MODELING OF THE BONE-IMPLANT HEALING; MECHANOBIOLOGY OF OSTEOBLASTS POPULATION IN PRESENCE OF ENDOTHELIAL CELLS

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1. INTRODUCTION

Bone tissue formation decomposes into three stages: production, maturation and mineralization (Sims N 2000). In mature adult bone, these stages take place at the same time in order to keep the equilibrium between production and mineralization of the bone matrix. In a first step, osteoblasts secrete collagen fibers without mineralization in order to form a fin layer of osteoid tissue. This stage is followed by an augmentation on the mineralization velocity in order to keep up with the collagen fabrication. In a last step, the velocity of synthesis of collagen decreases but the mineralization continues for the osteoid tissue to be fully mineralized (Luo G 1997).

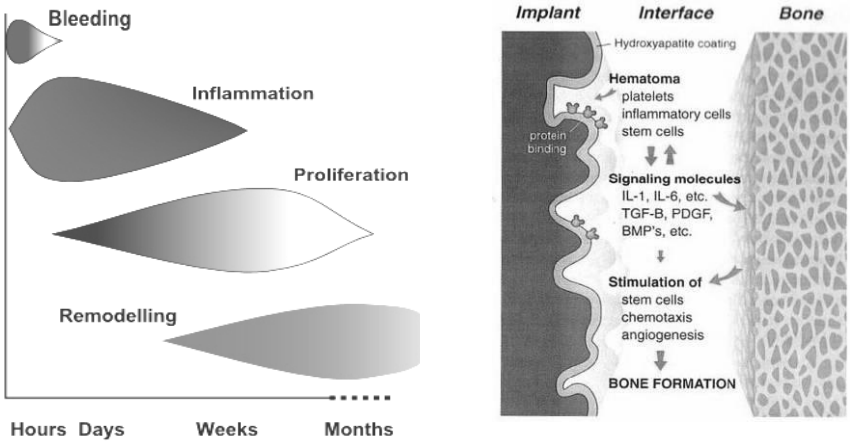


Figure 1 – (a) Tissue repair phases and timescale, (b) periprosthetic healing (Overgaard S 2000)

In order to initiate mineralization, there should be a sufficient initial concentration of Ca^{2+} and PO_4^{3-} ions to induce the precipitations of calcium phosphate, leading to the formation of hydroxyapatite crystals. This is realized by the matrix membranous vesicles (Anderson 1980). The hydroxyapatite crystals present in the matrix environment, increase in groups, and then fuse to calcify the matrix. A mineralization wave then propagates in the new formed osteoid.

The bone healing process is done normally by three stages. The first stage is the inflammation, which is an immunatury defense process due to an aggression. A hematoma is formed on the lesion site of the bone tissue from the first hours until three weeks after the traumatism. Leucocytes, fibroblasts and osteoblasts infiltrate the site under the influence of different elements like prostaglandins. This leads to the constitution of granulation tissue, the development of a vascularised tissue and the migration of mesenchymal cells. The local vasodilatation increases the blood circulation to help the evacuation of dead cells and toxins from one part, and on another part to bring and activate the necessary element for healing: growth factors, nutriments and oxygen. This phase permits to clean the traumatism area. The second stage is reparation. During the first two days after the traumatism, osteoblasts proliferate from the periosteum and colonize in the traumatism area. After two days, the hematoma is colonized and osteoblasts begin bone formation. About three weeks later and until three months, a bone callus is formed from the osteoide substance. After three weeks

of the traumatism, bone remodeling stage begins and it is the last stage of bone healing. On this level, we can find the transformation of immature bone into lamellar bone. It is shown that the duration and the intensity of the phenomena applied to this phase could vary by the variation of mechanical constraints applied on the tissue. Bone tissue needs a certain amplitude and frequency of mechanical solicitations to heal. There is an open problem on the threshold of these solicitations.

Periprosthetic healing is related to the intramembranous healing. We do not observe a cartilaginous phase in this type and the formation of connective fibrous tissue is generally followed by the formation of osteoid tissue (Sims N 2000). Groups of mesenchymal cells presented in a highly vascularised region would differentiate into osteoblasts. These cells begin to synthesize the osteoid matrix where meshenchymal cells continue to differentiate into osteoblasts. Blood vessels are then incorporated between the trabelcular bones lamellas including the bone hematopoietic marrow. In a last stage, bone tissue is progressively replaced with mature bone. It is highly sensitive to different conditions to certain conditions like the mechanical stability of the implant (Søballe K 1992), the presence and the dimension of the gap between the bone and the implant (Bobyn JD 1980). The access of the extracellular fluid to the surface of the implant, the site of implementation and the density of the bone surrounded the implant. The micro-movements of the interface bone-implant seem that it would favorites the apparition of fibrous tissue and the healing around the implant is highly influenced by growth factors (Overgaard S 2000).

In our methodology, reactive transports in deformable porous media have been associated to computational cell biology (cellular migration and proliferation in presence of anabolic growth factors). The populations of osteoblasts and endothelial cells, the phases of bone growth factors, angiogenic factors and fibronectin have been taken into account to propose a set of governing equations describing the process of intramembranous healing.

2. MODELLING METHODOLOGY

Interactions in the model are described in Figure 2 (Ambard 2005, Guérin 2009 , Khalil 2011) . The matrix of the neo-formed tissue is a two phase biological medium: a solid phase and a liquid phase representing the extracellular fluid in which evaluate all biological entities. This biphasic medium is modeled by a formulation of a saturated porous deformable medium by taking into consideration the effect of pressure and deformation.

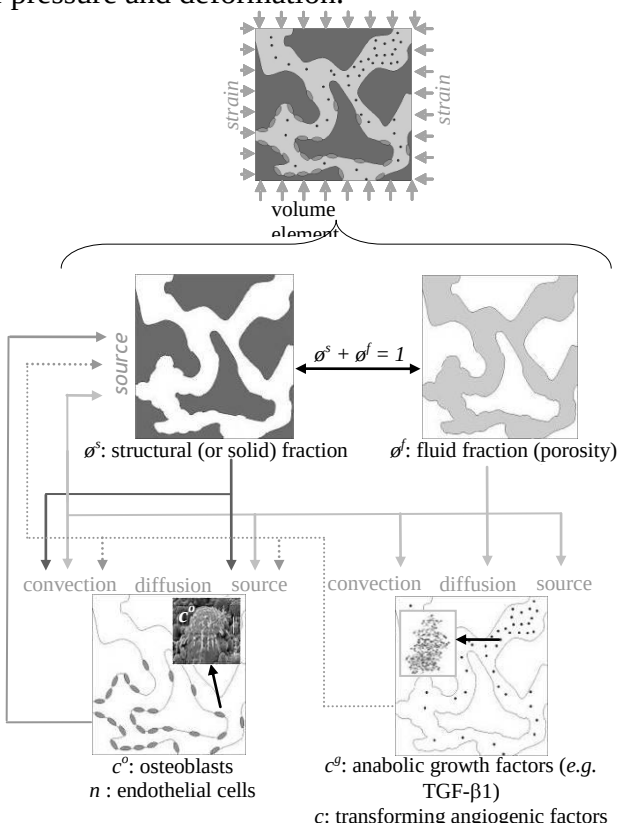


Figure 2: The biological tissue was modeled as a multiphasic reactive porous medium and its healing was due to complex interactions between endothelial cells, osteoblasts population, fluid phase, structural phase and growth factors.

2.1 Poromechanics

Porous medium modeling was first introduced by Terzaghi (Terzaghi K 1947) and developed by Biot (Biot MA 1963). Continuous porous medium is a medium composed by a solid matrix and by a saturated space composed of interstitial fluid. The matrix is constituted by a solid part filled with numerous pores. From this representation, we could define the porosity ϕ^f as the fraction of fluid volume over the total saturated volume and the solid fraction ϕ^s as the matrix solid volume over the total volume. These fractions are represented by the equation (1).

$$\phi^s + \phi^f = 1 \tag{1}$$

The elastic porous medium is modeled by a spatio-temporal superposition of a porous solid matrix and a saturating fluid. Under rapid solicitations, the fluid does not have the time to elapse between connected pores. The drained behavior concerns the response to a permanent or a transitory state; also, it concerns a quasi-static state. This behavioral hypothesis would constitute the main frame of our macroscopic formulation. The behavior laws of a deformable porous medium are linear combination between the average stress tensor of the solid medium fraction and the average stress tensor of the fluid medium fraction. We use the decomposition of stress tensor to intervene the effective solid and fluid tensor on the medium. Thus, we use the decomposition of the stress tensor on an elementary volume by the following way:

$$\overline{\overline{\sigma}} = \phi^s \cdot \overline{\overline{\sigma^s}} + \phi^f \cdot \overline{\overline{\sigma^f}} \tag{2}$$

The superposition principle is used to predict the response of the porous medium to the hydrostatic pressure and external strains successively. This allows the poroelastic governing equation (3) of a volume element to be obtained. K^{sm}, E^{sm}, ν^{sm} are the intrinsic mechanical properties of the constitutive material of the structural skeleton, i.e. compressibility coefficient, the Young modulus and Poisson ratio. K^e, E^e, ν^e, and μ^e (Lamé coefficient) are the effective mechanical properties of the porous medium.

$$\overline{\overline{\sigma}} = \frac{\nu^e E^e}{\left(1-2\nu^e\right)\cdot\left(1+\nu^e\right)} \cdot \operatorname{trace}\overline{\overline{\varepsilon}} \cdot \overline{\overline{I}} + \frac{E^e}{1+\nu^e} \cdot \overline{\overline{\varepsilon}} - \left(1 - \frac{K^e}{K^{sm}}\right) \cdot p^f \cdot \overline{\overline{I}} \quad K^e = \frac{E^e}{3\left(1-2\nu^e\right)} \quad K^{sm} = \frac{E^{sm}}{3\left(1-2\nu^{sm}\right)} \tag{3}$$

The governing equation (3) can be rewritten in the form (4) which involves the Biot coefficient *b*. When the intrinsic structural matrix of the tissue volume element is incompressible, K^{sm} tends to infinite and *b* is equal to 1. This assumption will be used in the following and finally, the volume variation of tissue volume element will be due to external mechanical strain and fluid pressure gradients.

$$\overline{\overline{\sigma}} = \left(K^e - \frac{2\mu^e}{3}\right) \cdot \operatorname{trace}\overline{\overline{\varepsilon}} \cdot \overline{\overline{I}} + 2\mu^e \overline{\overline{\varepsilon}} - b \cdot p^f \cdot \overline{\overline{I}} \tag{4}$$

In quasi-static behaviour, kinetic energies are neglected facing strain energies and dissipative energies. Assumptions of small strains and incompressible phases (solid phase and fluid phase) validate the following. The coupling equation (4), is joined to conservation equations (5) and (6) and Darcy's law (7) to obtain the set of poroelastic governing equations.

$$\vec{0} = \overrightarrow{\operatorname{div}\overline{\overline{\sigma}}} + \overrightarrow{f_v} \quad \text{with} \quad \overrightarrow{f_v} : \text{volume force} \tag{5}$$

$$\frac{d(trace\overline{\overline{\varepsilon}})}{dt} = div\left(\overrightarrow{q^{f/s}}\right) = \frac{d}{dt}\left(J\phi^f\right) \quad J = 1 + trace\overline{\overline{\varepsilon}} \tag{6}$$

$$\overrightarrow{q^{f/s}} = -\frac{\kappa^e}{\mu} \cdot \overrightarrow{\operatorname{grad} p^f} \tag{7}$$

In quasi-static the porosity ϕ^f (or structural fraction ϕ^s) can be relied to the mechanical transform (*J*) of the porous substrate as expressed by equation (8).

$$\phi^f = 1 - \frac{\left(1-\phi_0^f\right)}{J}\phi_0^s = J\phi^s \quad (8)$$

The solutions of previous governing equations are the kinematics admissible displacement field U and the admissible pressure field p^f.

2.2 Transport equations of endothelial cells

The mathematical model of endothelial cells migration was based on previous mathematical model of angiogenesis (Anderson A. R. A. 1998). We proposed that the bone-implant interface is a continuous non-porous medium. We assume that the motion of endothelial cells (at or near a capillary sprout tip) is influenced by three factors: random motility (analogous to molecular diffusion), chemotaxis in response to *TAF* gradients and haptotaxis in response to fibronectin gradients. To derive the partial differential equation governing endothelial cells motion, we first consider the total cell flux and then use the conservation equation for cells density. The three contributions to the endothelial cells flux q^n, are given by: $q^n = q_{random} + q_{chemo} + q_{hapto}$ (9)

The random flux is expressed by equation (10). It describes the random motility or the passive migration of endothelial cells at or near the sprout tips, n is the endothelial cells concentration and D^n is a diffusion coefficient. The haptotactic flux is expressed by equation (11) involving h^n the haptotactic coefficient and f the concentration of *FF*. This allows taking into account an active migration due to adhesion gradient. The chemotactic active migration is described by equation (12). The response of endothelial cells is influenced by the gradient of *TAF* which concentration is c.

$$q_{random} = -D_n \cdot \nabla n \quad (10) \qquad q_{hapto} = h^n \cdot n \cdot \nabla f \quad (11) \qquad q_{chemo} = \chi^n(c).n.\nabla c \quad (12)$$

The chemotactic coefficient $\chi^n(c)$ is a receptor kinetic law in the form of equation (13). It reflects a biological result showing that the chemotactic sensitivity decreases when the TAF concentration increases. Other parameters are the initial chemotactic coefficient $\chi^n{}_0$ and a positive constant $k^n{}_1$.

$$x^n(c) = x_0^n \frac{k_1^n}{k_1^n + c} \quad (13)$$

The conservation equation of endothelial cells population is given by equation (14) involving the source term Ω^n. This term allows the proliferation process to be modeled by using the logistic law (1) where α^n is the proliferation coefficient and $N^n{}_1$ is a concentration threshold.

$$\frac{\partial n}{\partial t} + \nabla q^n = \Omega^n \quad \Omega^n = \alpha^n \cdot n \cdot \left(N_1^n - n\right) \quad (14)$$

Finally, the governing law of endothelial cells population is expressed by equation (15).

$$\frac{\partial n}{\partial t} = D^n \Delta n - \nabla\left[\chi^n(c) \cdot n \cdot \nabla c\right] - \nabla\left[h^n(c) \cdot n \cdot \nabla f\right] + \alpha^n \cdot n \cdot \left(N_1^n - n\right) \quad (15)$$

2.3 Modeling of Transforming Angiogenic Factors (*TAF*)

TAF are diffusible factors modeled as a continuous population where the principal variable is the concentration c. To derive the *TAF* equation, we first have to consider the initial event which is the secretion of *TAF* by inflammatory cells. Once secreted, *TAF* diffuse into surrounding tissue and extracellular matrix and set up a concentration gradient between the implant and any pre-existing vasculature. During this initial stage, where the *TAF* diffuse into the surrounding tissue (with some natural decay), we assume that the *TAF* concentration c satisfies an equation of the form:

$$\frac{\partial c}{\partial t} = D^c \Delta c + \Omega^c(n, c) \quad (16)$$

D^c is the *TAF* diffusion coefficient and Ω^c the decay rate. We assume that the steady state of this equation establishes the *TAF* gradient between the implant and the nearby vessels and it provides the initial conditions for the *TAF* concentration. As the endothelial cells migrate through the extracellular matrix in response to this steady-state gradient (Stokes C. L. 1990), there are some uptakes and bindings of *TAF* by cells (Ausprunk D. H. 1977, Hanahan 1997). This is modeled by an

uptake function involving the uptake rate λ^c into Ω^c. Thus, the conservation of *TAF* was given by equation (17).

$$\frac{\partial c}{\partial t} = D^c \Delta c - \lambda^c \cdot n \cdot c \tag{17}$$

2.4 Modeling of fibronectin factors (*FF*)

Fibronectin is known to be present in most mammalian tissues and has been identified as a component of the extracellular matrix. In addition to this pre-existing fibronectin, it is known that the endothelial cells themselves produce and secrete fibronectins. Equation (18) describes the random diffusion by the Laplacian of concentration Δf while the source term was involving the secretion factor ω^f and the uptake factor μ^f due to cells activity.

$$\frac{\partial f}{\partial t} = D^f \Delta f + \Omega^f (n, f) \qquad \Omega^f (n, f) = \omega^f \cdot n - \mu^f \cdot n \cdot f \tag{18}$$

2.5 Influence of the fluid phase

Endothelial cells, *TAF* and *FF* are related to the presence of interstitial fluid. The behavior of the fluid phase is dependent upon the structural phase and is involved into the extracellular matrix formation. The strains *J* and ϕf are then included into the equations. The solid deformation on *TAF* and *FF* is considered negligible due to their solubility in the fluid phase; thus, the mechanical transform (*J*) is only considered in the endothelial cells equation. Finally, the set of governing equations describing the endothelial cells population is written as follows:

$$\frac{\partial}{\partial t}\left(\phi^f . J . n\right) = \phi^f \left(D^n \Delta n - \nabla\left[\chi^n (c) . n . \nabla c\right] - \nabla\left[h^n . n . \nabla f\right]\right) + \alpha^n . \phi^{f2} . n . \left(N_1^n - n\right) \tag{19}$$

$$\frac{\partial}{\partial t}\left(\phi^f c\right) = D^c \cdot \phi^f \cdot \Delta c + q^{f/s} \cdot \nabla c - \lambda^c \cdot \phi^{f2} \cdot n \cdot c \tag{20}$$

$$\frac{\partial}{\partial t}\left(\phi^f . f\right) = D^f . \phi^f . \Delta f + \phi^f . \left(\omega^f . n - \mu^f . \phi^f . n . f\right) \tag{21}$$

2.6 Modelling of the osteoblast cells population

The osteoblastic cellular population is modeled as a continuous phase. We assume the volume was negligible comparing to the volume of the solid and the fluid fractions. The osteoblasts concentration C^o is defined by the relation (22), involving the solid fraction (or mineralized fraction) ϕ^s and osteoblasts cells population n^o.

$$C^o = \frac{n^o}{\left(1 - \phi^s\right)} \tag{22}$$

The mass conservation is expressed by equation (23). The left term represents the local increase of cells population, and the right term represents the sum of cells crossing the boundary of the volume element and the local cells source. The conservation equation is expressed by convection-diffusion-reaction type equation (24).

$$\frac{\partial}{\partial t}\int_v \left[C^o \cdot \left(1 - \phi^s\right)\right] \mathrm{d}v = \int_s \left(\overrightarrow{q^o} \cdot \vec{n}\right) \mathrm{d}s + \int_v \Omega^o \ \mathrm{d}v \tag{23}$$

$$L_o \frac{\partial C^o}{\partial t} = D_o \Delta C^o - C_o \nabla C^o + \Omega^o \tag{24}$$

The diffusion term D_o and the convection term C_o represent the flux of cellular migration. The passive cellular migration is a random migration. The active migration corresponds to a chemotactic migration where osteoblasts are guided by the gradient of anabolic growth factors (*e.g. TGF-β1*), and to a haptotactic migration where osteoblasts are guided by the gradient of adhesion sites. Theses

adhesion sites increase with the formation of extracellular matrix ϕ^s. The flux q^o of osteoblasts is expressed by the equation (25).

$$\overrightarrow{q^o} = D^o \vec{\nabla} C^o - \chi^o . C^o . \vec{\nabla} C^g - \rho^s . h^o . C^o . \vec{\nabla} \phi^s \tag{25}$$

The reactive term Ω^o corresponding to the proliferation is expressed by equation (26). The proliferation logistic law involves the proliferation rate α^o, the maximum concentration $C^o{}_m$ and the concentration of endothelial cells and bone growth factors. The autocrine and paracrine action modes are taken into account. The role of physiological concentration of growth factors $C^g{}_p$ and endothelial cells threshold n_l have similar mathematical expression in equation (29). This last point allows representing cellular renewal and equilibrium between proliferation and cellular death (or apoptosis).

$$\Omega^o = \alpha^o \cdot \phi^{f4} \cdot C^o \cdot \left(C^o_m - C^o\right) \cdot \left(C^g - C^g_p\right) \cdot \left(n - n_l\right) \tag{26}$$

To take into account the influence of substrate deformation, the strain tensor of the volume element is added. Finally, the conservation equation of the osteoblasts population is given by equations (27) and (28).

$$\frac{\partial}{\partial t}\left(\phi^f \cdot J \cdot C^o\right) = div\overrightarrow{q^o} + \Omega^o \tag{27}$$

$$\frac{\partial}{\partial t}\left(\phi^f . J . C^0\right) + [\chi^0 . \nabla C^g + \rho^s . h^o . \nabla \phi^s] . \phi^f . \nabla C^o = D^o . \phi^f . \Delta C^o - \phi^f . C^o . \left[\chi^0 . \nabla C^g + \rho^s . h^o . \nabla \phi^s\right] + \Omega^0 \tag{28}$$

Endothelial cells provide oxygen and nutrients supply and waste elimination. The endothelial cells play a major role in the source term of osteoblasts. This direct role on the synthesis of osteoblasts in conjunction with anabolic growth factors (*TGF-β1*) also induces an indirect role in the synthesis of osseous matrix.

2.7 Modelling the phase of anabolic growth factors (*e.g. TGF-β1*)

The anabolic growth factors are diffusible factors considered as a continuous phase of concentration C^g. The concentration per volume element is defined by equation (32) involving the solid fraction ϕ^s and the *TGF-β1* quantity n^g. The volume phase of growth factors is considered negligible.

$$C^g = \frac{n^g}{\left(1 - \phi^s\right)} \tag{30}$$

As previously explained, the conservation equation (32) leads to the convection-diffusion-reaction equation (31).

$$\frac{\partial}{\partial t}\int_v \left[C^g \cdot \left(1 - \phi^s\right)\right] \mathrm{d}v = \int_s \left(\overrightarrow{q^g} \cdot \vec{n}\right) \mathrm{d}s + \int_v \Omega^g \ \mathrm{d}v \qquad L_g \frac{\partial C^g}{\partial t} = D_g \Delta C^g - C_g \nabla C^g + \Omega^g \tag{31}$$

The flux is modeled by a diffusion flux D_g and by a convective flux C_g. These two fluxes represent the random diffusion and the transport by the fluid phase into the porous volume element.

$$\overrightarrow{q^g} = D^g \vec{\nabla} C^g + C^g \cdot \overrightarrow{q^{f/s}} \tag{32}$$

The secretion of growth factors by osteoblasts and endothelial cells is taken into account in the source term; α^g being the synthesis factor. The consumption by osteoblasts and endothelial cells is modeled by the decay velocity d^g. This logistic law implies that the more growth factors are present in the volume element, the more osteoblasts and endothelial cells might use these growth factors. The limitation is given by the physiological concentration $C^g{}_p$. Assuming that the volume element does not involve any fluid source, the conservation equation of the phase of anabolic growth factors is expressed by equation (34).

$$\Omega^g = \alpha^g . \phi^{f2} . C^o . n - d^g . \phi^{f3} . C^o . n . \left(C^g - C^g_p\right) \tag{33}$$

$$\frac{\partial\left(\phi^f C^g\right)}{\partial t} = D^g \phi^f \Delta C^g + q^f \nabla C^g + \Omega^g \tag{34}$$

2.8 Modeling of the tissue consolidation (reactive medium)

The conservation equation of the osseous matrix is written by taking into account the biological process of mineral matrix synthesis due to osteoblasts. This process is expressed by the source term in equation (35) involving the coefficient of matrix synthesis α^s, the fluid fraction, and the concentration of anabolic growth factors. The governing equation of the structural fraction evolution is then obtained.

$$\Omega^{\phi^s} = \alpha^s.\phi^{f2}.C^o.\left(C^g - C_p^g\right) \quad \frac{\partial \phi^s}{\partial t} = \Omega^{\phi^s} \tag{35}$$

To take into consideration the evolution of tissue permeability during healing, the Kozeny-Carman model expressed by equation (36) was used (Arramon YP 2001). This model maintains the relationship between the permeability and the porosity ϕ^f (or fluid phase) to be expressed.

$$\frac{\kappa^s}{\mu} = \frac{a \cdot \left(\phi^f\right)^b}{10^{-2} \cdot s^2} \qquad s = 323 \cdot \phi^f - 939 \cdot \phi^{f2} + 1340 \cdot \phi^{f3} - 1010 \cdot \phi^{f4} + 288 \cdot \phi^{f5} \tag{36}$$

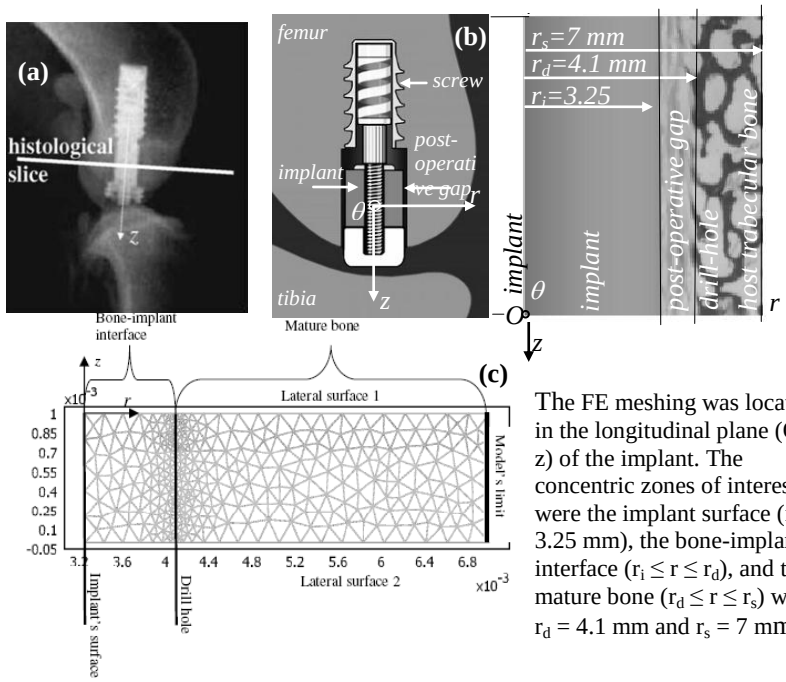
To manage the transition from fibrous tissue to cortical bone, coefficients *a* and *b* are 2.592 $\times 10^{-2}$ and 4.668 respectively (Arramon YP, 2001). During healing, the effective mechanical properties of neo-formed tissue are increasing. The evolving porosity is used to update the effective Young modulus E^e and the effective Poisson ratio ν^e by using equations (37) respectively (Arramon YP 2001).

$$E^e\left(\phi^s\right) = E_0^e \cdot \left(\phi^s\right)^c \qquad \nu^e\left(\phi^s\right) = \nu_0^e \cdot \left(\phi^s\right)^d \tag{37}$$

The governing laws are shown in **Erreur ! Source du renvoi introuvable.** for E^e_0 = 1220 MPa and ν^e_0 = 0.17. Coefficients *c* and *d* are 1.9 and 0.271 respectively. The mature host bone surrounding the implant is modeled by a non-evolutive Young modulus of 5000 MPa and a Poisson ratio of 0.266.

3. APPLICATION TO A CANINE MICROMOTION IMPLANT

The application concerns a reference experimental implant (canine micromotion implant) developed within the framework of an international collaboration (K. Søballe - Denmark, J.E. Bechtold - USA).



The FE meshing was located in the longitudinal plane (O, r, z) of the implant. The concentric zones of interest were the implant surface (r_i = 3.25 mm), the bone-implant interface ($r_i \leq r \leq r_d$), and the mature bone ($r_d \leq r \leq r_s$) with r_d = 4.1 mm and r_s = 7 mm.

Figure 3 (a) Implant x-ray; (b) schematic description, (c) FE model

The implant is located in the medial condyle of knees of skeletally mature dogs for 8 weeks In case of unstable implant the maximum motion magnitude is 500μm. The evaluation of the healing process is achieved by histomorphometry and push-out tests. Image analysis allows the average radial distribution of solid fraction to be quantified. This distribution is characterized by the solid fraction at the implant surface, into the post-operative gap and close from the drill-hole. The periprosthetic zone of interest includes three domains: the trabecular host bone, the post-operative gap, and an active zone where bioactive properties of the implant interact with growth factors and cellular flux. The post-operative gap was between r_i and r_d and the host bone was between r_d and r_s. The implant could be "stable" which correspond to a healing process without mechanical deformations, or "unstable"; a configuration that take into consideration deformations of the porous medium under mechanical loadings. The healing induces a consolidation starting from fibrous tissue to immature bone involving osteoid matrix and a time healing of 8 weeks.

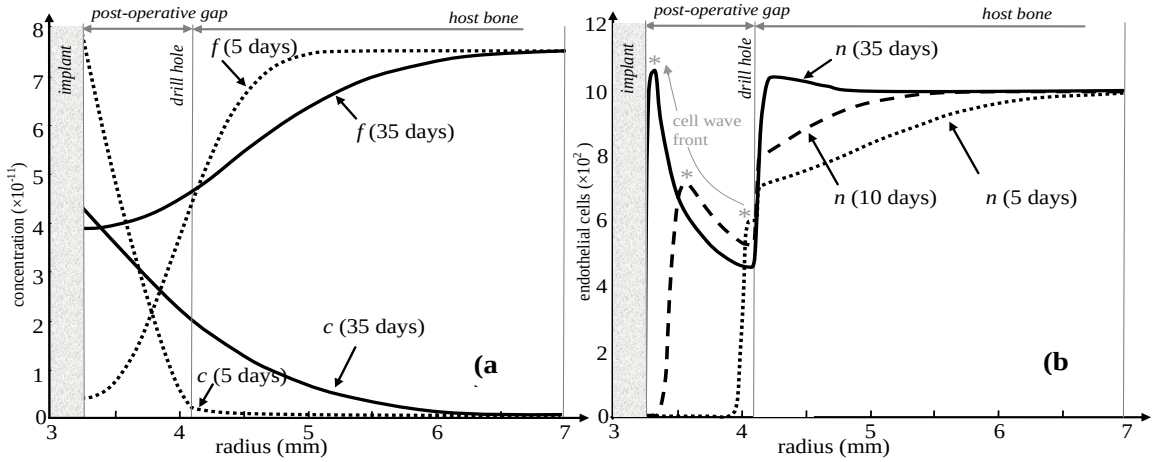


Figure 4: Radial distribution patterns of endothelial cells, transforming angiogenic factors (TAF) and fibronectin factors (FF) at 5 days (····), 10 days (– –) and 35 days (─)

As shown in Figure 4 *TAF* diffuse towards the host bone and the concentration is divided by two at the implant surface after five weeks. At the same time, *FF* shows a significant increase at the implant surface since starting from zero, a concentration of 4×10^{-11} moles is found. After five weeks, *TAF* and *FF* show monotonic distribution patterns whereas a wave front migration of cells from the host bone towards the implant is predicted. At ten days, the population peak is located at mid-gap and developed an oscillation. At twenty days, the endothelial cells reach the implant and at thirty-five days, the cells concentration is significant and oscillation is increasing with time.

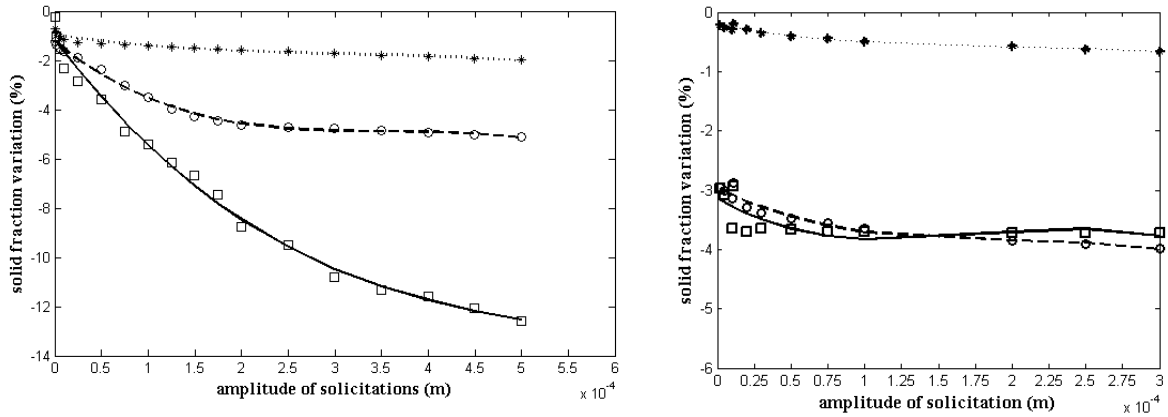


Figure 5 – (a) Influence of shear (half sine) on the structural fraction, (b)Influence of radial compressive strain

The reference was the stable implant. The implant motion tended to decrease the amount of neo-formed bone tissue especially at the implant surface (-12%). Radial displacement imposed at the boundary of the host bone tended to decrease the bone tissue formation but without a significant influence.

4. CONCLUSION

We have proposed an original set of governing equations associating poromechanics to computational cell biology to predict the neo formation of tissue in the periprosthetic healing. We investigated the influence of a daily axial and radial mechanical stimulus of our canine experimental model. Initial concentrations of endothelial cells in the host bone and transforming angiogenic factors at the implant surface had predominant and favorable effects on the final endothelial cells concentration at the implant surface and into the post-operative gap. Chemotaxis played a favorable role on the concentration of endothelial cells at the implant surface.

The numerical model provided results in good agreement with in-vivo studies (Bechtold JE 2001, 2002), especially for shear motion. The axial micromotion tended to decrease the bone formation at the implant surface from 5 to 13%. Even if biological tissues (ligaments, muscles) surrounding the arthroplasty might modify the mechanical stimuli locally; our model did not predict a significant influence of the radial strain.

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