

NUMERICAL SIMULATION OF PERI-IMPLANT TISSUE DIFFERENTIATION IN A BONE CHAMBER

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INTRODUCTION: Although it is well known that mechanical loading interacts with tissue differentiation processes, the exact mechanisms are not yet fully understood. A combined approach, consisting of animal experiments and numerical modeling can contribute to a better understanding of the mechano-regulation of tissue differentiation. For the interpretation of the experimental results, one must pay attention to the fact that the bone adaptive response seems to be site-specific and species-specific. To overcome these problems, a repeated sampling bone chamber was developed (figure 1). The goal of the present study is twofold: (1) the numerical modelling of tissue differentiation inside the bone chamber. (2) the assessment of the feasibility of the mathematical model for mechanically induced tissue differentiation developed by Prendergast *et al.* [1] and Huiskes *et al.* [2] in situations besides fracture healing.

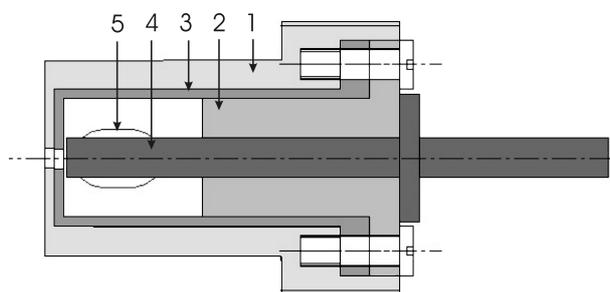


Fig. 1: Assembly drawing of the bone chamber. After insertion of the outer bone chamber (1, outer diameter = 10 mm), there is a healing period of six weeks to assure rigid fixation. After six weeks the inner bone chamber (3) together with the teflon bearing (2) and the test implant (4) are inserted and the experiment can start. Tissue can grow in the chamber via three perforations (5).

METHODS: A 2D axisymmetric and a simplified 3D finite element model were created of the tissue inside the bone chamber (figure 2). At the beginning of the differentiation simulation, the entire chamber was assumed to be filled with granulation tissue. The tissues were modelled as biphasic tissues, their properties are summarised in table 1. Two types of loading regimes were applied in a displacement controlled manner: a sine (frequency 1 Hz) with an amplitude of 50 μm and 160 μm respectively. These correspond to the loading conditions of the animal

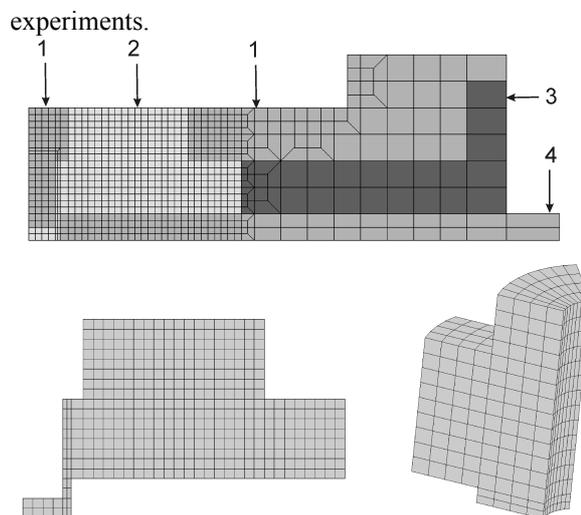


Fig. 2: Axisymmetric finite element model of the entire bone chamber (upper). The outer and inner chamber (1), the tissue inside the chamber (2), the teflon bearing (3) and the test implant (4). Both a 2D and 3D model of the tissue inside the chamber are shown (under).

Table 1. Material properties of the biphasic tissues used in the simulation.

	fibrous tissue	cartilage	bone
E-modulus [MPa]	1	10	1000
Poisson ratio	0.17	0.17	0.3
Permeability [$\text{m}^4(\text{Ns})^{-1}$]	10^{-14}	$5 \cdot 10^{-15}$	10^{-13}

For the simulation of the tissue differentiation, the model of Prendergast *et al.* [1] and Huiskes *et al.* [2] was implemented. From the FE model, the maximal distortional strain and relative fluid velocity were calculated. Depending on these stimuli a tissue phenotype for each element was predicted. To avoid numerical instabilities during the simulations, a smoothing procedure proposed by Lacroix *et al.* [3] was implemented.

At the beginning of the differentiation process, mesenchymal cells enter the bone chamber through the perforations. Their differentiation into fibroblasts, chondroblasts or osteoblasts was assumed to be entirely dependent on the local mechanical stimulus. The migration of mesenchymal cells was modelled by means of the diffusion equation (n representing the cell density, t the time and D the diffusion coefficient):

$$D \nabla^2 n = dn/dt \quad (1)$$

The diffusion coefficient was chosen in such a way that there is a complete coverage of the chamber by mesenchymal cells in six weeks. The results of the diffusion analysis were read before every loading cycle and a rule of mixtures [3] was applied to calculate the average material properties, based on the local mesenchymal cell concentration. Figure 3 shows the entire modelling scheme.

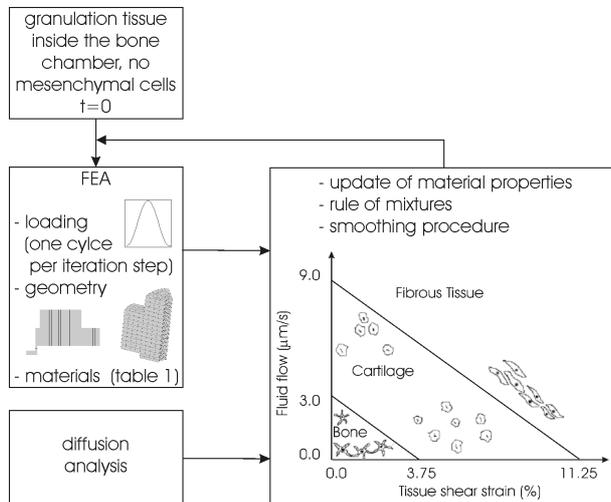


Fig. 3: Simulation scheme. Overview of the entire modelling procedure.

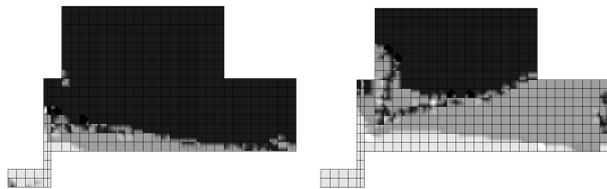


Fig. 4: Tissue types inside the bone chamber after six weeks for the loading regimes with a displacement of 50 μm (left) and a displacement of 160 μm (right). Black represents bone, gray represents cartilage and white is fibrous tissue.

RESULTS: Figure 4 shows the situation in the bone chamber after six weeks of loading for both of the loading conditions. Under a displacement of 50 μm , the granulation tissue was able to differentiate into bone in a large volume of the chamber. At the interface between the tissue and the implant, the conditions were such that the formation of cartilage was favored. At the bottom of the chamber, high strains and fluid velocity inhibited any tissue differentiation beyond fibrous tissue. This observation corresponds with the results of the animal experiments. Moreover, the predicted ingrowth pattern resembles the ingrowth pattern observed during the animal experiments (figure 5). The second loading condition (160 μm) has not yet been experimentally investigated. The simulations predict that the tissue will only differentiate into bone in the perforations of the chamber. The rest of the chamber is filled with fibrous tissue and cartilage.

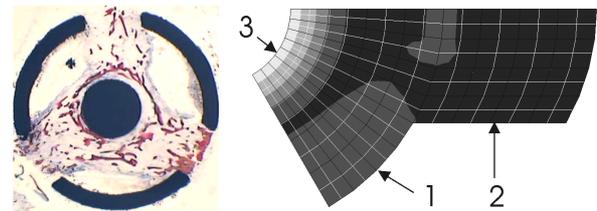


Fig. 5: Tissue ingrowth in the bone chamber. Comparison of a histological section and the result of the numerical simulation. There is a qualitative resemblance in the ingrowth pattern. (1 - immature bone, 2 - mature bone, 3 - fibrous tissue & cartilage)

DISCUSSION & CONCLUSIONS: When comparing the results of the 2D and 3D simulations with the experimental results, a qualitative resemblance in tissue phenotype is seen, in spite of the fact that some simplifications were made. These simplifications comprehend the geometry of the models, the boundary conditions, the differentiation model that was implemented and the presumed behavior of the mesenchymal cells. Due to the limited number of animals in the pilot experiment, only a qualitative comparison was possible. Expansion of the mathematical model with more biological factors, such as cell proliferation, cell apoptosis and the influence of growth factors might allow the simulation of the observed inter-animal differences.

In conclusion, this study is a first step in the simulation of the process of peri-implant tissue differentiation inside a bone chamber. The implemented model succeeds in predicting this process in a qualitative way.

REFERENCES: ¹ P.J. Prendergast *et al.* (1997) *J Biomech* **30**:539-548. ² R. Huiskes *et al.* (1997) *J of Mat Sc: Mat in Med* **8**:785-788. ³ D.Lacroix *et al.* (2002) *Med Biol Eng Comp* **40**:14-21.

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