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ORIGINAL PAPER

# Enhanced trabecular micro-architecture of the femoral neck in hip osteoarthritis vs. healthy controls: a micro-computer tomography study in postmenopausal women

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**Abstract**
*Purpose* A controversial relationship between osteoarthritis (OA) and bone fragility has been attracting considerable attention. However, despite interest in the effects of OA on femoral neck fracture risk and numerous studies analysing the changes in the arthritic femoral head, there is insufficient data about femoral neck 3D bone micro-architecture in individuals with hip osteoarthritis. We compared trabecular micro-architecture of the femoral neck between postmenopausal women with coxarthrosis and controls to explore whether coxarthrosis may indicate reduced bone fragility from the trabecular micro-architectural perspective.
*Methods* The study sample included nine women with hip osteoarthritis and 13 age-matched controls. The femoral neck sections were scanned using micro-computed tomography, evaluating the cancellous bone from the superolateral and inferomedial neck subregions.
*Results* Osteoarthritic subjects demonstrated a general trend of improved trabecular micro-architecture in both analysed subregions when compared with age-matched controls. In particular, several architectural properties that are important predictors of cancellous bone strength showed significantly better values in the OA group, even after adjusting for bone volume fraction. Namely, the OA group expressed higher trabecular connectivity ($p=0.008$), lower SMI indicating more plate-like structure ($p=0.005$), and reduced anisotropy ($p=0.006$) particularly in the inferomedial neck. Osteoarthritic cases also trended towards higher BV/TV, particularly in the

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superolateral neck. All micro-architectural parameters displayed significant regional heterogeneity ($p \leq 0.01$), with the inferomedial neck region showing more favourable values than the superolateral region.

*Conclusions* Enhanced trabecular micro-architecture of the femoral neck in postmenopausal osteoarthritic subjects suggests reduced cancellous bone fragility in comparison with their age-matched healthy controls.

## Introduction

Osteoarthritis (OA) is a topic of many debates concerning its relationship with osteoporosis and bone fragility. Clinical data mainly show that osteoarthritis and osteoporosis rarely coexist in the same individual [1, 2]. Reduced incidence of the femoral neck fracture in osteoarthritic hips [3] has led to a common belief that osteoarthritis may have a protective role against osteoporosis and bone fragility [1, 2, 4]. However, the opposite observations showing presence of osteoporosis in the hips of OA patients were also reported [5, 6].

Most researchers analysed bone mineral density (BMD) and bone geometry in individuals with OA [7, 8]. Additionally, it has been suggested that the architecture of cancellous bone plays an important role in hip fracture risk in both osteoarthritic and osteoporotic women [9]. However, micromorphometric analyses have been carried out infrequently. The majority of such studies have focussed on histomorphometric features in the femoral heads of osteoarthritic femora—analysing their relation to age [4] and mechanical properties [10], comparing them with healthy controls [11, 12] and with osteoporotic specimens [13–15]. In contrast to a number of research studies analysing the OA changes in the femoral head, and although there is a clear clinical interest in the relationship between OA and risk of femoral neck fracture, quantitative data about the bone structure of the femoral neck in patients with OA are surprisingly rare. Few studies have addressed this issue at the level of histomorphometry and compared OA patients with healthy controls [16–18] or hip fracture cases [9]. Moreover, the data on three-dimensional structure of the femoral neck trabecular bone in osteoarthritis are limited to pQCT studies that compared the OA with hip fracture cases [19, 20]. So far there has been no micro-CT data on the femoral neck structure in two biomechanically relevant sites of the femoral neck (inferomedial neck and superolateral neck) in OA vs. healthy cases.

In this study we investigated how the trabecular micro-architecture differs between osteoarthritic cases and age-matched controls in the femoral neck of postmenopausal women. We postulated that the hip osteoarthritis would be associated with a reduced degree of bone fragility of the femoral neck, from the perspective of trabecular micro-architecture.

## Material and methods

### Selection and preparation of specimens

The study sample included 22 postmenopausal Caucasian women divided into two groups: a hip osteoarthritis group ($n=9$, age 69±11 years) and a control group ($n=13$, age 72±8 years). The femoral necks of osteoarthritic cases were taken from those who had undergone hip arthroplasty for severe osteoarthritis at the Clinic for Orthopaedic Surgery and Traumatology (Clinical Centre of Serbia, Belgrade). The control specimens were obtained during autopsy (Institute of Forensic Medicine, School of Medicine, University of Belgrade). The control cases were devoid of macroscopic and radiological signs of bone pathological changes and had no history of musculoskeletal diseases and medications known to interfere with bone metabolism. There was no difference in age between the cases with osteoarthritis and controls ($t$-test, $p=0.175$). All activities were approved by institutional review boards and administrative units.

Bone samples were stored in 70 % ethyl alcohol for a minimum of two weeks and were then manually cleaned of adherent soft tissue. The section of the femoral neck was obtained using a water-cooled diamond saw (Exakt, Germany).

### Micro-CT imaging

The bone specimens were put in a sample holder with a consistent proximal-distal orientation and scanned using μCT40 micro-computed tomography (Scanco Medical, Switzerland) at the Department of Osteology and Biomechanics (University Medical Centre Hamburg-Eppendorf). Images were obtained at 70 kV and 114 μA at isotropic resolution of 18 μm, 2,048×2,048 pixels per slice. The integration time per projection was 300 ms.

Two regions of interest on the neck section were analysed using micro-CT: the inferomedial and the superolateral half of the femoral neck (Fig. 1). The following micro-architectural parameters of the trabecular bone were automatically evaluated using the built-in program of the micro CT with direct 3D morphometry: bone volume fraction (BV/TV), connectivity density (Conn.D, 1/mm$^3$), structure model index (SMI), trabecular number (Tb.N, 1/mm), trabecular thickness (Tb.Th, mm), trabecular separation (Tb.Sp, mm), and degree of anisotropy (DA).

### Statistical analysis

The Kolmogorov-Smirnov test was used to estimate the normality of the data distribution. The effects of the group and region on micro-architectural parameters were assessed

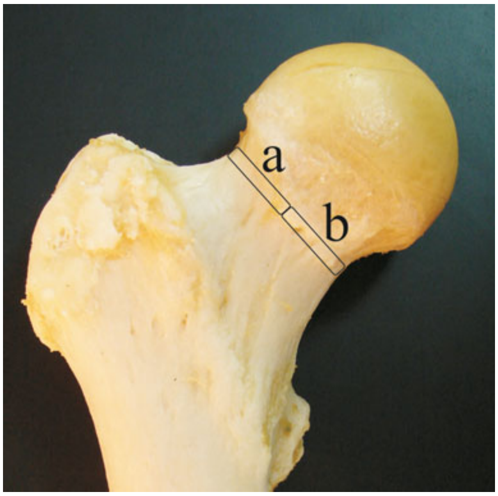


**Fig. 1** The proximal femur. Regions of interest: superolateral neck (**a**), inferomedial neck (**b**)

by using ANOVA for repeated measurements. In order to assess the differences in micro-architectural parameters between OA and control cases, the group was defined as *between-subject factor*, while the region was set as *within-subject factor* to follow its effects on micro-CT parameters within individuals. Afterwards, all micro-architectural parameters were adjusted for BV/TV which was defined as *covariate* (ANCOVA), to check whether architectural differences were independent of bone mass. All analyses were conducted in SPSS statistical software (version 15.0) and the results were considered statistically significant at the 0.05 level.

## Results

We analysed the cancellous bone samples from 22 postmenopausal women divided into a hip osteoarthritis group (OA) and a control group in two biomechanically relevant subregions of the femoral neck (superolateral and inferomedial neck). Although osteoarthritic subjects displayed greater variability, they demonstrated a clear trend of improved trabecular micro-architecture when compared with age- and sex-matched controls (Table 1; Fig. 2). Namely, the osteoarthritic cases expressed notably higher connectivity density ($p=0.008$), significantly lower SMI ($p=0.005$) and significantly reduced anisotropy ($p=0.006$). The same inter-group differences remained after allowing for the effects of BV/TV (Conn.D: $p=0.018$, SMI: $p=0.002$, DA: $p=0.002$).

The osteoarthritic cases also trended towards higher bone volume fraction although without reaching statistical significance in our sample. In particular, the superolateral neck's BV/TV was about 50 % higher than in the control group (0.13 vs. 0.09).

### Inter-site differences

Our results have also shown that all micro-architectural parameters were largely dependent on the region ($p<0.05$), where the inferomedial neck steadily displayed better micro-architecture than the superolateral region (Table 1; Fig. 2). In particular, the bone volume fraction, connectivity density and degree of anisotropy were more than 30 % improved in the inferomedial neck. Namely, inter-site comparisons demonstrated 33 %

**Table 1** Trabecular micro-architecture in the superolateral and inferomedial femoral neck of postmenopausal women with osteoarthritis and the control group

| Parameter | Region | Control group (CL), mean (SD) | Osteoarthritis group (OA), mean (SD) | CL–OA[a] | | SL-IM[b] |
|---|---|---|---|---|---|---|
| | | | | % difference | *p* | *p* |
| BV/TV | Superolateral | 0.09 (0.03) | 0.13 (0.11) | −51.98 | 0.261 | <0.001 |
| | Inferomedial | 0.15 (0.04) | 0.17 (0.10) | −12.71 | | |
| ConnD | Superolateral | 0.52 (0.37) | 1.76 (1.34) | −238.29 | 0.008 | 0.001 |
| | Inferomedial | 0.85 (0.60) | 2.62 (2.28) | −210.18 | | |
| SMI | Superolateral | 2.65 (0.36) | 1.78 (0.95) | 32.79 | 0.005 | 0.010 |
| | Inferomedial | 2.29 (0.41) | 1.49 (0.91) | 35.22 | | |
| Tb.N | Superolateral | 1.25 (0.05) | 1.20 (0.16) | 4.43 | 0.761 | 0.015 |
| | Inferomedial | 1.28 (0.07) | 1.37 (0.28) | −6.91 | | |
| Tb.Th | Superolateral | 0.20 (0.05) | 0.22 (0.07) | −9.87 | 0.759 | 0.009 |
| | Inferomedial | 0.26 (0.07) | 0.23 (0.05) | 13.29 | | |
| Tb.Sp | Superolateral | 0.67 (0.29) | 0.88 (0.12) | −30.61 | 0.098 | 0.004 |
| | Inferomedial | 0.65 (0.27) | 0.78 (0.11) | −19.87 | | |
| DA | Superolateral | 1.72 (0.26) | 1.48 (0.40) | 13.59 | 0.006 | <0.001 |
| | Inferomedial | 2.27 (0.25) | 1.95 (0.18) | 14.26 | | |

[a] CL-OA Control vs. osteoarthritic cases: % of difference in each region, and significance of the effect of the group on micro-CT parameters regardless of the region

[b] SL-IM Superolateral vs. inferomedial region: significance of the effect of the region on micro-CT parameters

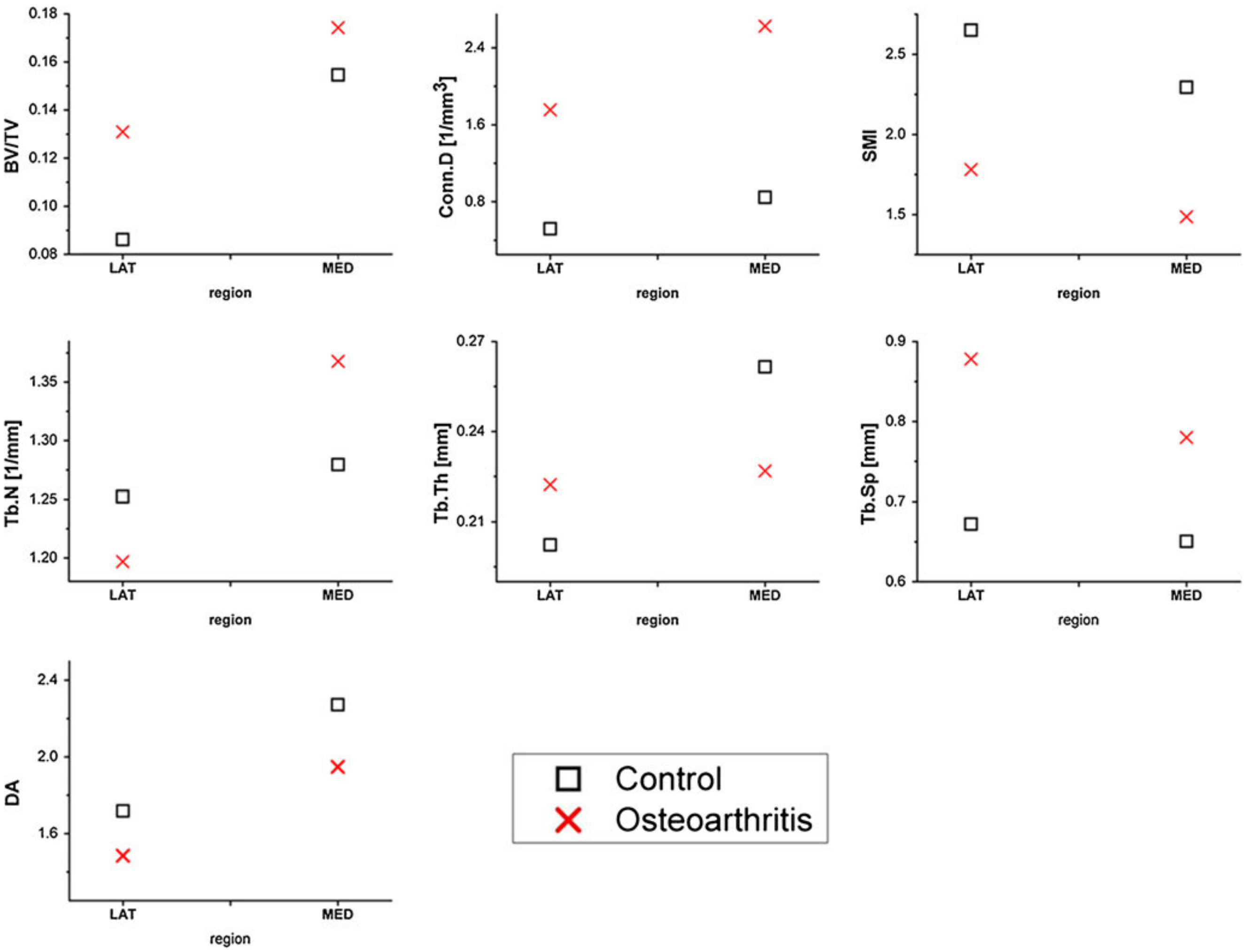


**Fig. 2** Trabecular micro-architectural parameters in the superolateral and inferomedial regions of the femoral neck in osteoarthritic and normal age-matched postmenopausal women

higher bone volume fraction in the inferomedial region in controls, and even 80 % higher values in the inferomedial neck of osteoarthritic cases. In both groups the trabeculae expressed about 50 % reduction in connectivity and nearly 30 % lower anisotropy in the superolateral region.

## Discussion

Due to the prevailing interest in subchondral bone of the femoral head, there are still limited and inconsistent data in the literature about the micro-architecture of the femoral neck in osteoarthritis, particularly in comparison to healthy controls. Overall, our micro-CT study revealed enhanced trabecular micro-architecture in the regions of the femoral neck in postmenopausal women with hip osteoarthritis when compared to the control group. These results confirm previous findings from conventional histomorphometric analysis about denser cancellous bone in the femoral neck in hiparthrosis [16], and contrast another study that reported smaller trabecular bone area in the neck of osteoarthritic femora than in controls [17].

Although Jordan et al. and Neilson et al. [16, 17] did not find evidence for inter-site differences in the femoral neck trabeculae, our results showed regional heterogeneity in all bone micro-architectural parameters in both osteoarthritic and normal femora. Our observation of enhanced micro-architecture in the inferomedial neck is in line with the common belief that this region is well adapted to withstand high compressive stresses [21–24]. In contrast to the quite well preserved inferomedial neck, the less heavily loaded superolateral neck suffers greater deterioration in advanced age [21–23]. In addition, our study showed subtle differences in the pattern of regional heterogeneity of some micro-architectural parameters between OA femora and controls (Table 1; Fig. 2); for instance, the OA cases showed less pronounced inter-site differences in BV/TV when compared to controls, suggesting that their BV/TV increases, particularly in the superolateral region.

Significantly better connectivity and predominance of plate-like trabeculae (low SMI) in both femoral regions in OA patients indicate improved cancellous micro-architecture of the femoral neck in coxarthrosis. In particular, changes in SMI are considered to have disproportionately large effects on bone strength [25]. The degree of anisotropy denotes the level of trabecular alignment which is believed to correspond to principal stress directions and, therefore, may indicate a specific loading pattern [21, 22]. A reduced degree of anisotropy in osteoarthritic femora (particularly in the inferomedial region) depicts more random spatial organisation of the trabeculae in the hiparthrosis patients than in controls. Together with other micro-structural features, lower anisotropy may be beneficial against fracture, since it enhances bone resistance to forces originating from unusual directions such as those originating from falls [21, 22, 26].

Previous studies have shown clear trends of trabecular micro-architectural deterioration during aging in women [21]. Combined consideration of micro-architectural data from several histological, micro-CT and pQCT studies in elderly individuals [9, 19–22] suggest three levels of the trabecular architecture in the femoral neck (osteoporotic, healthy aged, osteoarthritic). Namely, although female population is subject to "normal" trabecular deterioration with aging, some elderly women are affected more severely [22], which may lead to increased susceptibility to fracture. This is in contrast to women who develop hiparthrosis and appear to be to some extent "protected" from the age-related deterioration in cancellous bone structure. From the micro-architectural point of view, our results indirectly support the thesis that net bone loss is lower in aged individuals with OA [2]. Such micro-architectural pattern that we observed in osteoarthritic bone, especially the changes in degree of anisotropy, may be associated with intensive remodelling, but with positive bone balance. This assumption is supported by previous data showing that in osteoarthritic patients various biochemical and cellular factors boost remodelling not only in subchondral bone [27] but also in deeper trabecular bone [28, 29]. Fazzalari [11] noted that increased bone remodelling must be biomechanically influenced, since the femoral neck is remote from the OA lesion. Hence, new biomechanical conditions in OA including changed size and orientation of the joint resultant forces [30, 31] may change the loading pattern of the affected joint [8] and together with the changes in subchondral bone may influence the strains experienced by the femoral neck. It would change the pattern of bone remodelling [32], with subsequent bone structural adaptation reflected in changed trabecular micro-architecture [8] as observed in our study. It is interesting to note that in the observed group differences in trabecular connectivity, shape and anisotropy remained even after adjusting for the effects of BV/TV, denoting that those micro-organisational parameters were independent of bone mass in discriminating osteoarthritic patients from controls.

Our findings seem to contrast data from the study on early knee osteoarthritis [33] that reported decreased mechanical properties of subchondral bone of tibial condyles. However, we analysed bone micro-structure of the femoral neck (in severe hip osteoarthritis) that undergoes a different mechanical loading pattern than the tibial condyles in knee osteoarthritis, which prevents reliable comparisons. In addition, it has to be considered that mechanical properties of trabecular bone depend not only on bone micro-architecture but also on material properties of the bone matrix [34]. Our study focussed on micro-architectural basis of bone strength exclusively. The limitations of our study are related to its cross-sectional nature, i.e., it cannot track an individual during aging and disease progression. Bone fragility is estimated indirectly as reflected in micro-architectural parameters. However, a relation between micro-architectural parameters and bone fragility was shown in a recent micro-CT study on hip fracture cases [22]. Further studies on other aspects of bone quality (including cortical bone characteristics) are necessary to provide a more complete picture of the relationship between OA and femoral neck fragility.

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