

## Fracture Fixation Determines the Pathway of Osseous Repair: A bilateral femur fracture model in a rat

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### Introduction

In humans, rigid internal fracture fixation leads to primary bone healing (intramembranous ossification), whereas secondary healing (endochondral ossification) is stimulated by interfragmentary motion at the fracture site and is characterized by a cartilaginous callus intermediary. We sought to investigate factors influencing the pathway of fracture repair and establish a bilateral femur fracture model that would concurrently induce both repair pathways in one animal. Specifically, healing induced by two variants of a novel, locked intramedullary nail were compared to rigid fracture fixation via contralateral compression plating.

### Methods

On an IACUC-approved protocol, 17 five-month old, male Sprague-Dawley (SD) rats underwent bilateral open transverse mid-shaft femur fracture with predrilling and an osteotome. All were treated by rigid fixation with plate and screws on one side. On the contralateral side, 8 animals underwent fixation with a custom static locked intramedullary nail (Figure 1) and 8 received a dynamized IM nail with a single distal screw. 5 animals in each group were survived 24 weeks with serial radiographs. Callus was quantified on lateral radiographs using a ratio of callus to cortical bone width. One animal from each group was euthanized for histology at 10, 21, and 28 days. Histomorphometric analysis was performed to compare callus size and tissue differentiation.



Figure 1: Post-op AP radiograph of a Sprague-Dawley rat after bilateral fracture surgery and fixation with a static locked intramedullary nail and contralateral plate and screws.

### Results

One animal died intraoperatively due to an anesthetic overdose. Two plated femurs failed and the animals were euthanized (one at 6 weeks and one at 10 days). The static locked nail group showed early callus, but 0/5 achieved definitive radiographic union by 24 weeks. Definitive radiographic union was achieved in 3/4 dynamized nails; the non-union occurred in a nail that broke at its screw sites and lost reduction. Definitive radiographic union was obtained in 6/9 plated fractures. Dynamized nails had a higher union rate than locked nails (75% vs 0%,  $p=0.048$ ), but there was no difference in union rate between dynamized nails and plates ( $p=1.00$ ). There was an apparent trend towards more rapid healing with internal fixation by plates and screws than dynamized nailing (9.67 vs. 12 weeks respectively,  $p=0.1389$ ).

Peak callus size was greater in femurs treated with intramedullary nails than those treated with plates and screws (callus indices of 1.92 in dynamized nails and 1.68 in static locked nails vs. 1.11 in plates,  $p<0.01$ ); however, there was no difference in peak callus size between the different nail types (1.92 vs. 1.68,  $p=0.2764$ ). Plated fractures featured less radiographic callus than either nail variant at all timepoints after 3 weeks ( $p<0.05$ ; see Figure 2).

Histologically, plated femurs had less absolute callus size than nailed femurs at 10, 21, and 28 days. Nailed femurs featured more fibrocytes at each timepoint. Nailed femurs harvested at 28 days featured more chondrocytes than plated femurs ( $1.89 \text{ mm}^2$  vs.  $0.27 \text{ mm}^2$ ,  $p=0.0041$ , pictured in Figure 8). There was no difference in callus size or tissue type between the nail variants at 10 or 21 days; however, femurs treated with a dynamized nail had more histologic callus than femurs treated

with static locked nails at 28 days ( $42.5 \text{ mm}^2$  vs.  $19.1 \text{ mm}^2$ ,  $p=0.016$ ). Figure 3 displays histologic cross-sections from femurs harvested from the same animal at post-op day 28; there is significantly more callus, chondrocytes, and fibrocytes in the nailed femur compared to the plated femur.

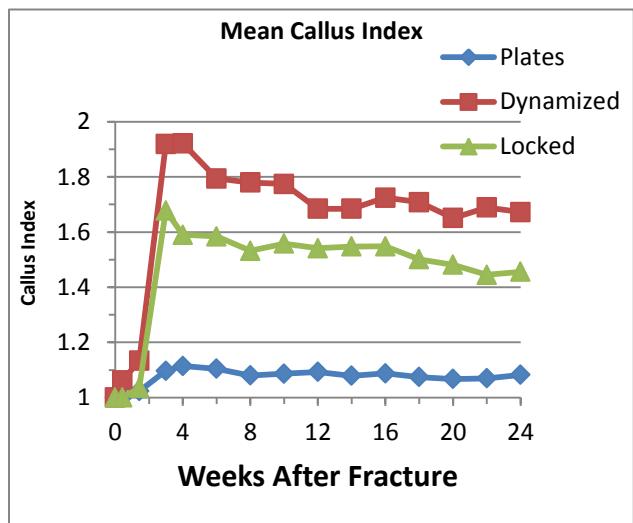


Figure 2: Mean radiographic callus index of each treatment group at each radiographic timepoint. Plates featured less radiographic callus than either nail variant.

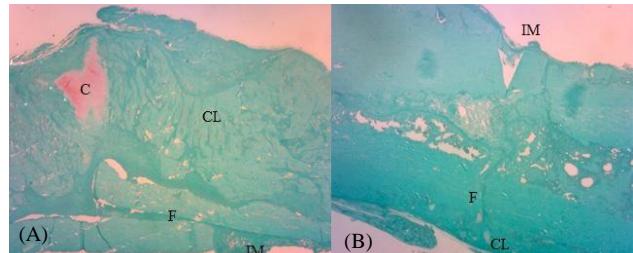


Figure 3: Longitudinal cross sections of fractures 28 days after treatment with (A) a dynamized nail and (B) a plate with screws. F=fracture site, C=cartilage, CL=callus, IM=intramedullary canal.

### Conclusion

As in humans, the rigidity of fracture fixation in SD rats determined the pathway of fracture healing. IM nailing allowed interfragmentary motion that stimulated endochondral ossification, while plated femurs provided rigid fixation and healed via intramembranous ossification (as evidenced by differences in radiographic and histologic callus formation). The static locked IM nail did not result in radiographic union; however, union occurred with the dynamized variant. Controlled axial loading through the fracture site induced endochondral ossification and facilitated radiographic union in the SD rat femur fracture.

### Significance:

The creation of a bilateral fracture model that simultaneously induces both endochondral and intramembranous ossification will facilitate study of the differential effects of external and systemic stimuli on each healing pathway and provides for the establishment of biologically based treatment strategies for specific patient populations.