MECHANICAL CHARACTERIZATION OF COLLAGEN-FIBRIN COMPOSITES FOR VASCULAR TISSUE ENGINEERING

by

Shaneen Lashay Rowe

An Abstract of a Thesis Submitted to the Graduate

Faculty of Rensselaer Polytechnic Institute

in Partial Fulfillment of the

Requirements for the degree of

DOCTOR OF PHILOSOPHY

Major Subject: Biomedical Engineering

The original of the complete thesis is on file
In the Rensselaer Polytechnic Institute Library

Examining Committee:

Jan P. Stegemann, PhD, Thesis Adviser

Natacha DePaola, PhD, Member

Rahmi Ozisik, PhD, Member

Deepak Vashishth, PhD, Member

Rensselaer Polytechnic Institute
Troy, New York

June 2007
(For Graduation August 2007)

ABSTRACT

Blood vessel substitutes are needed as improved replacements for native vessels that have been narrowed or occluded with the progression of atherosclerotic disease. Blood vessel substitutes engineered from naturally derived proteins can provide a suitable scaffold for replacement of small diameter (< 6 mm) vessels. However, mimicking of *in vivo* mechanical properties has proved elusive. Microstructure is an important contributor to the properties of engineered tissues. Previous research has shown that collagen-fibrin mixed composite scaffolds demonstrate improved tensile mechanical properties relative to pure protein scaffolds. It is hypothesized that features of the microstructure are responsible for these improvements. In this investigation, the relationship between microstructure and mechanical properties in cell-populated gels created from collagen, fibrin or a mixture of these two proteins was examined. Specific microstructural features were identified and correlated with tensile and viscoelastic properties. This allowed us to determine candidate features which could be varied to produce more mechanically robust matrices. Towards this end, comparative mixed scaffolds were created by manipulating the microstructure of the composite system. To do this, we: 1) increased the concentration of the fibrin protein, 2) increased the concentration of thrombin, the enzyme used to polymerize fibrin and 3) used ancrod, a thrombin-like enzyme, to polymerize fibrin. These changes in mixed construct preparation resulted in changes to the scaffold architecture and mechanical properties. Variations in structural features were quantified and correlated with increases or decreases in tensile and viscoelastic properties. Decreases in fiber diameter were related to increased strength, while an increase in the number of bundles was linked to increased stiffness and strength. The number of bundles was also correlated with increased energy storage, elasticity, decreased deformation and slowed relaxation. These changes in mechanical behavior were prevalent in mixed scaffolds. These results demonstrate that further improvements in mechanical properties can be made by a targeted manipulation of scaffold architecture. An understanding of the relevant structural features will lead to the rational design of protein scaffolds with the necessary microstructural characteristics required for enhanced macroscopic function. An improvement in the mechanical properties of these scaffolds is a step towards replacement of damaged blood vessels.