Correlation between pre-operative periprosthetic bone density and post-operative bone loss in THA can be explained by strain-adaptive remodelling

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Abstract

Periprosthetic adaptive bone remodelling after total hip arthroplasty can be simulated in computer models, combining bone remodelling theory with finite element analysis. Patient specific three-dimensional finite element models of retrieved bone specimens from an earlier bone densitometry (DEXA) study were constructed and bone remodelling simulations performed. Results of the simulations were analysed both qualitatively and quantitatively. Patterns of predicted bone loss corresponded very well with the DEXA measurements on the retrievals. The amount of predicted bone loss, measured quantitatively by simulating DEXA on finite element models, was found to be inversely correlated with the initial bone mineral content. It was concluded that the same clinically observed correlation can therefore be explained by mechanically induced remodelling. This finding extends the applicability of numerical pre-clinical testing to the analysis of interaction between implant design and initial state of the bone. © 1999 Elsevier Science Ltd. All rights reserved.

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1. Introduction

Periprosthetic bone loss is recognized as a common complication of total hip replacement (Jacobs et al., 1993). It is a problem requiring attention in the follow up of clinical cases and in the design process of new hip prostheses. In clinical practice it was observed predominantly around cementless hip stems (Engh et al., 1987; Kiratli et al., 1996). Bone loss affects the strength of the femur and increases the risk of bone fracture. Femoral components without proper proximal support experience higher loading and the risk of fatigue fracture of the stem is increased (Engh et al., 1990). Apart from affecting the longevity of the primary reconstruction, reduced bone stock presents serious problems for revision surgery. For all the above reasons periprosthetic bone loss has been studied extensively. Earlier radiographic studies were soon followed by more sensitive and more precise dual energy X-ray absorptiometry (DEXA) investigations (Engh et al., 1987,1990; Kiratli et al., 1991,1992; McCarthy et al., 1991; Kilgus et al., 1993).

Adaptive bone remodelling due to stress shielding was identified as one of the important causes of the resorption. This was confirmed by patient studies and animal experiments, which showed that the observed effects of implant design parameters can indeed be explained as consequences of stress shielding (Engh et al., 1987; Engh and Bobyn, 1988; Maistrelli et al., 1991). As a process controlled by mechanical stimuli, adaptive bone remodelling can be simulated in computer models which combine bone remodelling theories with finite element analysis (Cowin, 1993; Carter et al., 1987; Hart et al., 1984; Huiskes et al., 1987,1992). The practical value of these models was established in a number of studies...
(Huiskes, 1993, 1996; Weinans et al., 1993; van Rietbergen et al., 1993) and the potential of the method to serve as a tool for pre-clinical testing of innovative design concepts was demonstrated (Huiskes and van Rietbergen, 1995). The studies employing these models largely provided reasonable predictions of adaptive bone changes in a generic bone (Huiskes, 1993; Huiskes et al., 1992; Huiskes and van Rietbergen, 1995). However, the only validation done so far was based on animal experiments (Weinans et al., 1993; van Rietbergen et al., 1993). Parameters involved in the model are species dependent, so their use in human models requires separate validation.

The objective of this study was to evaluate the bone remodelling procedures (Huiskes et al., 1992) by comparing computer predictions with measurements in a retrieval study (Engh et al., 1992). In addition, we wanted to check whether predicted bone loss correlates with the pre-operative density of the bone, as it did in the clinical cases (Engh et al., 1992; Sychterz and Engh, 1996), to see if this finding could be explained by strain adaptive remodelling.

2. Materials and methods

2.1. Experimental data

The study was based on a retrieval study (Engh et al., 1992), in which ten femora obtained at autopsies of five elderly patients who had Anatomic Medullary Locking (AML, DePuy Inc., Warsaw, IN, USA) prostheses in situ for 17 – 84 months were investigated. For each subject both the femur operated on in vivo and the contralateral one were examined (these will be referred to as the actual and the control bones, respectively). A prosthesis identical to the one used in the in vivo operation was implanted post mortem into each control bone before the measurements were performed. The specimens were analysed for periprosthetic bone stock using dual X-ray absorptiometry (DEXA) (Engh et al., 1992, 1994, 1995) and videodensitometry (McGovern et al., 1994). The analysis performed was based on the assumption that the control bone represents the immediate post-operative condition with sufficient accuracy. The study was conducted according to the relevant laws and regulations (Engh et al., 1992).

DEXA measurements were performed on both the actual and control bones. The periprosthetic bone was divided into 10 mm zones and in each of these zones the bone was scanned in anteroposterior (AP) and mediolateral (ML) directions. Sixty bone mineral content (BMC) values (in grams of bone material) were obtained for each bone, 15 for each (medial, lateral, anterior and posterior) side of the implant. After the DEXA scanning, the bones were sectioned from proximal to distal at 5 mm increments, starting 10 mm distal to the implant’s collar (Fig. 1). Contact radiographs of the transverse sections were obtained, providing 28–30 cross-sectional images per bone. Follow-up clinical radiographs were available for all cases and were used for qualitative evaluation of the extent of post-operative bone remodelling (Engh et al., 1992).

2.2. Construction of the FE model

The geometry of the model was derived from the radiographs of transverse cross-sections. As the patient specific information was available only for the sectioned parts of the bones (distal to the level 10 mm below the implants’ collars — Fig. 1), the construction of the remaining (proximal) part of the model had to be based on the geometry of a ‘typical’ femur (Huiskes and van Rietbergen, 1995). Case specific models of four control bones from the retrieval study were constructed in this manner; the model for the fifth case could not be constructed due to the damage of the specimen and consequent lack of bone geometry data. Finite element models of AML prostheses in appropriate sizes were constructed from engineering blueprints. The position of the implant was determined for each case from the cross-sectional images and AP radiographs. Models of intact bone consisted of 2302
of reducing the dilute values of the apparent densities with the primary aim of DEXA measurements were used to correct the absolute layer of the bone represented by one layer of elements. The DEXA measurements were used to correct the absolute values of the apparent densities with the primary aim of reducing the differences between DEXA data and density measurements simulated in the FE models of the intact bones in the following way. First, the cortical bone density was estimated for each case from the DEXA measurements. DEXA simulation software was used for estimating the volume of bone within individual scanning windows in order to calculate average apparent densities from the measured BMC. Then the first estimate of the densities of individual elements was produced on the basis of the average greyscale value in the corresponding part of the cross-sectional images. Case specific cortical bone density was associated with the highest greyscale value and bone density of 0.2 g cm$^{-3}$ with the lowest greyscale. A linear relationship between the greyscale of the contact radiograph and apparent density of the bone was assumed. Densities of elements in the inner (medullary) part of the bone had to be extrapolated from the densities of the surrounding elements, because the implant was ‘obstructing’ this part of the cross-sectional images. This first estimate of the density was then corrected in order to get simulated DEXA readings of the model as closely as possible to the real measurements performed on the control bones. The densities of elements in individual layers (each corresponding to one set of DEXA measurements) were uniformly increased or decreased to yield the minimum error (defined as the sum of squares of the differences of the simulated and real DEXA measurements in the particular layer). The Golden section optimization algorithm (Press et al., 1992) was employed. The density was limited by the minimum and maximum densities 0.05 and 1.75 g cm$^{-3}$, respectively. The density of the proximal part of the bone was derived from computed tomography (CT) scans of the ‘typical’ (Huiskes and van Rietbergen, 1995) bone by assigning densities to greyyscale values in a linear fashion, with densities ranging between the case specific value of cortical bone and the minimal value 0.05 g cm$^{-3}$. Young’s moduli of the elements representing the bone were determined from their apparent densities using cubic relationship proposed by Carter and Hayes (1977), $E = c p^3$, where $c = 3790$ MPa g$^{-3}$ cm$^{-9}$. Poisson’s ratio of bone was set to 0.35 and the material was assumed to be linearly elastic and isotropic. The interface between the bone and the implant was assumed to be fully bonded along the coated part of the stem. Along its uncoated distal part a layer of non-linear gap elements (MARC Analysis, Palo Alto, CA, USA) was placed and frictionless contact was assumed.

The model was loaded with a superposition of three loading cases. Two cases represented the loading during level walking at the time of heel strike and at 45% of the gait cycle, the third represented the loading during stair ascent at 70° flexion. The loading consisted of the hip joint contact force and three muscle forces (gluteus minimus, medius, and maximus). The magnitudes and directions of the forces were used as in a previous study (Huiskes and van Rietbergen, 1995) with forces applied to the femoral head and the greater trochanter, and scaled to reflect the individual patient body weight. The loads were identical (in terms of magnitudes as well as lines of action) in both the pre- and post-operative models. The model was constrained at the distal surface in all three directions. The elastic modulus of the implant material (CoCrMo alloy) was set to 200 GPa, Poisson’s ratio 0.3, and the material was assumed to be linearly elastic.

### 2.3. Bone remodelling simulation

This was based on the strain adaptive remodelling theory formulated and implemented as described earlier (Huiskes et al., 1987,1989; Weinans et al., 1992,1993; van Rietbergen et al., 1993). The remodelling procedure employed was identical to the one used in previous studies (Huiskes and van Rietbergen, 1995; Huiskes et al., 1992), including an iteration process required for the non-linear condition at the bone–implant interface. Only internal remodelling was assumed. A threshold level, under which no reaction occurs, of 75% of the physiological strain energy was used. This value produced realistic results in previous human simulations (Huiskes et al., 1992; Huiskes, 1993; Huiskes and van Rietbergen, 1995). The simulation procedure was applied to the models and 30 remodelling increments were calculated. Adaptive bone remodelling changes were predicted in terms of the time varying density of the elements of the models.

### 2.4. Simulation of radiographic and DEXA examinations

This was performed on the FE models in order to obtain the results of the remodelling simulations in a form comparable with the data of the retrieval study. The volume of the model was divided by three mutually perpendicular systems of equispaced parallel planes into rectangular voxels. In an iterative process an element in which each voxel lays was identified and the density of that element assigned to the voxel. Summing the mass of voxels along projection lines produces simulated radiographic images of the FE model. Similarly, total mass of voxels within an arbitrary volume represents the amount...
of bone mineral as clinically measured with DEXA. Visualizing the density information of one layer of voxels produces an image similar to a radiograph of a transverse section of a bone. When simulating DEXA measurements, the control volumes corresponding with the scanning windows, used in the experimental measurements on the control bones, were used.

3. Results

Simulated radiographs (anteroposterior) of the models at different stages of the adaptation process were generated in order to assess the overall progress of the remodelling changes (Figs. 2 and 3). Patterns of density changes visible in the simulated radiographs were consistent with clinical observations. Progressive bone loss in the proximal part of the bone is clearly visible, with the biggest reduction of bone mass in the proximal–medial region and distal to the greater trochanter. This remodelling pattern corresponds well with the radiographs of retrieved specimens. Densification around the tip of the implant was predicted in two of the four cases, one of which is shown in Fig. 3. Corresponding changes were not reported for the retrieved specimens. In all four cases some densification was predicted at the proximal lateral end of the implant in the region of the greater trochanter, where muscle forces (abductors) — which encourage bone retention — were applied. A similar phenomenon can be seen in some of the clinical radiographs, even though the extent of bone retention (or even densification) is overestimated in the model. The region of the pronounced proximal resorption was limited by the junction of the porous and smooth implant surfaces. The simulation overestimated bone resorption in the region of the lesser trochanter. In all four cases this part of the bone disappeared completely in the course of the remodelling simulation.

Patterns of bone loss at the bone–implant interface, which can be seen in simulated radiographs of transverse cross-sections (Fig. 4), were similar to those present in some of the cross-sectional radiographs of the retrieved specimens. Gradual filling of the gaps between the implant and the bone is the most apparent feature of both real and simulated cross-sectional images.

In order to quantitatively compare the predictions and the results from the retrieval study, DEXA measurements of the models were simulated. These simulated DEXA measurements were performed for all remodelling increments and BMC values (60 scanning windows for each model) predicted for multiple time instants (experimental measurements provided values for only two time instants — the assumed state of the bone after implantation and at the time of death). The patterns of bone loss along the stem observed in the retrieval study, showing pronounced decreases in BMC in the part of the bone proximal to the border of porous coating, were reproduced in the simulation. Nevertheless, direct comparison

Fig. 2. Simulated radiographs at remodelling increments 0, 5, 9 and 13 (case 2 GK) show the progress of bone adaptation. Characteristic patterns of proximal bone loss and distal bone retention in the retrieved specimens are well reproduced.
of DEXA measurements in individual scanning windows did not provide much useful information. There were differences at the level of individual scanning windows between the initial state of the model and the control bone as well as some inconsistencies in the experimental data, probably caused by the lack of initial symmetry at a local level, or by differences in the position of the implant in the treated and control bones. These made the comparison at the level of individual scanning windows inconclusive.

Rather than comparing the data at a local level, a compound measure of the total bone mass in the model was calculated as a sum of BMC values obtained from simulated DEXA measurements in the lateral direction. The development of the adaptation process in time (Fig. 5) showed, in all four cases, a gradual decrease of the total BMC towards an equilibrium state. The rate at which the bone was lost differed for individual cases. Models with lower initial BMC lost more bone and at a higher rate than the denser bones. The amount of bone loss showed a strong inverse correlation with the initial state of the bone (Fig. 6). The same relationship was reported in the original study (Engh et al., 1992) and later reaffirmed by another retrieval study (Sychterz and Engh, 1996). While the general trend was well reproduced in the simulations, the slope of the linear relationship was higher in the retrievals. This indicates that while for the cases with lower initial BMC the bone loss predicted for the equilibrium state is close to reality, for the ones with higher initial BMC it is overestimated. If the values of bone loss at an earlier remodelling time, rather than at equilibrium, are considered, the correspondence between the predictions and experimental measurements is very good (Fig. 6).

4. Discussion

The aim of this study was to test the validity of the predictions of a finite element based bone remodelling simulation procedure and to examine whether the correlation between the initial state of the bone and the amount of eventual bone loss could be explained by strain adaptive remodelling. Models were constructed of four specimens investigated in the retrieval study (Engh et al., 1992) with their individual geometric and bone density distribution characteristics represented. Post-operative adaptive bone remodelling was simulated and periprosthetic bone resorption predicted. The bone remodelling changes were analysed qualitatively and quantitatively. Bone densitometry data from the human retrieval study were used for comparison.

The study differs from earlier ones in several aspects. The use of quantitative densitometric information in both the construction of the models and in the analysis of the predictions is unique. The earlier studies usually...
modelled a ‘typical’ bone whereas in this project case specific models were employed. This increases the potential of the models to provide more insight into the behaviour of the remodelling procedures and was essential when the initial state of the bone was examined as a factor in the remodelling process. The latter could not have been done with a model of a typical bone, as the differences of the initial state of the bone cannot be represented simply by scaling the density of the whole model of a typical bone without affecting the validity of the results.

Construction of the models and the analysis of the DEXA measurements on the retrievals were based on the assumption that the contralateral bone represented the pre-operative state of the treated bone. Although this assumption is not unreasonable, it is clear that it is not absolutely correct. Differences between contralateral bones have been described in the literature (Kiratli et al., 1991; Kale et al., 1995) and the limited validity of the assumption of the bilateral symmetry established. Apart from pathological changes, which led to the operation, the state of both bones might have been affected by altered loading related to the pain-induced changes in the subjects’ posture and movement patterns. Such changes have been described (Bryan et al., 1996) and attributed to the general disuse of the affected limb. Only a fully prospective bone densitometry study, which would
provide accurate description of the development of both bones, would make more accurate assessment of actual changes possible.

The retrieval study provided detailed descriptions of the bones along the stem of the implant. Since the case-specific information (cross-sectional images and DEXA) was not available for the proximal part of the bone it had to be approximated on the basis of a typical bone. Although the bone characteristics are well reproduced in the important areas of the main load transfer around the stem, some inaccuracies in the proximal part may have affected the load transfer, especially in the reference situation.

A linear relationship was assumed between the grey-scale of the contact radiographs and apparent density of the bone when assigning densities to the elements of the model on the basis of the cross-sectional images. This is a simplification of the complex relationship between the bone mineral content and the greyscale of an image obtained by digitizing a transilluminated radiograph of a bone cross-section with a camera (McGovern et al., 1994). The error caused by this simplification is thought to be less significant than the inevitable error related to the representation of the density distribution by homogeneous elements. The fact that the density of the elements of the model had to be derived from two different datasets (cross-sectional images and DEXA) caused some difficulties. All possible measures were employed to reconstruct the density field and achieve correspondence between the models and the specimens. DEXA-based optimization eliminated the most pronounced differences between real DEXA readings and the ones simulated with the models. In the future it would be advantageous to have a detailed description of the whole bone, for example in the form of pre-operative CT scans.

The boundary conditions used in the finite element calculations inevitably simplify the real situation. The loading of the bone was represented by three loading cases, each corresponding with a certain daily activity. Of all the muscles acting on the proximal femur only those attached to the greater trochanter were represented. Even though the use of site-specific remodelling theory (with the loads applied to the reference and actual models being identical) lessens the significance of precise representation of the loading (Huiskes et al., 1987), the fact that some parts of the bone are locally underloaded may lead to unrealistic adaptive changes. This was the case for the lesser trochanters which, being unloaded, were completely resorbed in the simulations. Greater realism of muscle loading is an obvious area for improvement.

Full ingrowth along the porous coated surface of the implant was assumed from the very beginning of the post-implantation adaptation process. In reality osseointegration of the implant is not instantaneous and does not occur over the whole porous coated surface. The fact that the implant was surrounded in the model by a thin layer of elements with densities assigned according to the contact radiographs of the control bone (with a gap in some places, separating the post mortem inserted implant from the bone) at least partly compensated for this simplification. These elements represented either a gap filled with very flexible cancellous bone or cortical bone in direct contact with the implant.

Another factor which affects the predictions of the model is the dead-zone threshold; or, in other words, bone reactivity. It has been shown that higher bone reactivity produces more bone resorption (Huiskes et al., 1992). This parameter was set to the same value for all cases in our simulations and the value used was based on the experience from previous simulation studies. It is possible that reactivity, which may be variable between individuals, and subject to factors like age or progress of bone disease, was in fact different in the real bones.

Apart from correspondence between the simulations and corresponding specimens in general patterns of spatial distribution of bone loss, other phenomena known from clinical practice were observed in the simulated radiographs. For example hypertrophy was seen at the tip of the stem, and the zone of bone loss was limited by the border of the porous coating (Engh and Bobyn, 1988). Almost complete resorption predicted in the region of the lesser trochanter, which is not consistent with clinical observations, can be attributed to the fact that no forces were applied to this part of the model. The absence of forces, which in the model have bone-conserving effects similar to those they have in real bone, led to unrealistic bone loss in this area.

The relationship between initial BMC and bone loss was examined. The simulations showed an inverse relationship between these two quantities, the same as found in retrieval studies (Engh et al., 1992; Sychterz and Engh, 1996). Even though the trend of the relationship was reproduced, the slope of the relationship for the equilibrium state was smaller than the one found for the retrievals. While the predictions of bone loss were similar to the experimental findings in the cases with lower initial BMC, for the denser bones the bone loss at equilibrium state was overestimated. If an earlier remodelling time is considered, rather than the equilibrium state, the correspondence in the slope of the bone loss versus initial BMC was excellent.

We believe that the problems of technical precision, mentioned earlier in this discussion, are not the main cause of the bone loss overestimation at equilibrium state. The finding that this overestimation is higher in cases in which the equilibrium is reached later (the rate of bone loss is lower) leads us to the hypothesis that the adaptive process is limited to a certain finite post-operative period. This idea is supported by an earlier validation study, relative to canine hip replacement (Weinans et al., 1993), in which the minimum error of the computer prediction was also found at an earlier post-operative
time than when the equilibrium state of the model was reached. The hypothesized cut-off time after which the adaptive process does not continue is indicated in Fig. 5 by a vertical line at time 60. This reduction of the time given to the remodelling process produces relatively more bone loss in cases with higher rates of bone loss (lower initial BMC) while limiting the amount of bone loss in cases with slower progress of the adaptation process (higher initial BMC). We hypothesize that the bone does not ‘remember’ its pre-operative internal mechanical environment after a certain time and terminates the adaptive process even though the original (‘forgotten’) state is not fully re-established. This hypothesis of limited bone ‘memory’ will require further investigation.

The fact that the results of remodelling simulations show correlation between the eventual bone loss and initial density of the bone indicates that the same correlation which was observed in the clinical cases can be explained by strain adaptive remodelling. We acknowledge that there are important biological factors at work as well, but it is a fact that the mechanical factors alone can largely explain the adaptive changes observed post-operatively. It must be added, though, that our results do not give an explanation for the real biomechanical mechanisms the model is supposed to represent; the model is phenomenological in nature, not mechanistic.

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References


