Can Additional Experimental Data in Humans Verify the Finite Element-Based Bone Remodeling Algorithm?

Christian Wong*, P. Martin Gehrchen and Thomas Kiaer

Spine Section, Department of Orthopaedic Surgery, University Hospital of Copenhagen, Blegdamsvej 9, 2100 Copenhagen, Denmark

Abstract: A finite element-based bone remodeling study in human was conducted in the lumbar spine. This was done to examine the validity of the bone remodeling algorithm by comparing to experimental data. A non-linear 3-D finite element model of the normal ligamentous lumbar spine of L3 to L5 was generated. Two different material configurations were assigned to the finite element model. Two analyses with the non-site specific iterative bone remodeling algorithm were conducted with strain energy density as remodeling signal. The experimental data was bone mineral content measurements in the lumbar spine of 87 test subjects. The finite element-based bone remodeling data were compared to the experimental bone mineral content data. For both bone remodeling analyses there were a statistical significant difference between the bone remodeling data and experimental data for 6 out of 8 regions of interest. The bone remodeling data showed too small agreement to confirm the validity of the bone remodeling algorithm.

INTRODUCTION

Many scientific papers have been published concerning adaptive bone remodeling (BR) algorithms [1-11]. BR has been used as a mathematical method to predict changes in bone stock, when inserting different prosthesis designs to obtain an optimal design [12]. It seems, however, that the general focus has been on elaborating on the mathematical theories with little subsequent experimental evaluation – not at least in the spine [1-3], but even in the hip and knee, where the majority of the studies have been conducted [4,8,9]. Some studies have had no experimental data at all [2,3,13,14] and some studies have used inconsistent experimental data with small sample sizes [4,8]. Additionally, some papers have been uncritical when validating the BR algorithm accepting large differences between the BR and experimental data [1,4]. Based on these circumstances, we undertook an evaluation study in a previous publication [15]. We compared systematic experimental *prospective* bone mineral content (BMC) data in the operated spine with resembling data generated using the adaptive BR algorithm [15]. There were unexpectedly no agreement between the experimental BMC and generated BR data, and we could not confirm the BR algorithm hypothesis. However, the number of included patients was small, so the impact of the study could be questioned. For this reason, we found it relevant to perform yet another study this time including a larger number of test subjects. In this study we included 87 healthy human test subjects in a cross-sectional BMC study in the lumbar spine. As in our previous study we applied the finite element-based (FE) iterative BR algorithm to the lumbar spine, and did a comparison between results from the FE-based BR algorithm and the experimental BMC measurements for a broader evaluation of the BR algorithm.

*Address correspondence to this author at the Dept. of Orthopaedics, University Hospital of Hvidovre, Kettegård Alle 30, 2650 Hvidovre, Denmark; Tel: +45 36 32 23 33; Fax: +45 36 32 37 82;
E-mail: chwo123@gmail.com

MATERIAL AND METHODS

Finite Element Model

FE analyses were performed by the finite element code COSMOS/M®. The 3-dimensional FE model included the third, forth and fifth lumbar vertebrae of the ligamentous spine. The FE model is illustrated in Fig. (**1**).

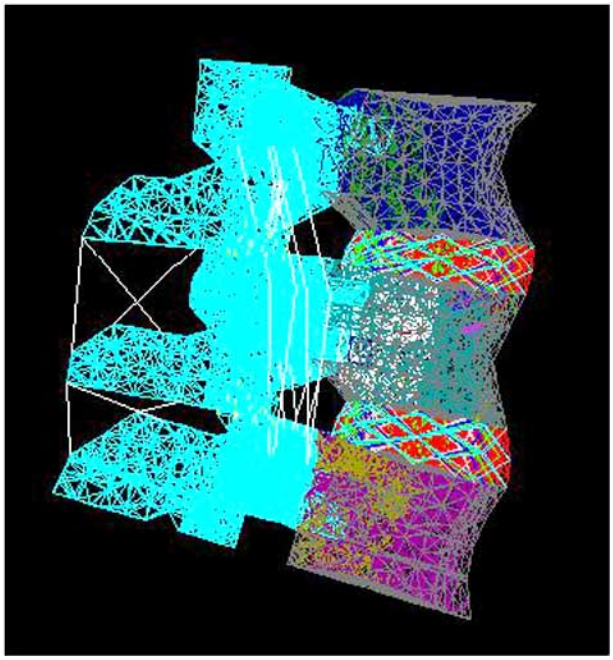

Fig. (1). Finite element model of L3 to L5 lateral view.

The bony structures were generated by segmentation of a data set of computed tomography from the Visible Human Project® [16]. Segmentation is a data reduction tool to simplify the geometrical shape of the bony structures of the spine without losing accuracy. This was necessary for the FE

1876-5327/10

code to handle the large amount of data. The FE model had a total of 14512 volumetric elements. All volumetric elements were high order tetrahedral elements. The Young's modulus for cortical bone was set to 12000 MPa and had a Poission's ratio at 0.3. There were two FE models in regards of the material properties for trabecular bone; one with a uniform distribution of Young's modulus of 100 MPa and a Poission's ratio at 0.2. This was called the *uniform FE model*. The other FE model was called the *subdivided FE model*. The material properties of L4 for this model were subdivided into 8 regions of interest (ROI). Each ROI had an area of 1 cm^2 in the frontal plane. The 8 ROI of L4 for the FE model are illustrated in Fig. (**2**).

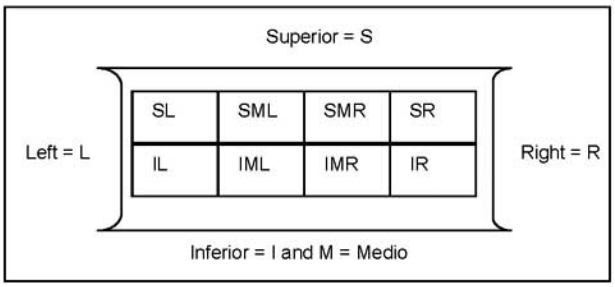

Fig. (2). 8 regions of the 4th vertebral body in the frontal plane.

The material properties of the 8 ROI were based on BMC measurements of the 87 test subjects. They were generated by conversion of BMC data to compressive modulus based on a mathematical relationship from the study by Keller *et al.* (1989) [17];

$$S = 1.30 * BMC_{dexa}^{2.00}$$

The relationship had a correlation coefficient of 0.90 (r2=0.90). The material properties of L3 and L5 were also based on the BMC data, but had one uniform material property within each vertebral body (see Table **1**).

The FE model also consisted of the intervertebral discs between L3-4 and L4-5. They were divided into a nucleus and an annulus fibrosis. The nucleus was defined as an incompressible fluid. The annulus fibrosis consisted of 4 concentric rings of fibres embedded in ground substance. The thickness of the fibres increased from the innermost layer outwards with the square of the distance to the disc centre in accordance with Smit *et al.* (1999) [18]. The overall volume of the fibres was 16 % of the annulus volume in accordance with Shirazi-Adl (1984) [19]. The fibres were modelled in a criss-cross pattern with linear 2-node uni-axial elements (TRUSS3D). The ligamentous structures consisted of 7 ligaments. The bony insertion points of the ligaments were connected manually. The ligaments were modelled with TRUSS3D elements with material non-linearity. Since tension forces were relatively low while at rest, the ligaments were assumed to be initially unstressed and were defined to be active in tension only according to Shirazi-Adl (1986) [20]. Cross-sectional area of the ligaments was adapted in accordance with Goel *et al.* (1995) [21]. The facet joints were also included in the FE model. They were defined with 3 dimensional non-linear node-to-node contact elements (GAP) and had an average of 19 elements each. The effect of the compliant facet cartilage layer was incorporated by non-linear TRUSS3D elements active in compression only [22].

The FE model is described in detail and validated by comparing results to experimental Instron® tests in a previous published study [23]. Convergence test for the FE model was performed. This was performed to ensure, that the FE model had an appropriate number of elements. When this test is performed, the number of elements in the FE model is increased until a certain point, where the calculated results converge to the one exact solution, thus giving the appropriate number of elements to use for the FE model.

The load cases used were a simulation of a 'daily loading cycle'. It consisted of three separate load cases. These were applied to the superior layer surface of L3 and consisted of an uni-axial compression load of 424.7 N, a 10 Nm flexion and 10 Nm extension moment load for the BR algorithms in accordance to Grosland *et al.* (1998) [3], who performed a similar BR study. The FE models were constrained on the inferior surface of L5. Non-linear static analyses were performed for all three load cases.

FE-based Adaptive Bone Remodeling

In this study we used the *non-site specific* iterative BR algorithm proposed by Huiskes *et al.* (1987, 1989) [5,6]. The following sets of equations were used to simulate the BR process:

$$d\rho/dt = \tau_{osteolysis} * (S_{t,i} - (1 - s) * S_{ref})^{\alpha}$$

$$\text{if } S_{t,i} < (1-s) * S_{ref}$$

$$d\rho/dt = 0$$

$$\text{if } (1-s) * S_{ref} \leq S_{t,i} \leq (1+s) * S_{ref}$$

$$d\rho/dt = \tau_{osteogenese} * (S_{t,i} - (1 + s) * S_{ref})^{\beta}$$

$$\text{if } S_{t,i} > (1+s) * S_{ref}$$

$$\text{for } \rho_{minimum} < \rho < \rho_{cortical\ bone}$$

St,i was the actual BR signal for the specific location, i, to be remodelled at the time t. The BR signal was determined for the daily loading cycle as the strain energy density (SED) for the location i over the apparent density. The BR constants (α and β) were unknown, since they have never been experimentally verified. They were arbitrarily set to 1 as in earlier studies of the spine [1,2]. The time constant was determined in a way that the maximal change in density did not exceed 0.25 of the density of the previous BR iteration in accordance to Goel *et al.* [1,2]. The time constant and the BR constants together determined the rate of the remodeling process; however, the changes in density had to be kept small to control the BR algorithm and this ensured that the BR data converged to the exact solution, thus giving the appropriate number of iterations to use for the BR algorithm. s represented the dead zone, where no BR was taking place and was set to 0.75 in accordance to Huiskes (1993) [8]. The dead zone was the threshold level, where the changes in the biomechanical scenario would not give rise to BR changes in the bone. This simulated the homeostatic situation, where daily living occur. The reference signal, Sref, was taken as the average SED for the FE model [1,6]. The BR algorithms were applied to the middle vertebral body of L4, since the boundary conditions were applied on the adjacent vertebrae. The processes of FE analysis and BR were iterative, and repeated until the total SED reached a minimum 1. This was

the criterion of convergence for the BR process to be regarded as the ideal mathematical state for process of osteogenesis.

Dual Energy X-Ray Absorptiometry of the Lumbar Spine

The experimental part of the study was performed using the XR-26 Mark II dual energy x-ray absorptiometer. The bone densitometer was calibrated every morning using a 77-step calibration standard according to the recommendations of the manufacturer. Test subjects were voluntary members of staff, medical students and patients of the University Hospital of Copenhagen. Informed consent was obtained from every test subject. None of the test subjects had previous surgery of the spine, medical disease or medication known to affect the bone quality. Eighty-seven healthy subjects were included. All test subjects were scanned once. They had a mean age of 39.3 years (range 21-70), and the female:male ratio was 1:1. The subjects had a mean height and weight of 173.76 cm and 72.13 kg, respectively. All measurements of the healthy test subjects were performed using the anterio-posterior (AP) spine scan option of the bone densitometer. This was a semi-automatic procedure, which ensured the test subjects were placed in the same way.

RESULTS

The cross-sectional BMC measurements from the eighty-seven test subjects are listed in Table **1**. The table includes the mean BMC measurements and calculated compressive moduli for the third, forth and fifth lumbar vertebrae.

Table 1. BMC and E (Compressive) Modulus for the 87 Healthy Test Subjects

Vertebral Body (n=87)	L3	L4	L5
BMC (g/cm^2)	2,72	3,06	3,21
E Modulus (MPa)	96,47	121,44	134,14

The bone remodeling algorithm was evaluated by comparing simulated BMC data for the two FE models and BMC data for the 8 ROI. Convergence for the non-site specific BR algorithm was achieved when reaching a global minimum at iteration number 7 for the *subdivided FE model* and 43 for the *uniform FE model.* The FE-based and experimentally measured BMC data are compared in Fig. (**3**).

In Fig. (**3**) the BMC data are represented by the mean and 95% confidence limits for the mean. The mean of the BMC data were significantly different for both the subdivided and the uniform FE model in all regions except in region IL and IR

DISCUSSION

The purpose of this study was to evaluate the validity of the adaptive FE-based bone remodeling algorithm using SED as remodeling signal. We included an experimental material

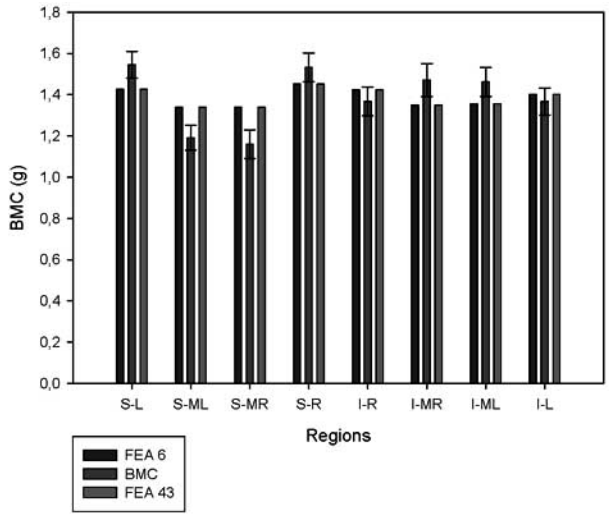

Fig. (3). Comparison between the FE-based BR data (FEA 6 and 43) and BMC data (with standard deviation).

of rather large size with a representative distribution in age and gender to substantiate the hypothesis. This has never have been done before for the purpose of evaluation of the BR algorithm. We found a significant difference within 6 out of 8 ROI, when comparing experimental BMC data with data from the FE-based BR algorithm. Therefore we could not confirm the validity of the BR algorithm. This result confirms an earlier study by this group, where there were no similarities between prospective experimental data in the operated spine compared to data of the BR algorithm [15]. Even so, we have had considerations concerning the set-up of the present study as it could be thought to cause some degree of influence to the bone remodeling algorithm, thus to the comparison of experimental data, which would influence the conclusion above. The FE-based bone remodeling algorithm may be influenced by several factors. Weinans *et al.* (1989) divided the factors into three [24], and the implications of the factors are discussed below:

The Geometric Configuration

External remodeling of the shape of the vertebral body was not carried out. However, the geometric model in this study was set up to resemble a general representative model in dimensions and shape. This coincides with the experimental material of this study, which also was a general representation of the material data. Also, an earlier study has shown, that external bone remodeling only change the shape marginally, indicating that it would have equally minor influence on the internal bone remodeling algorithm [1].

The Loading and Boundary Conditions

The loads in this study were chosen in accordance with previous BR studies [1,3]. Studies examining spinal loads indicate that much higher loads take place *in vivo* [25]. Furthermore, mechanical boundary conditions as the spinal muscles increase stability and decrease stresses in the spine [26,27]. The muscles were excluded in this study. The full range of daily activities was represented by three load cases

in this study. This must be considered to be a simplified average estimate, thus affecting the BR algorithm.

The Density Distribution

The initial material distribution has been shown to affect the iterative BR results [9,24]. Several factors might have affected the material distribution of the spine, which was based on BMC measurements; the use of scanner type (DEXA or DPA) [17], the error of rotation in the BMC scans, the precision in measuring the ROI's and the material distributions determined by mathematical approximation. However, we included both the experimental heterogeneous BMC-based material distribution and a uniform homogenous material distribution to examining the effects of different material distribution. Indeed all mentioned factors have an impact on the FE-derived stress and strain results thus influencing the FE-based BR algorithm.

Several factors of the mathematical BR algorithm could cause the differences in the comparison to the experimental data. SED was used as the striving BR signal. Other remodeling signals could as well have been used in the remodeling algorithm thus affecting the density distribution 28. However, SED was used as BR signal as it seem to be the remodeling signal with best experimental verification of its influence [1,5,7,28]. Huiskes *et al.* (1992) examined the effects of the dead zone by increasing bone reactivity. He found that the total bone loss increased, but the pattern of bone loss was similar [12]. Furthermore, the time constant τ was variable, determining the change in density in each time step and controlling the rate of convergence. Especially if the time constant was overestimated, it could affect the density distribution. However, we ensured an adequate time constant by performing additional iterative BR cycles both before and after the convergence criterion with even lower values for the time constant. This ensured that a global minimum was reached instead of a local minimum.

Notwithstanding these reservations mentioned above it appeared that the FE-based BR and experimental BMC data had a statistical significant difference for the regions of interest. Conclusively, too small agreement was seen between FE-based BR and experimental BMC data in the lumbar spine to substantiate the BR algorithm. We have now in two studies not been able to confirm the FE-based BR algorithm in the spine. This would suggest that future research in this field wisely should be focused on experimental evaluation – also in the hip and knee region. The experimental evaluation in the hip and knee region in humans seems to be somewhat unsystematic and uncritical. For example Van Lenthe *et al.* used a different prosthesis design for the FE model than used when generating the experimental data [4]. Kerner *et al.*, Huiskes *et al.* and Skinner *et al.* had different time lengths of implantation and different prosthesis designs in the experimental data-set [8-11] Weinans *et al.* and van Rietbergen *et al.* evaluated the BR algorithm in the animal studies. They used the contralateral bone as a reference for the BR simulation, assuming bilateral symmetry and measuring the contralateral bone after implantation of the prosthesis and after harvesting the animals [7,11]. Furthermore, some studies have accepted large differences between predicted and experimental data, still claiming coherency between the FE-based BR and experimental data [1,4].

CONCLUSION

Conclusively, it is recognized that many factors (medication, disease, age, gender, metabolic and hormonal factors and more) influence the biological BR. However, they were not included since these factors are, as of yet, not fully understood. If in fact a single mechanical signal determines the biological BR as postulated in the adaptive BR algorithm, it must induce or mediate all the factors that influence the biological BR. This study could not substantiate such a bone remodeling hypothesis. However, maybe by including even more parameters some mathematical relationship between the biological BR and the mathematical remodeling algorithm could exist. Again, this study could not substantiate this hypothesis.

DISCLOSURE

This study is approved by the local Research Ethics Committee of Copenhagen, Denmark. All included patients have signed patient consent forms and anonymity is ensured. All copyrights are given to the Open Spine Journal and no copied material is submitted.

REFERENCE

[1] Goel VK, Ramirez SA, Kong W, Gilbertson LG. Cancellous bone Young's modulus variation within the vertebral body of a ligamentous lumbar spine--application of bone adaptive remodeling concepts. J Biomech Eng 1995; 117: 266-71.

[2] Goel VK, Seenivasan G. Applying bone-adaptive remodeling theory to ligamentous spine - preliminary results of partial nucleotomy and stabilization. IEEE Eng Med Biol 1994;August/September: 508-16.

[3] Grosland N, Goel VK, Grobler LJ, Griffin SL. Biomechanical basis for bone growth around an interbody fusion cage. Louisiana: New Orleans, 1998: pp. 654-654.

[4] van Lenthe GH, Waal Malefijt MC, Huiskes R. Stress shielding after total knee replacement may cause bone resorption in the distal femur. J Bone Joint Surg Br 1997; 79: 117-22.

[5] Huiskes R, Weinans H, Dalstra M. Adaptive bone remodeling and biomechanical design considerations for noncemented total hip arthroplasty. Orthopedics 1989; 12: 1255-67.

[6] Huiskes R, Weinans H, Grootenboer HJ, Dalstra M, Fudala B, Slooff TJ. Adaptive bone-remodeling theory applied to prosthetic-design analysis. J Biomech 1987; 20: 1135-50.

[7] Weinans H, Huiskes R, van Rietbergen B, Sumner DR, Turner TM, Galante JO. Adaptive bone remodeling around bonded noncemented total hip arthroplasty: a comparison between animal experiments and computer simulation. J Orthop Res 1993; 11: 500-13.

[8] Huiskes R. Stress shielding and bone resorption in THA: clinical *versus* computer- simulation studies. Acta Orthop Belg 1993; 59 (Suppl 1): 118-29.

[9] Kerner J, Huiskes R, van Lenthe GH, *et al.* Correlation between pre-operative periprosthetic bone density and post- operative bone loss in THA can be explained by strain-adaptive remodeling. J Biomech 1999; 32: 695-703.

[10] Skinner HB, Kilgus DJ, Keyak J, Shimaoka EE, Kim AS, Tipton JS. Correlation of computed finite element stresses to bone density after remodeling around cementless femoral implants. Clin Orthop 1994; 178-89.

[11] van Rietbergen B, Huiskes R, Weinans H, Sumner DR, Turner TM, Galante JO. ESB Research Award 1992. The mechanism of bone

remodeling and resorption around press-fitted THA stems. J Biomech 1993; 26: 369-82.
[12] Huiskes R, Weinans H, van Rietbergen B. The relationship between stress shielding and bone resorption around total hip stems and the effects of flexible materials. Clin Orthop 1992; 124-34.
[13] Huiskes R. The various stress patterns of press-fit, ingrown, and cemented femoral stems. Clin Orthop 1990; 27-38.
[14] Huiskes R, van Rietbergen B. Preclinical testing of total hip stems. The effects of coating placement. Clin Orthop 1995; 64-76.
[15] Wong C, Gehrchen PM, Kiaer T. Can experimental data in human verify the bone remodeling algorithm? Spine 2008; 33(26): 2875-2880.
[16] Ackerman MJ. The visible human project. J Biocommun 1991; 18: 14.
[17] Keller TS, Hansson TH, Abram AC, Spengler DM, Panjabi MM. Regional variations in the compressive properties of lumbar vertebral trabeculae. Effects of disc degeneration. Spine 1989; 14: 1012-9.
[18] Smit TH, Odgaard A, Schneider E. Structure and function of vertebral trabecular bone. Spine 1997; 22: 2823-33.
[19] Shirazi-Adl SA, Shrivastava SC, Ahmed AM. Stress analysis of the lumbar disc-body unit in compression. A three- dimensional nonlinear finite element study. Spine 1984; 9: 120-34.
[20] Shirazi-Adl A, Ahmed AM, Shrivastava SC. Mechanical response of a lumbar motion segment in axial torque alone and combined with compression. Spine 1986; 11: 914-27.
[21] Goel VK, Monroe BT, Gilbertson LG, Brinckmann P. Interlaminar shear stresses and laminae separation in a disc. Finite element analysis of the L3-L4 motion segment subjected to axial compressive loads. Spine 1995; 20: 689-98.
[22] Shirazi-Adl A, Drouin G. Load-bearing role of facets in a lumbar segment under sagittal plane loadings. J Biomech 1987; 20: 601-13.
[23] Wong C, Gehrchen PM, Darvann T, Boisen-Møller F, Kiaer T. Non-liniear finite element analysis and biomechanical evaluation of the lumbar spine. IEEE Trans Med Imaging 2003; 22: 742-6.
[24] Weinans H, Huiskes R, Grootenboer HJ. Convergence and uniqueness of adaptive bone remodeling. 1989: 310.
[25] Han JS, Goel VK, Ahn JY, *et al.* Loads in the spinal structures during lifting: development of a three- dimensional comprehensive biomechanical model. Eur Spine J 1995; 4: 153-68.
[26] Goel VK, Kong W, Han JS, Weinstein JN, Gilbertson LG. A combined finite element and optimization investigation of lumbar spine mechanics with and without muscles. Spine 1993; 18: 1531-41.
[27] Kong WZ, Goel VK, Gilbertson LG, Weinstein JN. Effects of muscle dysfunction on lumbar spine mechanics. A finite element study based on a two motion segments model. Spine 1996; 21: 2197-206.
[28] Brown TD, Pedersen DR, Gray ML, Brand RA, Rubin CT. Toward an identification of mechanical parameters initiating periosteal remodeling: a combined experimental and analytic approach. J Biomech 1990; 23: 893-905.

Received: November 17, 2009 Revised: December 24, 2009 Accepted: December 27, 2009