowledge as to how externally applied forces at the tissue level are transmitted to the cell in both native and engineered tissue systems
- Goal: gain a quantitative understanding of the biomechanical events that occur during in-vitro tissue formation and the remodeling within a synthetic fibrous scaffold
- Hypothesis: cellular deformations within ES-PEUU scaffolds are likely a complex function of scaffold mechanical properties, architecture, and cellular coupling with the surrounding polymer fibers

Specimen Fabrication and Preparation

Biaxial Stretch and Test Device

QuickTime™ and a
TIFF (Uncompressed) decompressor
are needed to see this picture.

Confocal Imaging

Cellular Deformations and Scaffold Stretch Protocols

QuickTime™ and a
TIFF (Uncompressed) decompressor
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Scaffold Fiber Kinematical Analysis

- Affine fiber deformation transformation model to gain understanding of how the fibers deform as a function of macroscopic scaffold strain
- The rotation of fibers originally at an angle theta to the angle beta in the deformed state is given by

$$\beta = \tan^{-1}\left[\frac{U_{PD}}{U_{XD}}\tan(\theta)\right]$$

- The angular fiber distribution in the deformed state R(β) can be related to the original angular distribution R(θ) by

$$R(\beta) = R(\theta)\left[\frac{U_{PD}^2\cos^2(\theta) + U_{XD}^2\sin^2(\theta)}{U_{PD}U_{XD}}\right]$$

U_{PD}=extensional stretch along the preferred directions

U_{XD}=extensional stretch along cross-preferred direction

Highlighted Results

QuickTime™ and a

- Cell nuclei align primarily in the plane of the scaffold and rotated in the direction of deformation
- A plateau in the change in NAR was observed at approximately 60% strain corresponding to a transition from a wavy fiber architecture to a interconnected, web-like, fiber morphology
  - Indicating that nuclei deformations are dominated by local fiber straightening as opposed to macro tissue level deformations

Conclusions and Looking Forward

- Tissue engineering still faces many challenges in repairing or replacing tissues that serve primarily biomechanical functions
- Through cell micro-integrated elastomeric scaffolds, we can
  - Characterize the mechanical behavior of electrospun PEUU and cellular response to global deformation
- The cell micro-integrated ES-PEUU scaffolds exhibited micro fiber morphologies and kinematics that were shown to directly influence local cellular deformations
- Biodegradable synthetic polymers as scaffolds have been proven successful, but the unique micromechanics of various scaffolds induce different cell deformation responses, which could correlate to difference in cell proliferation and function
- Although a great deal can be learned from ES-PEUU scaffolds, it is still a goal throughout the tissue engineering community to understand how organ-level deformations translate to microstructural deformations and cellular mechanical stimuli

Many of life's failures are people who did not realize how close they were to success when they gave up.

~Thomas A. Edison