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Early Changes of Articular Cartilage and Subchondral Bone in The DMM Mouse Model of Osteoarthritis

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Introduction

- Recent findings suggested that subchondral changes might precede cartilage degeneration during OA.
- Gene expression of subchondral bone in a rat model was reported dramatically dysregulated before noticeable articular cartilage damage.

Introduction

◆However, how articular cartilage and subchondral bone changes during the time-course of OA in the predominant model of post-traumatic OA—the DMM model, has not yet been fully described.

◆Understanding the articular cartilage and subchondral bone changes (especially in the early stage) in this commonly used mouse model will provide more information on the

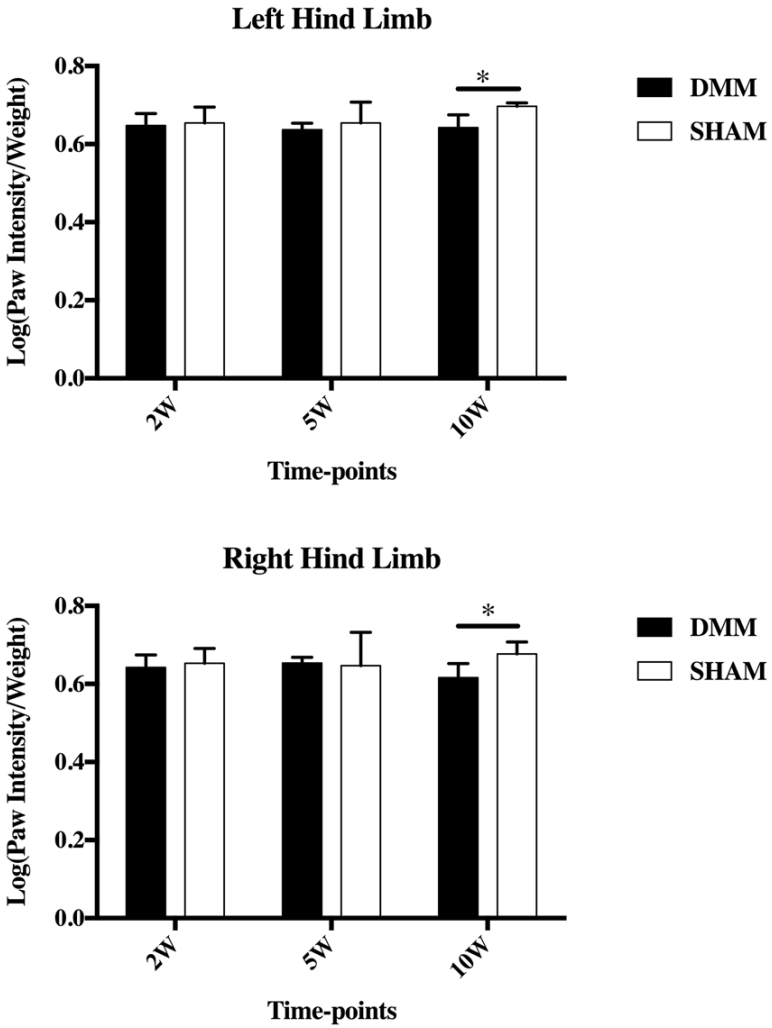
Materials and Methods

12W C57BL/6 mice

- Group 1 Sham group,
- Group2 DMM group（Left leg），

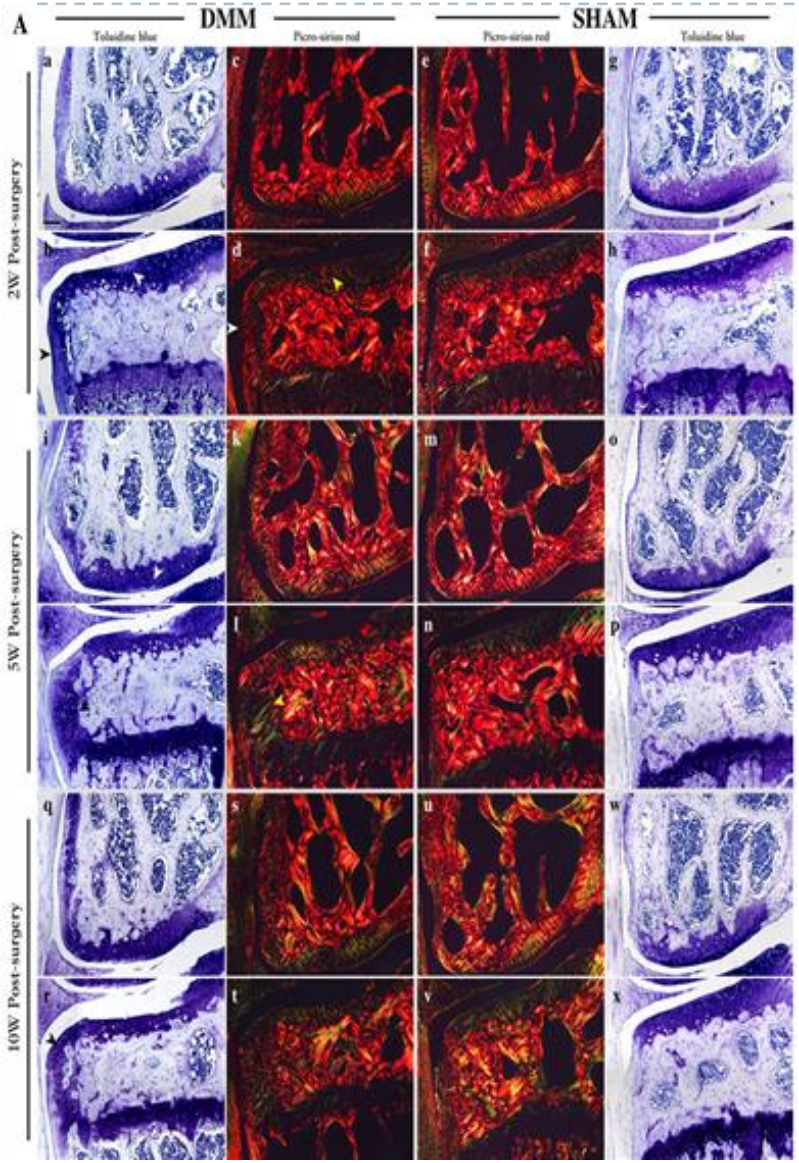
Three termination time-points (2, 5 and 10 weeks post-surgery)

Results (Gait analysis)



Gait disparity only occurred at 10 weeks post-surgery in the DMM group compared to SHAM but not at 2- and 5-week time-points after surgery.

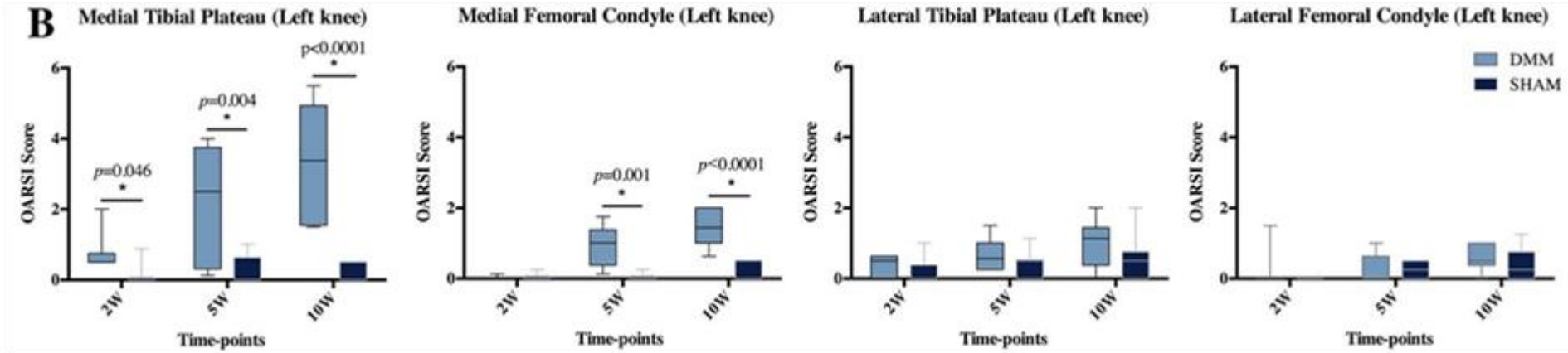
Results（toluidine blue (TB)、picrosirius red (PR) staining



◆Proteoglycan loss (b, white arrow)

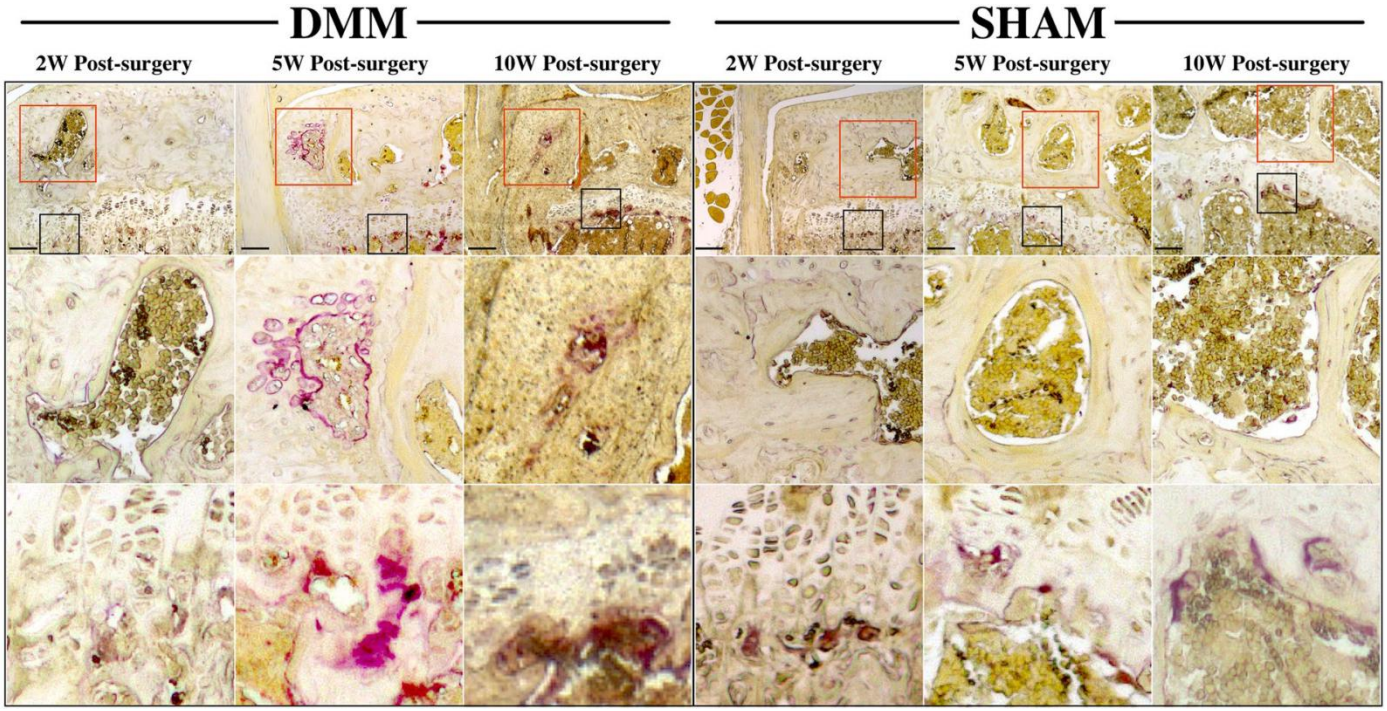
◆Cartilagenous osteophyte formation (b, black arrow)

Results（toluidine blue (TB)、picrosirius red (PR) staining



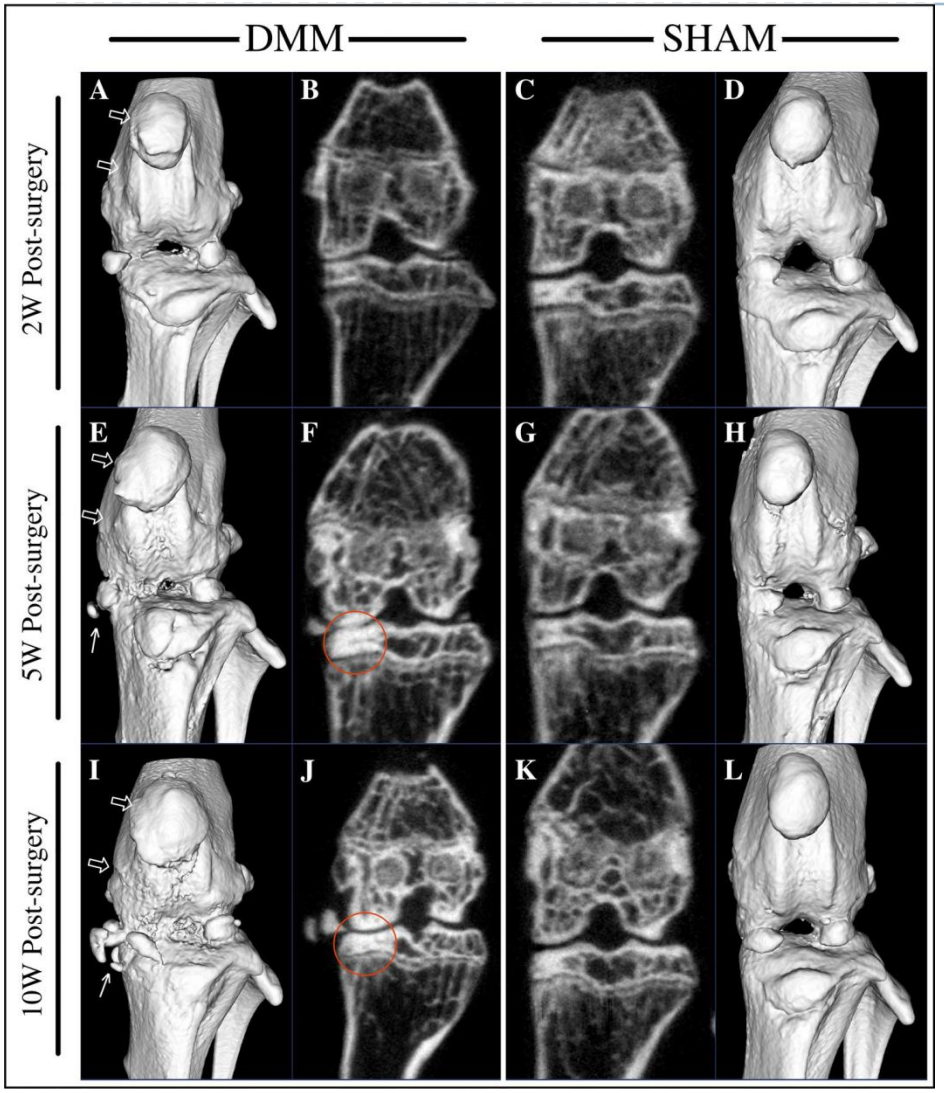
◆OARSI scores of the medial tibial plateau of DMM mice were increased at all time-points

Results（TRAP staining）



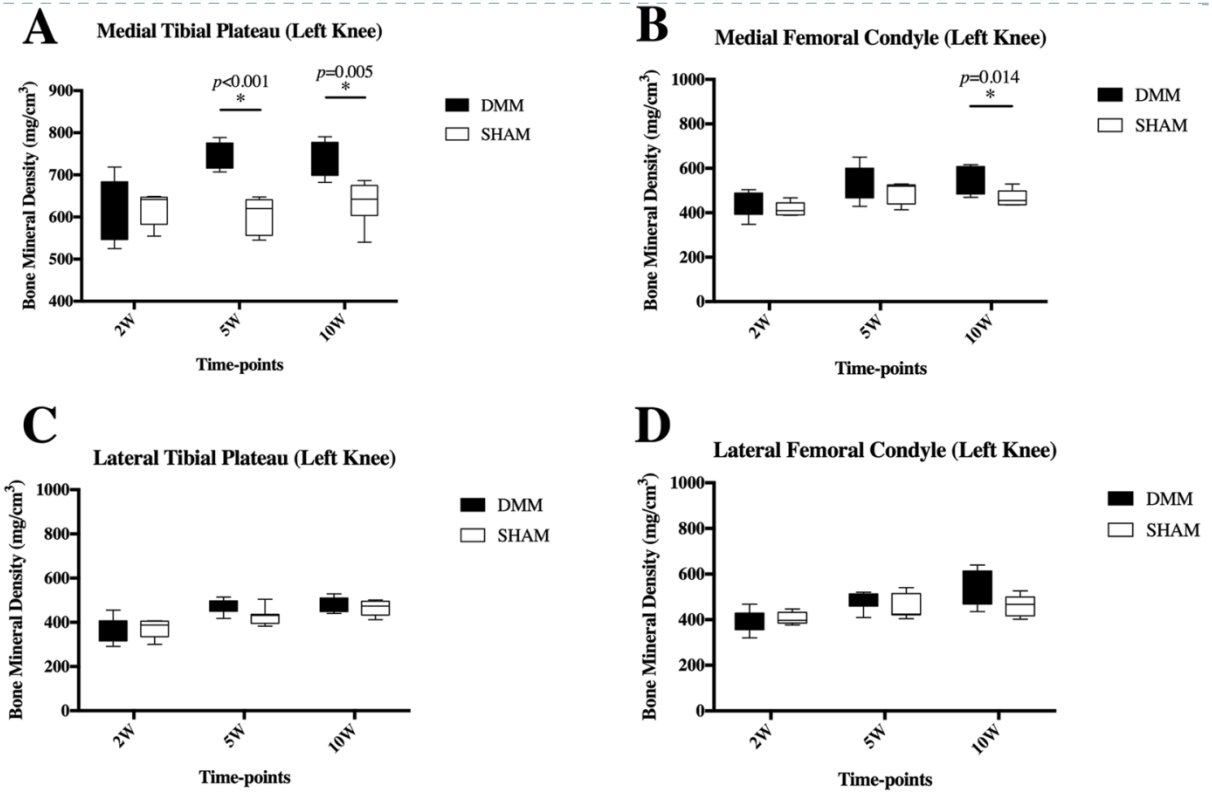
- Osteoclast activity in the subchondral bone appeared increased at 5- and 10-week following DMM surgery,mostly within the osteophyte (red rectangle)

Results (μCT 3D joint reconstruction)



- Micro-CT analyses demonstrated that joint condition deteriorated through the time course in DMM mice, presenting with osteophyte formation (E,I, arrow) around the joint. A coronal plane that represents the middle of the joint showed bone sclerosis in the medial tibial plateau at 5 and 10 weeks post-surgery in DMM mice.

Results

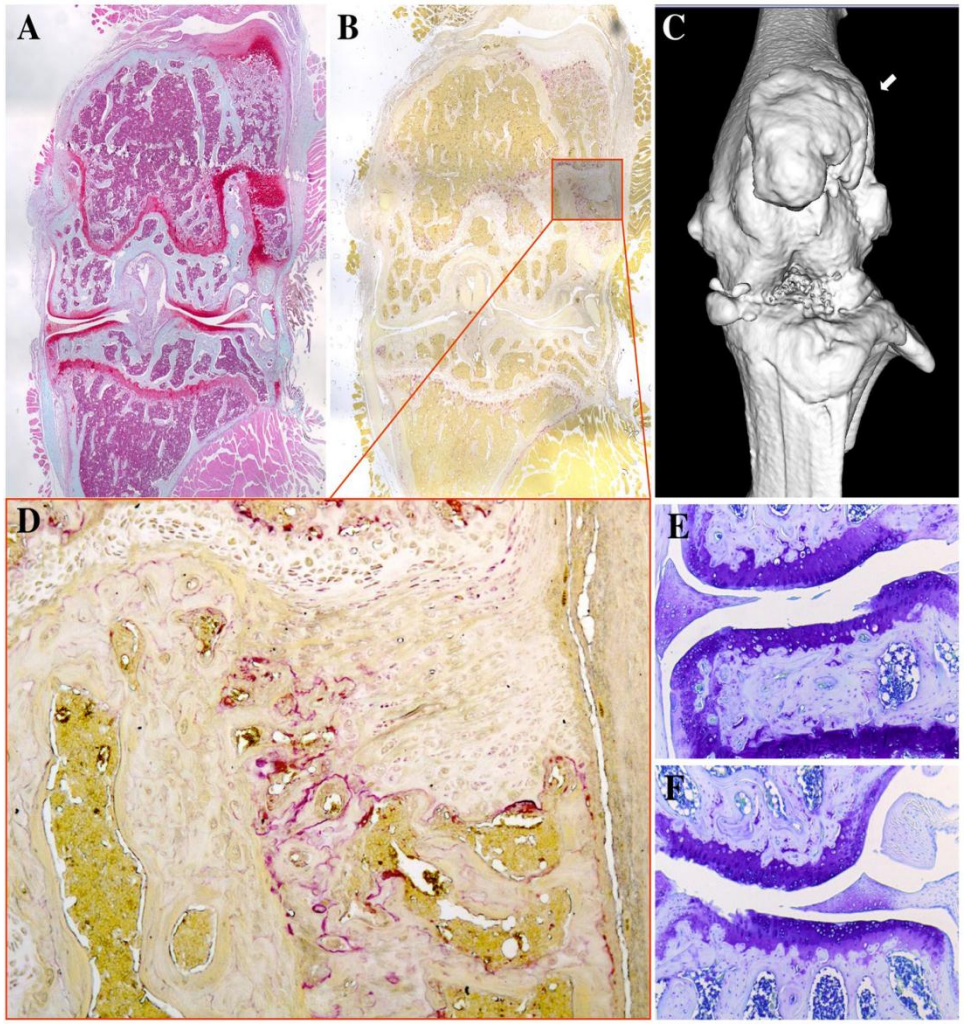


- Clearer differences were detected between DMM and SHAM at both 5 and 10 weeks post-surgery with higher BMDs in DMM mice.
- BMDs of the MFC were higher in DMM mice 10 weeks after surgery

Discussion

- It has been reported that a large number of genes were dysregulated as early as 6 hours after DMM surgery by microarray analysis of gene expressed in the whole joint, including known pathogenic OA genes *Mmp3, Adamts5,*and *Ccl2.*
- BV/TV of MTP at 2 weeks post-surgery was significantly higher in DMM mice, suggesting that increased bone remodeling occurred at very early stages (earlier than 2 weeks post-surgery) of OA in DMM mouse model.

Discussion



Another finding of note is the subluxation/dislocation of the patella that occurred in some of the mice following DMM surgery as early as 2 weeks post-surgery.but this complication hasn’ t been reported yet to our knowledge. It is possibly one of the reasons that surgical outcomes of DMM vary from lab to lab, and from individual to individual. So we exclude those

Conclusion

This study suggests that subchondral bone changes might occur at the same time as (and possibly earlier than) cartilage changes. Further investigation of early subchondral bone changes driven by osteoclasts/osteoblasts/osteocytes activities as well as gene and protein expressions in the subchondral bone at the early time-points is needed for a better understanding of the molecular mechanism driving bone changes during the initiation of OA in the DMM model