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An ex vivo model to study transport processes and fluid flow in loaded bone.

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Abstract
Load-induced fluid flow has been postulated to provide a mechanism for the transmission of mechanical signals (e.g. via shear stresses, enhancement of molecular transport, and/or electrical effects) and the subsequent elicitation of a functional adaptation response (e.g. modeling, remodeling, homeostasis) in bone. Although indirect evidence for such fluid flow phenomena can be found in the literature pertaining to strain generated potentials, actual measurement of fluid displacements in cortical bone is inherently difficult. This problem motivated us to develop and introduce an ex vivo perfusion model for the study of transport processes and fluid flow within bone under controlled mechanical loading conditions. To this end, a closed-loop system of perfusion was established in the explanted forelimb of the adult Swiss alpine sheep. Immediately prior to mechanical loading, a bolus of tracer was introduced intraarterially into the system. Thereafter, the forelimb of the left or right side (randomized) was loaded cyclically, via Schanz screws inserted through the metaphyses, producing a peak compressive strain of 0.2% at the middiaphysis of the anterior metacarpal cortex. In paired experiments with perfusion times totalling 2, 4, 8 and 16 min, the concentration of tracer measured at the middiaphysis of the cortex in cross section was significantly higher in the loaded bone than in the unloaded contralateral control. Fluorometric measurements of procion red concentration in the anterior aspect alone showed an enhancement in transport at early stages of loading (8 cycles, 2 min) but no effect in transport after higher number of cycles or increased perfusion times, respectively. This reflects both the small size of the molecular tracer, which would be expected to be transported rapidly by way of diffusive mechanisms alone, as well as the loading mode to which the anterior aspect was exposed. Thus, using our new model it could be shown that load-induced fluid flow represents a powerful mechanism to enhance molecular transport within the lacunocanalicular system of compact bone tissue. Based on these as well as previous studies, it appears that the degree of this effect is dependent on tracer size as well as the mechanical loading mode to which a given area of tissue is exposed.

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