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Review Article

Tensile trabeculae - Myth or Reality?

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Abstract

Understanding of the functional role of the trabecular bone is very important for the analysis and computer-aided simulations of bone remodelling processes. The aspired wide clinical applications remain a remote future despite a great number of developed up-to-date approaches and theories and collected data on both material properties of the trabecular bone and its reaction to various stimuli. It is widely accepted that the mechanical loading plays the major role for the structure of the cancellous bone. The *in vivo* loading conditions of the cancellous bone are not known. Hence, for the computer-aided analysis and modelling of the trabecular bone specimens, simplified loading conditions are used. Also for the analysis of the cancellous bone as a part of a whole bone simplified loading conditions are assumed based on previous research without questioning its accuracy or relevance to the real *in vivo* conditions. In particular, the bending loading of the bone, which originates from the well-known observations made more than a century ago that have evolved in the trajectorial theory or "tensile trabeculae tradition", is often assumed to reflect the physiological loading conditions of bones. Some studies show that the bending or tensile-compressive orthogonal loading conditions for the cancellous bone may lead to plausible results. However, some other research works suggest that the presence of the tensile trabecular structures (particularly in the proximal femur) is doubtful and the bending loading conditions in bone should be treated with caution. Moreover, the loading conditions with compensated (or minimised) bending also produce results that correlate with the material distribution in the bone. The purpose of this review is to analyse some of the data and ideas available in the literature and to discuss the question of the major factors that define the shape and structure of the trabecular bone during the process of functional adaptation.

Keywords: Compressive Trabecular Structures, Bending-minimised Loading, Finite Element Analysis, Functional Loading of Trabecular Bone, Cancellous Bone Anisotropy, Compressive Loading of Bone

Material properties of cancellous bone

Understanding of the functional role of the trabecular bone is very important for the analysis and computer-aided simulations of bone remodelling processes. These simulations can find research and clinical applications in such fields as individualised fracture modelling and prognosis, simulation of implant osseointegration, development of the osteoporosis and its treatment, etc. The benefits for the patients and healthcare system rendered by the computer-aided analyses and simulations are beyond any doubt. Still the aspired wide clinical applications of the computer-aided simulations remain a remote future mainly because the modelling of the physiological loading conditions is an unsolved task. We review the collected data on material properties of the cancellous bone and its reaction to the mechanical stimulus and discuss several theories and modelling approaches.

The trabecular bone has been the most extensively investigated biological material using both experiment and computer simulations. On a tissue level (or material level), the elastic modulus of the trabecular bone material has been investigated in many studies (see the review by Guo[1] that compares the tissue mechanical properties of the cortical and cancellous bone). The elastic modulus of the trabecular bone tissue has often been suggested to be close to that of the cortical bone tissue[2,3], but "the exact values of modulus for cancellous tissue are still uncertain"[1].

However, modelling of the trabecular bone relevant for the orthopaedic research is done considering the bone on the continuum (or apparent) level. At this level, the trabecular bone is described by the material properties averaged over a charac-

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teristic bone volume omitting specific modelling of rods and plates composing the cancellous bone. A large selection of literature on trabecular bone properties on the continuum level is reviewed by van Rietbergen und Huiskes[4]. Based on the review, the mechanical behaviour of the cancellous bone can be described well as a linear elastic material characteristic for normal daily locomotion with strains not exceeding 3000 $\mu\varepsilon$ and at strain rates of the magnitudes of $10^{-3} – 10^{-1}$ strain per second. At such strain rates the contribution of the bone marrow to the stiffness as well as the viscoelastic behaviour can be neglected. The elastic behaviour of the cancellous bone can be modelled as anisotropic (requiring an experimental determination of 21 material constants), orthotropic (9 material constants), or isotropic (2 material constants). In general, cancellous bone is anisotropic. However, the limitations of the experimental studies cannot capture all required material constants.

Using micro finite element (μFE) method, some of the experimental limitations can be overcome. Using high resolution images of cancellous bone, finite element (FE) models of the complex trabecular structures can be generated and FE simulations of a real or imaginary experiment can be performed by applying corresponding boundary conditions to the FE model. Using μFE technique and applying homogeneous linear elastic and isotropic material properties, "it was found in many studies that, indeed, most of the anisotropy of cancellous bone at the apparent level is due to its trabecular structure only"[4]. Cancellous bone is often assumed to have orthotropic properties based on the observation that the trabecular structures can be described by a second-rank fabric tensor. Van Rietbergen and Huiskes review several studies that support the orthotropy assumption based on the μFE results. In particular, in the study by Odgaard et al.[5] the close alignment of the principal directions of mechanical properties form μFE analysis and fabric directions from morphometry analyses was found. On the one hand, this means that the orthotropic representation of the stiffness matrix of the cancellous bone gives a good approximation of the material properties of the bone. On the other hand, this offers a means to extract material properties of cancellous bone form the imaging data. But it also reinforces the idea of the interdependence of the structural and material properties of the cancellous bone, which is connected to the idea that the distribution of bone material serves primarily the mechanical purpose.

Martin gives an overview of the multi-functionality of the bone as a tissue and an organ[6]. Although the bone may be considered as a reservoir of minerals (essential e.g. for muscle function), bone in vertebrates is primarily a mechanical organ. Thus, the structure of bones is guided by the minimisation of the bone weight and maintaining weight-bearing ability regardless of the animal size. The metabolic processes and the substances such as hormones may accelerate or decelerate the remodelling processes in bone but the remodelling is guided primarily by the mechanical stimulus. Thereby the mechanism of the bone remodelling is discussed as a crucial phenomenon serving the two purposes of optimally adjusting the bone geometry to the mechanical loads and repairing the microscopic damage due to these loads.

Motivated by the findings of several authors who demonstrated a linear relationship between the Young's modulus of the cancellous bone and the yield strength, Turner investigated the hypothesis that "cancellous bone alters its structure to maintain uniform, isotropic peak strains"[7]. He evaluated the relationships between mechanical properties of cancellous bone and trabecular architecture using previously collected data for bovine bone and found that over 90% of the variance in yield strength and 70-78% of the variance in Young's modulus can be explained by the combination of the apparent density and the normalized anisotropy constant. Therefore, the trabecular architecture seems to be determined by the distribution of the peak principal stresses in the cancellous bone: "the anisotropy of fabric must exactly cancel the anisotropy of the peak principal stresses imposed upon cancellous bone", in order to reach the goal of cancellous bone adaptation[7]. A comparison of this bone adaptation hypothesis to the hypotheses based on the strain energy density as a major adaptation stimulus was also given.

An experimental study of the failure mechanisms of trabecular bone can shed some light on the question of the bone function. Fyhrie and Schaffler applied compressive loads to cube-shaped specimens of cancellous bone harvested from human lumbar vertebrae in the main loading direction of the bone[8]. In their study, high compressive strain of 15% was applied in the anatomical direction in order to achieve certain failure. The strain value significantly exceeded the previously reported failure strain of trabecular bone (2-3%). As a result, a complicated failure pattern was observed at the microscopic level. As reported in this study, the trabeculae oriented in the main loading direction have suffered damage to the bone matrix but "retained their shape and general architecture". In contrast, the trabeculae oriented transversely to the main direction of the loading direction suffered an overt fracture. Such a loss of structural integrity leads not only to the loss of the load bearing function by these trabeculae but also to the interruption of the nutrients supply to the vital tissue and must be followed by a rapid resorption. These experimental findings of Fyhrie and Schaffler are supported by the observations of Mosekilde who analysed the trabecular structures using scanning electron microscopy[9]. For this study the specimens were obtained from a central part of lumbar vertebrae of normal human subjects (26-90 years old), cleaned from marrow, and prepared so that no organic bone material was removed. In this study the evidence of the formation of small calluses around some vertical trabeculae was presented indicating the damage repair process. These trabeculae were oriented in the main loading direction of the vertebrae and were mostly found in older subjects presumably overloaded in old osteoporotic subjects. Disconnected trabeculae were oriented horizontally (transversal to the main loading direction). In the disconnected trabeculae an "aggressive" osteoclastic resorption was observed. Both these studies reflect the complicated failure pattern in the cancellous bone, which is crucial for the maintenance of the cancellous bone structure, and reveal the mechanisms, by which high compressive loading can be withstood by the cancellous bone without a significant loss of the functionality.

Thus, putting together the remarkable remodelling ability of bone, the inner structure of cancellous bone closely adapted to its loading, the failure mechanisms, and failure repair mechanisms of the trabecular bone, we can derive the functional loading of the bone in accordance with its mechanical function of weight-bearing. Indeed, knowing the material properties of the cancellous bone and its architecture we can conclude about the major loading, which the bone was adapted to. This becomes more transparent if the comparison with the design of a technical structure is made. For a technical structure the material properties and the loading conditions determine its structural design. Reversely, the loading of the light-weight structure of bone can be determined by the properties of the bone and its architecture taking into account its remodelling ability. In the following hypotheses and problems with the determination of the loading conditions for the modelling of cancellous bone and the bone remodelling processes are discussed.

Functional loading of cancellous bone

As seen from the studies reviewed in the previous section, it is well established that the structure of cancellous bone is adapted to its mechanical function. This notion is of particular importance for the medical or research applications because it can be used to model biological processes in bone using the FE method, for example, in osteoporosis research or in preoperative analysis of prostheses integration. Due to the recent developments, the FE method became numerically very accurate with broad possibilities of generating complex geometries. However, in order to arrive at a reasonable computational model of cancellous bone remodelling, one has to specify this mechanical function accurately and derive some numerically accessible remodelling criteria that correspond to the mechanical function.

Several FE-oriented theories that try to relate mechanical stimuli to the adaptation of the bone inner structure or density distribution[10] and of the bone shape[11] have been suggested. The exact mechanical stimuli triggering the bone remodelling and tissue differentiation are still under discussion in the biomechanics community. Two major concepts of bone remodelling have been suggested: strain-adaptive and damage-adaptive bone remodelling. The strain-adaptive remodelling theories relate the local strain in the bone to the local density of the bone material or to the geometry of the bone. Thereby, the strain-based remodelling stimulus can be formulated based on the local strain, strain energy density, von Mises stress, effective, or energy stress. Initially, the role of the remodelling stimulus transducer was assigned to the bone lining cells that can be transformed into osteoblasts or osteoclasts. Recent studies show that the bone remodelling can be controlled also by the nervous system[12,13]. The damage-adaptive remodelling theories relate fatigue damage accumulation in the bone to the remodelling stimulus. On the basis of the two bone remodelling concepts, a combined strain and micro-damage remodelling algorithm has been proposed recently[14].

The nature of the mechanoregulation models on the basis of the mechanobiological studies is phenomenological. For example, Huiskes and co-authors have proposed a theoretical framework for strain-related trabecular bone maintenance and adaptation and tested it in a 2D model[15] and in a 3D model[16]. In these works the strain energy density (SED) is used as a measure of the remodelling stimulus for the bone trabeculae. In the mathematical formulation several other parameters and coefficients are also included that weight SED and determine the time dependence of the remodelling process. Initial trabecular bone model consists of a fine regular orthogonal grid of isotropic homogeneous material (in the 2D model it forms a square-shaped structure and in the 3D model – a cube). According to the remodelling procedure, the material is loaded in compression in the vertical direction and in tension in the transversal direction(s). The magnitudes of the cyclic compressive and tensile loads are the same. Note that SED is insensitive to the sign of the local stress or strain value (conventionally positive for the tensile and negative for the compressive stress/strain). The FE simulation arrives at a homeostatic state with a grid that is coarser than the initial one. This coarse grid resembles however the initial orthogonal configuration of the "tensile" and "compressive" trabeculae in the horizontal and vertical directions correspondingly. Some irregularity of the grid, which is evident in the homeostatic state, appears probably due to the mathematical formulation of the osteoclastic activity using a stochastic function. The reaction to the changed loading is also investigated. Uniformly reduced loads led to the uniform thinning of the trabeculae. A uniform change to the load application directions (the applied tensile and compressive loads remained orthogonal) led to the corresponding reorientation of the trabecular grid. A reduction of the load in the transversal directions led to the formation of the anisotropic configuration with only a few transversal trabeculae.

The results of the discussed model show that this simple model can be tuned to show any desired remodelling pattern within the framework by an appropriate adjustment of both the parameters of the mathematical formulation and loading conditions. However, the results seem to be an artefact of the model: for example, the same results of the coarse grid could be obtained assuming only tensile loading in both orthogonal directions or only compressive loading in both directions. Also, this model is very difficult to tune for the prediction of the real anisotropy of the cancellous bone under physiological conditions (especially keeping in mind the fact that the physiological loading is not really known) and capture the variety of the patterns in the structure of the cancellous bone. In the discussed framework an assumption of the trajectorial theory is made a priory that the trabecular structures appear on the orthogonal patterns of tensile and compressive stresses.

Another example of the computer simulation of trabecular bone remodelling consistent with the idea of the existence of tensile and compressive trabeculae is presented in studies by e.g. Tsubota et al.[17,18] In this study von Mises equivalent stress was used as a driving force for the surface remodelling of the trabeculae in the proximal femur. As a representative daily loading condition three load cases were adopted from an older study by Beaupre et al.[19]. The loading conditions were formulated in accordance with the “bending bone belief” disregarding the compensation of bending loading by muscles. The stochastic component was included in the model during the initial stage of the modelling when “the cancellous bone part was filled with a random pattern of circular trabeculae”. The results obtained by Tsubota et al. show anisotropic trabecular structures appearing due to three different loading conditions in 2D and 3D models and also due to a combination of the loading conditions. However, the results of this study show inconsistency with the proposition that the marked trabecular structures in the trochanter major region are the tensile trabeculae. The true tensile trabecular structures in both 2D and 3D models appear in the proximity of the superior trochanter major where the abductor muscle forces are applied. In region 3, where the “tensile trabeculae” are supposed to be according to the proposal of the trajectorial theory, the tensile loading appears only for loading case of the extreme abduction.

These biomechanical studies use mechanical stimuli modelled by simplified or generalised mechanical loading and have drifted away from the issues of the real loading environment of the tissues within the biological structures at the macro-level such as bones in the musculoskeletal system. Thereby, the question of the loading macro-environment of bones plays an important role in modelling and simulation of osteogenic processes, especially in considerations of complex processes such as osseointegration of an implant under complex loading conditions during everyday locomotion. Indeed, the loading on the macro level provides the mechanical environment for bone adaptation and remodelling processes.

The question of the bone loading in the musculoskeletal system has not been unambiguously answered. There have been two opinions regarding the physiological loading of bones. One of them states that bending is the main loaded state of long bones. Bending and tension are also considered to be a stimulus for bone remodelling shown in experimental studies. For example, the work by Liskova and Hert is often cited as an evidence of bone formation under tension as well as under compression[20]. They applied cyclic bending to rabbit tibias for certain limited time during the day and found the extensive new bone formation on both tensile and compressive sides of the bone. However, they also showed that on posterior and anterior sides (in the neutral plane of the bending) of the loaded tibias of rabbits, there is a 9-16% decrease of cortical bone thickness. According to their drawings, the control tibias have balanced an increase of the cortical thickness. Note that most of the test animals (65 out of 70) in the study were young growing animals; some animals were excluded from the data analysis, it is not indicated if they were young or adult. The “bending bone belief”[21] originates form the “obvious” resemblance of the trabecular structures in proximal femur with the principal stress trajectories in Cullmann’s crane reported by Wolff over a century ago[22]. In the trajectorial theory, the fine trabecular structures in the cancellous bone are interpreted as tension and compression patterns crossing at right angles. Since then, many investigations, in particular of proximal femur, showed that the trabeculae may cross at different angles and hence do not correspond to the principal stress lines[23-25]. Many authors have doubted the presence of tensile stresses in the femoral neck[23,25-27].

The alternative opinion states that, due to the light-weight design principle, the bones are built to carry mainly compressive loading whereas ligaments and muscles take over the tensile loading (see review[21] for details and more references). Bending compensation provided by the soft tissues leads to the significantly reduced stress level in bone cross-sections and more uniform stress distribution. The uniform stress distribution means balanced loading of the bone during every particular loading conditions and absence or only a minimised amount of unloaded bone, which is practical and economical from the point of view of nourishment and energy required for locomotion[6].

Mostly compressive loading of bones in physiological loading conditions

From the point of view of mainly compressive loading, bones are adapted to bending loading by avoiding it. Pauwels described four ways, in which the bone adapts to be not subjected to bending and tension[28]: tension cording, spontaneous adjustment of posture (transferring the centre of gravity over the supporting limb), distribution of the material in the bone cross-section (growth of the bone in width, as he called it), and adjustment of the shape of the bone (growth of the bone in length, as he called it). Frost’s Mechanostat theory[29] follows the same path concerning the structural adaptation of bones. Bending initiates bone remodelling processes that result in compressive structures. The four ways of bone adaptation to avoid bending are applied continuously and simultaneously during the function of the locomotion system. The result seen in the CT images of bones is the product of these adaptations up to the point in time when the CT was done. This means that the bone available for the consideration is optimised in terms of shape and structure for certain loading conditions in which in which the bending loading is compensated by the muscles.

In order to test the hypothesis of minimisation of bending loading (compensation of the tensile loading) of bones through the muscular action, a 3D FE model[21] of a human femur was generated based on a set of CT data. The model was minimally constrained in order to ensure physiological loading conditions. The muscle forces for a human femur during normal gait and sitting down (peak hip joint forces) were obtained such that the bone is loaded predominantly in compression. The obtained values of muscular forces were found to be in the physiological range. Based on the premises of bones being “predominantly compressive structures”, the obtained results showed that a tensile-stress-free loading leads to the significant reduction of the stress level in the bone and the stress distribution in the bone corresponds to the material distribution in cortical and in cancellous bone. This conclusion was based on the analysis of the compressive stress distribution in femur for two physiological loading conditions[21].

In particular, for the cancellous bone it was found that the pat-

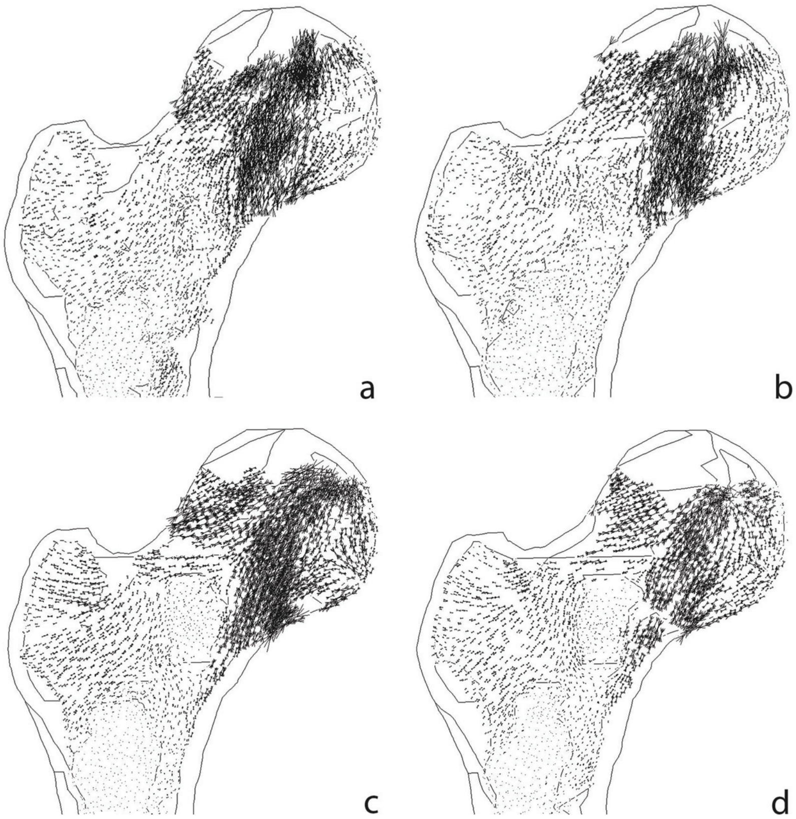

Figure 1. Vector plot of the third principal stress in the cancellous bone of the proximal femur – frontal cross-sections: every cross-section plot is obtained by selecting a 0.8 mm thick slice of nodes; the nodes at the very top of the femoral head are unselected for this representation, to reduce artefacts due to the nodal application of the loads to the model; not to scale; **a, b** cross-sections near the femoral head centre 6mm apart correspond to the load case during normal gait; **c, d** cross-sections near the femoral head centre 6mm apart correspond to the load case during sitting down.

terns of the higher compressive stresses agree with the concentration of the trabecular structures in bone. This can be seen explicitly in the vector plots of the third principal stress in cancellous bone in the frontal (Figure 1) and in transversal (Figure 2) cross-sections of the described 3D FE model. In these plots the qualitative picture of the compressive stress patterns due to the bending-minimised load cases is shown (for the quantitative stress distribution see the contour plots in the review[21]). In the frontal cross-sections (Figure 1), one can see a marked compressive structure in the region of the medial group of trabeculae (according to Ward's classification as used by Whitehouse and Dyson[25]) with no qualitative difference between the two load cases. Clearly they reflect the main load bearing direction. The lateral group of trabeculae (according to Ward's classification as used by Whitehouse and Dyson[25]) is described as the trabecular structures along the upper cortical wall of the femoral neck springing from the structures along the epiphyseal scar in the femoral head and flowing into the lateral part of the intertrochanteric arches. In these regions, the two load cases produce two distinct patterns of the compressive stresses. In the upper plots for the gait the compressive stress vectors are parallel to the cortex of femoral neck (Figure 1 a, b) and in the lower plots for sitting down the stress vectors are oblique to the cortex of femoral neck (Figure 1 c, d). This may explain the findings by Whitehouse and Dyson[25] that the trabeculae in this region "were seen to vary in character from place to place", which "suggests that the word 'lateral' should be used in a geographical sense, referring to a region in the bone and not to a coherent structural system of trabeculae". The variation in the trabecular structure may have been dictated by its functional loading during different load cases and variation of the load-bearing direction. Thus, the resulting trabecular structure is a superposition of the structures, which fulfil the compressive load bearing function for every single load case.

The same structural superposition is evident in the transversal plots (Figure 2). According to the obtained FE results, the loading during gait leads to the preferred anterior-posterior direction of the formation of the trabeculae in the region of trochanter major (Figure 2a). In the corresponding cross-section during the sitting down (Figure 2c), the loading pattern of the trabeculae in the medial-lateral direction is emphasised. In the region of trochanter minor (Figure 2 b, d), differences in the compressive vector orientation is also present. This result shows a clear correlation to the anatomical structures observed in human bones and provides a biomechanical explanation for the anisotropic trabecular architecture of the proximal femur.

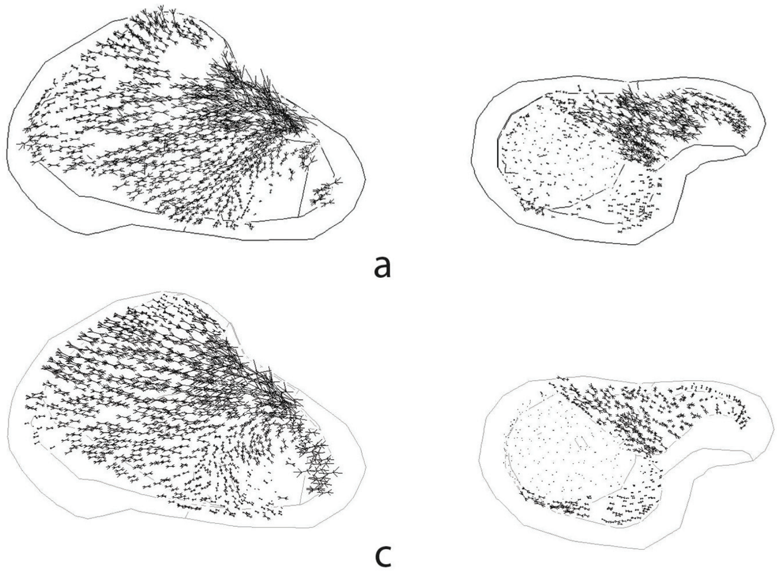

Figure 2. Vector plot of the third principal stress in the cancellous bone of the proximal femur – transversal cross-sections at the level of trochanter major (**a, c**) and trochanter minor (**b, d**): every cross-section plot is obtained by selecting a 0.8 mm thick slice of nodes; not to scale; **a, b** cross-sections correspond to the load case during normal gait; **c, d** cross-sections correspond to the load case during sitting down.

In summary, the comparison of the two load cases, which were obtained based on the bending minimisation principle, reflects the close interplay of the physiological loading and the bone structure postulated above. The functional loading and the bone structure are the two integral parts of the whole musculoskeletal system and the physiological superposition of all load cases contributes to the structure of the cancellous bone.

Conclusion

Currently, there is no agreement on the fundamental bone-remodelling signal, other than it is a "mechanical stimulus". The well-documented remodelling that was detected in laboratory conditions in numerous animal experiments, for sportsmen, and astronauts are examples of the functional adaptation. Bone tissue can withstand both tension and compression and remodelling processes have been observed under the tensile and compressive loading. Consequently, bending has been widely accepted as a physiological loading of bone. However, the bones of ordinary people with more or less stable daily activities are also the results of the functional adaptation.

In our research the physiological loading of bones is defined as a normal every-day loading, which the bone is adapted to and which causes a physiological stress distribution with minimised amount of unloaded or under-loaded material (the loading is evenly distributed throughout the structure). This definition is based on the widely accepted view that biological systems are optimised light-weight structures. It takes into account that the bone needs a functional stimulus in order to not only adjust its structure to the changing loading but also to sustain it during the steady state remodelling. In the optimised light-weight skeletal structures of highly mobile animals and humans the bending loading of bones (with its inherent variation in stress) is avoided/compensated for. It does not exclude occasional bending but "predominantly compressive" loading means that the stimuli of this occasional loading are not consistent or prolonged enough in the considered physiological case, otherwise they would lead to a different structure as shown by numerous *in vivo* experiments, in which bone remodelling is evoked by the experimental loading conditions that are new for the bone.

This definition of the physiological loading is taken as the basis for the determination of the loading of a musculoskeletal system[21] and the predominantly compressive loading for a human femur was obtained for two loading conditions. The FE results show that the compressive stress distribution in the bone corresponds to the material distribution. In particular for the cancellous bone of the proximal femur, the vector plots of the third principal stress correlate with the trabecular directions in the cancellous bone. Moreover, the results indicate the marked differences between compressive stress patterns for the different load cases. These may be considered as the different principal directions of the load-bearing trabecular structures. The anisotropic structure of cancellous bone may be explained by the superposition of these directions for different daily activities. Thus, the irrefutable fact that the musculoskeletal system is optimised as a light-weight structure provides a major argument for the point that the trabecular bone formation takes place on the pathways of the compressive stresses.

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