Uncoupling of Bone Formation with Resorption in Osteoarthritis Subchondral Bone in Postmenopausal Women - Associated with Osteocyte Dysfunction?

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INTRODUCTION
Osteoarthritis (OA) is not only a disease of articular cartilage but also subchondral bone. Subchondral bone plays an important role in OA initiation and progression. Osteoarthritic subchondral bone is characterized by sclerotic bone and osteophyte formation. Such excessive bone formation was once attributed to osteoblastic dysfunction. Osteocytes compose over 90% of bone cells and are thought to negatively regulate osteoblast differentiation. Yet few studies have been done to investigate the role of osteocytes in OA subchondral bone pathology. This study aimed to characterize the morphology and function of osteocytes in osteoarthritic subchondral bone of human beings.

MATERIALS AND METHODS
Total 20 postmenopausal women aged >50, who suffered from the end-stage OA and hip fracture, were recruited for arthroplasty in authors’ institute (OA n=10; fracture n=10). The age of the patients was 56±18 years for OA patients and 70±12 years for fracture patients. The bone specimens were collected with informed consent for radiological and histological evaluations sequentially. The morphology of osteocyte lacunae was evaluated by nano-CT and histology; the function of osteocytes was measured by the percentage of sclerostin-positive osteocytes lacunae under immunohistochemistry.

RESULTS
Subchondral bone formation was uncoupled with resorption in OA group; whereas it was coupled in fracture group (arrow). Such uncoupled bone formation with resorption in OA group led to higher BV/TV and thicker trabeculae as compared with fracture group (p<0.05 for both) (Fig.1.). The osteocyte lacunae embedded in OA bone matrix was smaller but its number was much more than fracture group (p<0.05 for both), which were echoed by routine histology (Fig.2.). The clustered osteoblasts were also noted (Block arrow). The percentage of sclerostin-positive osteocytes was significantly lower in OA than that in fracture (p<0.05), whereas the percentage of osteocalcin-positive cells was higher in OA than that in fracture (p<0.05) (Fig.3.).

CONCLUSION
This study firstly revealed aberrant morphology of osteocyte lacunae and alter function of sclerostin secretion in osteoarthritic bone, which was associated with osteoblastic dysfunction and excessive bone formation in OA. Osteocytes dysfunction might result in erroneous osteoblast differentiation or result from erroneous transition from osteoblast to osteocyte. The causative effect of osteocytes and its sclerostin secretion in OA bone pathology was further investigated in a spontaneous OA model of guinea pigs. It might provide a scientific foundation for a potential therapeutic strategy for OA.

REFERENCE

ACKNOWLEDGEMENT
This study was supported by University Seeding Fund (Ref No. HKU10400853).