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Numerical prediction of peri-implant bone adaptation: Comparison of mechanical stimuli and sensitivity to modeling parameters

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ABSTRACT

Long term durability of osseointegrated implants depends on bone adaptation to stress and strain occurring in proximity of the prosthesis. Mechanical overloading, as well as disuse, may reduce the stability of implants by provoking bone resorption. However, an appropriate mechanical environment can improve integration. Several studies have focused on the definition of numerical methods to predict bone peri-implant adaptation to the mechanical environment. Existing adaptation models differ notably in the type of mechanical variable adopted as stimulus but also in the bounds and shape of the adaptation rate equation. However, a general comparison of the different approaches on a common benchmark case is still missing and general guidelines to determine physically sound parameters still need to be developed. This current work addresses these themes in two steps. Firstly, the histograms of effective stress, strain and strain energy density are compared for rat tibiae in physiological (homeostatic) conditions. According to the Mechanostat, the ideal stimulus should present a clearly defined, position and tissue invariant lazy zone in homeostatic conditions. Our results highlight that only the octahedral shear strain presents this characteristic and can thus be considered the optimal choice for implementation of a continuum level bone adaptation model. Secondly, critical modeling parameters such as lazy zone bounds, type of rate equation and bone overloading response are classified depending on their influence on the numerical predictions of bone adaptation. Guidelines are proposed to establish the dominant model parameters based on experimental and simulated data.

1. Introduction

The process of bone adaptation to mechanical stimulations is often modeled at the continuum scale through the Mechanostat [1]. This theory postulates that a specific mechanical stimulus occurring in bone is kept within a physiological range (i.e. the lazy zone, LZ) through the variation of bone mass [2,3] which in turns affect the distribution of elastic modulus in the bone structure. These phenomenological adaptation models represent at the continuum scale the net result of the local bone adaptation process: the sensor network formed by osteocytes and their complex signaling is described by a mechanical measure of the stress and strain in a control volume (the "stimulus") while the activity of the osteoblasts and osteoclasts resulting in different rates of local bone apposition and resorption are represented by the rate of change of bone density at the continuum scale (the "bone apposition rate"). In extreme conditions, when bone is overloaded, continuous damage accumulation supersedes the capacity of bone to adapt and repair itself, which is represented in the adaptation models by a fast reduction of bone stiffness and/or mass above a certain overloading threshold. Several adaptation models have been implemented in order to evaluate the integration of implants, for example in dentistry [4–6] by considering both bone apposition and resorption due to overloading. The interplay between these phenomena has been seen to regulate the peri-implant marginal loss and determine the long term stability of dental implants [7,8].

Despite their versatility, these phenomenological approaches rely on many assumptions that are difficult to verify by experimentation and rarely discussed [9], such as: the choice of a mechanical signal which drives the bone adaptation ('stimulus'), the relation between the bone adaptation rate and the stimulus, the limits of bone adaptation and the size of the zone of stimulus diffusion in non-local models.

Indeed, the first open question concerns the choice of the mechanical variable used as a triggering signal. Investigations

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studying signals based on strain [1,10], strain energy density [2] or stress [11,12] all lead to satisfying results in specific applications when properly calibrated, however, there is no clear agreement on which regulation signal provides the best consistency in a general sense. Moreover, signal selection and the definition of bone apposition and resorption thresholds are not frequently discussed and comparisons are rare [5,13].

The mathematical form of the adaptation law which relates the level of mechanical stimulus to the bone apposition or resorption rate is also an open question. In order to preserve the natural structure of bone under physiological conditions, continuum level isotropic bone adaptation models must at least exhibit a region of homeostasis by defining a so-called lazy zone (LZ). The LZ represent an equilibrium condition at which normal bone turnover occurs, i.e. the resorption rate controlled by osteoclasts is equal to the apposition rate due to osteoblasts activity. The limits of the LZ and the bone overloading threshold are critical variables that control the adaptation process by governing the transition between bone resorption, homeostasis , apposition and damage. However, because of their potential dependency on species, location and biovariability, those bounds are difficult to determine and are only rarely defined on a rigorous experimental basis [14]. Furthermore, the dependence of bone adaptation rate on the mechanical stimulus has been formulated through linear [15], quadratic [16] or piecewise functions including a rate saturation [17], but the sensitivity of the obtained predictions to these different mathematical forms remains unclear.

Since bone adaptation is assumed to be driven by cell mechanotransduction [18], several adaptation models involve a spatial averaging of the stimulus over a zone of influence (ZOI) [3,19,20] to represent diffusion processes. The size of the ZOI affects the accuracy of numerical predictions but this dependence is scarcely investigated.

Furthermore, the pre-implantation bone structure and geometry differs significantly among one group of individuals, which limits the validity of predictions based on an average representative geometry. Biovariability is expected to induce a significant scatter in results of bone adaptation and this point is seldom discussed.

This work aims at establishing guidelines for the definition of the hypothesis needed to obtain accurate predictions of bone adaptation around implants. The modeling parameters, adaptation theories and mechanical stimuli are classified as critical, important or negligible with respect to their influence on results and methods are proposed to choose the values of the dominant parameters. The ‘loaded implant’ animal model is adopted as a benchmark [21]. This animal model allows investigating the effects of a controlled external stimulation of the bone tissue surrounding two transcutaneous implants inserted in the proximal part of rats' tibiae [22,23]. The ‘loaded implant’ model was chosen here as it allows a precise control of the loading history and implant placement but also because it closely mimics the difficulties found in clinical implantations in which a complex three dimensional stress state with local stress concentrators are commonly observed. Different mechanical stimuli are compared on the benchmark of full tibiae being subjected to physiological loading conditions. Assuming that the Mechanostat hypothesis is valid, a clear lazy zone should be able to be observed in the distribution of proper adaptation mechanical stimuli under such conditions. Moreover, the LZ of the ideal mechanical stimulus should also satisfy the criteria of location independence, tissue independence and specimen independence. The stimulus which best satisfies these conditions is identified and used in combination with a specimen-specific adaptation algorithm to predict bone peri-implant adaptation. A sensitivity study subsequently highlights the dependence of bone adaptation results on the LZ, on the adaptation law, on the ZOI, on the load level and on biovariability.

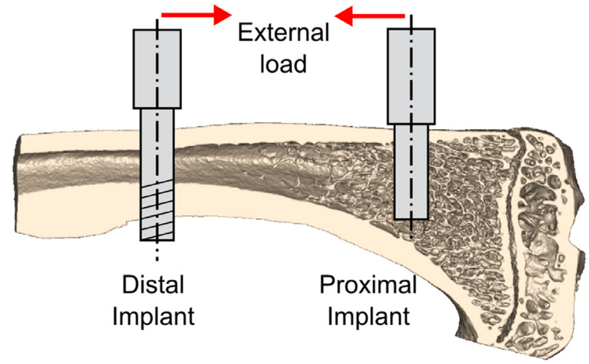

Fig. 1. Working principle of the ‘loaded implant’ model: two titanium implants are screwed mono and bi-cortically into the proximal part of the rat tibia (view cut). A controlled stimulation is provided daily by pulling the implants heads together.

2. Materials and methods

2.1. Animal model

Two transcutaneous Ti implants were screwed mono- and bi-cortically into the right tibia of female Sprague-Dawley rats (Fig. 1) following the procedures described in [22,23]. After two weeks of integration, five animals were euthanized. This ‘basal’ group represented the pre-stimulation integration state of the ‘loaded implant’ model and was used as a basis for bone adaptation simulation. The remaining animals (‘stimulated group’) were subjected to a controlled external load of 5 N, applied on a daily basis to force the implant's heads together and to stimulate the bone tissue around them. The load was applied with the following schedule: 1 Hz sinusoidal cycle from 0 N to 5 N, 900 cycles/day, 5 days/week for 4 weeks (total of 20 days of stimulation) with a progressive increase of load amplitude during the first week (+1 N/day). After sacrifice, all tibiae were dissected, cleared of their soft tissue coverage and frozen at −21 °C. The specimens were then thawed out and analyzed using a high resolution CT imaging system (μCT-40, Scanco Medical AG, Brüttisellen, Switzerland, isotropic voxel size: 20 μm). The technical aspects of surgery, implant design, activation setup and CT imaging that characterize the ‘loaded implant’ model are described in detail in [22–24].

2.2. Finite element models

Continuum-level specimen-specific FE models of bare and implanted rat tibiae were generated from CT scans through a verified and validated procedure [24]. The CT images were segmented to isolate the continuum bone and implants domains and processed with an open-source FE model generator to quality second order tetrahedral meshes. These models represent the whole bone structure as a continuum, elastic, isotropic and inhomogeneous material. The local average BMD is calculated in each element of the model using the mean BMD of the CT voxels contained in the elements. To avoid potential checkerboard patterns and oscillations, the BMD field is then averaged at the nodes of the mesh to obtain a continuous description. Subsequently, the integration points were assigned their material properties by interpolation of the nodal BMD and by using the density-elasticity relationship developed by Cory et al. [25]. Five whole tibiae were processed to generate specimen-specific FE models, which were then subjected to a gait-based loading condition that had been shown to generate a sound physiological pattern of deformation [26] (Fig. 2a). These specimens were adopted as the benchmark for the comparison of mechanical stimuli.