Characterization of a Transtibial Amputation Model of Osseointegrated Implant Infection

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Purpose: Osseointegrated (OI) prostheses have major advantages to traditional socket-based prostheses, yet a difficult barrier to widespread implementation is infection and challenges with treating OI-associated infections. To address this critical problem, a preclinical animal model must exist of the human model to test potential interventions. We describe a novel rabbit model of OI implant-related infection that can act as a platform for rapid translation and development of therapeutic approaches to combat these uniquely challenging infections.

Methods: Studies were conducted as a single-stage amputation via exposure, transection, reaming, and tapping of the tibia, followed by placement of a 3.5 mm x 75 mm Ti-6Al-4V cortical screw implant. The remaining muscle and skin were closed and a prosthetic attached to the screw. Comprehensive complete blood cell hematology and clinical chemistry and imaging performed up to 8 weeks. High-resolution micro CT and histology were conducted at terminal end points. Separately, pharmacokinetic testing of intraosseous vancomycin delivery was performed with 30 mg/kg vancomycin in 5 mL saline delivered over 30 minutes via peripheral IV cannula or intraosseous administration via 18-G needle. Serum and bone marrow collection was conducted across a period of 5 hours. Statistical analyses (2-way analysis of variance) were performed in GraphPad Prism 10 software.

Results: Hematology and clinical chemistry results indicate normal ranges over the study course. Aseptic loosening of the implant was observed in 3 rabbits (38%), likely due to anatomical features of the rabbit tibia. Terminal micro CT and histology demonstrate osseointegration between the threads of the implanted screw within the medullary cavity. Pharmacokinetic data determined intraosseous vancomycin delivery results in significantly lower vancomycin concentrations systemically as compared to IV delivery of vancomycin ($P<0.05$) and higher peak vancomycin concentration within the tibial canal.

Conclusion: This work-in-progress translational model has demonstrated a reproducible small animal model of OI transtibial amputation that successfully recreates the bone-skin-implant interface, material-bone interactions to match human OI, and a similar immune response. Preclinical efficacy of intraosseous administration of vancomycin compared to traditional IV vancomycin delivery will be investigated, with potential for rapid translation to clinical studies.