Developing a Novel Porcine Meta-Critical-Sized Bone Defect Model for Clinical Translation

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Purpose: Segmental bone defects (SBDs) from high-energy trauma can result in infection and nonunion. Surgeons are continuously looking for effective methods to treat SBDs. Robust preclinical models that can test emerging surgical strategies and adjunctive therapies are an important research tool. Most critical-sized defect (CSD) models have been in small animals. Several ovine and canine preclinical models have been reported. In contrast, porcine CSD models are largely undeveloped. Porcine models offer the advantage of marked immunologic fidelity to the human injury response. Here we describe our progress developing a porcine CSD model.

Methods: Eight adult Yucatan Minipigs (YMPs) were subjected to a 25-mm SBD in the midtibial diaphysis via resection through an anterior approach and treated with a custom made intramedullary nail (IMN). Four YMPs were subjected to a 25-mm SBD and treated with a 7-hole 3.5-mm compression plate on the lateral tibial surface and an adjunctive 7 hole 1/3 tubular plate on the anteromedial tibial surface (small ORIF [open reduction and internal fixation]). An additional 4 YMPs were subjected to a 40-mm SBD and treated with an 8-hole 3.5-mm compression plate and an 8-hole 1/3 tubular plate placed in an identical manner as the smaller defect (large ORIF). IMN pigs were sacrificed at 6 months after surgery. Small ORIF and large ORIF groups were sacrificed 3 months after surgery. Serial radiographs were taken monthly until sacrifice. Three orthopaedic trauma surgeons recorded modified radiographic union scale in tibial fractures (mRUST) scores on all specimens. Mean mRUST for each group at each time point was calculated. Union was confirmed at sacrifice by direct observation.

Results: Mean mRUST scores for the IMN, small ORIF, and large ORIF groups at 1 month were 6.2 ± 1.5, 7.1 ± 1.1, and 5.3 ± 1.1 ($P > 0.2$). At 4 months, only 1 of 8 IMNs healed with a mean mRUST of 8.5 ± 1.4. Three of 4 small ORIFs had healed with a mean mRUST of 11.6 ± 1.8 ($P < 0.0001$ compared to IMN). The fourth pig was progressing to union (mRUST 9.5) at the time of sacrifice. All 4 of the large ORIFs were sacrificed at 3 months due to flail nonunions of the affected leg. Fracture healing was slow but progressive in the small ORIF group. Monthly interval mRUST scores were 1 month = 7.1 ± 1.1; 2 months = 9.5 ± 0.9, 3 months = 10.8 ± 1.3, 4 months = 11.7 ± 1.8 (1 mo vs 2 mo $P < 0.00001$; 2 mo vs 3 mo $P = 0.0002$; 3 mo vs 4 mo $P = 0.0571$).

Conclusion: We have developed a "meta-CSD" model in which healing was arrested with IMN fixation but successful with rigid internal fixation in the smaller defect. This model offers a variety of options to test therapies that can promote healing using IMN fixation, or to investigate concomitant conditions that may arrest healing (ie, muscle injury, hemorrhagic shock, diabetes) using rigid internal fixation with the smaller defect.