MECHANICAL AND BIOCHEMICAL CHARACTERIZATION OF SELF-ASSEMBLING TENDON CONSTRUCTS

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Quantification of the influence of mechanical interventions on soft biological tissues is confounded by the complex *in vivo* environment. Correlations between experimental manipulations and changes on a specific tissue morphology can be a direct influence of the applied stimulus or a result induced by changes within the surrounding tissues. To address this issue, an *in vitro* tendon-like construct was created that allows for application of controlled mechanical interventions. Tendon fibroblasts, under the proper conditions, can be influenced to proliferate to confluence and delaminate from the substrate, assembling into a cylinder held together by the extracellular matrix secreted by the cells.[1] When tested to failure in tension, the constructs display the mechanical response characteristics of tendons. (Figure 1) The nominal stress-strain response is initially non-linear (the toe region). At a critical stiffness the specimen response becomes linear and continues at this same stiffness until just prior to failure. The ultimate tensile stress and tangent modulus of the constructs is similar to that of embryonic chick tendon.

Currently, methods to quantify the effects of mechanical interventions on these constructs are being developed. The constructs express similar proteins as neonatal and adult tendons as illustrated by western blot analysis. Experiments to show the effect of tension on the protein distribution are underway. Preliminary results have indicated that the stiffness of the constructs increases with time. This evolution of stiffness is also seen during tendon development, but whether similar mechanisms are occurring in the constructs, which include increases in collagen fibril diameter and cross-link density, warrants further elucidation.

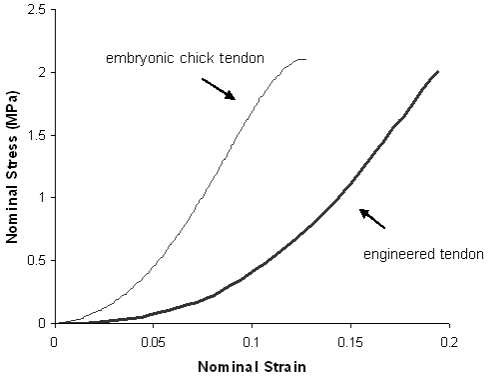

Figure 1. Stress-strain responses of tendon construct and embryonic chicken extensor tendon (14 days *in ovo*).[2] The tendon constructs were strained until failure at a rate of 0.05 s^{-1}. While the toe region of the engineered tendon is elongated, the tangent moduli and ultimate tensile strengths of both tissues are similar. The tangent modulus measured at a strain of 0.16, within the linear region of the response, is 20 MPa. The constructs are mechanically similar to embryonic chicken extensor tendons which have a tangent modulus of 27 MPa.[2]

References

[1] S. Calve et al. "Engineering of Functional Tendon." *Submitted for publication to Tissue Engineering, 2003.*
[2] D.J. McBride, R.L. Trelstad, and F.H. Silver, "Structural and Mechanical Assessment of Developing Chick Tendon." *International Journal of Biological Macromolecules,* v. 10, p. 194-200, 1988.