# Subchondral bone remodelling spatially linked to the overlying cartilage degeneration in osteoarthritis progression.

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Early diagnosis of osteoarthritis (OA), before to the onset of irreversible changes is crucial for understanding the disease process and identifying potential disease-modifying treatments from the earliest stage. However, the spatial relationships between cartilage lesion severity (CLS) and microstructural changes in the subchondral plate and trabecular bone remain elusive.

In this study, we collected femoral heads from hip arthroplasty for primary osteoarthritis (OA group) and femoral neck fracture (non-OA controls). The specimens were assessed for cartilage lesions using Outerbridge classification and entire femoral heads were micro-CT scanned and analysed. Principal component analysis (PCA) was employed to assess differences between OA and non-OA samples, and the spatial relationship between CLS and subchondral bone changes.

The mapping of the trabecular bone microstructure in OA patients with low CLS revealed trabecular organisation resembling non-OA patients, whereas clear differences were identifiable in subchondral plate architecture. It was reported that the greater articular cartilage deterioration in OA was regionally-linked with lower BV/TV, TMD and thickness, and greater BS/BV and porosity in the subchondral plate; and with thinner, less separated trabeculae with greater BMD and BS/BV in the trabecular bone. Our findings suggest that impairment of subchondral bone microstructure in early stage of OA is more readily discernible in the cortical plate and that morphological characterisation of the femoral head bone microstructure may allow for earlier OA diagnosis and monitoring of progression.

### Abstract

Osteoarthritis (OA) is a degenerative joint disease that affects both cartilage and subchondral bone [1, 2]. The osteochondral junction is the transition between soft and hard tissues and so is critical in absorbing the stresses during joint loading. Abnormal loading leads to microfractures within the osteochondral junction and within the subchondral bone. With progression of OA, as results of changes in the loading pattern, bone remodelling and resorption occur in the joint [3]. This weakens the physical environment that supports the overlying cartilage. In this study, we examined the changes in local distribution of volumetric bone mineral density (vBMD) in the subchondral bone, and the biomechanical properties of the overlying cartilage with an aim to understand the effect of subchondral bone remodelling on the overlying cartilage degeneration.

Human femoral heads were collected during total hip replacement operation due to OA. Cartilage was graded using ICRS classification, and the mechanical property of cartilage was measure by non-destructive cyclic indentation. To determine the remodelling of the subchondral bone, a peripheral quantitative CT (pQCT) was used to assess the vBMD distribution within the subchondral bone. Non-parametric Kruskal-Wallis method was used for statistical analysis (p= 0.05).

The examination of retrieved tissues revealed cartilage in different stages of degeneration, from normal to severely abnormal. Subchondral vBMD decreased with cartilage ICRS grade from 576 to  $253 \text{ mg/cm}^3$  confirming bone remodeling in all samples. Dynamic modulus of cartilage was mapped and showed a weak positive correlation to ICRS grades ( $3.34\pm0.93$ ,  $2.86\pm1.11$ ,  $4.64\pm4.37$  and  $5.56\pm1.83$  N/mm for grade I,II,II and IV respectively), and a moderate positive correlation to subchondral vBMD (*r*=0.59), confirming the concurrence of cartilage biomechanics, degeneration and SCB remodelling.

In summary, subchondral bone provides mechanical support to the overlying cartilage. There is a direct correlation between the cartilage degeneration and the subchondral bone remodelling. Subchondral bone remodelling is an integral part of the pathology of OA, and structural, biochemical and biomechanical changes in the subchondral bone is association with OA progression.

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## **Reference:**

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Early diagnosis of osteoarthritis (OA), before to the onset of irreversible changes is crucial for understanding the disease process and identifying potential disease-modifying treatments from the earliest stage. OA is a whole joint disease and affects both cartilage and the underlying subchondral bone. However, the spatial relationships between cartilage lesion severity (CLS) and

microstructural changes in the subchondral plate and trabecular bone remain elusive. Herein, we collected femoral heads from hip arthroplasty for primary osteoarthritis (n=7) and femoral neck fracture (n=6; non-OA controls) cases. Samples were regionally assessed for cartilage lesions by visual inspection using Outerbridge classification and entire femoral heads were micro-CT scanned. Scans of each femoral head were divided into 4 quadrants followed by morphometric analysis of subchondral plate and trabecular bone in each quadrant. Principal component analysis (PCA), a data reduction method, was employed to assess differences between OA and non-OA samples, and the spatial relationship between CLS and subchondral bone changes. Mapping of the trabecular bone microstructure in OA patients with low CLS revealed trabecular organisation resembling non-OA patients, whereas clear differences were identifiable in subchondral plate architecture. The OA-related changes in subchondral plate architecture were summarised in the first principle component (PC1) which correlated with cartilage lesion severity in all quadrants, whilst by comparison such associations in trabecular bone were most prominent in the higher weight-bearing regions of the femoral head. Greater articular cartilage deterioration in OA was regionally-linked with lower BV/TV, TMD and thickness, and greater BS/BV and porosity in the subchondral plate; and with thinner, less separated trabeculae with greater BMD and BS/BV in the trabecular bone. Our findings suggest that impairment of subchondral bone microstructure in early stage of OA is more readily discernible in the cortical plate and that morphological characterisation of the femoral head bone microstructure may allow for earlier OA diagnosis and monitoring of progression.