LONGITUDINAL SUBCHONDRAL BONE MICROSTRUCTURE AND JOINT LOADING IN RATS WITH POST-TRAUMATIC KNEE OSTEOARTHRITIS

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Introduction

Osteoarthritis is a disease of the whole joint with concurrent degeneration of cartilage and subchondral bone. Mechanical loading is believed to contribute to disease onset and progression [1]. Destabilization of the Medial Meniscus (*DMM*) is often used to trigger post-traumatic osteoarthritis in preclinical studies [2]. We longitudinally imaged subchondral bone and estimated joint loading using musculoskeletal modeling in rats with DMM. We hypothesized that DMM alters loading and subchondral bone microstructure in the medial tibia.

Materials and methods

Unilateral DMM or sham surgery was performed in male Sprague-Dawley rats (n=6 rats/group). **Longitudinal *in vivo* micro-CT**: The operated knee was imaged every other week for 6 weeks (Skyscan 1076, Bruker, 18µm, 65kV, 150µA, 2000ms, 0.8°, Al 1mm). After image reconstruction and filtering, subchondral bone microstructure was analyzed on the tibial medial plateau (*BV/TV*: bone volume fraction, *BS/BV*: specific bone surface, *Tb.Th*: trabecular thickness, *Tb.Sp*: trabecular separation, *Tb.N*: trabecular number, *Sb.Pl.Th*: subchondral bone plate thickness) [3]. **Musculoskeletal model:** 8 weeks after surgery, rat gait was recorded using biplanar fluoroscopy and ground reaction forces (several trials per rat) [4]. With these data, peak medial force and associated adduction angle were estimated with musculoskeletal modeling [5,6]. **Histology and *ex vivo* micro-CT**: Rats were sacrificed 8 weeks after surgery. All dissected knees were scanned as described above, and knee histology was performed (safranin-O staining) in half of the animals. **Statistics**: linear mixed-effects models were used for *in vivo* parameters and musculoskeletal outputs, and Wilcoxon rank-sum tests for *ex vivo* parameters.

Results

At 2 and 4 weeks, Sb.Pl.Th was higher in DMM versus sham. There was no interaction of time and surgery for other parameters (see **Fig 1**).

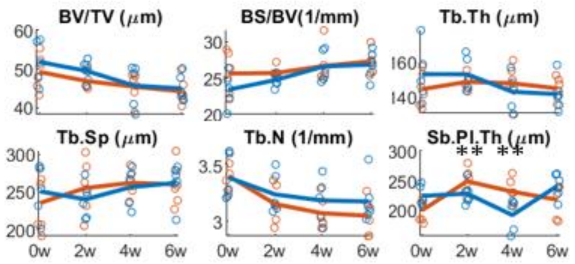

*Figure 1: Evolution of subchondral bone parameters following knee surgery (in vivo scans, from 0 to 6 weeks). n=6 rats per group. Sham in blue, DMM in red. **p<0.01*

8 weeks after surgery, there were fewer and thicker trabeculae in DMM versus sham. Histology confirmed abnormal cartilage and bone structure (proteoglycan loss, bone cyst) (see **Fig. 2**).

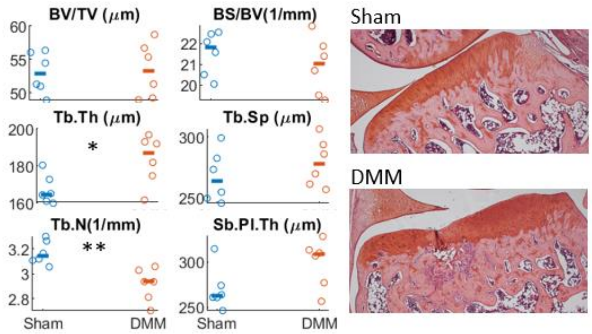

*Figure 2: LEFT: Subchondral bone parameters based on ex vivo scan (left) n=6 rats per group *p<0.05; **p<0.01; RIGHT: histological sections of the medial plateau in rat with sham surgery and DMM (right).*

There was no difference in peak force on the medial compartment 8 weeks after surgery. Adduction angle was lower in DMM versus sham (see **Fig. 3**).

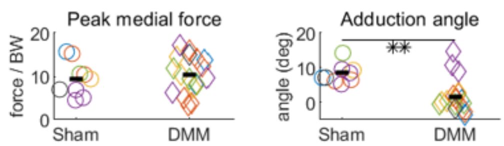

*Figure 3: musculoskeletal outputs. N=6 rats, n=18 trials for sham; N=6, n=9 for DMM. BW=body weight; **p<0.01.*

Discussion

DMM altered subchondral bone microstructure, resulting in fewer and thicker trabeculae. The musculoskeletal analysis showed no overloading of the medial compartment with DMM, but knee adduction angle was reduced. Although loading was not altered at joint level, it might be altered at tissue level. A finite element analysis of the knee joint could determine if local mechanical cues are associated with altered bone adaptation.

References

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