Prospects of computer models for the prediction of osteoporotic bone fracture risk

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Prospects of computer models for the prediction of osteoporotic bone fracture risk

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Abstract. Bone fractures are major problems for osteoporosis patients. To avoid such fractures, more information is needed about the factors that determine the bone fracture risk. In this chapter, it is discussed how recently developed finite element computer models that can represent the trabecular architecture in full detail can provide such information. It is concluded that a computer modeling approach to this problem is feasible, required and promising. It is expected that, eventually, such models can be used as a basis for an accurate diagnosis of the bone fracture risk.

1. The problem: increased fracture risk due to reduced bone stock

From an engineering point of view, bone tissue is a remarkable material. It displays a fascinating wide variation in architecture, varying from dense and compact (cortical bone) to highly porous architectures (trabecular bone), build of rods and plates. Even more intriguing are its dynamic capabilities; it can grow, adapt and repair itself, enabling it to last a lifetime. The dynamic, adaptive capabilities of bone are not easily recognized in the healthy mature skeleton. During lifetime, only gradual changes in bone architecture and bone mass occur, with a mild reduction of bone mass after the age of 30 as the most obvious one. For almost one third of women in the US over age 65 (and a smaller percentage of men) however, a much larger decline in bone mass of 20-40% is found by the age of 65 [1,2]. This condition of excessive bone loss, usually in combination with a deteriorated bone architecture, is called osteoporosis, and is a result of metabolic diseases. The inferior mechanical quality of osteoporotic bone leads to an increased risk of bone fractures. Such fractures, usually the first symptoms of osteoporosis, most commonly occur at the femoral neck, vertebral bodies and the distal radius. As a public health issue, osteoporosis is now considered an epidemic, directly attributing to over 1.2 million fractures annually in the US alone [3,4]. For a 50 year old woman today, the risk of a hip fracture in her remaining lifetime is about 17% [5]. By the age of 70, 40% of US women will experience a fracture due to osteoporosis [6]. With the increase in the average age, the number of bone fractures will become an increasing problem for society. It is estimated that the number of hip fractures will increase to over 6.2 million worldwide in 2050 [7]. Such bone fractures are catastrophic events, the one year mortality rate from hip fractures is 25% and the probability of an older patient to regain the previous level of function after a hip fracture is less than 30% [8-10].

Apart from metabolic diseases, bone stock is also threatened by the load adaptive mechanism itself when the loading of the bone is decreased. A state of reduced mechanical loading of bone throughout the body is experienced for example by astronauts and by

patients subjected to long bed rests or immobilization [11-13]. The loss of bone stock under conditions of micro-gravity is a limiting factor for long-duration space flights, whereas bone loss after bed rest or immobilization can lead to the need of a long rehabilitation period to recover at least some of the bone lost. At a more local level, dramatic bone loss due to unloading is often seen after orthopedic treatment, in particular around medullary implants [14-16]. In this case mechanical unloading is a consequence of the fact that the relatively stiff implant now carries part of the load that was formerly carried by the surrounding bone alone ('stress shielding'). This form of bone loss has been recognized as a factor that can seriously threaten the success of hip arthroplasties (See the chapters by Huiskes and by Weinans and Sumner in this issue). It also limits the success of revision operations, since the bone stock that is left can be insufficient for the fixation of a new implant. Bone loss due to stress shielding is a problem in particular for patients who received the implant after a hip fracture due to osteoporosis, since in these cases the bone stock is already at a minimum.

2. The need for a better diagnosis of bone fracture risk

Until a safe and effective therapy has been developed that can stop or even reverse the process of bone loss, the prevention of osteoporotic bone fractures should be the primary goal of treatment [6]. This requires an accurate diagnosis of the load carrying capacity ('quality') of bones. This capacity depends on two factors. First the strength of the bone tissue itself (yield stress) which, in turn, is highly correlated with the stiffness (elastic modulus) and the degree of mineralization of the tissue. The second is morphology. This includes the external and internal shape of the bone as well as the arrangement of the trabecular architecture. Trabecular architecture can be represented by two qualities. First the volume fraction, which determines the volume of bone tissue per unit of volume. This quality may also be expressed in the total mass per unit of bone volume, which is called the apparent density, and comprises the degree of mineralization as well. Second the directionality of the trabecular architecture, which determines its anisotropy.

Most diagnostic methods presently used to determine bone mechanical quality are based on the only material property that can be clinically measured in a noninvasive way: the bone apparent density. In fact, osteoporosis is often defined purely in terms of bone density as "a condition whereby the density of bone is two times the standard deviation less than the average density of a representative population at the age of 30". In practice, however, this is not a very accurate definition, since it does not account for the role of architecture in bone strength. Consequently, it is possible that people with a low bone mass but a strong architecture receive unnecessary treatment whereas people at risk of bone fractures are not recognized.

For a more accurate and reliable diagnosis of bone quality, it will be necessary to determine *mechanical* parameters of the bone, in particular its elastic properties and strength, since these are the parameters that determine the fracture risk. With standard engineering techniques, these parameters are measured from mechanical tests on a sample of the material. Because it is not desirable to take out a bone sample for mechanical test experiments from patients who may already suffer from insufficient bone stock, the diagnosis of bone mechanical properties must be based on parameters that can be measured *in vivo*. Preferably these should be parameters that can be measured in a relatively easy way, such as bone density and morphological parameters that can be measured from radiographs. So far, however, no accurate relationships between morphological and mechanical parameters have been found, and it has been questioned if accurate relationships based on such parameters can exist at all. Recently, new imaging techniques have been introduced that allow for the

assessment of bone architecture in its full three-dimensional detail, rather than by its volume fraction only [17,18]. With these techniques it is possible to reconstruct the bone architecture in a computer. Such a reconstruction can be used as a basis for the geometry of finite element models from which mechanical properties of the bone can be calculated. The feasibility and prospects of using such microstructural finite element models based on computer reconstruction for a better quantification of *in vivo* bone quality is discussed in the next paragraph.

3. Feasibility of computer models for the diagnosis of bone fracture risk

In older studies that aimed to calculate the stiffness or strength of trabecular bone from microstructural finite element models, generalized, and thus simplified, models were used to represent the trabecular architecture [19,20]. It can be questioned, however, if this is a good approach; it is well possible that as many aspects of bone behavior are due to irregularities in its structure as there are due to regularities.

With recently developed computer techniques, more realistic finite element models of trabecular bone are available, that can represent the trabecular architecture in the same detail as the computer reconstruction [21-23]. The geometry of these finite element models is defined by computer reconstructions created from images of sequential cross sections of trabecular bone samples, obtained from serial sectioning techniques or micro-CT scanners, which are digitized and stored in a computer in a three-dimensional voxel grid. These computer reconstructions can be converted to finite element models by simply converting all bone voxels in the reconstruction to equally sized brick elements. These finite element models can be used to simulate classical mechanical tests, from which the elastic constants of the specimen as a whole can be calculated (Fig. 1) [23-25]. It has been demonstrated that the results obtained from these computer simulations can compare very well to those obtained from accurate compression tests and, by this comparison, these models can provide

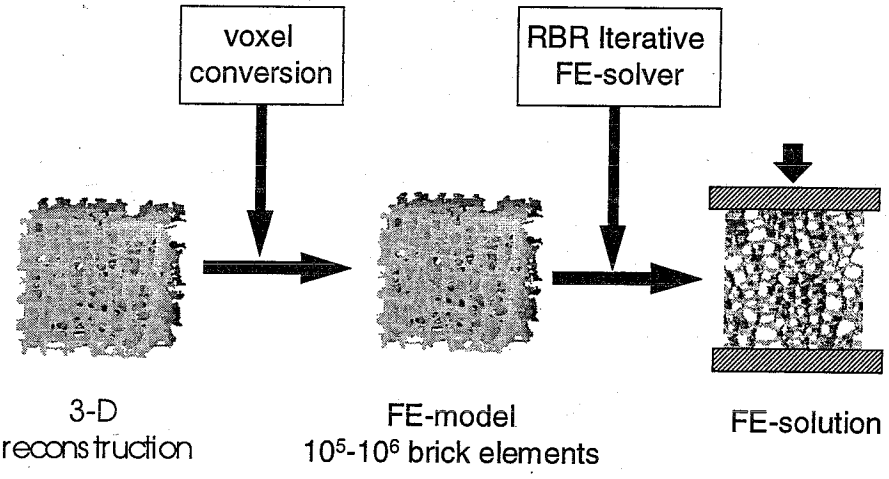

Fig. 1 Summary of the microstructural FE-approach for the calculation of mechanical properties of trabecular bone. A three-dimensional computer reconstruction of a trabecular bone specimen (left) is converted to a FE-model by simply converting all bone voxels in the reconstruction to equally sized brick elements in the FE-model. The resulting FE-model (middle) has exactly the same geometry as the reconstruction it is based on. For a 10 mm specimen, the FE-model consists of on the order of 10^5 to 10^6 elements. Problems of this size can not be solved with standard FE-codes. Instead, special-purpose solvers must be used [27]. By applying the appropriate boundary conditions, the FE-models can be used to simulate compression test experiments and, after solving the corresponding FE-problem, to calculate the elastic properties of the specimen and the local loading conditions in trabeculae of the specimen (right).

information about the tissue elastic properties (Fig. 2) [25]. In addition, these computer models allow for the simulation of experiments that can not be done with real bone specimens, in particular shear experiments. By simulating three compression and three shear experiments, it is possible to obtain a complete characterization of all elastic constants of a bone specimen, and to determine its orthotropic principal directions (Fig. 3) [26]. A demonstration of these techniques can be found in the chapter by Ulrich et al. in this book.

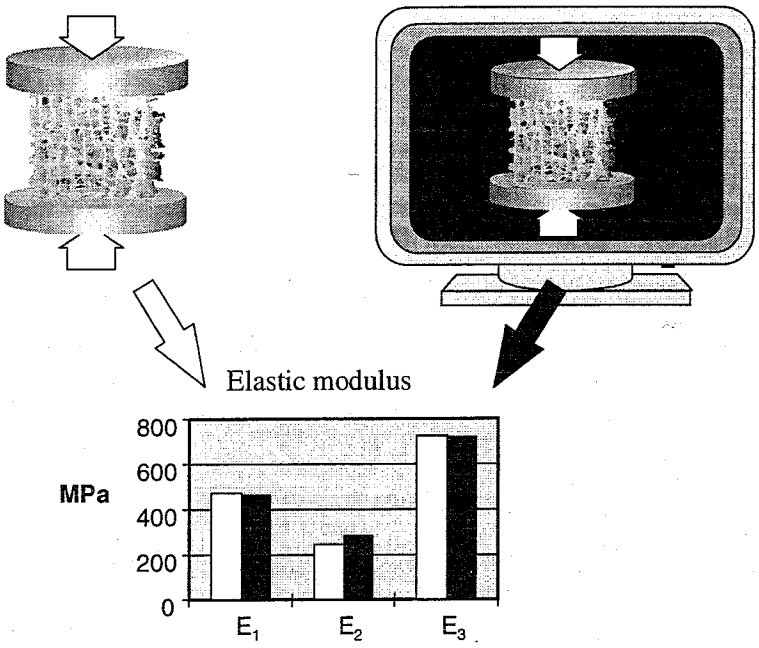

Fig. 2 The elastic moduli measured in a compression test (white bars) compared to those calculated from FE-simulations of these experiments (black bars) for the same specimen after it was reconstructed and converted to a FE-model. The best agreement between both results was found if the tissue modulus in the FE-model was set to 14.6 GPa. [25]

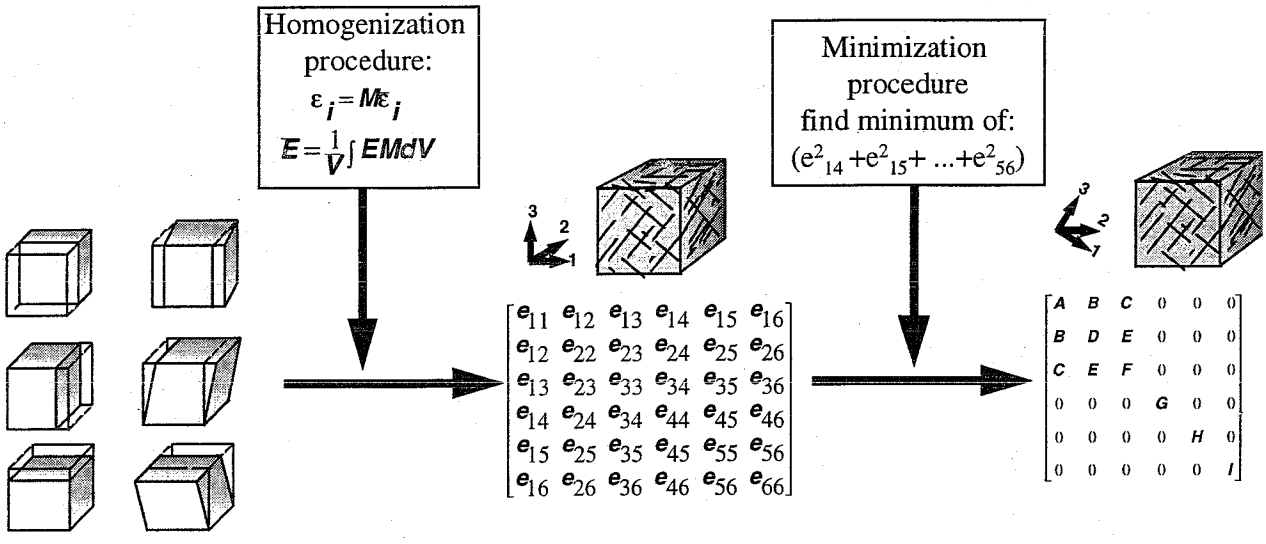

Fig. 3 Overview of the procedure to find the best orthotropic elastic constants and symmetries for a bone specimen. Six FE-analyses are performed representing six different uni-axial strain loading case (left). From the results of these analyses, the full stiffness matrix for the specimen as a whole can be calculated (middle). This stiffness matrix is used as input for an optimization procedure that searches for the coordinate transformation that gives the best orthotropic representation of this stiffness matrix [26]. As a result, nine orthotropic elastic constants and orthotropic main directions of the specimen are found.

The computer reconstructions of trabecular bone not only allow for an accurate determination of mechanical parameters, but can also be used to determine morphological parameters and thus, can be used as well to find relationships between these parameters if a sufficient large set of reconstructed specimens is available. Many inaccuracies and uncertainties are involved with other methods used earlier for the measurement of these parameters. These can be eliminated when using computer models. It is likely that parameters measured from these models offer a better basis for finding such relationships. In an earlier study, using a limited number of specimens, it was found that, indeed, accurate relationships could be found between bone elastic constants and fabric parameters (Fig. 4) [28]. More recent studies have confirmed that accurate relationships can exist as well for a larger and more diverse set of specimens [29]. However, it will be necessary to analyze a much larger set of specimens than is now available before it can be concluded that general relationships exist.

Finally, the finite element models offer unique possibilities for the assessment of local tissue loading in bone specimens due to externally applied forces. Information about the local tissue loading can be used to define the 'efficacy' of trabecular architectures, i.e. how well a certain architecture is adapted to the external loading (Fig. 5). This information is of great importance for a better understanding and prediction of mechanically induced processes that take place at this level, in particular bone fracture.

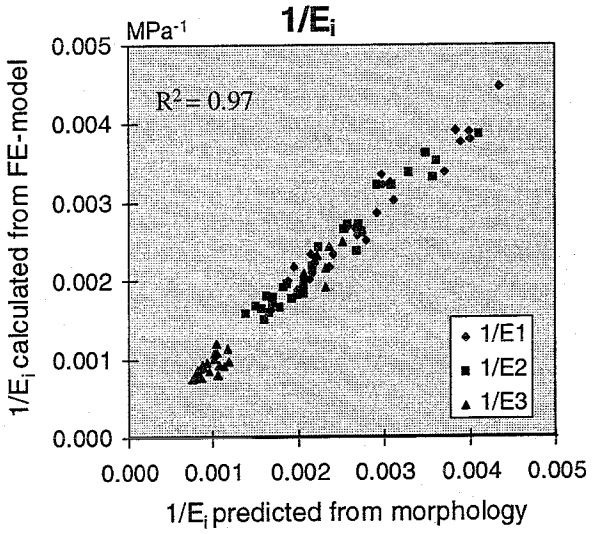

Fig. 4. Correlation of Young's moduli calculated from FE-analyses with those predicted from morphology and volume fraction for a set of 29 specimens [28]

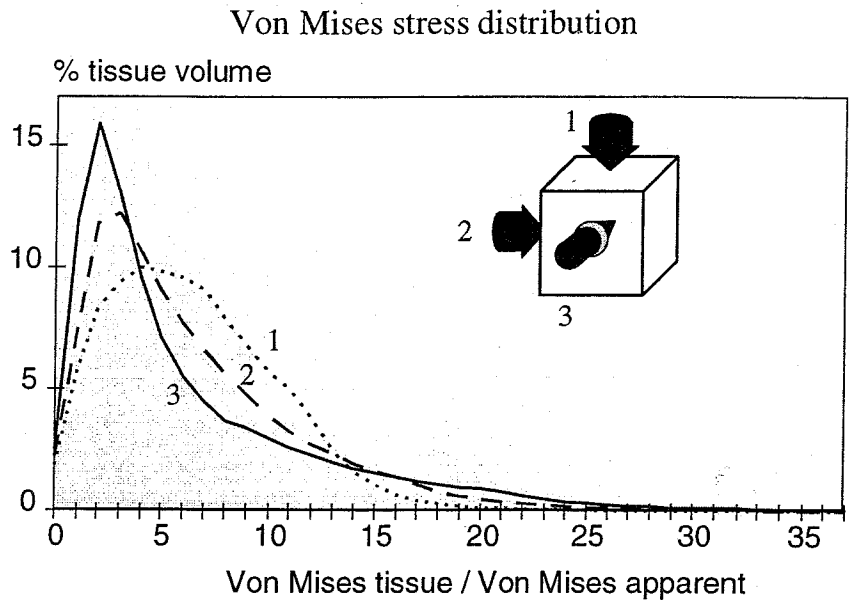

Fig. 5 The Von Mises stress distribution in a bone specimen when loaded in three orthogonal directions. The 1-direction corresponds with the anatomical loading direction. When the specimen is loaded in this direction, the distribution curve is less 'peaked' and less wide than when it is loaded in the other directions. This indicates that when loaded in the 1-direction, more bone tissue is loaded in a physiological range and a smaller percentage of the tissue material is subjected to high stress values. In other words, the trabecular architecture is better suited or more efficient for carrying loads in the 1-direction than in the other directions.

4. Conclusions

Looking at the results obtained so far, we conclude that, indeed, this computer modeling approach is feasible. With these techniques, it is possible to obtain quantitative information about the elastic properties and local loading conditions of trabecular bone; information which is essential for the prediction of bone fracture risk. Since no other methods exist that can provide such accurate and complete information, there is clearly a need for these methods.

Eventually, these computer methods can be used in the clinic to predict bone fracture risk, such that preventive measures can be taken in time when needed. To make this possible, three problems will have to be solved. First, the resolution of scanners used in the clinic must be increased to the level of those of the micro-CT and micro-MRI scanners now used in laboratories. Second, the bone tissue material properties must be quantified from the images as well, for example by finding relationships between the bone mineral content measured from the gray-value of image pixels and the tissue material properties. Third a reliable failure criterion for trabecular bone must be established, based on the tissue loading conditions calculated from the finite element models. It is expected that a diagnosis of bone fracture risk based on this information can be much more accurate than based on bone mass only, as it is common now.

A more immediate purpose is the use of these computer models to bridge the gap between morphological and mechanical parameters. Such relationships can be of great importance for the practical assessment of mechanical quality of bone from CT-, MRI- or even plain radiographic images. In this way it will be possible to translate morphological parameters to mechanical parameters, which adds to the importance of the former.

References

[1] P. Rüegsegger, M.A. Dambacher, E. Rüegsegger, J.A. Fischer, M. Anliker, Bone loss in pre-menopausal and postmenopausal women. A cross-sectional and longitudinal study using quantitative computed tomography, *J. Bone Joint Surg. Am.* **66**, (1984) 1015-1023

[2] L.J. Melton, E.A. Chrischilles, C. Cooper,A.W. Lane, B.L. Riggs, Perspective. How many women have osteoporosis? *J. Bone Miner. Res.* **7**(9), (1992) 1005-1010

[3] B.L. Rigss, and L.J. Melton, The prevention and treatment of osteoporosis. *N. Engl. J. Med.* **327**, (1992), 620-627

[4] J. Stevenson, Pathogenesis, prevention, and treatment of osteoporosis, *Obst Gyn.*, **75**, (1990), 36S-40S

[5] P.J. Meunier, Prevention of hip fractures, *Am. J. Med.*, **95(A)**, (1993), 75S-78S

[6] Conference report, consensus, development conference, prophylaxis and treatment of osteoporosis, *Am. J. Med.* **94**, (1993), 656-660

[7] C. Cooper, G. Campion, and L.J. Melton, Hip fractures in the elderly: A world-wide projection. *Osteoporosis Int.* **2**, (1992), 285-289

[8] J. Magaziner, E.M. Simonsick, T.M. Kasher, J.R. Hebel, J.E. Kenzora, Survival experience of aged hip fracture patients. *Am. J. Public Health*, **79**, (1989), 274-278,

[9] E.A. Chrischilles, C.D. Butler, C.S. Davis, R.B. Wallace, A model of lifetime osteoporosis impact. *Arch. Intern. Med.* **151**, (1991) 2026-2032,

[10] C. Cooper, E.J. Atkinson, S.J. Jacobsen, W.M. O'fallon, L.J. Melton, Population-based study of survival after osteoporotic fractures, *Am. J. Epidemiol.* **137**, (1993), 1001-1005,

[11] P.C. Rambout, C.S. Leach, and G.D. Whedon, A study of metabolic balance in crew members of Skylab IV *Acta Astronautica*, **6**, (1979), 1313-1322

[12] F.E. Tilton, J.J. Degioanni, and V.S. Schneider, Long-term follow-up of Skylab bone demineralization *Aviat. Space Environ. Med.*, **51**, (1980), 1209-1213

[13] A.D. LeBlanc, V.S. Schneider, H.J. Evans, D.A. Engelbretson, and J.M. Krebs, Bone mineral loss and recovery after 17 weeks of bed rest. *J. Bone Min. Res.* **5**(8), (1990), 843-850

[14] C.A. Engh, J.D. Bobyn, and A.H. Glassman, Porous coated hip replacement: the factors governing bone ingrowth, stress shielding, and clinical results. *J. Bone Jt. Surg.*, **69-B**, (1987), 45-55

[15] J.O. Galante, Clinical results with the HPG cementless total hip prosthesis. In: Non-cemented total hip arthroplasty, Ed. by Fitzgerald, R., Raven Press, New York, 427-431, 1988

[16] A. Rosenberg, Cementless total hip arthroplasty: femoral remodeling and clinical experience, *Orthopaedics*, **12**(9), (1990), 1223-1233

[17] L.A. Feldkamp, S.A. Goldstein, A.M. Parfitt, G. Jesion, and M. Kleerekoper, The direct examination of three dimensional bone architecture in vitro by computed tomography. *J. Bone Min. Res.* **4**, (1989), 3-11.

[18] A. Odgaard, K. Andersen, F. Melsen, and H.J.G. Gundersen, A direct method for fast three-dimensional serial reconstruction. *J. Microscopy* **159**, (1990), 335-342.

[19] G.S. Beaupré, and W.C. Hayes, Finite element analysis of a three-dimensional open-celled model for trabecular bone, *J. Biomech. Eng.*, **107**, (1985), 249-256

[20] L.J. Gibson, The mechanical behavior of cancellous bone, *J. Biomech.* **18**, (1985), 317-328

[21] D.P. Fyhrie, M.S. Hamid, R.F. Kuo, and S.M. Lang, Direct three-dimensional finite element analysis of human vertebral cancellous bone. *Trans. 38th Ann. Meeting Orthop. Res. Soc.* 551, 1992

[22] S.J. Hollister, D.P. Fyhrie, K.J. Jepsen, and S.A. Goldstein, Application of homogenization theory to the study of trabecular bone mechanics. *J. Biomech.* **24**, (1991), 825-839.

[23] B. Van Rietbergen, H. Weinans, R. Huiskes, and A. Odgaard, A new method to determine trabecular bone elastic properties and loading using micromechanical finite-element models. *J. Biomech.*, **28**, (1995), 69-81

[24] B. Van Rietbergen, R. Huiskes, H. Weinans, A. Odgaard, and J. Kabel, The role of trabecular architecture in the anisotropic mechanical properties of bone, in Bone structure and remodeling (ed. by Odgaard, A. and Weinans, H.), World Scientific, Singapore, 1995

[25] B. Van Rietbergen, A. Odgaard, J. Kabel and R. Huiskes, Determination of tissue elastic properties by comparison of experimental and finite element results, *10th Conference of the ESB,* 327, 1996

[26] B. Van Rietbergen, A. Odgaard, J. Kabel, and R. Huiskes, Direct mechanics assessment of mechanical symmetries and properties of trabecular bone architecture. *J. Biomech.* **29**, (1996), 1653-1657

[27] B. Van Rietbergen, H. Weinans, R. Huiskes, and B.J.W. Polman, Computational strategies for iterative solution of large FEM applications employing voxel data. *Int. J. Num. Meth. Eng.*, **39**, (1996), 2743-2767

[28] B. Van Rietbergen, A. Odgaard, J. Kabel, and R. Huiskes, The inherent mechanical quality of trabecular bone architecture can be accurately predicted from fabric and apparent density, *Trans. 42nd Ann. Meeting Orthop. Res. Soc.* 82, 1996

[29] J. Kabel, B. Van Rietbergen, A. Odgaard, and R. Huiskes, Fabric and volume fraction can accurately predict mechanical properties for a wide range of trabecular architectures, *Trans. 43rd Ann. Meeting Orthop. Res. Soc.*, 1996 (accepted)

[30] H. Weinans, B. Van Rietbergen, A. Odgaard and R. Huiskes, Loss of trabecular bone strength due to small changes in bone mass, *Bone*, **19S,** 167S

[31] B. Van Rietbergen, H. Weinans and R. Huiskes, Trabecular bone quality measured from mechanical characteristics of trabecular architecture, *Bone*, **19S**, 166S