Biologically Compatible Volume-Filling Medical Foam for Local Antibiotic Delivery in Fractures

Olivia Pyke[1], Jacqueline Linn[1], Amelia Stoner[1], Jacob Singer[1], Cody Plaisance[1], Renata Impastato[1], Steven Dow[1], Kirk McGilvray[1], Lynn Pezzanite[1], Nicholas Alfonso[2]
[1]Colorado State University, Fort Collins, CO, [2]University of Colorado, Aurora, CO
opyke@colostate.edu

Disclosures: This work was supported by the Orthopedic Trauma Association Full Member Basic Grant and University of Colorado Department of Orthopedics Seed Funding Grant.

INTRODUCTION: Fracture-related infection (FRI) following open fractures remains the most common and devastating complication, with rates ranging as high as 52%.[1] Delayed treatment can also lead to increased morbidity.[2] Standard of care remains expedited systemic antibiotics and surgical irrigation/debridement. However, systemic antibiotic penetration to critically injured tissues can often not achieve therapeutic levels due to devascularization. For these reasons, local antibiotic delivery to the wound bed as a topical powder has gained popularity, as it achieves rapid and high local antibiotic concentrations. However, powders present clinical challenges as they are easily suctioned/blown from incisions, have uneven distribution in complex wound geometries, and inconsistent pharmacokinetics. To overcome these limitations, we developed a flowable, non-solidifying absorbable biopolymer-based Medical Foam (MF) designed to enable efficient, uniform, and topical delivery of antibiotics *in situ*.

METHODS: The MF consists of two biopolymers, Chitosan and Pluronic F-127, and is aerated to create a flowable, temporally stable foam. Bacterial bioburden was assessed in skeletally mature male Sprague Dawley rats using a radial fracture segmental defect model. The fracture was infected with *S. aureus* via 1) an inoculated K-wire, which recapitulated the metal used in fracture repairs, and 2) a surgical mesh, to prevent the immediate clearance of the infection. The infection was immediately treated with 25 mg vancomycin powder or MF (VANC FOAM in Figure 1 graphs), with or without systemic antibiotics (50 mg/kg cefazolin), compared to systemic cefazolin alone or no treatment (n = 10, 6 groups). Rats were imaged daily for 72 hours via In Vivo Imaging System (IVIS) Spectrum, and quantitative cultures were performed to detect/quantify bacteria (total flux p/s). Local concentrations were quantified via Liquid Chromatography-Mass Spectrometry (LC-MS). Photon flux, quantitative counts were compared via one-way ANOVA with *post hoc* Tukey's adjustment (Prism v9.1.1, $p<0.05$). After euthanasia, wound bed tissue was collected for pharmacokinetics and quantitate cultures pending.

RESULTS SECTION: Studies to date indicate higher quantitative bacterial loads in untreated controls compared to all local and systemic treatments. Local treatments reduced counts further than systemic cefazolin. As seen in Figure 1, local vancomycin in MF achieved a similar reduction in bacterial counts compared to powder, with improved distribution and ease of application to the fracture bed site. Pharmacokinetics, imaging, histology, and final data analyses are pending.

DISCUSSION: A recent meta-analysis[3] indicated that local antibiotic powder delivery reduced the incidence of overall infections in both open and closed fractures, regardless of fracture severity or antibiotic class. The MF approach achieved similar concentrations and reduced bacterial counts, while being easier to apply, addressing a critical need to treat fracture wounds in both civilian and military populations. Exploration of optimized strategies for local antibiotic application could represent a paradigm shift in care for open musculoskeletal injuries, helping to decrease FRI.

SIGNIFICANCE/CLINICAL RELEVANCE: Effective local antibiotic delivery is critical for preventing FRIs, particularly in devascularized tissues where systemic therapy fails to reach therapeutic levels. This study introduces a flowable, absorbable MF for localized antibiotic delivery, offering temporal and uniform spatial distribution, ease of application, and the potential to reduce infection rates in both civilian and military trauma care.

REFERENCES:
[1] Coombs, J., Billow, D., Cereijo, C., Patterson, B., & Pinney, S. (2022). Current Concept Review: Risk Factors for Infection Following Open Fractures. *Orthopedic Research and Reviews*, *Volume 14*, 383–391. https://doi.org/10.2147/orr.s384845
[2] D'Souza, E. W., MacGregor, A. J., Dougherty, A. L., Olson, A. S., Champion, H. R., & Galarneau, M. R. (2022). Combat injury profiles among U.S. military personnel who survived serious wounds in Iraq and Afghanistan: A latent class analysis. *PLoS ONE*, *17*(4), e0266588. https://doi.org/10.1371/journal.pone.0266588
[3] Awad, M. E., Chung, J. Y., Griffin, N., Stoneback, J. W., & Alfonso, N. A. (2023). Prophylactic Intrawound Antibiotics Significantly Reduce the Risk of Deep Infections in Fracture Fixation: Subgroup Meta-analyses of the Type of Fracture, Antibiotics, and Organism. *Journal of Orthopaedic Trauma*, *37*(10), e400–e409. https://doi.org/10.1097/BOT.0000000000002641

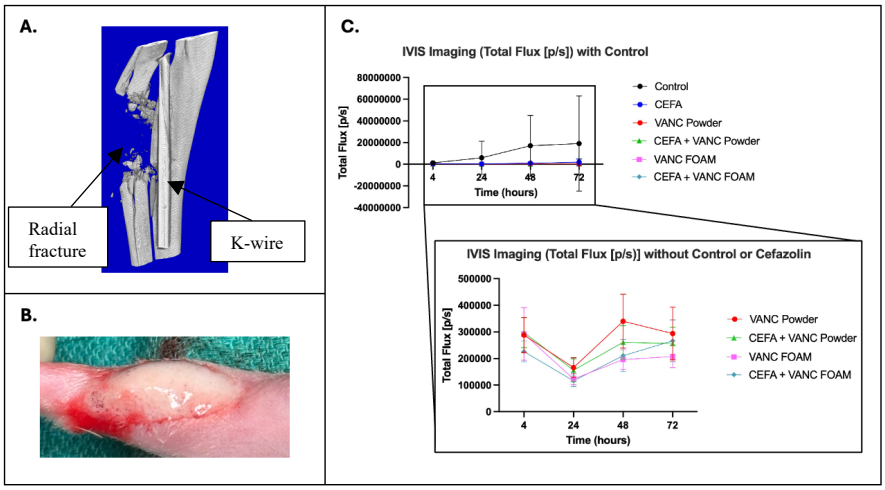

Figure 1: **A.** uCT image showing the radial fracture via rongeurs with k-wire placement. **B.** Medical Foam filling the wound site prior to surgical closure. **C.** IVIS data results showing the treatments with control and a closer look at the MF treatment results.