A Generalized Large Deformation Constitutive Model for Forming Tissues in Needled Non-Woven Scaffolds

Michael S. Sacks
Center for Cardiovascular Simulation, ICES/Biomedical Engineering, UT Austin

In order to evaluate the mechanical quality of forming engineered soft tissues, it is essential to predict the forming extracellular matrix (ECM) phase mechanical properties from the overall composite response. Without a proper formulation, it is impossible to know, in a quantitative sense, to what degree the measured mechanical response is influenced by the remaining scaffold component. Previous modeling efforts have resulted in a descriptive mechanical model for intact needle non-woven (NNW) scaffolds (Fig. 1). When applied to tissue-scaffold composites using the rule of mixtures, however, this model was not able to account for the observed increases in stiffness of the composite and substantially underestimated the predicted composite stiffness compared to the experimentally measured values. The models was also restricted to small deformations, and the meso-scale composite model relies heavily on an empirically determined coupling factor to account for observed scaffold-ECM interactions. Moreover, structural measurements indicated that scaffolds experience reduced volume fractions. Further, after extended in vivo durations, the scaffold becomes highly fragmented and discontinuous. Both previous model formulations do not account for such scaffold changes and may ultimately underestimate tissue properties. In this work, we develop a structural constitutive model that separates the scaffold mechanical contributions to enable estimation of forming engineered tissue mechanical properties for NNW scaffolds. The new model is proposed with the following assumptions:

1. The strain energies of the scaffold, ECM, and scaffold-ECM interactions are additive.
2. A measurable amount of scaffold will degrade with time, but the overall continuity of the scaffold phase will remain intact.
3. The scaffold remains in intimate contact with the ECM phase.
4. The ECM phase can be modeled as an incompressible anisotropic soft tissue.
5. Scaffold-ECM interactions manifest as shearing and extensional effects between the scaffold fibers that are in effect embedded in the ECM.
6. Scaffold-ECM interactions are additive and thus can be separated.

NNW scaffolds were seeded with vascular smooth muscle cells and incubated for up to 4 weeks using standard methods. Another group of NNW scaffolds were imbedded with PAM gels of graduated, known stiffnesses to calibrate the model with a known standard. Both groups were subjected to biaxial mechanical evaluation. A strong relationship between effective scaffold fiber stiffness and matrix shear modulus was found. Additionally, the model was shown to estimate the PAM gel shear moduli accurately. When applied to the implanted NNW scaffolds, we found little changes from 0 to 7 day during the initial implant period, even though the scaffold and collagen mass increased (Fig. 2).

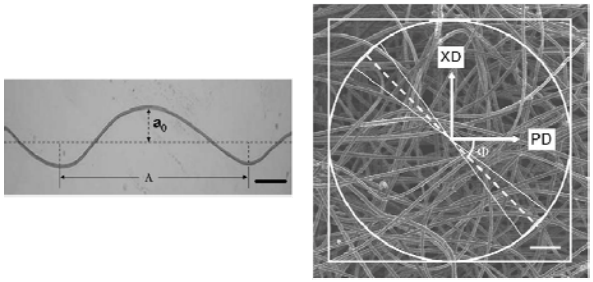

Figure 1 – NNW scaffold fiber geometry and local preferred (PD) and cross-preferred (XD) directions.

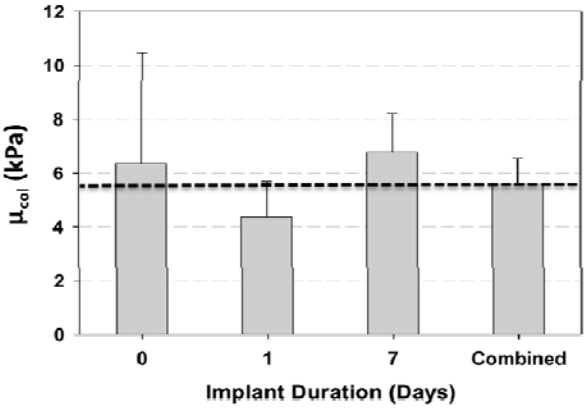

Figure 2 – Predicted collagen fiber moduli from initial to 7 days.

We hope that the insights gained from our simulations will be used to guide the design of scaffolds and selection of process variables so that the resulting engineered tissues mimic the non-linear mechanical behavior of the native tissues.

Acknowledgements: NIH R01 HL068816.