Three-dimensional microarchitecture of the proximal femur in osteoarthritis and rheumatoid arthritis

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Abstract

BACKGROUND: The main reason for reducing the life of joint prosthesis is prosthetic loosening. In addition to prosthesis design, surgical technique, prosthetic material and the resulting wear particles, bone quality also plays a very important role in prosthetic loosening. Bone tissue microstructure has an important impact on bone quality. Recently, the quantification of bone architecture based on micro-CT has been widely used in the research of various bone diseases.

OBJECTIVE: To observe the osteoarthritis- and rheumatoid arthritis-related changes in the properties of the proximal femur based on micro-CT, thus to compare the bone microstructure in osteoarthritis and rheumatoid arthritis patients.

METHODS: Femoral heads were collected from primary osteoarthritis (*n*=10) and rheumatoid arthritis (*n*=7) patients undergoing total hip replacement. A 10-mm segment of the femoral neck was cut from each individual femur, perpendicular to the main trabecular direction on X-ray films. The specimens were analyzed by using micro-CT system. After scanning, the data were transferred to three-dimensional images, and then detailed structural parameters of the cortical bone, cancellous bone and femoral neck were statistically analyzed based on novel unbiased, model-free three-dimensional methods.

RESULTS AND CONCLUSION: There was no significant difference in the microstructure of the femoral head (cortical bone, cancellous bone and the entire) between the primary osteoarthritis and rheumatoid arthritis groups. The overall microstructure properties of the femoral neck were similar to those of the cancellous bone. Primary osteoarthritis patients were characterized by a more loss of the connectivity to the trabecular bone, an increase in degree of anisotropy for the cortical bone, but a decrease in degree of anisotropy for the cancellous bone and the entire trabecular bone, when compared to the rheumatoid arthritis group. These findings show that there is no difference in the microstructure of the cortical bone, the cancellous bone and the entire femoral neck between patients with primary osteoarthritis and rheumatoid arthritis, suggesting that primary osteoarthritis and rheumatoid arthritis have a similar trend of global microarchitectural degeneration in the femoral neck.

Subject headings: Osteoarthritis; Hip; Arthritis, Rheumatoid; Femur Neck
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INTRODUCTION

Osteoarthritis and rheumatoid arthritis are the common bone diseases[1]. There are more and more evidences showing that primary osteoarthritis might initially be a bone disease rather than a cartilage disease[2-6]. It is demonstrated that the femoral neck in patients with osteoarthritis has increased cancellous bone area, connectivity and trabecular thickness which may all protect the femoral neck against fractures[7-10]. Osteoporosis (primary or secondary), a result of an imbalance in bone metabolism, is a condition of excessive bone loss, usually combined with deterioration of bone architecture[11]. Rheumatoid arthritis is a major cause of secondary osteoporosis and is frequently associated with both para-articular and generalized osteoporosis[12]. There are many studies demonstrating that rheumatoid arthritis shows high bone turnover and the same decreased bone mineral density as primary osteoporosis[12-18]. Patients with rheumatoid arthritis are at increased risk of fractures. Total hip replacement is the only treatment in advanced stages of both diseases. The main reason for reducing the life of joint prosthesis is prosthetic loosening and peri-prosthetic bone fracture. In addition to prosthesis design, surgical technique, prosthetic material and the resulting wear particles and other factors, bone

quality also plays a very important role in prosthetic loosening.

Bone tissue microstructure has an important impact on bone quality. Disease-associated changes in the quantity and distribution of cortical and cancellous bone around the femoral neck may contribute to enhance hip fragility in osteoporosis[19-20]. There are divergent views on the relative contributions of cortical and trabecular compartments to bone strength[21-23]. The results from Rivadeneira's study indicated that fragility fractures of the hip are mainly caused by cortical instability and that bone strength and instability are the function of the thickness of the cortices relative to the diameter of the bone[24]. There is no evidence of abnormalities of bone mass/structure in the femoral neck which is away from the site involved in hip osteoarthritis[25-26].

Recent quantification of bone architecture based on micro-CT has been widely used in the research of various bone diseases[27-29]. However, to our knowledge, there is no study that uses the micro-CT method to compare the integrity (total) microstructural distribution of cortical and trabecular bone of the femoral neck between osteoarthritis and rheumatoid arthritis (secondary osteoporosis). Accordingly, the aim of this study was to compare three-dimensional microarchitecture of trabecular bone and cortical bone of the femoral neck between osteoarthritis and rheumatoid arthritis. Our study has been the first to use high-resolution micro-CT to obtain microstructural data of the total (general) distribution of cortical and trabecular bone of the femoral neck. This study aimed to seek further insight into better understanding diseases-related changes in the properties of cancellous and cortical bone tissues, thus provideing important information for clinical diagnosis, prophylaxis and treatment of clinical diseases and for design, fixation and durability of joint prostheses.

MATERIALS AND METHODS

Design

Histology *in vitro* and comparative observation.

Time and setting

The experiment was performed at the Orthopaedic Research Laboratory, Department of Orthopaedic Surgery, Odense University Hospital, University of Southern Denmark between September 2011 and September 2014.

Subjects

Human femur neck samples: human proximal femoral necks including heads were harvested from patients undergoing total hip replacements at the Department of Orthopaedic Surgery and Traumatology, Odense University Hospital. These were 7 female patients with rheumatoid arthritis (average age 67.14 years; range 52–86 years), and 10 female patients with osteoarthritis (average age 68.86 years; range 58–82 years). Prior to experiments, all written documents were obtained from patients who agreed to donate femoral necks/heads, and all written informed consents were obtained from all subjects to offer cadavers for anatomical education and research. Thus, this study included two groups: osteoarthritis and rheumatoid arthritis. All patients and donors were Caucasian. The inclusion criteria: a strict criteria for selecting samples was used, all osteoarthritis and rheumatoid arthritis samples had clinical and radiological diagnosis to confirm the diseases. They were also checked with roentgenographic, biochemical or histological evidence to rule out other bone diseases than osteoarthritis and rheumatoid arthritis. Congenital or acquired dysplasia, gout or avascular necrosis were excluded from the osteoarthritis and rheumatoid arthritis groupS. This study was approved by the Department of Orthopaedic Surgery and Traumatology, Odense University Hospital, and the Ethic Committee of the Region of Southern Denmark (ID: S-VF-20040094).

Reagents and instruments

Equipment	Source
vivaCT 40	Scanco Medical AG., Zurich, Switzerland
Exakt saw	Exakt Apparatebau GmbH & Co. KG, Norderstedt, Germany
MX-20 DC10 (X Ray)	Faxitron, USA

Methods

Sample preparation

According to total hip replacement procedure, the femur head was sawed off between trachantal minor and major. The femur head samples were stored in sealed plastic bag and kept in −20 ℃ for future preparation. The proximal femurs were cleaned of soft connective tissue with a scalpel. Before the specimens were harvested, the orientation of the trabeculae in the femoral neck was determined from an anterior-posterior contact radiograph. In each X-ray image, the main trabecular direction was identified by the operator and the angle between the tangent line of the inferior cortical bone of the femoral neck and the main trabecular direction was measured. A 10-mm segment of the femoral neck was cut at the base of femoral head and at the base of femoral neck, perpendicular to the main trabecular direction of each individual femur, using Exakt saw (Exakt Apparatebau GmbH & Co. KG, Norderstedt, Germany) (**Figure 1**).

Micro-CT scanning and three-dimensional microstructural analysis

The specimens were analyzed by cone-beam micro-CT system (vivaCT 40, Scanco Medical AG., Zurich, Switzerland). The entire cortical and cancellous bone was scanned continuously with a tube voltage of 70 kV, tube current of 84 μA. Data from each three-dimensional image consisted of approximately micro-CT slide images (512× 512 pixels) with 16-bit grey levels.

After scanning, the micro-CT image data were transferred to a workstation, and the entire cortical and trabecular region of the femoral head were selected and segmented using an individual density threshold value. The cortical bone was defined by removing the osteophyte at the periosteal surface

Figure 1 A femoral head sample with osteoarthritis (A and B) and the femoral neck scanning specimen was cut according to the main trabecular direction (MTD; C)
Note: The thickness of scanning specimen was 10 mm.

operator. We binarized the image to separate pure bone from background or pores, using a single threshold.

of the cortex and the pores at the endosteal surface of the cortex by the same Based on the three-dimensional reconstructions of the total cortical (Co) and trabecular (Tb) bone, mean bone density (MBD, mg HA/ccm), bone surface (BS, mm^2), bone volume (BV, mm^3), total volume (TV, mm^3), thickness (Th*, mm), number (N*, mm^{-1}), separation (Sp,mm), were analyzed. MBD, BS, BV, and TV were calculated using tetrahedrons corresponding to the enclosed volume of the triangulated surface. BS/BV, BS/TV, BV/TV were calculated. Th*, N*, and Sp of the cortical and trabecular bone were based on direct measurement by a distance transformation method. The structure model index (SMI) is a parameter that quantified the characteristic form of a three-dimensional described structure in terms of the plate-like or rod-like nature of the complete structure. Connectivity density (CD, mm^{-3}) is a topological parameter that estimate the number of trabecular connections per cubic millimeter. The degree of anisotropy (DA) defines the direction and magnitude of the preferred orientation of trabeculae and uses the ratio between the maximum and minimum radii of the mean intercept length ellipsoid. All the above parameters were computed in three-dimensional without model assumptions required for two-dimensional analysis. Cross sectional area (CSA) was calculated according to two-dimensional reconstruction data, and the value was the mean value of three different cross sections (top, middle and bottom).

Main outcome measures

The entire microstructure of the femoral neck and measurement indicators.

Statistical analysis

All statistical analyses were completed using SPSS 16.0 software (SPSS, Chicago, IL, USA). Data were presented as mean±SD. Normality of the distributions was assessed using the *Kolmogorov-Smirnov* test with the significance level set at 0.05. Differences of these properties between the two groups were analyzed using independent-samples *t* test. The data were not normally distributed, so non-parametric tests (Mann-Whitney *U* test) were performed. Bivariate correlation analysis and linear regression analysis were conducted to assess the association of different properties between the groups. A value of $P < 0.05$ was considered significant.

RESULTS

Difference in the three-dimensional microstructure of femoral neck specimens between osteoarthritis and rheumatoid arthritis groups

All the data were not distributed normally. Analyses of variation in the microstructural properties of different regions in the two groups are summarized in **Table 1**.

The patients with osteoarthritis were older than those with rheumatoid arthritis, but there was no significant difference. The entire cortical bone of the femoral neck in patients with rheumatoid arthritis had higher BV/TV, Co.Th*, Co.N* and Co.CD, lower Co.Sp, Co.DA and CSA than those with osteoarthritis, but there was no significant difference between the two groups. The entire trabecular bone in the rheumatoid arthritis group had higher BV/TV, Tb.N*, Tb.CD, Tb.DA and CSA, lower Tb.Th*, Tb.Sp than that in the osteoarthritis group, but there was no significant difference between the two groups. Properties of the femoral neck were similar to those of the trabecular bone. This decrease in bone volume in the osteoarthritis group resulted from the decreased amount of cortical and trabecular bone tissues as well as a consequent increase in dispersion degree. The osteoarthritis group was also characterized by a loss of the connectivity, an increase in DA for the cortical bone, but a decrease in DA for the cancellous bone and the entire trabecular bone when compared to the rheumatoid arthritis group.

Relations between the microstructural parameters of femoral neck specimens in osteoarthritis and rheumatoid arthritis groups

Among all the parameters, BV/TV had the strong correlation with Th*, Sp, SMI, and N* for the entire femoral head, cortical and trabecular bone in both osteoarthritis and rheumatoid arthritis groups. For all the three regions of rheumatoid arthritis and osteoarthritis patients, we found a BV/TV-related increase in Th* and a BV/TV-related decrease in Sp and SMI. But for the correlation between BV/TV and N*, there was no consistent tendency in the three regions of osteoarthritis

Table 1 Microstructural parameters for the femoral neck in osteoarthritis (OA) *vs*. rheumatoid arthritis (RA) patients ($\bar{x}$±s)

Microstructural properties of the femoral neck	Total			Co			Tb		
	RA (*n*=7)	OA (*n*=10)	*P*	RA (*n*=7)	OA (*n*=10)	*P*	RA (*n*=7)	OA (*n*=10)	*P*
Age (years)	67.14±13.20	68.86±8.09	0.81	67.14±13.20	68.86±8.09	0.81	67.14±13.20	68.86±8.09	0.81
BS/BV (mm^{-1})	9.50±1.32	9.26±1.28	0.65	3.54±1.18	3.46±0.94	0.48	15.47±2.41	14.98±2.00	0.91
BS/TV (mm^{-1})	2.97±0.32	2.62±0.24	0.26	3.19±0.91	3.04±0.67	0.37	2.74±0.52	2.49±0.25	0.28
BV/TV (%)	0.54±0.30	0.53±0.25	0.39	0.91±0.05	0.89±0.05	0.84	0.18±0.05	0.17±0.03	0.49
Thickness (mm)	0.43±0.16	0.44±0.27	0.79	0.69±0.25	0.67±0.18	0.86	0.18±0.02	0.19±0.02	0.56
Number (mm^{-1})	2.31±0.53	2.09±0.55	0.41	2.89±0.81	2.83±0.58	0.66	1.74±0.65	1.45±0.24	0.29
Separation (mm)	0.47±0.22	0.54±0.28	0.35	0.24±0.01	0.25±0.09	0.77	0.70±0.22	0.78±0.11	0.28
Structure model index (0−3)	–	–	0.63	–	–	0.62	1.76±0.72	1.75±0.54	0.87
Connectivity density (mm^{-3})	11.82±5.43	7.98±3.23	0.10	10.96 ±5.96	8.05 ±5.30	0.17	12.68±6.47	8.78±3.20	0.13
Degree of anisotropy	1.41±0.12	1.39±0.15	0.79	1.37 ±0.24	1.38 ±0.12	0.80	1.45±0.13	1.43±0.05	0.79
Cross sectional area (mm^2)	673.11±162.97	72.40±292.99	0.41	97.68±17.81	151.82±15.32	0.79	565.67±289.62	543.68±267.93	0.63

Note: There was no significant difference in bone microstructural parameters in any region between RA and OA group. The results of integrity femoral neck bone properties were similar to the trabecular bone. Compared to the RA group, the OA group was also characterized by a loss of the connectivity, an increase in the degree of anisotropy for the cortical bone, but a decrease in the degree of anisotropy for the entire femoral head and trabecular bone. Total=total femoral neck, Co=cortical part of femoral neck, Tb=trabecular part of femoral neck, BS=bone surface, BV=bone volume, TV=total volume. "–"=negative value.

and rheumatoid arthritis groups. The significant correlations between Sp and N* were also found in the three regions of osteoarthritis and rheumatoid arthritis groups.

DISCUSSION

This study investigated the bone microarchitectural changes of the femoral neck in patients with osteoarthritis and rheumatoid arthritis. It was an interesting observation that there were no significant differences in the microarchitectural parameters of the entire femoral neck between osteoarthritis and rheumatoid arthritis groups. These results did not support our hypothesis that the microarchitecture was significantly different between osteoarthritis and rheumatoid arthritis patients. Thus, our data might suggest that osteoarthritis and rheumatoid arthritis had a similar trend of global bone microarchitectural degeneration in the femoral neck, despite marked erosion in rheumatoid arthritis, but the local difference could not be eliminated.

We did not find significant differences in bone quality and trabecular microarchitecture between patients with osteoarthritis and rheumatoid arthritis in integrity, cortical and trabecular bone properties of the femoral neck. To our knowledge, this is the first study evaluating the three-dimensional structure of the femoral neck in patients with rheumatoid arthritis using micro-CT.

It is a surprising finding that the global microarchitecture of the cancellous bone in the femoral neck did not differ between osteoarthritis and rheumatoid arthritis patients, despite apparent erosion in rheumatoid arthritis bone. As it is generally believed that rheumatoid arthritis is a major cause of secondary osteoporosis, and thus the deteriorated microarchitecture of cancellous bone should be typically characterized as decreased bone density (volume fraction), transformation of cancellous bone structure into extremely rod-like. However, our data did not support this assumption. The global changes in cancellous bone and cortical bone were similar in the femoral necks of osteoarthritis and rheumatoid arthritis patients, but this did not propose that local changes were similar as well. Given the fact that rheumatoid arthritis-induced erosion particularly close to the joint surface was apparent, there were significant differences in local microarchitecture of bone tissues. Nevertheless, our current data suggest a similar trend of global microarchitectural degeneration in osteoarthritis and rheumatoid arthritis patients.

Femoral neck fracture is one of the most common fractures in osteoporosis patients. Rheumatoid arthritis is a major cause of secondary osteoporosis and is frequently associated with both paraarticular and generalized osteoporosis[12]. Femoral neck fracture is attributed to the loss of both cortical and trabecular bone mass[30-33]. Bone mass in osteoarthritis patients is higher than that in normal subjects[1]. It is demonstrated that the femoral neck in patients with osteoarthritis has increased cancellous bone area, connectivity and trabecular thickness which may all protect the neck against fractures[9, 29]. Although several studies have found that the microstructural changes of the femoral neck not only exist in the trabecular bone but also in the cortical bone which determine that the bone strength of femoral neck play the crucial role in prevalence of femoral neck fracture, these studies did not investigate the integrity structure of femoral neck[1, 2, 4, 8-10, 20, 29]. This study was the first to measure the three-dimensional microstructural parameters of the entire femoral neck instead of partial specimens from some part of the femoral neck. We think that it is of great significance for assessing the effects of changes in the bone properties on femoral neck fracture.

In this study, the microarchitectural parameters measured were not different between the two groups. The bone volume fraction of the aging control was similar to that of the aging tibial cancellous bone. The structure type of the control group was typical rod-like, and was similar to what was reported earlier in human aging tibial cancellous bone[5]. In general, the decreased bone tissues in the osteoarthritis and rheumatoid arthritis groups were compensated during aging and disease processes, resulting in severe bone loss with aging. According to our data, the entire cortical bone of the femoral neck in patients with rheumatoid arthritis increased by 2.19% in BV/TV,

2.89% in Co.Th*, 2.07% in Co.N* and 26.55% in Co.CD, respectively; declined by 4.16% in Co.Sp, 0.7% in Co.DA compared to osteoarthritis patients. The bone properties of the trabecular bone and the entire femoral neck were similar to those of the cortical bone. The change of BV/TV was associated with change in Co.Th, Co.N, and Co.Sp in our findings which are in line with previous studies[1-2, 5-10].

It seems our findings are not in agreement with the results of previous studies that there are more bone quality in osteoarthritis patients that osteoporosis patients[9, 20, 29]. We think the discrepancy of our findings can be interpreted by several causes. First, in all almost previous studies, for assessing cortical and trabecular bone structures and their possible regional variability in the femoral neck, the osteoporosis specimen was taken from osteoporotic hip fracture (primary osteoporosis) instead of secondary osteoporosis[1-2, 4, 7, 20, 29]. Rheumatoid arthritis is a major cause of secondary osteoporosis and is frequently associated with both paraarticular and generalized osteoporosis. Rheumatoid arthritis is an autoimmune disorder of unknown etiology characterized by progressive damage of synovial-lined joints and variable extra-articular manifestations. Detailed microarchitecture of the cancellous bone and cortical bone in rheumatoid arthritis patients is still not well known[12, 18, 34-35]. The factors of rheumatoid arthritis-induced osteoporosis are more complex than primary osteoporosis. Generalized bone loss may be influenced by immobility, the inflammatory process and treatments such as steroids, while paraarticular loss is probably due to local release of inflammatory agents such as cytokines from the rheumatoid synovium and articular immobility. Determinants of bone mass in rheumatoid arthritis are multifactorial such as sex and menopausal status, disease duration, disease activity, and reduced mobility and function[18-36]. Due to this, it is possibly inapposite that the changes of bone microstructure in rheumatoid arthritis-induced secondary osteoporosis are similar to those in primary osteoporosis. Although there are many studies demonstrating that rheumatoid arthritis shows high bone turnover and the same decreased bone mineral density[12-17], we did not find any studies addressing the difference in three-dimensional bone microstructure between primary osteoporosis and rheumatoid arthritis using micro-CT. Hence, we think if there is another study group of primary osteoporosis as control group, it is very helpful to detect the difference. But it is regretful that it is very difficult to perfectly obtain the entire femoral neck from osteoporotic hip fracture patients due to the operation or fracture damage of the specimen. Secondly, it is well accepted that age-related bone loss is an important factor leading to enhanced bone fragility and fracture risk in the elderly[37-39]. Age-related changes of trabecular bone include a decrease in BV/TV, Tb.N and Conn.D, an increase in Tb.Sp, a shift from plate-like trabeculae to rod-like structure. With normal aging, this thin cortical zone in the femoral neck becomes substantially thinner[40-43]. Although rheumatoid arthritis patients possibly have osteoporotic changes of bone microstructure, patients with rheumatoid arthritis have a mean age of 67.1 years, who are younger than those with primary osteoarthritis (an average age of 68.2 years).

There are several limitations needed to be discussed. Firstly, there was a small sample-size in each group. Apparently, if more samples were included in the study, the results were possibly more convincing. Secondly, no mechanical test was performed, since these valuable samples were used for another study to investigate ultrastructure of bone tissues. The relative contributions of cortical and trabecular bone is important to maintain the bone strength at the femoral neck[23, 31-32]. Hence, our study was the first to scan the entire femoral neck once, and calculated the three-dimensional parameters of whole cortical and trabecular part in every specimen. According to our method not applied in previous studies, we could easily assess the global properties of the femoral neck, cortical bone and trabecular bone, and analyze the difference between osteoarthritis and rheumatoid arthritis. The relative importance of cortical and trabecular bone to the femoral neck strength has been reported in studies that have used several experimental methods[44-47]. All the studies have taken one part of the femoral neck (cortical or trabecular bone) as interesting specimen, which cannot veritably reflect the general change in the femoral neck in human body and produce bias. In human beings, trabecular bone density of the femoral neck declines twice as much as does cortical thickness or cortical bone density[48]. Moreover, an analytical study found that, at the mid-femoral neck, 50% of the applied load, either during gait or during a sideways fall, was supported by the trabecular bone[32]. But in our study there was no difference in the tendency of changes in cortical, trabecular and entire femoral neck both in osteoarthritis and rheumatoid arthritis patients. We think both cortical and trabecular bones play the same important role in the ability of femoral neck to sustain stresses produced by falls. If with mechanical test, we possibly get the association between microarchitectrual properties and mechanical properties in osteoarthritis and rheumatoid arthritis, and know which part of femoral neck play its different role in change of bone strength while with tension or torsion by falls.

In conclusion, this study demonstrated that there were no significant differences in the global microarchitectural parameters of the femoral neck between osteoarthritis and rheumatoid arthritis. These results might suggest that osteoarthritis and rheumatoid arthritis have a similar trend of global microarchitectural degeneration in the femoral neck, despite marked erosion in the bone of rheumatoid arthritis and osteophyte formation in the bone of osteoarthritis, but the local difference cannot be eliminated. The bone loss with aging in the osteoarthritis and rheumatoid arthritis was not as serious as that of osteoporosis according to literature reports, suggesting a compensation effect of the diseases that increase

REFERENCES

[1] Sun SS, Ma HL, Liu CL. Difference in femoral head and neck material properties between osteoarthritis and osteoporosis. Clin Biomech. 2008;23:S39-S47.

[2] Issever AS, Burghardt A, Patel V, et al. A micro-computed tomography study of the trabecular bone structure in the femoral head. J Musculoskelet Neuronal Interact. 2003; 3(2):176-184.
[3] Radin EL, Rose RM. Role of subchondral bone in the initiation and progression of cartilage damage. Clin Orthop. 1986;213:34-40.
[4] Li BH, Aspden RM. Mechanical and material properties of the subchondral bone plate from the femoral head of patients with osteoarthritis or osteoporosis. Ann Rheum Dis. 1997;56:247-254.
[5] Ding M, Christian Danielsen C, Hvid I. Bone density does not reflect mechanical properties in early-stage arthrosis. Acta Orthop Scand. 2001;72(2):181-185.
[6] Dieppe P, Cushnaghan J, Young P, et al. Prediction of the progression of joint space narrowing in osteoarthritis of the knee by bone scintigraphy. Ann Rheum Dis. 1993;52: 557-563.
[7] Chappard C, Peyrin F, Bonnassie A, et al. Subchondral bone micro-architectural alterations in osteoarthritis: a synchrotron micro-computed tomography study. Osteoarthritis Cartilage. 2006;14(3):215-223.
[8] Cooper C, Cook PL, Osmond C, et al. Osteoarthritis of the hip and osteoporosis of the proximal femur. Ann Rheum Dis. 1991;50:540-542.
[9] Dequeker J, Johnell O. Osteoathritis protects against femoral neck fracture: the MEDOS study experience. Bone. 1993;14:S51-S56.
[10] Verstraeten A, Van Ermen H, Haghebaert G, et al. Osteoarthrosis retards the development of osteoporosis. Observation of the coexistence of osteoarthrosis and osteoporosis. Clin Orthop. 1991;264:169-177.
[11] Gong H, Zhang M, Yeung HY, et al. Regional variations in microstructural properties of vertebral trabeculae with aging. J Bone Miner Metab. 2005;23:174-180.
[12] Inaba M, Nagata M, Goto H, et al. Preferential reductions of paraarticular trabecular bone component in ultradistal radius and of calcaneus ultrasonography in early-stage rheumatoid arthritis. Osteoporos Int. 2003;14(8):683-687.
[13] Korczowska I, Olewicz-Gawlik A, Trefler J, et al. Does low-dose and short-term glucocorticoids treatment increase the risk of osteoporosis in rheumatoid arthritis female patients? Clin Rheumatol. 2008;27(5):565-572.
[14] Böttcher J, Pfeil A, Mentzel H, et al. Peripheral bone status in rheumatoid arthritis evaluated by digital X-ray radiogrammetry and compared with multisite quantitative ultrasound. Calcif Tissue Int. 2006;78(1):25-34.
[15] Enokida M, Yamasaki D, Okano T, et al. Bone mass changes of tibial and vertebral bones in young and adult rats with collagen-induced arthritis. Bone. 2001;28(1): 87-93.
[16] Le Corroller T, Pithioux M, Chaari F, et al. Bone texture analysis is correlated with three-dimensional microarchitecture and mechanical properties of trabecular bone in osteoporotic femurs. J Bone Miner Metab. 2013; 31(1):82-88.
[17] Ollivier M, Le Corroller T, Blanc G, et al. Radiographic bone texture analysis is correlated with 3D microarchitecture in the femoral head, and improves the estimation of the femoral neck fracture risk when combined with bone mineral density. Eur J Radiol. 2013; 82(9):1494-1498.
[18] Deodhar AA, Woolf AD. Bone mass measurement and bone metabolism in rheumatoid arthritis: a review. Br J Rheumatol. 1996;35(4):309-322.
[19] Homminga J, Van-Rietbergen B, Lochmuller EM, et al. The osteoporotic vertebral structure is well adapted to the loads of daily life, but not to infrequent "error" loads. Bone. 2004; 34: 510-516.
[20] Blain H, Chavassieux P, Portero-Muzy N, et al. Cortical and trabecular bone distribution in the femoral neck in osteoporosis and osteoarthritis. Bone. 2008;43(5):862-868.
[21] Mayhew PM, Thomas CD, Clement JG, et al. Relation between age, femoral neck cortical stability, and hip fracture risk. Lancet. 2005;366:129-135.
[22] Basso T, Klaksvik J, Syversen U, et al. A biomechanical comparison of composite femurs and cadaver femurs used in experiments on operated hip fractures. J Biomech. 2014; 18;47(16):3898-3902.
[23] Bouxsein ML, Fajardo RF. Cortical stability of the femoral neck and hip fracture risk. Lancet. 2005;366:1532-1534.
[24] Rivadeneira F, Zillikens MC. Femoral neck BMD is a strong predictor of hip fracture susceptibility in elderly men and women because it detects cortical bone instability: the rotterdam study. J Bone Miner Res. 2007;22:1781-1790.
[25] Fazzalari NL, Parkinson IH. Femoral trabecular bone of osteoarthritic and normal subjects in an age and sex matched group. Osteoarth Cart. 1998;6:377-382.
[26] Fazzalari NL, Moore RJ, Manthey BA, et al. Comparative study of iliac crest and subchondral femoral bone in osteoarthritis patients. Bone. 1992;13:331-335.
[27] Hildebrand T, Rüegsegger P. Quantification of bone microarchitecture with the structure model index. Comput Methods Biomech Biomed Engin. 1997;1(1):15-23.
[28] Odgaard A. Three-dimensional methods for quantification of cancellous bone architecture. Bone. 1997;20(4):315-328.
[29] Tanck E, Bakker AD, Kregting S, et al. Predictive value of femoral head heterogeneity for fracture risk. Bone. 2009; 44(4):590-595.
[30] Duque G, Troen BR. Understanding the mechanisms of senile osteoporosis: new facts for a major geriatric syndrome. J Am Geriatr Soc. 2008;56:935-941.
[31] Bell KL, Loveridge N, Power J et al. Structure of the femoral neck in hip fracture: Cortical bone loss in the inferoanterior to superoposterior axis. J Bone Miner Res 1999;14: 111-119.
[32] Lotz JC, Cheal EJ, Hayes WC. Stress distribution within the proximal femur during fait and falls: implications for osteoporotic fracture. Osteoporos Int. 1995;5:252-261.
[33] Bell KL, Loveridge N, Power J, et al. Regional differences in cortical porosity in the fractured femoral neck. Bone. 1999; 24:57-64.
[34] Lane NE, Pressman AR, Star VL, et al. Rheumatoid arthritis and bone mineral density in elderly women. The study of osteoporotic fractures research group. J Bone Miner Res. 1995;10(2):257-263.
[35] Aguila LA, Lopes MR, Pretti FZ, et al. Clinical and laboratory features of overlap syndromes of idiopathic inflammatory myopathies associated with systemic lupus erythematosus, systemic sclerosis, or rheumatoid arthritis. Clin Rheumatol. 2014;33(8):1093-1098.
[36] Heidari B, Hassanjani Roushan MR. Rheumatoid arthritis and osteoporosis. Caspian J Intern Med. 2012;3(3): 445-446.
[37] Chen H, Kubo KY. Bone three-dimensional microstructural features of the common osteoporotic fracture sites. World J Orthop. 2014;18;5(4):486-495.
[38] Chen H, Zhou X, Fujita H, et al. Age-related changes in trabecular and cortical bone microstructure. Int J Endocrinol. 2013;2013:213234.

[39] Courtland HW, Kennedy OD, Wu Y, et al. Low levels of plasma IGF-1 inhibit intracortical bone remodeling during aging. Age (Dordr). 2013;35(5):1691-1703.
[40] Giambini H, Wang HJ, Zhao C, et al. Anterior and posterior variations in mechanical properties of human vertebrae measured by nanoindentation. J Biomech. 2013;46(3): 456-461.
[41] Chen H, Zhou X, Washimi Y, et al. Three-dimensional microstructure of the bone in a hamster model of senile osteoporosis. Bone 2008;43:494-500.
[42] Popp AW, Buffat H, Eberli U, et al. Microstructural parameters of bone evaluated using HR-pQCT correlate with the DXA-derived cortical index and the trabecular bone score in a cohort of randomly selected premenopausal women. PLoS One. 2014;9(2):e88946.
[43] Chiba K, Burghardt AJ, Osaki M, et al. Heterogeneity of bone microstructure in the femoral head in patients with osteoporosis: an ex vivo HR-pQCT study. Bone. 2013;56(1): 139-146.
[44] Nicks KM, Amin S, Melton LJ 3rd,et al. Three-dimensional structural analysis of the proximal femur in an age-stratified sample of women. Bone. 2013;55(1):179-188.
[45] Manske SL, Liu-Ambrose T, Cooper DM, et al. Cortical and trabecular bone in the femoral neck both contribute to proximal femur failure load prediction. Osteoporos Int. 2009; 20(3):445-453.
[46] Hordon LD, Peacock M. The architecture of cancellous and cortical bone in femoral neck fracture. Bone Miner. 1990;11: 335-345.
[47] Lang TF, Keyak JH, Heitz MW, et al. Volumetric quantitative computed tomography of the proximal femur: precision and relation to bone strength. Bone. 1997;21:101-108.
[48] Riggs BL, Melton LJ 3rd, Robb RA, et al. Population-based study of age and sex differences in bone volumetric density, size, geometry, and structure at different skeletal sites. J Bone Miner Res. 2004;19:1945-1954.

骨性关节炎与类风湿关节炎的股骨近端骨结构三维微观结构分析

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文章亮点：

1 对于骨关节炎和类风湿性关节炎股骨近端骨组织(包括皮质骨与松质骨)的三维微观结构观察的研究国内外均未见报道。
2 文章的目的是对比研究骨性关节炎与类风湿性关节炎间的骨微观结构差异性。
3 实验的创新性在于首次采用高分辨 micro-CT 技术分析股骨颈部位骨组织的整体、松质骨和皮质骨的微观结构。

关键词：
组织构建；骨组织工程；微观结构；股骨颈；骨关节炎；类风湿性关节炎；微观CT；皮质骨；松质骨；骨质疏松；髋关节；骨组织
主题词：
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摘要

背景：人工关节假体松动的原因除了手术技术、假体设计及其产生的磨损颗粒等因素以外，假体周围的骨质量也起着极为重要的作用。骨微观结构是影响骨质量主要因素，应用技术分析组织微观结构目前已初步用于各种骨骼疾病的研究。

目的：应用 micro-CT 技术，观察类风湿性关节炎与骨性关节炎股骨近端骨组织性能变化，对比研究两者之间的骨微观结构差异。

方法：收集原发性骨关节病和类风湿性关节炎患者因行全髋关节置换而切除的股骨头(骨性关节炎 10 个，类风湿关节炎 7 个)。根据每个股骨头标本 X 射线上主要骨小梁方向，取材并制作来自于股骨颈骨组织的 10 mm 标本，然后进行 micro-CT 扫描，数据转换成 3D 图像数据后，分析两组之间皮质骨、松质骨以及股骨颈整体的骨微结构参数，做统计学处理。

结果与结论：骨性关节炎与类风湿性关节炎的股骨颈骨组织的微结构(皮质骨、松质骨以及整体)差异无显著性意义；两种疾病的股骨颈骨组织的整体微结构特点与松质骨结构特点相近。与类风湿患者相比，骨关节炎患者骨小梁的连接性密度丢失较多，皮质骨的骨小梁定向分布程度升高，而松质骨和整体的骨小梁定向分布程度降低。结果证实，骨性关节炎与类风湿性关节炎的皮质骨、松质骨以及整体股骨颈骨组织的微结构无显著差异，这提示两种疾病的股骨颈整体的微结构退变是相同的。

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利益冲突：文章及内容不涉及相关利益冲突。

伦理要求：参与研究的患病个体及其家属自愿参加，所有参与者均对实验过程完全知情同意，在充分了解实验的前提下签署“知情同意书”。研究方案获南丹麦地区伦理委员会批准(ID: S-VF-20040094)。

学术术语：原发性、继发性骨质疏松症–此病是骨代谢失衡造成的，会有过量的骨丢失，通常伴有骨微观结构破坏。类风湿性关节炎往往造成继发性骨质疏松，经常伴有关节周围及全身的骨质疏松。大量研究证实类风湿关节炎有更高的骨转换，与原发骨质疏松症相同的骨密度下降。

作者声明：文章为原创作品，无抄袭剽窃，无泄密及署名和专利争议，内容及数据真实，文责自负。

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