Introduction: Postoperative spinal wound infections are a significant problem despite improved surgical techniques, systemic antibiotic prophylaxis, and reduced operating time. Infection rates are 1-5% in the non-compromised patient population undergoing elective posterior spinal surgery. Due to numerous systemic and local factors, this infection with Staphylococcus aureus in the traumatized spine occurs at a rate of 6-12%. Frequent returns to the operating room for irrigation and debridements and the need for long term intravenous antibiotics lead to significant morbidity for the patient and pressures healthcare facilities with tremendous costs. Local hematoma harboring bacteria at the end of a procedure, combined with systemic malnutrition, tissue hypoxia, compromised skin under a stabilizing brace, and poor wound healing while patients are bedridden are important factors for this increased risk of infection.

Materials and Methods: Using an FDA-approved biodegradable polymer (poly(lactic-co-glycolic-acid) or PLGA) we created resorbable microspheres (~10 micrometers, resorption in 3-10 days) facilitating a reliable, controlled release delivery system for gentamicin to wounds and hematoma. Efficacy of the microspheres in prevention of spinal wound infections was tested using a well published spinal implant infection model in New Zealand White rabbits. Prior to application in an animal model, pharmacokinetics of the release were studied in-vitro and in-vivo. All rabbits were given intravenous prophylactic ceftriaxone (20 mg/kg) prior to surgery to mimic preoperative prophylaxis in humans. Three non-contiguous surgical incisions were made in each rabbit overlying the T-13, L-3, and L-6 vertebrae. At each site the spinous process was removed to create a ‘dead space’ defect to allow for implantation of a 1 cm Ti90/Al6/V4 rod. Two treatment sites and one control site were randomly assigned to each rabbit. Control sites were treated with a flowable hemostatic agent (Surgifoam, Johnson & Johnson) and the non-antibiotic PLGA resomer while Surgifoam and gentamicin microspheres were used in the treatment sites. Wounds were then challenged with 10^6 CFU S. aureus (ATCC 25923) prior to closure of the fascia and skin incisions. After 7 days, postoperative wound infection was assessed using standard tissue sampling and bacterial quantification techniques (fascia, implant, hematoma and bone) to test our hypothesis that both incidence as well as severity of postoperative spinal wound infection can be reduced using controlled, local delivery of gentamicin using microsphere technology.

Results: Local delivery of gentamicin-microspheres resulted in controlled bactericidal levels of 20ug/ml hematoma for 48hrs, while powdered delivery of equal amounts of gentamicin resulted in cytotoxic ‘burst’-levels above 130ug/ml for the first 24hrs (levels >100ug/ml are shown to be toxic for osteoblastic fusion formation). After establishing a reliable infection in 92% of all challenged control sites, gentamicin-microsphere treatment reduced incidence of infection down to 43% (p<0.01 – Chi-square). Sites were considered to have a positive biomaterial-centered infection if both the implant and one of the deep tissues (hematoma and/or bone) were found to be infected. Biomaterial-centered infections were found in 58% of the control sites while only 28% of sites treated with gentamicin-microspheres were found to be infected in this fashion (p<0.01 – Chi-square).

Discussion: Local delivery of antibiotics to wounds and hematomas in the spine is an intuitively attractive option to sterilize the local environment where intravenous antibiotic prophylaxis cannot reach (hypoxic, devitalized tissue, dead space and pooled hematoma lacking vascular flow). Powdered delivery, however, leads to cytotoxic levels of aminoglycosides (>100ug/ml) and is of only short duration. Gentamicin-microsphere controlled delivery successfully reduced the incidence and severity of S.aureus postoperative spinal wound infection while bactericidal levels of gentamicin remained at 20ug/ml for a prolonged period of time.

Clinical investigation in postoperative spine wounds in traumatized patients will be pursued to prove clinical efficacy and potentially allow this treatment to become the standard of care as an adjuvant in the at-risk patient population.