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In vivo demonstration of load-induced fluid flow in the rat tibia and its potential implications for processes associated with functional adaptation.

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Abstract
Load-induced extravascular fluid flow has been postulated to play a role in mechanotransduction of physiological loads at the cellular level. Furthermore, the displaced fluid serves as a carrier for metabolites, nutrients, mineral precursors and osteotropic agents important for cellular activity. We hypothesise that load-induced fluid flow enhances the transport of these key substances, thus helping to regulate cellular activity associated with processes of functional adaptation and remodelling. To test this hypothesis, molecular tracer methods developed previously by our group were applied in vivo to observe and quantify the effects of load-induced fluid flow under four-point-bending loads. Preterminal tracer transport studies were carried out on 24 skeletally mature Sprague Dawley rats. Mechanical loading enhanced the transport of both small- and larger-molecular-mass tracers within the bony tissue of the tibial mid-diaphysis. Mechanical loading showed a highly significant effect on the number of periosteocytic spaces exhibiting tracer within the cross section of each bone. For all loading rates studied, the concentration of Procion Red tracer was consistently higher in the tibia subjected to pure bending loads than in the unloaded, contralateral tibia. Furthermore, the enhancement of transport was highly site-specific. In bones subjected to pure bending loads, a greater number of periosteocytic spaces exhibited the presence of tracer in the tension band of the cross section than in the compression band; this may reflect the higher strains induced in the tension band compared with the compression band within the mid-diaphysis of the rat tibia. Regardless of loading mode, the mean difference between the loaded side and the unloaded contralateral control side decreased with increasing loading frequency. Whether this reflects the length of exposure to the tracer or specific frequency effects cannot be determined by this set of experiments. These in vivo experimental results corroborate those of previous ex vivo and in vitro studies. Strain-related differences in tracer distribution provide support for the hypothesis that load-induced fluid flow plays a regulatory role in processes associated with functional adaptation.

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