Title: Intrawound vancomycin powder does not alter in vivo titanium osseointegration in a murine model of joint arthroplasty

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Background:
Intrawound vancomycin powder is commonly used to prevent the development of superficial and deep wound infections in orthopaedic oncology. Investigators have demonstrated in vitro that vancomycin is cytotoxic to host cells required for healing such as osteoblasts, fibroblasts, myocytes, and endothelial cells. This data has generated concerns that the potential benefit of mitigating infection using vancomycin powder may not be worth the risk of perturbing biologic stability of orthopedic implants. There is a paucity of in vivo studies investigating the impact of vancomycin on osseointegration. The concern of impaired osseointegration is particularly relevant in the orthopaedic oncology population who may have diminished wound healing due to systemic illness and the use of chemotherapy.

Questions/Purposes:
Does vancomycin powder decrease osseointegration of titanium implants in a murine model of joint arthroplasty?
Is the impact of vancomycin on osseointegration early or sustained after the insult of local cytotoxic concentrations in the knee joint?

Methods:
A 6 x 0.8mm titanium pin was implanted retrograde into the distal femur of 10-week-old C57BL/6 mice. Mice were randomized to receive 4mg of intrawound vancomycin prior to wound closure (1g equivalent in humans). Animals were sacrificed at 2 and 4 weeks, and femurs were disarticulated, removed, and cleaned of all soft tissue. There were 5 mice in each group at each time point (N=20). Femurs were embedded in a resin block with the distal aspect exposed for “push-in” testing. An Instron hydraulic press was calibrated and used to quantify the force necessary to “push-in” the titanium implant, effectively disrupting the bone-implant interface. Peak values were recorded for each implant from curves in Figure 1.

Results:
Despite a small reduction in “push-in” force in the vancomycin treated group, there was no statistical difference at 2 weeks for control (21.4N) and vancomycin (16.9N) treated animals (p=0.6) (Figure 2). At 4 weeks, there was no difference in average “push-in” forces in control (36.4N) and vancomycin (36.2N) groups (p=0.9) (Figure 2).

Conclusion:
Investigators have demonstrated that vancomycin causes toxicity in vitro at concentrations used for intrawound application. In this murine model of titanium osseointegration, intra-wound vancomycin powder did not have a significant effect on osseointegration at 2 or 4 weeks post-operatively, as assessed by push-in force required for disruption of the bone-implant interface.
Figure 1). 2 week “push-in” curves for control (A) and vancomycin (B) treated animals. 4 week “push-in” curves for control (C) and vancomycin (D) treated animals.
Figure 2). Average push in force in Newtons (N) for control and vancomycin treated animals at 2 and 4 weeks.