IN SILICO ULTRASOUND STIMULATION OF OSTEOCYTE IN BONE LACUNO-CANALICULAR NETWORK

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Introduction

Osteocytes are known as the master orchestrator of bone remodeling being the mechanosensors of bone. They are dendritic cells, ubiquituous in the bone extracellular matrix (ECM) forming a complex micrometric 3D network. The space between the osteocytes and the ECM is called the pericellular matrix (PCM) and can be considered as a fluid. To relevantly analyze the mechanical stress induced by external stimulation such as physiological loading or ultrasound (US), this 3D micro-environment need to be taken into account. Several papers have been published on the interaction between lacuno-canalicular network (LCN) and physiological loading, currently represented as a gradient of pressure (30Pa/µm). However, to our knowledge, no study has been published on the action of ultrasound stimulation (USS) on osteocytes in a 3D configuration representative of their *in-vivo* micro-environment while ultrasound stimulation is clinically used in bone healing. To overcome this lack, we propose a first numerical finite-element model to investigate the effect of ultrasound stimulation on an 3D idealized geometry of the PCM.

Material and Methods

As currently admitted in the literature in the case of physiological loading, osteocytes are mainly sensitive to the fluid shear stress induced inside the PCM. Consequently, the goal of this study is to estimate the wall shear stress (WSS) applied on the osteocytes by ultrasound stimulation considered as harmonic acoustic wave. This configuration is modeled in the frequency domain with finite-element commercial software Comsol Multiphysics v6.0. The idealized 2D axisymmetric geometry is inspired from [1] (Figure 1a). The ECM and the osteocyte are considered as rigid bodies and the PCM as water. The boundary condition at the ends of the canaliculi is symmetry condition in order to represent a succession of osteocytes. The US loading is represented by the displacement of the ECM/PCM interface in the radial direction ($\mathbf{e}_r$), with an amplitude U_0 imposed at the frequency f.

Considering the dimensions of the system and the wavelength, the Thermoviscous Acoustics module and the Laminar flow module of Comsol Multiphysics are coupled to take into account the acoustic streaming induced in the PCM and to estimate the WSS at the osteocyte surface [2].

Results

Two parametric studies on U_0 and f were carried out in order to produce a WSS in the range [0.8-3] Pa defined by [3] to trigger the osteocytes remodeling response.

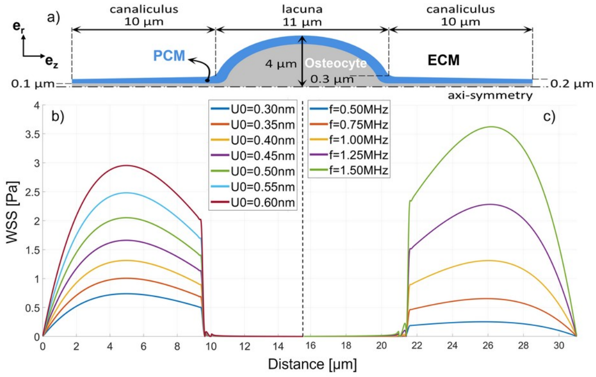

Figure 1: a) Geometrical 2D axisymmetric model; b) WSS at f=1 MHz for different values of U_0; c) WSS for different values of f at U_0=0.4 nm.

Figures 1b and 1c, clearly state that, whatever the amplitude and/or the frequency, WSS is quite zero at the osteocyte body whereas it mainly acts on the processes known as the privileged sites of mechanotransduction in osteocytes. Figure 1c confirms that the WSS increases with the frequency, i.e. the same level of stimulation will be reached for a lower loading by increasing the frequency.

Discussion

These results confirm that USS could reach WSS levels liable to trigger bone remodeling. However, more realistic boundary conditions and geometry will be investigated to be closer to the physiological environment, especially considering a network of osteocytes with irregular shape. In addition, the WSS reference range can be questioned because it was established for a physiological load that has different characteristics from USS (load direction and frequency). A WSS range dedicated to USS has yet to be defined. A better understanding of the interaction between US and LCN, will lead to a better interpretation of experimental and clinical observations on USS of bone regeneration in order to finally achieve an optimized therapeutic protocol.

References

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2 Muller and Bruus, *Phys. Rev. E*, 90,: 43016, 2014.
3 Weinbaum et al., *J. Biomech.*, 27: 339–360, 1994.