Influence of microcracks on interstitial fluid flows at the osteonal scale

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Résumé :

Les microfissures sont connues comme un facteur important qui stimule le remodelage de l'os. Ce travail étudie les conséquences de la présence d'une microfissure sur le comportement hydraulique osteonal. Un modèle poroélastique de type Biot a été développé. Les résultats numériques obtenus montrent que les microfissures pourraient modifier significativement les champs de vitesses des écoulements à l'intérieur des ostéons avoisinants. Ceci permetrait d'expliquer le mécanisme de "remodelage ciblé" par lequel les microfissures sont naturellement détectées et réparées.

Abstract :

It is well-known that microcracks act as a stimulus for bone remodelling. This paper proposes a quantitative evaluation of the strain-induced interstitial fluid velocities developing in osteons in presence of a microcrack in the interstitial bone tissue. Based on Biot theory in the low-frequency range, a poroelastic model is carried out to study the hydro-mechanical behaviour of cracked osteonal tissue. The finite element results show that the presence of a microcrack in the interstitial osteonal tissue may drastically reduce the fluid velocity inside the neighbouring osteons. This might explain the "targeted remodelling" mechanism in which microcracks are naturally detected and repaired

Mots clefs : **mécanotransduction ; ostéon ; milieu poreux**

1 Introduction

Cortical bone constitutes the outer shell of long bones. This live entity is continuously renewed by bone cells in response due to the loading generated by daily activity. This process, known as bone remodelling, is essential for proper bone functioning in both physiological and pathological conditions. Thus, linking bone loading to local tissue remodelling is an issue of great interest [7]. In particular, the nature of the signal sensed by bone cells is still in debate. Classical hypotheses stipulate that fluid shear stress [1], pericellular matrix deformation [15] and/or microcracks [10] do play a role in the triggering of the remodelling process. It has been particularly suggested that a microdamage occurring inside the osteonal volume may generate a cell transducing mechanism based on ruptured osteocyte processes [6]. Concomitantly, microcracks are likely to alter the fluid flow and convective transport through the bone tissue and thus modify the hydraulic vicinity of the sensitive cells. Some computational models have been proposed to consider this aspect (see *e.g* [5, 13]).

The aim of this paper is to propose a quantitative evaluation of the strain-induced interstitial fluid velocities in osteons when microcracks exist in interstitial bone tissue. The model deals with a representative cortical tissue seen as a three-dimensional fully-saturated poroelastic medium. This elementary volume contains a group of osteons surrounded by their cement lines and embedded in the interstitial bone matrix. This idealized structure is assumed to be homogeneous in the longitudinal direction of osteons by neglecting the influence of the Volkmann canals. Moreover, symmetric conditions are considered at the boundary of the representative cell. Under these assumptions, when mimicking mechanical stimulation (typically walking activity) by cyclic axial loading, an equivalent two-dimensional

simplification is possible. The motivation of these assumptions is to avoid the use of a more complex 3D model since our goal is to qualitatively question the hydraulic signals of bone remodelling. When adding a microcrack in the interstitial bone matrix that runs along the direction of osteons, the hydro-mechanical behaviour of neighboring osteons is numerically investigated, using a finite element method in the frequency domain. The implications of the simulations in the viewpoint of the bone remodelling mechanotransduction are drawn in a concluding discussion.

2 Statement of the problem

Description of the geometry. In osteonal bone matrix, Haversian canals run longitudinally through the bone cortex and are transversely inter-connected through Volkmann canals. Each osteon is developed concentrically around one Haversian canal, showing a cylindric shape. For simplification purposes, the osteonal zone considered here is assumed to be far enough from the transverse Volkmann canals, so that their influence can be neglected. Figure 1-A shows the idealized matrix of osteons containing Haversian canals. All osteons run along the vertical direction $\mathbf{e}_3$ and are modelled by thick-walled hollow cylinders. They are assumed to be identical and periodically distributed in the horizontal plane $(\mathbf{e}_1, \mathbf{e}_2)$ (see Fig. 1-B). Each osteon is coated by a thin layer representing the cement line. The tissue outside of the cement lines, *i.e.* the tissue that fill the space between the osteons, is made by old osteonal matrix and is hereafter called interstitial osteonal tissue. We consider a microrack existing within interstitial osteonal domain. According to *in vivo* observations [14], microcracks present an ellipsoid-like shape and they tend to run along the longitudinal direction of osteons. Furthermore, the longitudinal length of microcracks is often significantly greater than the other ones. Here, the microcrack is assumed to have its longitudinal axis perfectly aligned with $\mathbf{e}_3$-axis and is located equidistantly from its neighbouring osteons (see Fig. 1).

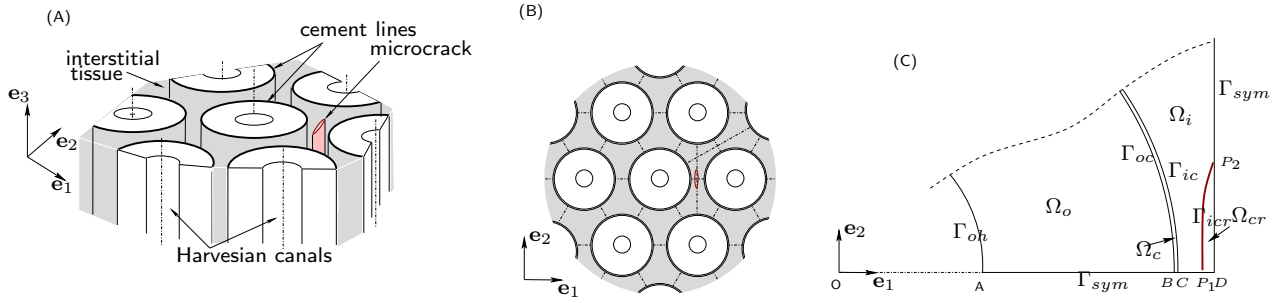

FIGURE 1 – Periodical osteon matrix with a microcrack

Governing equations. The porous components of bone material (osteons, cement lines and interstitial tissue) are considered as linear saturated anisotropic poroelastic media. Neglecting gravitational forces, the dynamic equations of an anisotropic poroelastic medium in the low-frequency range are :

$$\rho \ddot{\boldsymbol{u}} - \mathtt{div}\ \boldsymbol{\sigma} = \mathbf{0}, \tag{1}$$

$$\frac{1}{M}\dot{p} - \mathtt{div}\ (\boldsymbol{k}\,\mathtt{grad}\, p) + \boldsymbol{\alpha} : \dot{\boldsymbol{\epsilon}} = 0, \tag{2}$$

where $\rho = \phi\rho_f + (1-\phi)\rho_s$ is the mixture density which is defined from the porosity ϕ and the densities ρ_f and ρ_s of the fluid and solid phases respectively ; $\boldsymbol{u}$ and $\boldsymbol{\epsilon}$ are the displacement vector and the strain tensor of the solid phase respectively ; $\boldsymbol{\sigma}$ is the total stress tensor, p is the fluid pressure in saturated pores, $\boldsymbol{k}$ is the anisotropic permeability tensor ; $\boldsymbol{\alpha}$ is the Biot tensor and M is the Biot *modulus*. The stress tensor $\boldsymbol{\sigma}$ is linearly related to the skeleton strain $\boldsymbol{\epsilon}$ and to the fluid pressure p by :

$$\boldsymbol{\sigma} = \mathbb{C}\boldsymbol{\epsilon} - \boldsymbol{\alpha} p, \tag{3}$$

where $\mathbb{C}$ is the elastic tensor of the drained material. The permeability tensor $\boldsymbol{k}$ is a textural parameter allowing to quantify the ability of a porous material to transmit fluids through it described by the Darcy law :

$$\boldsymbol{v} = -\boldsymbol{k}\,\mathtt{grad}\,p, \tag{4}$$

where $\boldsymbol{v}$ is the filtration velocity vector defined by : $\boldsymbol{v} = \phi(\dot{\boldsymbol{u}}^f - \dot{\boldsymbol{u}})$; $\dot{\boldsymbol{u}}^f$ being the velocity of the interstitial fluid. The tensor $\boldsymbol{k}$ may be evaluated by $\boldsymbol{k} = \boldsymbol{\kappa}/\eta$ where $\boldsymbol{\kappa}$ is the intrinsic permeability tensor and η the pore fluid dynamic viscosity.

In the scope of this study, we are interested in investigating the hydraulical behaviour of the cortical tissue when submitted to an axial cyclic loading in the $\boldsymbol{e}_3$-direction. By making some supplement assumptions on the homogeneous deformation state of the system, the described 3D problem may be reduced to an equivalent 2D problem. Furthermore, as only cyclic loadings are considered, this 2D problem will be then resolved in the frequency domain by using the Comsol Multiphysics software. The detail of this mathematical development may be found in [12].

2.1 Numerical results and relevance to bone remodelling

Numerical parameters. The characteristic values of the osteonal tissue geometry are obtained from [3]. The *radii* of Haversian canals and osteons are $r_i = 30\,\mu$m and $r_o = 100\,\mu$m, respectively ; the thickness of the cement lines is $1\,\mu$m and the center-to-center distance between two adjacent osteons is $250\,\mu$m ; the size of the microcrack is given by $2b \times 2h$. In what follows, the material properties of all tissues (osteons, cement lines, interstitial tissues) are provided in Tab. 1. Only the permeability of the cement line is not the same as the one of the neighboring tissues ($\kappa^{(c)} = 10^{-21}\,\mathrm{m}^2$). Note that this very low permeability value indicates that the cement line is a quasi-impervious material.

ρ_s (kg.m^{-3})	E_1 (GPa)	E_2 (GPa)	E_3 (GPa)	G_{12} (GPa)	G_{13} (GPa)	G_{23} (GPa)	ν_{12} –	ν_{13} –	ν_{23} –
2000	15.9	E_1	20.3	$\frac{c_{11}-c_{12}}{2}$	6.9	6.9	0.328	0.25	ν_{13}
ρ_f (kg.m^{-3})	ϕ –	α_{11} –	α_{22} –	α_{33} –	κ_{11} (m^2)	κ_{22} (m^2)	κ_{33} (m^2)	η (Pa.s)	M (GPa)
1000	0.05	0.132	α_{11}	0.092	10^{-20}	10^{-20}	10^{-20}	10^{-3}	38.0

TABLE 1: Physical parameters considered for the tests [3]

As stated before, we consider a domain which is sufficiently large to avoid the influence of the crack to the symmetric conditions at the boundaries. In Fig. 2, the meshed domain used in the finite element simulation is presented.

The imposed vertical strain resulting from the mechanical activity is expressed by $\epsilon_{33} = \epsilon_0 e^{i\omega t}$, where ϵ_0 is the peak-to-peak magnitude and $\omega = 2\pi f_0$, f_0 being the loading frequency. The loading frequency is chosen through the strain rate $\dot{\epsilon} = \epsilon_0\, f_0$, in order to keep physiological strain rate values. Thus we consider $\dot{\epsilon} = 0.003\ \mathrm{s}^{-1}$ and $f_0 = 1$ Hz [12]. Furthermore, all the following simulations are presented through the isovalue curves of the maximal fluid velocity field during the compression loading phase.

Role of the interstitial fluid flow in bone remodelling. The osteocytes does respond to fluid flow stimulation and are considered as the best candidates to sense the mechanical *stimuli* [1], although the mechanism by which osteocytes perceive mechanical loads is still questioned. Classical hypotheses stipulate that the hydraulic environment of the mechano-sensitive is the key player in the bone remodelling expression. At the canalicular scale, the fluid flows between the osteocyte process and the *canaliculi* walls, this pore space being partially occupied by a fibrous pericellular matrix. By using

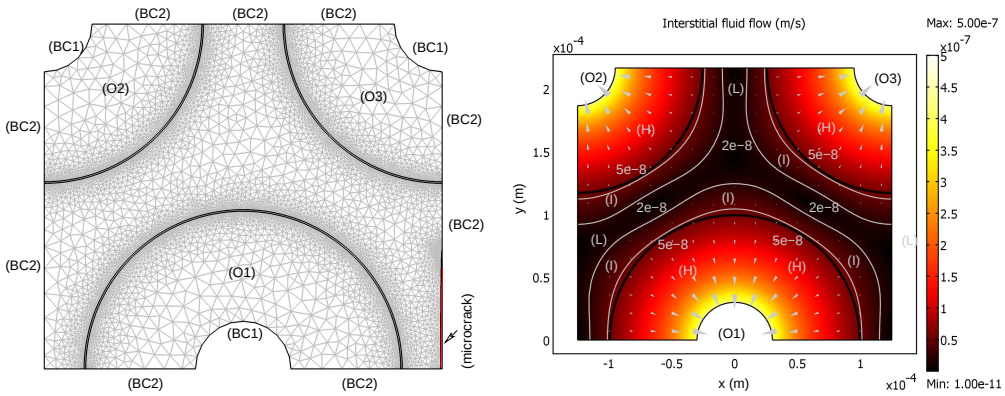

FIGURE 2 – 2D finite element mesh (left) and Case 1 : osteonal matrix without microcracks (right)

poroelastic models, some authors investigated the strain induced flow to correlate the cellular activity with the shear stress acting on the cell membrane [9]. These shear effects have been indeed shown to mechanically stimulate the bone cells. Moreover, the drag force caused by the pericellular fibres is thought to activate the cellular biochemical response through the interactions with the cytoskeleton [15]. Notwithstanding the nature of the remodelling fluid signal, shear effects or drag forces, the interstitial fluid velocity is involved in this process [15]. That is why our simulations will be presented in terms of fluid velocity profiles.

Figure 2 (right) presents the first test performed on a reference case considering an osteonal matrix without any microcracks. In the compression phase, the fluid tends to flow toward the Haversian canals where it reaches its maximum velocity. On the contrary, the fluid velocity remains very low at the (BC2) symmetry boundary. According to the Darcy law, the pressure inversely increases from its Haversian reference to reach its maximum in the interstitial tissues. Moreover, the velocity field is almost axisymmetric in the osteon.

In order to discuss about the fluid flow results in viewpoint of bone remodelling signals, we propose to distinguish 3 different ranges for the fluid velocity :

- "High-velocity zone" (H) - the fluid velocity induced by cyclic loading is sufficient to stimulate cells : $||\mathbf{v}|| > 5 \times 10^{-8}$ m.s^{-1} where $||\mathbf{v}||$ designates the fluid velocity vector norm ;
- "Low-velocity zone" (L) - the fluid velocity induced by the cyclic loading is not sufficient to stimulate cells : $||\mathbf{v}|| < 2 \times 10^{-8}$ m.s^{-1} ;
- "Intermediate zone" (I) : 2×10^{-8} m.s^{-1} $< ||\mathbf{v}|| < 5 \times 10^{-8}$ m.s^{-1}.

These bound values typically correspond to fluid shear stress effects of 1 Pa and 0.2 Pa, according to the procedure proposed by [8]. Note that these values correspond to the range of shear stress $(0.2 - 6$ Pa) activating bone cells [4]. By considering these ranges, the fluid velocity profiles presented in (Fig. 2) indicates that the osteocytes located in the zones neighboring the Haversian canals may be more stimulated than those located near the cement line or in the interstitial tissues. We might suggest that there is a hydraulic "inactive zone" outside of the osteon.

Microcracks and their implication in targeted bone remodelling. Sites of remodelling in cortical bone have been shown to occur in conjunction with microcracks [2]. In particular, it has been observed experimentally that a strong connection between microdamage, osteocyte viability and modulation of remodelling activity does exist and osteocyte apoptosis may play a role in the signalling mechanisms by which bone is remodelled after microcrack formation. Our hypothesis is that a microcrack, by modifying the hydraulic environment of osteocytes, does affect their stimulation. To investigate this avenue, we now consider the presence of a microcrack in the interstitial tissue.

In Fig. 3 (left), the fluid velocity field is plotted when considering the presence of a crack. The crack is oriented tangentially to the cement line of its neighbouring osteon (O1) and thus we consider that

$b \times h = 2\ \mu\text{m} \times 25\ \mu\text{m}$. In this case, the fluid tends not only to flow toward the Haversian canals but also toward the microcrack. As a consequence, an "inactive zone" interior to the osteon (O1) can be observed. Thus, the neighboring osteocytes of the osteon (O1) are directly affected by the presence of the microcrack existing beyond the cement line. Nevertheless, when moving away from the crack, the hydraulic behaviour inside the osteons is only very slightly modified. For instance, if the intermediate zone (I) reaches the peripheral volume of the osteon (O3), the osteon (O2) presents a similar velocity field to the one obtained for the no-crack case (Fig. 2). It means that the microcrack only has local effects.

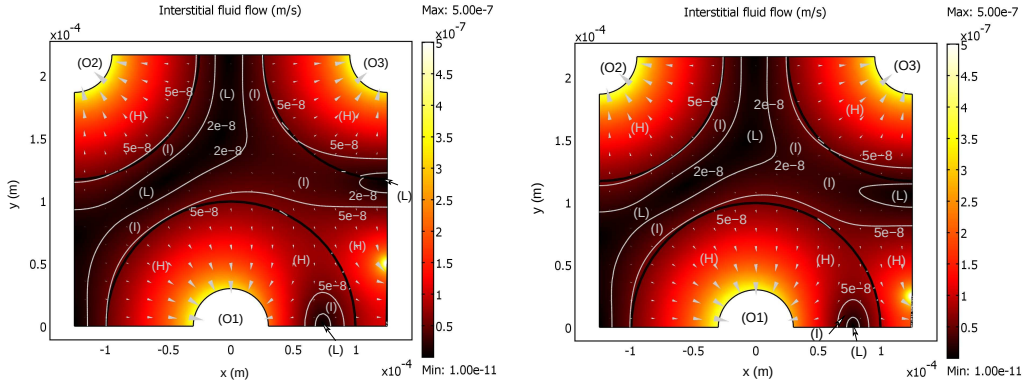

FIGURE 3 – Case 2 : $b \times h = 2\ \mu\text{m} \times 25\ \mu\text{m}$ (left) and Case 3 : $b \times h = 2\ \mu\text{m} \times 50\ \mu\text{m}$ (right)

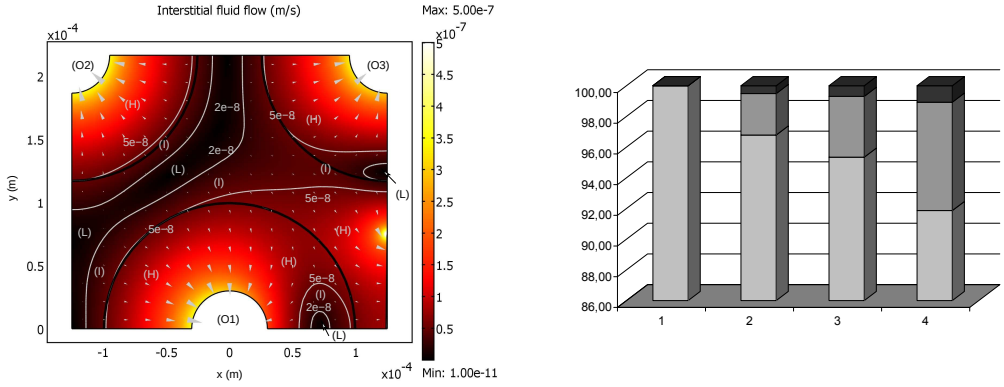

FIGURE 4 – Case 4 : $b \times h = 2\ \mu\text{m} \times 75\ \mu\text{m}$ (left) and percentages of the areas of the osteon (O1) with "High-" (light grey), "Intermediate-" (grey) and "Low-" (dark grey) velocities in 4 cases (right)

Let us now study the influence of the microcrack length. Figs. 3 and 4 present the numerical results corresponding to three microcrack sizes : $b \times h = 2\ \mu\text{m} \times 25\ \mu\text{m}$, $2\ \mu\text{m} \times 50\ \mu\text{m}$ and $2\ \mu\text{m} \times 75\ \mu\text{m}$. The longer the microcrack, the more extensive the "Low-velocity" (L) and "Intermediate" (I) zones are inside the osteons. For instance, in Fig. 4 (left), there is an "inactive area" that develops in the peripheral part of the osteon (O3).

When focusing on the closest osteon (O1), a quantitative analyze of the percentages of the areas corresponding to "High-", "Intermediate-" and "Low-" velocities is proposed in Fig. 4 (right). The cases 1-4 correspond to simulations of Figs. 3-4. Quantitatively, whatever the crack size, the part of the hydraulically low stimulated zone of the osteon only represents a few percents since more than 90 % of the osteon domain are characterized by a high fluid flow. This trend indicate that the consequence of the microcrack presence are focussed in a restricted area of the osteon domain.

3 Summary and discussion

Qualitatively, the obtained results in this study show that : i/ the crack presence has an influence on the osteons located in its vicinity ; ii/ the larger the crack, the more pronounced this influence is ; iii/ this phenomenon remains targeted in the close area of the crack since the fluid flow in the osteon (O2) does not significantly change, whatever the case.

Putting these test results back in the context of bone remodelling, the connection between a microcrack in the interstitial tissue and immediately neighboring osteons has been shown. A possible scenario could be that, when a microcrack develops inside the interstitial matrix, the fluid velocities in the closest osteons fall below a threshold value, limiting the osteocyte solicitation and thus initiating the lining cells activation. Moreover, since the hydraulic consequences of a damage inside a neighboring osteon are confined to a small area of the osteon, the idea that fluid environment may play a role in the targeting of remodelling is reinforced. Indeed, the remodelling process, which would so be targeted toward the location of the microcrack, could start.

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