

## Acute In Vivo Metrics of Joint Incongruity Following Articular Fracture Predict Posttraumatic Arthritis in Mice

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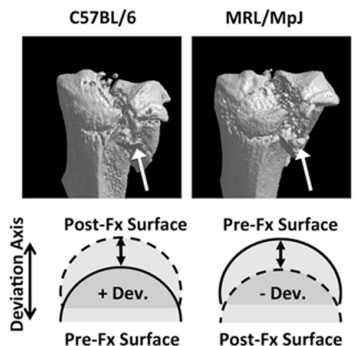
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**Purpose:** Posttraumatic arthritis (PTA) occurs commonly after articular fracture. Joint degeneration may arise in part from surface incongruity after injury. Radiographic classification systems do not account for 3-dimensional (3D) geometry of the joint surface. CT-based measures of joint fracture severity have been used to predict ankle PTA development. Interestingly, the MRL/MpJ “superhealer” mouse strain is protected from PTA following articular fracture, thus providing valuable insight into the progression of PTA. Currently, the relationship between initial injury severity, articular displacement, and PTA development following articular fracture remains unknown. The objective of this study was to develop in vivo micro CT metrics of joint incongruity after articular fracture to further characterize the pathomechanism of PTA.

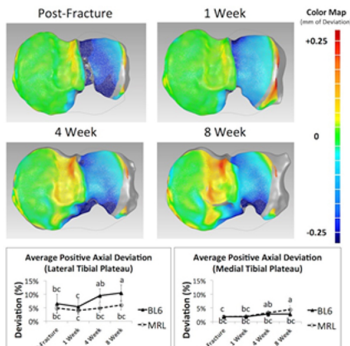
**Methods:** C57BL/6 and MRL/MpJ mice (n = 12/strain) received closed articular fractures (fx) of the tibia (Fig. 1). At 8 weeks, mice were sacrificed and assessed for arthritic changes (Mankin score). In vivo micro CT was performed pre- and post-fx, 1, 4, and 8 weeks post-fx. Displacements of the bone surface, or bone surface deviations (BSDs), were quantified for the lateral and medial tibial plateau (Fig. 1). Serum biomarkers of bone metabolism were measured pre- and post-fx to 6 weeks. BSDs were analyzed using analysis of variance and bone markers using nonparametric analyses.

**Results:** Temporal patterns in BSDs were significantly different between mice with larger average positive axial deviations found in C57BL/6 mice at 8 weeks post-fx ( $P = 0.01$ ; Fig. 2). Mankin scores were correlated to all BSDs in both mouse strains. Acute BSDs showed the strongest correlations with PTA development. In C57BL/6 mice, axial BSDs on post-fx day 0 were highly predictive of PTA severity at 8 weeks post-fx (Fig. 3). In contrast, MRL/MpJ mice post-fx day 0 BSDs did not predict PTA development. Serum PINP (procollagen I N-terminal propeptide), a bone formation marker, in the C57BL/6 mice was significantly lower than the MRL/MpJ mice post-fx ( $P = 0.005$ ), indicating a less robust acute response compared with the superhealer strain.

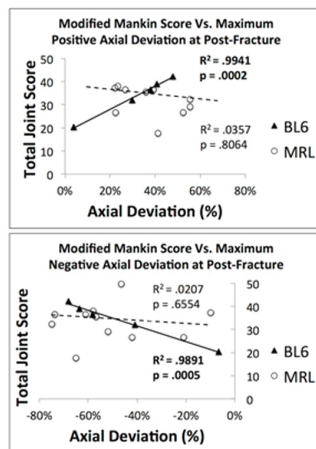
**Conclusion:** Acute displacements of the bone surface following articular fracture were predictive of arthritis development in C57BL/6 but not MRL/MpJ mice. C57BL/6 mice also showed an acute drop in serum PINP compared to MRL/MpJ mice. These findings suggest that MRL/MpJ mice undergo a unique mechanism of fracture healing following articular fracture and that joint incongruities secondary to articular fracture do not predispose MRL/MpJ mice to PTA development, whereas PTA development in C57BL/6 mice is predicted by acute bone displacements and decreased bone metabolism. In vivo CT metrics of joint incongruity provide a method for quantifying bone surface incongruities that have traditionally been difficult to measure. The translational potential of our joint incongruity metrics is high, as they could readily be applied to full-scale clinical CT scans.



**Figure 1.** (Top) Micro-CT images of representative fractures. (Bottom) Metrics of joint incongruity after intra-articular fracture. Reference surface = pre-fracture; test surface = post-fracture.



**Figure 2.** (Top) Representative color map of axial deviation with fracture healing. (Bottom) Significant strain-wise differences in fracture healing from post-fracture to 8 weeks.



**Figure 3.** Correlations between total joint Mankin score for arthritis at 8 weeks post-fracture and post-fracture joint incongruity.