

# IMPLANT USED AS DRUG DELIVERY SYSTEM : INFLUENCE OF PARTIAL BIOCOATING ON THE BONE REMODELING

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## Introduction

There is an actual trend to propose cementless hip implants to younger patients. The long term performance of implants has thus to be increased in particular for this type of patients. Beside the development of new materials with better wear properties, another way opens up with systemic pharmaceutical treatments targeting bone resorption e.g. [1]. However, this systemic therapy presents some drawbacks as important side effects e.g. (throat damage for bisphosphonates) or difficulty to determine appropriate dosage. To overcome these limitations, we propose a new concept of orthopedic implant which would be used not only as a mechanical supporting structure, but also as a drug delivery system. To this end, the stem of a cementless implant could be biocoated with a combination of carrier and drug (for example hydroxyapatite and bisphosphonate) that would enable to locally control the peri-implant bone remodeling.

In the present study, we propose first to theoretically validate the new concept of implant as drug delivery system using a bone remodeling model [2]. Secondly, we will evaluate the effect of a partial coating in order to gain a better control of the peri-implant remodeling.

## Material and Methods

**Bone adaptation model.** The adaptation model relates the rate of bone density  $\dot{\rho}$  to the mechanical stimulus  $\sigma$  (plastic yield stress) by a trilinear function:  $\dot{\rho} = v_d(\psi - \psi_d)$ , when  $\psi \geq \psi_d$  (densification);  $\dot{\rho} = v_r(\psi - \psi_r)$ , when  $\psi \leq \psi_r$  (resorption). Otherwise, the rate is zero when  $\sigma$  is in the equilibrium zone defined by  $\psi_r$  and  $\psi_d$ .  $v_r$  and  $v_d$  are the rates for resorption and densification. The bone remodeling parameters  $\psi_r$ ,  $\psi_d$ ,  $v_r$  and  $v_d$  were experimentally determined in a previous work [3].

**Model of biocoating effects.** Drugs used to control the disease of bone metabolism (e.g. bisphosphonate) affect the bone turnover [4]. These effects are modeled in the present study by changing the bone remodeling parameters  $\psi_r$ ,  $\psi_d$ ,  $v_r$  and  $v_d$  with the following relation:  $v_r(\kappa) = v_r + v_r^* \kappa$ ,

where  $v_r(\kappa)$  is the drug altered slope of resorption rate,  $v_r^*$  is the weight parameter representing the influence of the drug on the resorption rate and  $\kappa$  is a value between 0 and 1. The dependencies for  $\psi_r(\kappa)$ ,  $\psi_d(\kappa)$ , and  $v_d(\kappa)$  are defined in exactly the same way. The factor  $\kappa$  which is defined for each location in the bone, could be dependent upon the drug concentration or other biological properties. We use in the present study parameters ( $v_r^* = -v_r$ ,  $\psi_r^* = -\psi_r$ , and  $\kappa = 0.5$ ) corresponding to a drug concentration involving a two fold decrease of the bone resorption parameters,  $\psi_r$  and  $v_r$ .

**Application to hip arthroplasty.** We simulate the remodeling of bone surrounding a femoral stem using a finite element model [5]. This model accounts for major muscle forces corresponding to daily activities as gait cycle. Three different situations are simulated: A) the *standard case* corresponds to the stem without biocoating; B) the *full biocoating case* corresponds to a two fold decrease of the bone resorption parameters,  $\psi_r$  and  $v_r$  over the entire stem surface; C) the *partial biocoating case* corresponds to a two fold decrease of the bone resorption parameters,  $\psi_r$  and  $v_r$  on the proximal stem surface (Gruen zones 1 and 7).

## Results

The biocoating has significant effects on the peri-implant bone remodeling (Figure 1).

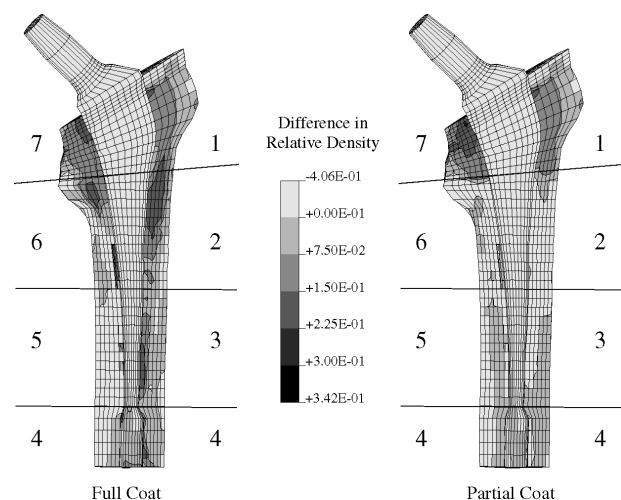


Fig. 1: Difference in relative bone density between the biocoated cases and the standard case

In both cases most regions have a higher density than in the standard case. The main differences between standard and biocoated stems appeared in the proximal region. The fully biocoated case results in a bone slightly denser in the medial proximal bone next to the implant and in the lateral distal outer region of the bone. The main difference between full biocoated and partial biocoated cases resides in the zones 2 and 6 and in particular in the lateral region next to the implant where the bone with a fully biocoated stem is 10 % denser. For the locally biocoated stem, a higher density in the Gruen zones 1 and 7 is achieved compared to the full biocoated stem. In the regions 3, 4 and 5, the fully biocoated stem results in a denser bone mainly located in lateral part with the higher increases next to the implant.

### **Discussion**

The presented results show that the developed model of biocoating allows us to simulate a bone-implant system with locally altered remodeling behavior. This work enables to validate the usefulness of the new concept of implant as drug delivery system. The numerical results clearly show that the bone density increases when the stem is fully biocoated in comparison to the standard case. This study also shows that a partial biocoating results in a more favorable bone remodeling situation. Indeed, in the case of full stem biocoating the major increase is located in the zones 1 and 7 but is inferior to the increase in density for the local stem biocoating. Moreover the full stem biocoating presents a higher bone density in the lower part of the implant which is not mechanically advantageous.

In conclusion, this concept of implant as drug delivery system seems a promising approach [6].

### **References**

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