Title: Systemic antibiotic absorption from calcium sulfate beads exceeds that from solid spacers used to treat hip and knee prosthetic joint infection (PJI)

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Introduction: Different methods exist for local antibiotic delivery during two stage revision arthroplasty for PJI. One such method, antibiotic-eluting calcium sulfate beads, has recently gained in popularity. While some investigation into the elution properties and local delivery of these antibiotics has been performed, there is a paucity of data evaluating their systemic absorption.

Methods: We prospectively collected data on 14 consecutive patients who successfully underwent a two-stage revision hip or knee arthroplasty for the treatment of PJI. During the first stage (explant), patients received an antibiotic impregnated spacer with or without calcium sulfate beads. During the second stage (reimplantation), patients received only antibiotic-impregnated calcium sulfate beads. Total amount of implanted tobramycin and daily serum tobramycin levels beginning on post-operative day (POD) #1 through hospital discharge were collected and recorded for both procedures. Paired T-tests were performed effectively using each subject as its own control across the two-stage revision.

Results: For the stage one procedure, the mean amount of total tobramycin implanted within the antibiotic laden spacer +/- additional calcium sulfate beads was  $4.3_g$  (range  $2.4_g$ - $7.2_g$ ). For the reimplantation, all patients had  $1.2_g$  tobramycin implanted in the form of drug eluting calcium sulfate beads. Mean POD#1 serum tobramycin levels were  $2.6_{\mu g/ml}$  and  $3.3_{\mu g/ml}$  for the first and second stage surgeries, respectively. Following the stage one procedure, POD#1 serum tobramycin levels were  $0.76_{\mu g/ml}$  per gram of tobramycin implanted; following the stage two procedure, the POD#1 serum tobramycin levels were  $2.7_{\mu g/ml}$  per gram of tobramycin implanted (p=0.014).

Conclusion: In this cohort of patients who underwent two-stage revision hip or knee arthroplasty for PJI, small doses of antibiotics added to calcium sulfate beads resulted in relatively high systemic serum antibiotic levels on POD#1. Surgeons should be aware of this systemic exposure when using calcium sulfate beads as a vehicle to deliver local antibiotics during the treatment of PJI.