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A PROPOSED ROLE FOR EXERCISE IN ERODIBLE IMPLANT INCORPORATION

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INTRODUCTION: Tissue engineered scaffolds require vascularization to 1) enhance nutrient exchange and 2) provide cells needed to build new tissue. Cell-seeded scaffolds—bioreactors-- require rapid penetration of vessels or enhanced fluid percolation to keep their contents alive until normal nutrient exchange can be established. Bone fluid flow (BFF) depends on a pumping system which drives percolation through its own matrix. Recent interest in the pumping mechanism has resulted in BFF models which link the pumps to bending of bone by muscle contraction and compression-tension cycles from weight-bearing during locomotion. We have proposed that capillary filtration, the source of the percolating fluid, is sufficiently enhanced by soliton pressure waves in blood driven by the muscle pump during exercise to provide a significant hydraulic pressure component to bone fluid percolating through bone and any bone-implanted scaffold. We present here a proposal and some preliminary results from a pilot project suggesting enhancement of capillary filtration by the muscle pump.

METHODS: Optical bone chambers were implanted in adult NZW female rabbits. Chamber construction and implantation were as usual[1]. At the third week post-op chamber ends were exposed and weekly intravital microscopy commenced. Transcutaneous electrical stimulation was administered with a ToneATronic® TENS at 85V, 80mA and 2Hz. The stimulator was applied externally over the gastrocnemius muscle. A fluorescence digital image was obtained before 30 minutes application of TENS after injection of FITC-D70. After stimulation RITC-D70 was injected. Blood samples were obtained from an aural vein in the ear opposite that being injected with the fluorescent dye after each injection. Blood concentration of dye was determined with a SPEX Fluoromax-3 spectrofluorometer for both serum (absolute concentration) and whole blood (to detect differences which would make fluorescence in vessels an inaccurate indicator of concentration due to RBC color contamination). For analysis 4 vessels were chosen and the average dye concentration profiles before and after 30 minutes of stimulation were obtained.

RESULTS: Results are shown in Figure 1. Extravasated dye levels in TENS rabbits were markedly higher than those in controls. Analysis of profiles using an erfc-based diffusion-convection discrimination model[2] showed that extravasation was convective.

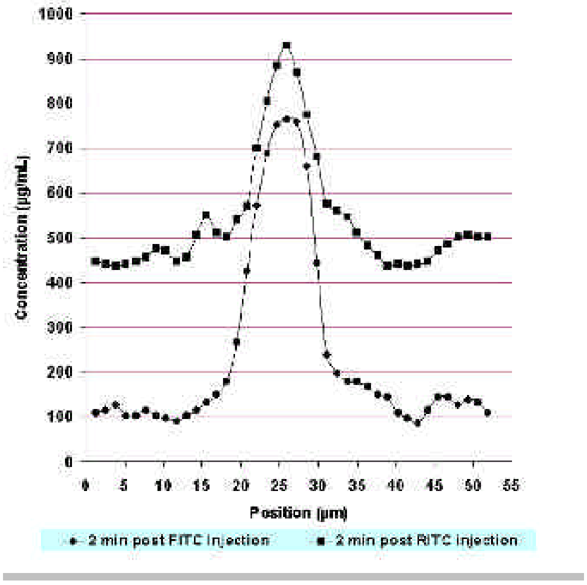

Fig. 1: Extravasation of fluorescent dyes pre- and post- 30 min. TENS. Peaks represent vessels.

DISCUSSION & CONCLUSIONS: These data are consistent with significant contribution to convective percolation of bone fluid through implanted scaffolds by muscle pump-driven extravasating fluid. They do not, however, answer two critical questions: 1) Is the magnitude of this convection a major component of flow through the scaffold? 2) What are the relative contributions of skeletal muscle-generated intravascular pressure solitons and incompressible fluid transmission of bone bending pressure to the convective flow observed? Additional studies with released gastrocnemius muscles are in progress.

REFERENCES: [1] Winet H (1989) *A horizontal intravital microscope bone chamber system for observing microcirculation* **Microvasc. Res. 37**: 105-114, [2] Nakamura Y, H Wayland (1975) *Macromolecular transport in the cat mesentery* **Microvasc. Res. 9**: 1-21.