

MODELING THE EFFECTS OF INTERSTITIAL FLUID FLOW ON A SINGLE OSTEOCYTE AND ITS PROCESSES

Eric J. Anderson

Dept. of Mechanical & Aerospace Engineering
Case Western Reserve University, Cleveland, OH 44106
Orthopaedic Research Center, Cleveland Clinic Foundation, Cleveland, OH 44195

Sathya Kaliyamoorthy

Orthopaedic Research Center, Cleveland Clinic Foundation
Cleveland, OH 44195

Melissa L. Knothe Tate

Depts. of Biomedical Engineering and Mechanical & Aerospace Engineering
Case Western Reserve University, Cleveland, OH 44106
Orthopaedic Research Center, Cleveland Clinic Foundation, Cleveland, OH 44195

ABSTRACT

In order to understand the manner in which local changes in mechanical environment are translated into cellular activity underlying tissue level bone adaptation, there is a need to explore fluid flow regimes at small scales such as the osteocyte. Recent developments provide impetus to model periosteocytic flow using computational fluid dynamics. In building this model, the local effects of fluid flow on the osteocyte cell body and its processes were analyzed. For each model, fluid flow was induced via a pressure gradient, and the CFD calculated, based on the Navier-Stokes equations, the shear stress at the cell-fluid interface and radial stress, acting normal to the cell surface. Based on the model, the osteocyte cell body is exposed primarily to effects of hydrodynamic pressure and the cell processes are exposed primarily to shear and radial stress, with highest stress gradients at sites where the process and the cell body intersect and where two cell processes join at the gap junction. Hence, this model simulates subcellular effects of fluid flow and suggests, for the first time to our knowledge, major differences in modes of loading between the domain of the cell body and that of the cell process.

INTRODUCTION

The lacunocanalicular system provides an ideal milieu for transfer of exogeneous and endogeneous signals via mechanical, electrical and chemical mechanisms. However, the fluid flow regimes that modulate this signal conveyance within the lacunocanalicular system are not understood; this is due in part to difficulty in understanding flow through a nanoscale system of pericellular pathways and to limitations in understanding the morphology and physiology of the osteocytes themselves. Confocal and electron micrographs of the pericellular channels reveal the annular space between osteocyte processes and the canaliculi walls (postulated dimension 14 to 100 nm). Understanding the fluid flow in

these spaces and its interaction with the cell (osteocyte) is of fundamental importance to understanding mechanotransduction from the system down to the cellular level.

METHODS

In order to explore fluid flow at the length scale of the cell, two models were developed to study (i) flow regimes within the annular space of a single canaliculus and (ii) within the pericellular space of a lacunocanalicular system including a highly idealized osteocyte and cell processes. Flow through the matrix microporosity was not included at this stage of modeling. The annular gap size between the osteocyte process and canalicular wall was defined to be $0.1\ \mu\text{m}$, the core diameter was $0.2\ \mu\text{m}$, and the channel length was $10\ \mu\text{m}$, respectively. The *lacunocanalicular model* was calculated for three cases, the simplest of which included two canaliculi that served as an inlet and outlet for flow, respectively. In two further iterations of the model, three canaliculi were joined to the lacuna and calculations were run (i) for the case where two canaliculi served as inlets and one as an outlet and (ii) for the case where one canaliculus served as an inlet and two as outlets for fluid flow. For both the case of the *canaliculus model* and the *lacunocanalicular model*, the interstitial fluid was idealized as water-like and appropriate properties were assigned to the fluid volumes, including density = $997\ \text{kg m}^{-3}$ and dynamic viscosity = $0.000855\ \text{kg m}^{-1}\ \text{s}^{-1}$. The boundary conditions were then set for the inlet and outlet of each model, where both the *canaliculus* and *lacunocanalicular* models were assigned an inlet pressure of 300 Pa and an outlet pressure of 0 Pa.

RESULTS

In the *canaliculus model*, both the pressure and shear stress are found to decrease with increasing annular radius, as expected. Wall shear stress displays a large gradient along the channel length of $10\ \mu\text{m}$ (Fig. 1), where values range from 7 to

nearly 1.75 dyn/cm^2 from inlet to outlet. Similarly, the pressure within the canaliculus is found to decrease across the channel, from 300 to 150 Pa, with distance from inlet to outlet, respectively, as governed by the given pressure gradient.

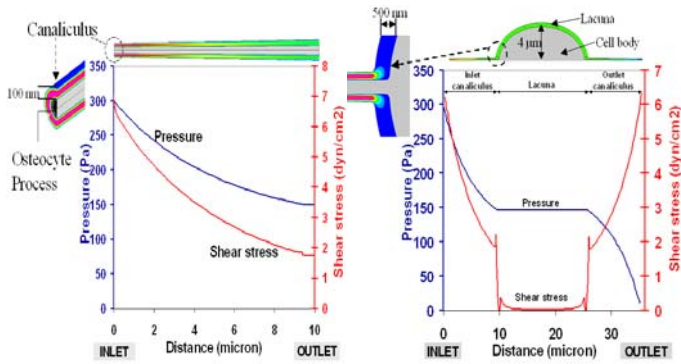


Fig. 1: - Canaliculus model

Fig. 2: Lacuna I (1 inlet, 1 outlet)

For all cases of the *lacunocanalicular model* the osteocyte was subjected to a sustained hydrodynamic pressure within the lacuna, with decreased stress values. Neither the number of canaliculi nor their designation as inlet or outlet had a significant effect on the qualitative relationship between the hydrodynamic pressures, which exerted a dominant effect, and the shear stresses at the surface of the cell body. However, the models did vary quantitatively, as the hydrodynamic pressure varied as a function of number of canaliculi, respectively, inlets and outlets.

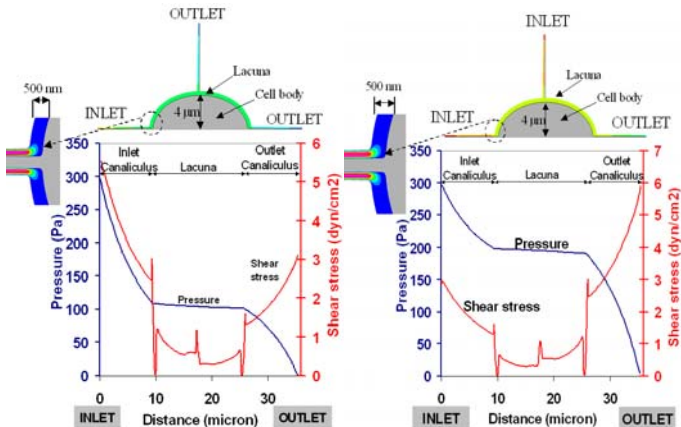


Fig. 3: Lacuna II (1 inlet, 2 outlet)

Fig. 4: Lacuna III (2 inlet, 1 outlet)

In comparison with the *canaliculus model*, the *lacunocanalicular models* with two canaliculi reveals similar results for fluid flow in each canaliculus; however, the variance in pressure abruptly ceases within the lacuna, where reduced stresses are sustained (Fig. 2). As the fluid moves from inlet to outlet, a sustained hydrodynamic pressure ($\sim 150 \text{ Pa}$) persists throughout the lacuna. Furthermore, as the pressure is sustained across the lacuna, the shear stresses decrease to near zero values. Thus, the model does not predict high gradients of stress along the surface of the osteocyte. From the inlet toward the lacuna, the wall shear stress decreases with pressure as observed in *canaliculus model* described above.

In the third case of the *lacunocanalicular model*, a third canaliculus was added as an outlet with a pressure of 0 Pa and corresponding mass flow rate (Fig. 3). With the addition of an extra outlet, the pressure within the lacuna decreased slightly

from that of the previous, where the chosen pathway shows no difference in the qualitative relationship between the canaliculus and lacuna. In this case, the hydrodynamic pressure within the lacuna is nearly sustained at 105 Pa, and the value of shear stress decreases to a reduced value on the osteocyte surface with an exception where the added canaliculus resides. This additional canaliculus causes the overall shear stress found within the lacuna to be higher than that of the previous models, where it varies between 0.3 and 1 dyn/cm^2 .

Analogous to the third lacunocanalicular model, the fourth case of the *lacunocanalicular model* showed a nearly sustained (slight drop throughout lacuna) hydrodynamic pressure within the lacuna with a decrease in wall shear stress at the cell surface (Fig. 4). The change in shear stress in the lacuna is opposite of the previous, where a slightly lower gradient of stress is found in the first half of the lacuna, with a higher gradient in the following section. This is to be expected as the added channel introduces flow at this point, thus increasing mass flow rate, velocity, and the wall shear stress found at the osteocyte surface.

In order to determine the robustness of the model, the variance in shear stress was determined corresponding to a range of pressures varying by an order of magnitude (3, 30, 300, and 3000 Pa). As in previous cases, the lacuna was subjected to sustained values of stress where high gradients of shear were found to increase with distance from the cell body. The stresses within the lacunae were comparable to the previous models, whereby magnitudes changed proportionally with pressure.

DISCUSSION

In conclusion, based on this new, nano-micro scale computational fluid dynamics model, the osteocyte cell body is exposed primarily to effects of hydrodynamic pressure within the lacuna and the cell processes are exposed primarily to shear and radial stresses within the canaliculi, with highest gradients in stress near and far from the cell body, at the sites of the junction with the cell body and gap junctions to other cells. Hence, this model simulates subcellular level effects of fluid flow and shows, for the first time to our knowledge, major differences in modes of loading between cellular regions remote to (*i.e.* cell processes) and near (*i.e.* cell body) cell-surface receptors and the cytoplasmic domain. This is expected to have profound implications for cell signaling and is being explored in a parallel, experimental study.

ACKNOWLEDGMENTS

This study is supported through a grant from the National Institutes of Health, NIAMS (AR049351-01).

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Keywords: Osteocyte, computational fluid dynamics, lacunocanalicular, nanofluidics, microfluidics, bone fluid flow