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Dynamic loading of immature epiphyseal cartilage pumps nutrients out of vascular canals

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ABSTRACT

The potential influence of mechanical loading on transvascular transport in vascularized soft tissues has not been explored extensively. This experimental investigation introduced and explored the hypothesis that dynamic mechanical loading can pump solutes out of blood vessels and into the surrounding tissue, leading to faster uptake and higher solute concentrations than could otherwise be achieved under unloaded conditions. Immature epiphyseal cartilage was used as a model tissue system, with fluorescein (332 Da), dextran (3, 10, and 70 kDa) and transferrin (80 kDa) as model solutes. Cartilage disks were either dynamically loaded ($\pm$10% compression over a 10% static offset strain, at 0.2 Hz) or maintained unloaded in solution for up to 20 h. Results demonstrated statistically significant solute uptake in dynamically loaded (DL) explants relative to passive diffusion (PD) controls for all solutes except unbound fluorescein, as evidenced by the DL:PD concentration ratios after 20 h (1.0 ± 0.2, 2.4 ± 1.1, 6.1 ± 3.3, 9.0 ± 4.0, and 5.5 ± 1.6 for fluorescein, 3, 10, and 70 kDa dextran, and transferrin). Significant uptake enhancements were also observed within the first 30 s of loading. Termination of dynamic loading produced dissipation of enhanced solute uptake back to PD control values. Confocal images confirmed that solute uptake occurred from cartilage canals into their surrounding extracellular matrix. The incidence of this loading-induced transvascular solute pumping mechanism may significantly alter our understanding of the interaction of mechanical loading and tissue metabolism.

1. Introduction

Solute transport in biological tissues is a fundamental process in support of cell metabolism, providing access to nutrients and a removal of waste products. In the native environment, solute exchange occurs primarily via the circulatory system, where it is understood that solutes transport down a concentration gradient from the blood stream into tissues. Over the years, considerable efforts have been made to explore the contributions of physiologic mechanisms for this exchange, such as passive diffusion, fluid convection, and transcytosis (Jennings and Florey, 1967; Michel and Curry, 1999; Pappenheimer, 1953; Pappenheimer and Soto-Rivera, 1948; Rippe and Haraldsson, 1994; Simionescu et al., 1975). However, the potential influence of mechanical loading on transvascular transport has not been explored significantly. This experimental investigation introduces and explores the hypothesis that cyclic mechanical loading can pump solutes out of blood vessels and into the surrounding tissue, leading to faster uptake and higher solute concentrations than could otherwise be achieved under unloaded conditions.

The concept of cyclic or dynamic loading enhancing solute transport in the extracellular matrix (ECM) of hydrated soft tissues has often been surmised to promote solute convection, induced by oscillatory interstitial fluid flow. Studies have generally shown that dynamic loading can increase the rate of solute transport in avascular tissue explants or hydrogels (Bonassar et al., 2001; Evans and Quinn, 2006; Lee et al., 2000; O'Hara et al., 1990). However, more recently, it has been demonstrated that dynamic loading can pump solutes into hydrogels from an external bath, promoting substantially higher concentrations than observed under passive diffusion alone (Albro et al., 2008). These concentration enhancements were observed to be as high as 15-fold over passive equilibrium values, demonstrating that solutes are being transported against their concentration gradient. This phenomenon was shown, on a theoretical basis, to result from the momentum exchange between solutes and the deforming solid matrix induced by dynamic loading (Albro et al., 2010; Mauck et al., 2003). As the matrix expands and recoils under loading, it is able to pull solutes from an external bathing solution into the tissue, in a manner akin to pumping.

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