HOW TO UNDERSTAND EFFECTS OF LIPUS ON BONE HEALING? A MULTISCALE COMPUTATIONAL STUDY

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Introduction

Bone is a complex biological tissue which remodels all along healing. Bone remodeling is the result of bone cells activation due to mechanical stresses. The osteocytes are thought to be the principal mechanosensory cells of bone. They are immersed in the lacuno-canalicular network (LCN) filled with interstitial fluid. There is theoretical and experimental evidence that their activation relies on the shear stress from fluid flowing through the osteocyte canaliculi.

Low Intensity Pulsed UltraSound (LIPUS) is a current clinical treatment to speed up or consolidate bone healing. But although it has been proven that LIPUS induces minimal thermal effects, debate is still opened to know how LIPUS mechanically stimulates bone regeneration. The aim of this preliminary study is to numerically investigate LIPUS stimulation from a tissue-scale model to a cellular-scale model in order to make the connection between *in vitro* studies and clinical observations.

Methods

Two numerical models were developed with the commercial software Comsol Multiphysics.

The first tissue-scale model (ModBone) is 2D and simulates the interaction of the ultrasound (US) stimulation with the cortical bone viewed as a biphasic medium: fluid in the vascular pores and an anisotropic poroelastic extracellular matrix (ECM) including the LCN. The geometry of the bone and of the vascular pores are deduced from RX images (22 µm). The whole domain is immersed in water (ρ_f=1000 kg.m^{-3}, K_f= 2.25 GPa). The wave propagation in the poroelastic matrix follows the Biot theory. The poroelastic coefficients are given in [1] for bone matrix with a LCN porosity of 5% and in [2] for the interstitial fluid. An US stimulation equivalent to what is clinically delivered is applied as boundary condition (I_{SATA} = 30 mW/cm², duty cycle = 20%, f = 1MHz).

The second model is the cellular-scale model (ModOst) including a 3D fluid-structure interaction model of one osteocyte immersed in the interstitial fluid of the LCN and embedded in the ECM. ECM and osteocyte were modeled as linearly elastic, isotropic materials. Interstitial fluid is modeled as viscous Newtonian fluid. Geometrical and mechanical characteristics are given in [2]. The pressure gradient obtained in ModBone is applied as boundary condition for the fluid.

Results

The US stimulation on ModBone induces pressure difference between the endosteum and the periosteum (Figure 1) and fluid shear stress in the LCN. The difference $\Delta P(t)$ between average pore pressure along endosteum P_{end} and average pore pressure along periosteum P_{per} is calculated over one US cycle. The time average value of $\Delta P(t)$ is equal to 300Pa and is applied in ModOst as fluid boundary condition.

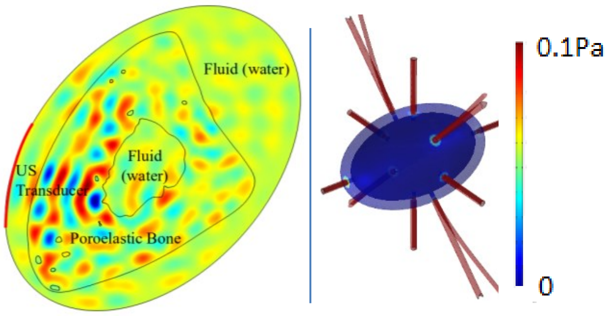

Figure 1: Fluid pressure in ModBone (left) and shear stress in ModOst (right)

In ModBone, fluid shear stress magnitude τ is calculated following [3]. Over one US cycle the average τ value over the cross section varies from 0 to 1.7 Pa with a local maximum of 20Pa. In ModOst, τ ranges between 0.1 Pa in osteocyte body and up to 1 Pa in canaliculi (Figure 1). These values agree well with [4].

Discussion

The effects of LIPUS on bone healing is a tricky question: they imply several scales and couple several physics. Both models presented in this study investigate qualitatively and quantitatively how the US stimulation generates fluid shear stresses in the LCN, sensed to be one of the key parameter in bone mechanotransduction. Nevertheless it is a preliminary study, the following points are still on going: effects of treatment duration over several cycles, boundary conditions at the endosteum and periosteum, the 3D reconstruction of vascular pore network.

References

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