BRIDGING ORGAN- AND TISSUE LEVEL COMPUTATIONAL MODELS OF BONE TO IMPROVE LOAD-INDUCED FLUID FLOW PREDICTIONS

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INTRODUCTION

Mechanical loading of bone has been shown to enhance extravascular molecular transport [1]. This convective transport of nutrients and bioactive molecules from the blood supply to the osteocytes embedded in the mineralized bone matrix, and between osteocytes, osteoblasts and osteoclasts, acts in addition to baseline diffusive and intracellular transport mechanisms. Due to the inaccessibility of the fluid spaces in bone for direct experimental observation, theoretical and computational models aid substantially in understanding the generation and effects of load-induced fluid movement.

Bone, like most biological tissues, is a highly hierarchical structure and possesses fluid spaces at several different length scales. It is therefore important to apply methods that are appropriate to simulate interstitial fluid flow effects at a given level of porosity. In our laboratory we have developed poroelastic finite element models to predict interstitial fluid movement in mechanically loaded bone on an organ level [2], and stochastically generated network models [3] to study the influence of cell density and connectivity on the bone tissue permeability on a tissue level. In this study we report on a method to integrate insights gained from tissue level simulations into calculations on an organ level in order to improve the accuracy of the computational predictions.

It has been reported that porosity of bone is site specific with respect to the distance from the bone surfaces (near endosteum, mid-cortex, or near periosteum), as well as with respect to the loading mode, to which a given area of the cross section is predominantly subjected to (*i.e.* tensile- or compressive load). In addition, porosity and permeability (one of the most important parameters for the prediction of interstitial fluid movement of a tissue) are intimately related. The goal of this study was to determine to what degree varying porosities in different aspects of the bone cross section affect the predicted macroscopic fluid movements. For this purpose we measured the site-specific porosities in a rat ulna, used these values to determine the local tissue permeability, which was then applied to predict the pore pressure distribution in a mechanically loaded bone model.

METHODS

The porosity attributed to the vascularity of a rat ulna was measured from high resolution μCT scans (6 μm, μCT 40, Scanco Medical AG, Switzerland). Photomicrographs from histological sections were used to measure the lacunocanalicular pore spaces and the osteocyte connectivity. The measured parameters served as input for stochastically generated network models [3] that allowed for the calculation of site specific, anisotropic permeability. These values, in turn, were used in an idealized, cylindrical bone model, representing a rat ulna, to calculate the fluid pore pressure in a bone subjected to a cyclic, combined compression-bending load acting at a frequency of 1 Hz.

RESULTS AND DISCUSSION

Most blood vessels within the bone cortex, and therefore the highest vascular porosity, were found in the region adjacent to the endosteal surface, as the analysis of the μCT scans showed. With respect to the lacunocanalicular porosity, the photomicrographs unveiled that for the specific case of the rat ulna the bone cortex can be divided into 3 concentric shells. Two of the shell layers are located near the endosteal and near the periosteal surfaces, respectively, where a relatively low number of osteocytes, and therefore low lacunocanalicular porosity, are arranged with a high degree of organization. A mid-cortex shell can be identified with a much lower degree of organization but higher number of osteocytes and therefore bigger porosity. A shell model incorporating these findings was therefore used for the parametric finite element study, whereas the site-specific material properties for each shell layer were calculated using the stochastically generated network models. While the overall pore fluid pressure distribution calculated with this poroelastic shell layer model was comparable to the pressure distribution determined with a model with uniform material parameters, local fluid pressures and fluid velocities changed significantly. Higher porosity and therefore permeability generally lead to lower fluid pressures, but higher fluid velocities. However, all calculated fluid velocities remained within the same order of magnitude.

CONCLUSIONS

This study confirmed the importance of site specific material parameters in the prediction of interstitial fluid flow in mechanically loaded bone. These insights will lead to the development of a next generation of computational models that will allow for a direct comparison with the results of experimental tracer studies.

REFERENCES

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ACKNOWLEDGEMENTS

This study was funded in part by a grant from the AO Research Foundation (04-S4)