Temporal bone volume changes in the humeral head subchondral bone in a rat rotator cuff tear arthropathy model

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INTRODUCTION: In the knee osteoarthritis (OA), the amount of subchondral bone in the affected joint is reduced, with bone resorption predominating in the early stages, followed by reversal and sclerotic changes in the advanced stages. However, it is unclear whether similar changes occur in OA of the shoulder joint, where mechanical stresses, such as a wider range of motion and a loss of weight loading, are unique. Rotator cuff tear arthropathy (CTA), secondary to a complete rotator cuff tear, is distinguished from primary shoulder OA by subchondral bone depression and femoralization of the humeral head, but its pathogenesis remains unclear. We established a modified CTA model (mCTA) in Sprague-Dawley (SD) rats (Ijuin T., et al., Osteoarthr Cartil Open, 2023) that the CTA phenotype could be reproduced by 4 weeks postoperatively (approximately 3 years of human lifetime equivalent) with reduced subchondral bone mass. Furthermore, we recently discovered that three days after mCTA treatment, M1 macrophages begin to increase in the synovium, and osteoclasts start to increase in the subchondral bone. We also demonstrated that the administration of bisphosphonates can prevent mCTA-induced changes by inhibiting these increases (Tawaratsumida H., et al., Osteoarthr Cartilage, 2024, in press). However, it is still unclear whether the subchondral bone becomes sclerotic in the late phase of CTA, such as 6 months later, as observed in knee OA models. In the present study, we examined whether this subchondral bone loss could change to sclerotic in the advanced stages of the mCTA model.

METHODS: For 12-week-old SD rats, an mCTA model was created in which the right shoulder underwent resection of the rotator cuff, long head of the biceps tendon, and superior glenoid arthrodesis, while the left shoulder was subjected to a sham procedure with a deltoid incision only. Shoulder joint sections were harvested at 4 weeks postoperatively and 6 months postoperatively (approximately 17 years of human lifetime equivalent). After toluidine blue staining, bone volume (BV/TV) was measured in three regions in the superior zone of the humeral head: the subchondral bone plate (SBP), cancellous bone (CB), and subchondral bone plate of the growth plate (SBP.GP). All animal experiments were conducted with the approval of the Ethical Review Committee of our institution.

RESULTS SECTION: At 4 weeks after mCTA, there was a significant decrease in BV/TV of all SBP, CB, and SBP.GP compared to sham shoulder. However, at 6 months, there was a significant increase in BV/TV for SBP ($P<0.05$), while BV/TV for CB and SBP.GP remained decreased (Fig.1,2). In the collapsed area after 6 months, osteoclasts had nearly disappeared, and instead, osteoblasts had increased, supporting the increase in the subchondral bone plate (Fig.3).

DISCUSSION: It has been suggested that the subchondral bone in human CTA is osteoporotic (Neer et al., 1983). Indeed, our quantitative analysis of the CT image of CTA cases (Tawaratsumida H., et al., *Osteoarthr Cartilage*, 2024, in press) demonstrated a significant decrease in the subchondral CB volume. However, in the present study, the SBP mass of the mCTA model increased at 6 months (advanced stage). This discrepancy with clinical evidence may be attributed to the fact that the shoulder is not loaded in a four-legged animal model. However, the subchondral CB remained reduced even after 6 months, which is consistent with the clinical findings of CTA and likely represents a characteristic difference from knee OA, in that it does not become sclerotic.

SIGNIFICANCE/CLINICAL RELEVANCE: By analyzing the phenotype of the late-stage (6 months) mCTA model and comparing it with evidence from knee OA models, it may be possible to uncover the specific molecular mechanisms in the shoulder joint that prevent sclerotic changes in the subchondral trabecular bone.

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IMAGES AND TABLES:

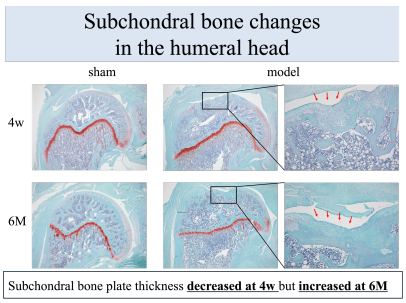

Fig.1

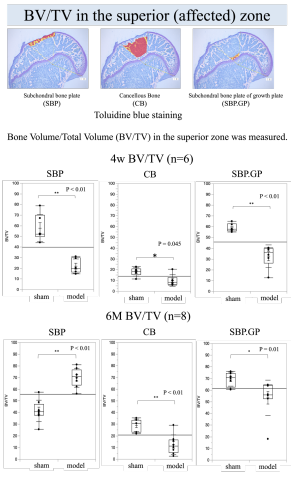

Fig.2

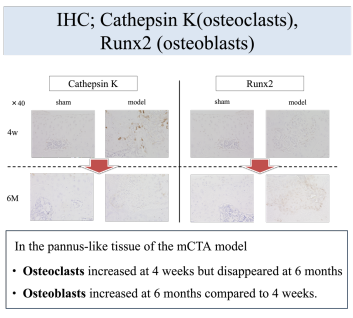

Fig.3