

# Tissue level microstructure and mechanical properties of the femoral head in the proximal femur of fracture patients

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**Abstract** This study aims to investigate the regional variations of trabecular morphological parameters and mechanical parameters of the femoral head, as well as to determine the relationship between trabecular morphological and mechanical parameters. Seven femoral heads from patients with fractured proximal femur were scanned using a micro-CT system. Each femoral head was divided into 12 sub-regions according to the trabecular orientation. One 125 mm<sup>3</sup> trabecular cubic model was reconstructed from each sub-region. A total of 81 trabecular models were reconstructed, except three destroyed sub-regions from two femoral heads during the surgery. Trabecular morphological parameters, i.e. trabecular separation (Tb.Sp), trabecular thickness (Tb.Th), specific bone surface (BS/BV), bone volume fraction (BV/TV), structural model index (SMI), and degree of anisotropy (DA) were measured. Micro-finite element analyses were performed for each cube to obtain the apparent Young's modulus and tissue level von Mises stress distribution under 1 % compressive strain along three orthogonal directions, respectively. Results revealed significant regional variations in the morphological

parameters ( $P < 0.05$ ). Young's moduli along the trabecular orientation were significantly higher than those along the other two directions. In general, trabecular mechanical properties in the medial region were lower than those in the lateral region. Trabecular mechanical parameters along the trabecular orientation were significantly correlated with BS/BV, BV/TV, Tb.Th, and DA. In this study, regional variations of microstructural features and mechanical properties in the femoral head of patients with proximal femur fracture were thoroughly investigated at the tissue level. The results of this study will help to elucidate the mechanism of femoral head fracture for reducing fracture risk and developing treatment strategies for the elderly.

**Keywords** Femoral head · Trabecular bone · Morphological parameters · Micro-finite element analysis · Apparent level · Tissue level

## 1 Introduction

Osteoporosis is one of the most common age-related diseases, often resulting in high rates of morbidity and mortality in the elderly population. Clinical symptoms of osteoporosis include thinner, easily broken, and lower volume of trabecular bone. The most serious consequence of osteoporosis is fracture as a result of greatly reduced bone strength [1–5].

The main determinants of bone strength include bone mineral density (BMD), bone mass, and microstructure [6–10]. In clinics, dual energy X-ray absorptiometry (DXA) is typically used to measure BMD for the diagnosis of bone quality [11]. However, DXA data cannot reflect the three-dimensional BMD information inside bones due to its planar images and low resolution [12–16]. Mechanical tests can

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only be performed for one time due to the destruction of samples during the test process. Alternatively, mechanical tests on a sample can be simulated by finite element analyses under different loading conditions without performing actual experiments. Trabecular microstructure is an important factor affecting bone strength. Trabecular microstructure in the target regions can be reconstructed accurately with a micro-CT system [17–20]. The tissue level mechanical properties of the trabecular bone inside the proximal femur can be accurately determined by micro-CT imaging-based micro-finite element analysis ( $\mu$ FEA).

Significant regional differences in proximal femoral trabecular morphology were found according to the micro-CT images. Measurements of cadaveric healthy Caucasians, aged 26–96 years, revealed that bone volume fraction (BV/TV) decreased, whereas the structural model index (SMI) significantly increased with aging in the regions of the femoral neck and the greater trochanter [21]. The increase in SMI, which indicates the transformation of the trabecular morphology from plate-like to more rod-like, could reflect low trabecular strength. Thus, the mechanical properties deteriorated. Significant differences in BV/TV, SMI, Tb.Sp, Tb.Th, and Tb.N between the medial and lateral femoral necks were found [15]. A study by Ascenzi et al. [22] suggested that trabecular thickness (Tb.Th) and specific bone surface (BS/BV) change significantly at the greater trochanter in healthy postmenopausal Caucasian women aged ranging from 52 to 77 years old. More discrete Tb.Th was found in the lower trochanter than in the upper trochanter. A study by Cui et al. [23] reported significant differences in BV/TV, Tb.Th, trabecular separation (Tb.Sp), trabecular number (Tb.N), and degree of anisotropy (DA) between the superior and inferior necks, as well as between the superior and inferior greater trochanters. The male cadaver donors were in the age range of 40–90 years without a history of musculoskeletal diseases [23]. Compression tests were conducted on cylindrical bone specimens from the femoral head, femoral neck, and Ward's triangle to determine the regional strength distribution of the trabecular bone within the proximal femur [14]. Significant differences were found in stiffness between the femoral head, femoral neck, and Ward's triangle as well as in Young's modulus between the femoral head and Ward's triangle [21].

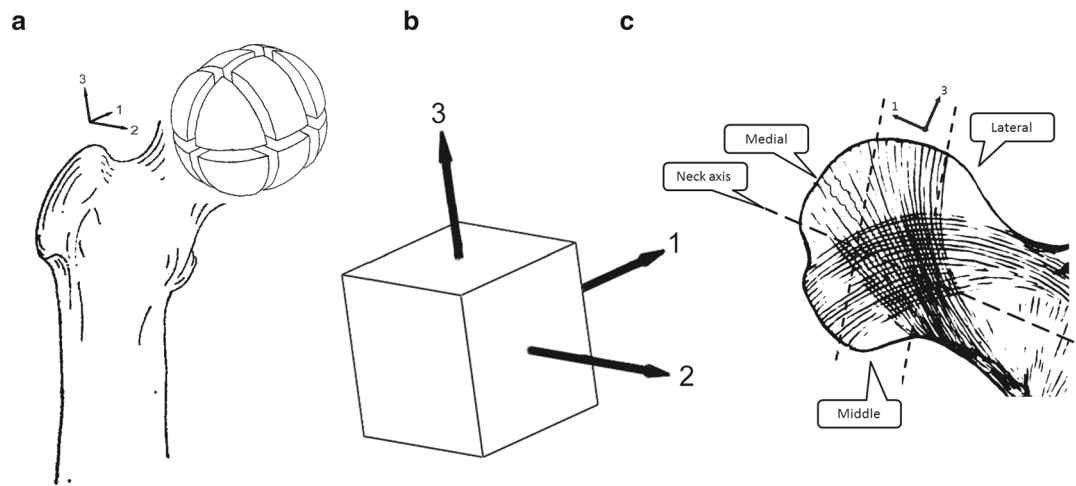
Although most studies focus mainly on femoral neck fracture, a high incidence of femoral head fracture also exists [24]. Knowledge about the microstructural degeneration of the femoral head may help elucidate the mechanism of fragile fracture as well as the trabecular morphologies and the mechanical properties of the femoral head. However, reports on the regional differences of microstructures and mechanical properties of the femoral head from proximal femoral fracture patients are few.

This study aims to determine the regional differences in trabecular morphological parameters of the femoral heads of patients with proximal femur fracture, as well as the apparent and tissue mechanical parameters under compressive loading conditions using  $\mu$ FEA. Consequently, the relationship between the trabecular microstructural characteristics and mechanical properties in fractured elderly patients can be determined. This study helps elucidate failure mechanisms of the trabecular bone within the proximal femur.

## 2 Materials and methods

Seven femoral heads from two male and five female Chinese patients were harvested by total hip arthroplasty surgeries in No. 1 Hospital of Jilin University (China). All patients had non-impact proximal femur fractures. The ages of the patients were  $80 \pm 6$  years, ranging from 72 to 88. The femoral heads were kept fresh by freezing in air-evacuated bags at  $-20^{\circ}\text{C}$ . Written informed consent to participate in this study was obtained from each enrolled patient. The ethical review committee of No.1 Hospital of Jilin University approved the conduct of the study and the procedure consent (No. 2012-064).

A micro-CT system (Skyscan 1076, SKYSCAN, Belgium) was used to evaluate the microstructure of the femoral heads. Localization of femoral heads was based on the femoral head axis that was determined by the fovea of the femoral head and the center of the femoral neck. The femoral head axis was parallel to the axis of the sample support. Each femoral head was scanned continuously at increments of  $38\ \mu\text{m}$  for 900 slices. The voxel size was  $38\ \mu\text{m} \times 38\ \mu\text{m} \times 38\ \mu\text{m}$ . Voltage and current sources were set to 79 kV and  $125\ \mu\text{A}$ , respectively. Each femoral head was divided into three regions along the femoral head from the fovea of the femoral head to the femoral neck, that is, medial region, middle region, and lateral region. Consequently, each region was divided into four sub-regions according to the horizontal plane and the coronal plane. Regional division is shown in Fig. 1a and 1c. A  $5\ \text{mm} \times 5\ \text{mm} \times 5\ \text{mm}$  cubic trabecular from the fovea of the femoral head to the femoral neck was reconstructed from each sub-region in the micro-CT images. The position of each model was determined such that at least one surface of the cube was perpendicular to the trabecular orientation. Two femoral heads could not be preserved intact during surgery, resulting in three broken sub-regions. Hence, a total of 81 trabecular bone models were reconstructed from seven femoral heads. Six morphological parameters of the trabecular bone were measured for each cubic bone model including Tb.Sp, Tb.Th, BS/BV, BV/TV, SMI, and DA [22–25].

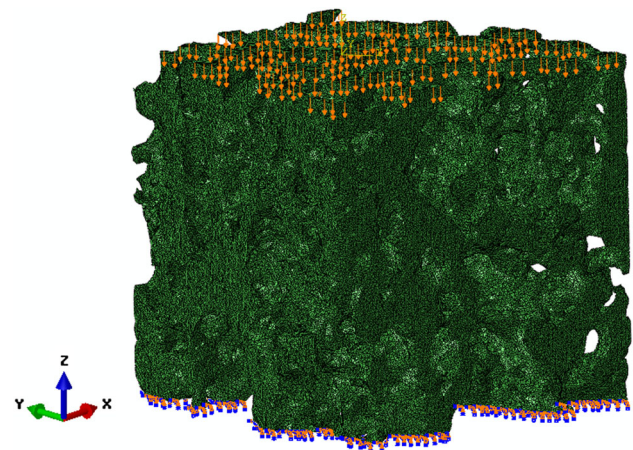


**Fig. 1** Regional division of a femoral head. **a** Segmentation method for a femoral head. **b** Definition of direction of bone blocks. **c** Front view of femoral head. The femoral head was divided into three regions according to trabecular orientation, namely, medial, middle, and lateral regions. Two beams of trabeculae were separated in the medial and lateral regions. The middle region is the cross structure of two beams of trabeculae. Each region was divided into four sub-regions. A whole femoral head was divided into 12 sub-regions, and one cubic bone model was extracted from each sub-region

Compression tests were simulated using  $\mu$ FEA in ABAQUS 6.11 (Dassault Inc.) along the three orthogonal directions of the bone cubes, respectively. Direction 1 was defined as the trabecular orientation, and direction 2 was defined as the direction that was perpendicular to the coronal plane. The remaining direction, orthogonal to direction 1 and direction 2, was defined as direction 3 (Fig. 1b). All cubic bone models were meshed with tetrahedral elements with sizes of 0.04–0.07 mm. The element numbers of the models ranged from 983119 to 3638354. The relationship between bone density and the grey value of the images can be determined by the calcium hydroxyapatite phantom of the micro-CT device. Models were conferred non-uniform linear elastic material properties by Young's moduli calculated from the grey values of the micro-CT images. Each element with a modulus below 5 MPa was assigned a modulus of 0.01 MPa (almost air) [26]. Given that a Young's modulus of 15 GPa contained almost all the bone materials, the remaining element moduli were grouped, requiring an adjustment of no more than 5 % for the moduli of every two adjacent groups. Approximately 174 modulus values were obtained [22,26]. The relationship between Young's modulus and trabecular density is shown as follows [27,28]. A constant Poisson's ratio of 0.3 was assumed [29].

$$E = \begin{cases} 6850 \times \rho^{1.49}, & \rho \leq 1.68 \\ 4293 \times \rho^{2.39}, & \rho \geq 1.68 \end{cases} \quad (\text{MPa}).$$

One percent strain was exerted on one surface of each bone cube along direction 1, with the opposite surface fully fixed [13]. The same condition was exerted along direction 2 and direction 3, respectively. A total of 243  $\mu$ FEAs were



**Fig. 2** A typical micro-finite element model of a trabecular bone cube from the middle region of the femoral head with boundary and loading conditions. One percent compressive strain was exerted on a surface, and the parallel surface was fully fixed. The orange arrows in the figure indicate loading points and directions. The loading directions refer to the local coordinate system that was set on the model surface. The pink signs indicate the fully fixed degree of freedom

conducted for 81 trabecular bones. Figure 2 shows an example of one finite element model of one cubic bone in the middle region with a loading direction in the trabecular orientation and boundary condition. Mechanical parameters under the compressive loading conditions along the three orthogonal directions were calculated including apparent Young's modulus and average tissue von Mises stress. The average von Mises stress of one trabecular bone specimen reflects its load-bearing capacity as a whole.

The regional differences in trabecular morphological parameters and mechanical parameters were analyzed. Considering that the distribution of parameters was unknown, non-parametric tests were performed for the differences among the parameters. Two independent sample non-parametric tests (Mann–Whitney U method) were performed to analyze the trabecular morphological differences in Tb.Sp, BS/BV, BV/TV, Tb.Th, SMI, and DA between each two regions. The same tests were also performed to analyze the regional differences in mechanical parameters along the direction 1 loading condition. In addition, the same tests for direction 2 and direction 3 loading conditions were conducted, respectively.

Multi-related sample non-parametric tests (Friedman method) were performed to analyze the differences in mechanical parameters under compression along the three orthogonal directions. When significant differences were found, two-related sample non-parametric tests (Wilcoxon method) were performed for each two directions.

Bivariate correlation tests (Pearson method) were performed to analyze the relationships between morphological parameters and mechanical parameters. All statistical analyses were performed using SPSS 17.0 (IBM Inc., USA), with a significance level of 0.05.

### 3 Results

The basic description of trabecular morphological parameters and mechanical parameters from proximal femoral fracture patients are shown in Fig. 3. DA and Tb.Th increased and BS/BV decreased from the medial to the lateral regions. SMI and BV/TV in the middle region were significantly higher than in the medial region, but the opposite trend is observed for Tb.Sp ( $P < 0.05$ ). Apparent Young's modulus and average tissue von Mises stress along direction 1 showed significant increase in strength from the medial to the lateral regions.

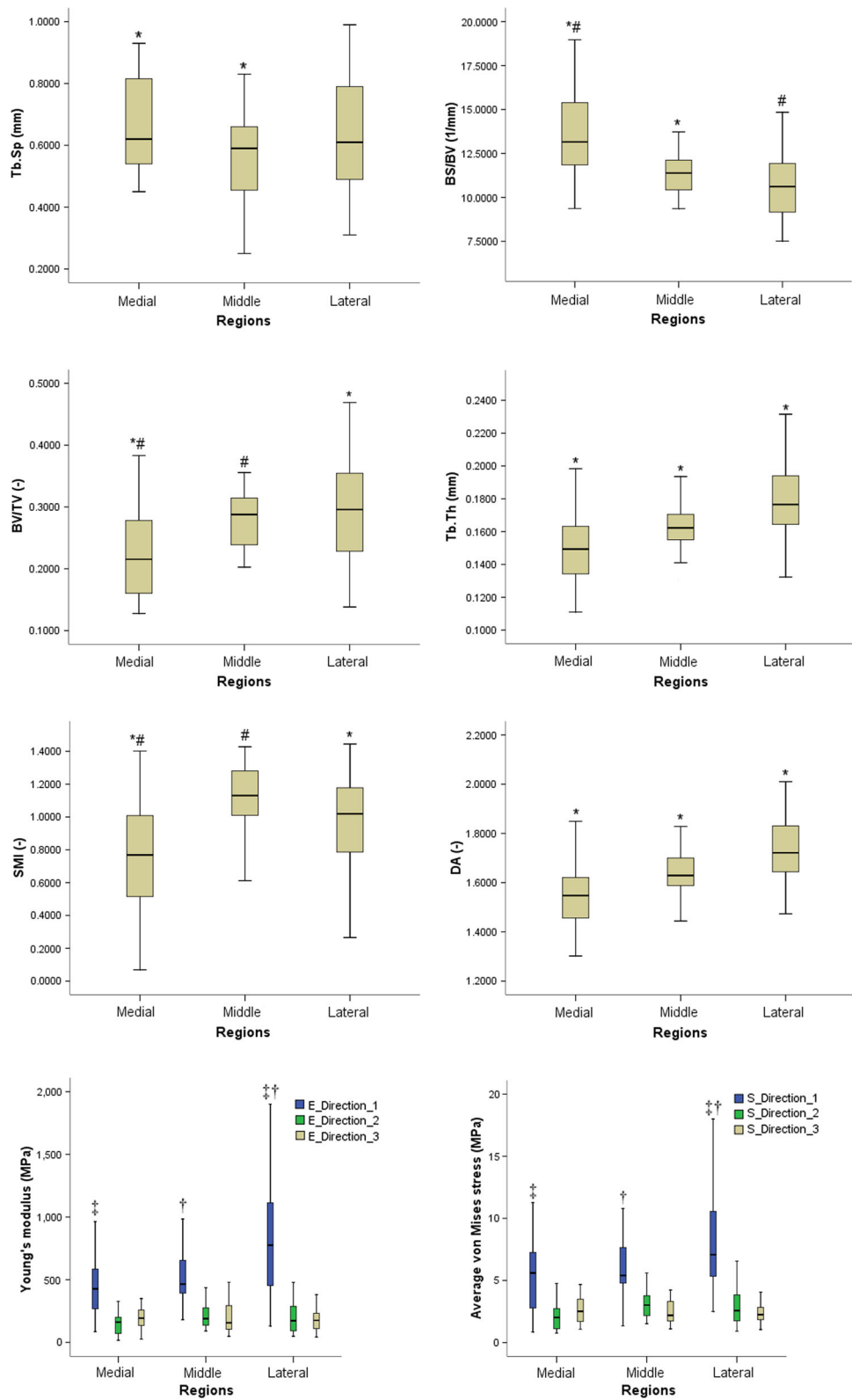
Morphological characteristics of trabecular bones in three typical regions and their von Mises stress distribution when loaded along the direction of trabecular orientation are shown in Fig. 4. Results showed that the bone in the lateral region was mainly composed of thick and plate-like trabeculae along the direction of trabecular orientation. Trabecular bone along the coronal axis was seriously degenerated and mainly composed of rod-like trabeculae. Many unconnected trabeculae were from the cross structures in the middle region. Trabecular bone in the medial region was mainly composed of plate-like structures along all directions. The plate-like trabeculae bore the most loads when 1 % compressive strain was exerted along direction 1, with an average von Mises stress of 8.1 MPa. Trabecular stresses in the medial region were

more evenly distributed compared with those in the lateral region, with an average of 4.92 MPa.

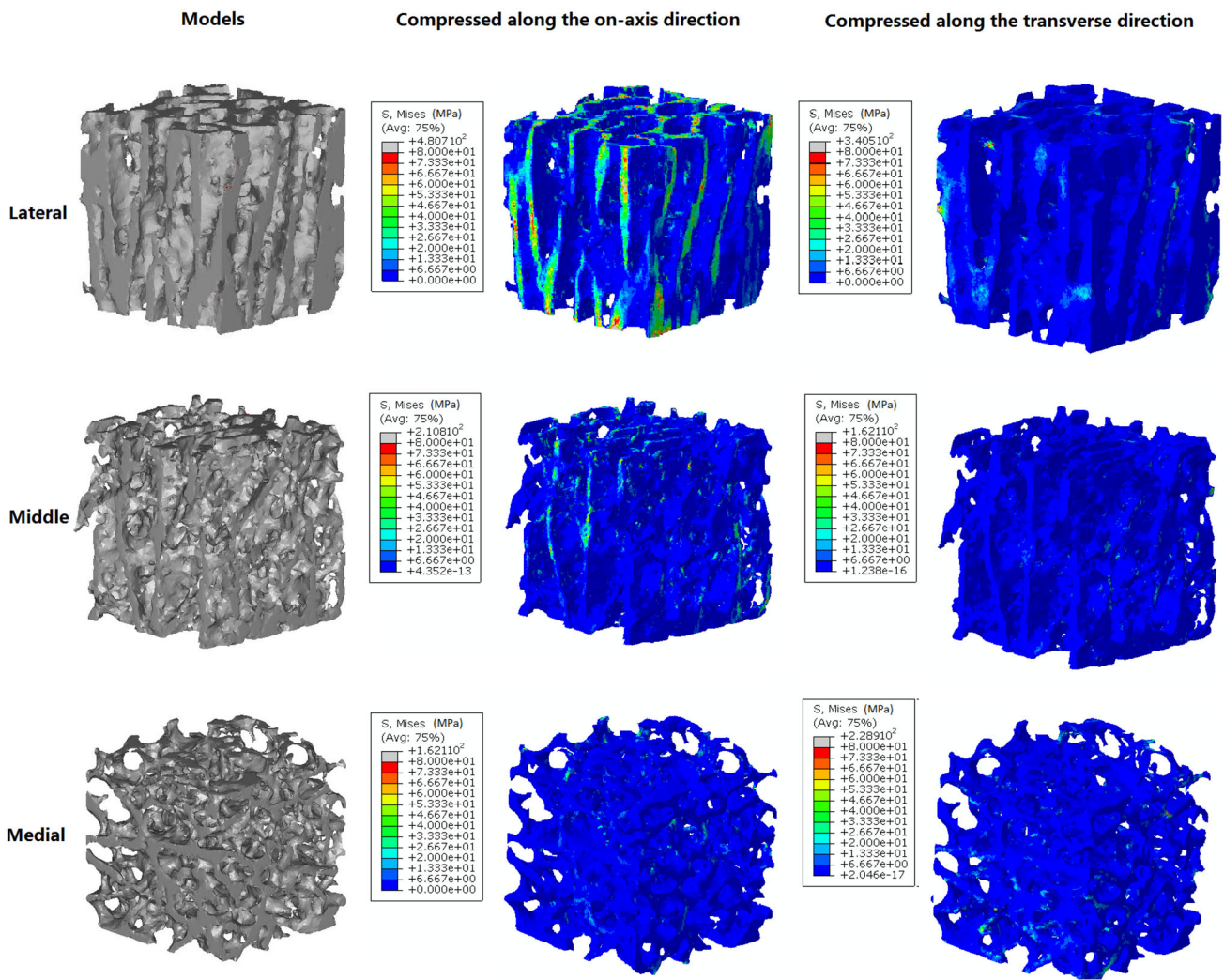
Two independent sample non-parametric tests (Mann–Whitney U method) were performed to analyze regional differences in all morphological parameters and mechanical parameters along the three orthogonal directions (Fig. 3). All morphological parameters in the medial region were significantly different from those in the middle and lateral regions, except Tb.Sp. Significant differences in Tb.Sp only existed between the medial and the middle regions. Morphological parameters in the lateral region were similar to those in the middle region, and significant differences only existed in Tb.Th ( $P = 0.009$ ) and DA ( $P = 0.031$ ). In addition, statistical regional differences were found in the mechanical parameters calculated from  $\mu$ FEA along direction 1 between the lateral and medial regions and the lateral and middle regions. However, no significant regional difference was found in the mechanical parameters along direction 2 or direction 3.

Multi-related sample non-parametric tests (Friedman method) were performed to analyze mechanical differences among the three orthogonal directions. Results showed that significant differences existed in the mechanical parameters along the three orthogonal directions. Two related sample non-parametric tests (Wilcoxon method) for each of the two directions were also performed. Results showed that significant differences existed between direction 1 and direction 2 in apparent Young's modulus, as well as between direction 1 and direction 3 (Fig. 3). In addition, no significant difference was found in apparent Young's modulus between direction 2 and direction 3. The same statistical method was performed to compare von Mises stresses under 1 % compressive strain. The results were similar with the apparent Young's modulus. Results from the microstructures and mechanical parameters of trabecular bone showed that direction 1 was the main loading direction during a gait process, and direction 2 and direction 3 were not the main loading directions. Therefore, direction 2 and direction 3 were defined as the transverse direction, and direction 1 was defined as the on-axis direction.

Bivariate correlation tests (Pearson method) were performed for all morphological parameters and mechanical parameters. Correlation coefficients between morphological parameters and mechanical parameters along the on-axis direction and the transverse direction were shown in Table 1. Significant correlations were found between the mechanical parameters along the on-axis direction and the morphological parameters BS/BV, BV/TV, Tb.Th and DA. Among these correlations, apparent Young's modulus was negatively correlated with BS/BV and positively correlated with BV/TV, Tb.Th, and DA. The correlations between von Mises stress and trabecular morphological parameters were simi-



**Fig. 3** Morphological parameters and mechanical parameters of trabecular bones (median and quartiles) in different regions of the femoral head. Charts with the same marker (\* or #) in each chart show significant differences in morphological parameters between these regions; ‡ significant difference in mechanical parameters along direction 1 between the medial and lateral regions; † significant difference in mechanical parameters along direction 1 between the middle and lateral regions



**Fig. 4** Typical cubic trabecular models from the lateral, middle, and medial regions and von Mises stress distribution of the trabecular cubes when compressed along the on-axis and transverse directions. Cubic trabecular models from lateral to medial regions are shown in the *left column*. The von Mises stress distribution along the on-axis direction of cubic trabecular models are also shown in the *middle column*, and those along the transverse direction of the same cubic trabecular models are in the *right column*. The trabecular bone in the lateral region was mainly composed of plate-like trabeculae along the trabecular orientation, and the trabeculae were very thick. Trabecular bone in the middle region was a cross structure with more unconnected and disordered trabeculae. Trabecular bone in the medial region was mainly composed of plate-like trabeculae along all directions because the medial region was in close contact with the acetabulum

**Table 1** Correlation coefficients between every morphological parameter and the mechanical parameters of trabecular bone

	Tb.Sp	BS/BV	BV/TV	Tb.Th	SMI	DA
$E_{On-axis}$	-0.04	-0.681*	0.444*	0.809*	0.139	0.382*
$\sigma_{On-axis}$	-0.017	-0.650*	0.444*	0.791*	0.148	0.399*
$E_{Transverse}$	-0.168	-0.018	0.072	-0.0123	0.098	-0.078
$\sigma_{Transverse}$	-0.248*	-0.043	0.138	-0.122	0.134	-0.018

\*  $P < 0.05$  (2-tailed)

lar to those between Young’s modulus and morphological parameters. No significant differences were found between morphological parameters and mechanical parameters along the transverse direction.

### 4 Discussion

In this study, trabecular morphological parameters and mechanical parameters in the medial, middle, and lateral

regions of femoral heads from proximal femoral fracture patients were obtained and analyzed using micro-CT and  $\mu$ FEA technologies. Based on the microstructural features of the trabecular bone, each femoral head was divided into 12 sub-regions. Various regional differences were found in the morphological and mechanical parameters of the trabecular bone blocks. Significant correlations between these two types of parameters were also found. Cubic bone models in different loading directions revealed anisotropic mechanical properties because trabeculae along the weight-bearing direction were mainly composed of compact plate-like structures. Consequently, trabeculae along the transverse direction were mainly composed of discrete rod-like structures. The mechanisms of femoral head fracture were analyzed based on the differences in regional mechanical properties, mechanical anisotropy, and the influence of microstructural features on mechanical properties. Results could provide references for predicting the fracture risk of femoral head.

A limitation of this study was the availability of samples. Performing micro-CT scanning for the proximal femurs of live individuals was impossible because of the excessive radiation and narrow shipping space of micro-CT devices. All samples collected were femoral heads from proximal femur fracture patients. Although most patients had femoral neck fractures, entire proximal femurs degenerated significantly. The femoral head, as an important part of the proximal femur, was at high risk of fracture. Microstructural features of trabecular bone in non-impact fractures were better understood by considering the femoral heads from total hip arthroplasty. This study was also useful for understanding the fracture mechanism in the elderly.

Previous studies showed that a significant decrease in BV/TV and Tb.Th led to intensified osteoporosis with aging. However, the morphological parameters of the trabecular bone not only change with age, but also vary with regions [23,30]. The average BV/TV in the elderly Caucasian with no proximal femur disease was suggested to be 0.306 in the medial region and 0.2895 in the lateral region [14], whereas the measured BV/TV were 0.23 and 0.29 in the medial and lateral regions, respectively. Results showed that the measurements in this study were quite similar to those of Nazarian et al. [14] in the lateral region. However, measurements in the medial region were 25 % lower than those in their study. These results indicated that the degeneration of the medial trabeculae of fracture patients was more serious than that of the lateral trabeculae. Therefore, the incidence of fracture in the medial region would be increased compared with that in the lateral region.

Figure 3 shows that Tb.Th increases and BS/BV decreases significantly from the medial to the lateral regions. Based on bone functional adaption to mechanical loading, bone tissue strength is maintained by increasing trabecular thickness

[23]. Results showed that the thickness of trabeculae in the medial region was significantly thinner than that in the lateral region, and the porosity in the medial region was statistically higher than that in the lateral region. In addition, the deterioration of the medial head was more serious than that of the lateral head.

SMI represents the three-dimensional microstructural features of the trabecular bone in terms of plate-like or rod-like structure. Changes in the trabecular bone from plate-like to rod-like structure can be observed clearly in the first column of Fig. 4. The trabecular morphology of the femoral head was mainly composed of plate-like trabeculae, even in the specimens of aged fracture patients. This phenomenon is different from the trabecular bone in the vertebral body [2].

Regional differences were revealed not only in the morphological parameters, but also in the mechanical parameters. The strength of the trabecular bone along the transverse loading direction was much lower than that along the on-axis direction in all regions according to the distribution of von Mises stress. In addition, no significant differences were found in von Mises stress along the transverse direction in the three regions. Once a large load was exerted on the femoral head along the transverse direction, it was susceptible to fracture. Therefore, the capacity of bearing load was quite poor under compressive stress distributed along the transverse direction, which may trigger a fracture.

Weight and gait loads were evenly transferred from the acetabulum to the surface of the medial head, which resulted in the lowest average stress of the trabecular bone along the on-axis direction in the medial region among the three regions. The average stress along the on-axis direction in the lateral region was statistically higher than that in the other two regions because of the thicker and plate-like trabeculae. When sudden impact was exerted along the on-axis direction in the lateral region, cracks were easily formed in the medial region. The stress distribution along the lateral region under on-axis compression condition was mainly concentrated on the plate-like trabecular bone. Therefore, the strength along the on-axis direction in the lateral region was much stronger than that in the medial region, and the micro-damage might be initiated from the medial region [31].

Several morphological parameters, as an important aspect affecting mechanical properties of cancellous bone, were significantly correlated with the mechanical parameters of the trabecular bone. Given that some fractured patients might not have osteoporosis [32,33], the influence of trabecular morphological parameters on their mechanical properties must be evaluated for a better prediction of fracture risk rather than considering BMD only. Table 1 showed that the mechanical parameters along the on-axis direction are significantly correlated with most of the morphological parameters.

Tb.Th was mostly correlated with the mechanical parameters of the femoral head, with a coefficient of 0.809.

BS/BV, BV/TV, and DA were still significantly correlated with the mechanical parameters. Among these parameters, BV/TV and DA were positively correlated with the apparent Young's modulus and von Mises parameters, and BS/BV was negatively correlated with the mechanical parameters. The influence of trabecular microstructural features on the mechanical properties was complicated. Any change on a morphological parameter will affect the trabecular mechanical properties, and the incidences were quite different. Tb.Th, BV/TV, and DA increased and BS/BV decreased from the medial to the lateral regions. All morphological parameters resulted in an increase in mechanical properties of the trabecular bone from the medial to the lateral regions, except DA. The DA behavior suggested that the disuse-mode trabecular bone remodeling process was mainly along the transverse orientation in the lateral region, resulting in high strength along the on-axis direction. However, the trabecular remodeling processes along all directions were homogeneous in the medial region, which weakened the strength in the medial region compared with that in the lateral region.

The introduction of micro-CT imaging technology,  $\mu$ FEA, and high performance computing cluster was an advanced and efficient means of observing the microarchitecture of the trabecular bone, and obtaining the mechanical parameters was possible. The number of elements in the cancellous bone model reconstructed from high resolution micro-CT images was generally more than three million. Such large-scale  $\mu$ FEAs could only be solved by high-performance computers. Accurate correlations between the mechanical parameters and the morphological parameters of the trabecular bone could be obtained through computation and analysis with a large sample size. In addition, exploring the mechanisms of fractures in the elderly is quite important.

In summary, significant regional differences in the microstructural features of the trabeculae were found inside the fractured femoral heads. As the mechanical properties of the trabecular bone were affected by their morphological properties, the mechanical properties also expressed significant regional differences. Fracture risk may be directly affected by trabecular degeneration with aging. When the deterioration of trabecular structures reaches a critical level, fractures will result. The fracture risk of the medial head was higher than the middle and lateral regions based on the analysis on the fracture patients. Mechanical properties along the transverse direction were in a poorer state than those along the on-axis direction. Therefore, transverse impact should be avoided by the elderly. Quantitative analysis of the early changing tendency of trabecular bone structures in the elderly may predict fracture risk, and possible treatment can be performed as early as possible. This study provides a deeper understanding of microstructures and the mechanical properties of the femoral head, as well as the mechanism of fractures.

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