Preliminary Data Demonstrates that Antimicrobial Photodynamic Therapy Is Effective in Eradicating MRSA in a Rodent Model of Contaminated High-Energy Open Fracture

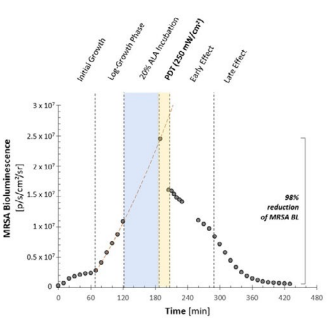
***Valentin Demidov, PhD**; Jonathan T. Elliott, PhD**;** Xinyue Han, PhD; J. Scott Sottosanti, B.Eng; Leah Gitajn, MD, MS*

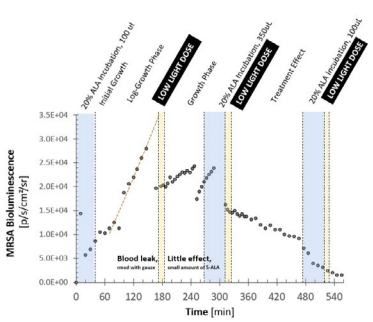
Purpose: Infection following high-energy open fracture is one of the most challenging complications in orthopaedic trauma, occurring in up to 50% of patients; for those patients, treatment failure remains unacceptably high at approximately 30%. Because of the associated wound contamination with high-energy mechanisms, along with the ubiquity of metallic implants, there is an ideal environment for planktonic bacteria to form biofilms, resulting in difficult to treat persistent infection. Antimicrobial photodynamic therapy (aPDT) involves the administration of a photosensitizing agent followed by treatment with light, generating free radicals that degrade microbe components and DNA. Here we demonstrate early results of treating contaminated open tibia fracture in a rat.

Methods: A blast overpressure tube is used to generate a high-energy pressure wave, impacting the lower leg of anesthetized rats and resulting in tibia fracture, skin laceration, and soft-tissue damage. Inoculum of bioluminescent strain of methicillin-resistant Staphylococcus aureus (MRSA; SAP231), containing ~108 colony forming units, were applied topically to the damaged bone and soft tissue. Bacteria were allowed to grow for 2-3 h, before being incubated with 20% 5-aminoluvulinic acid (5-ALA) and treated with either high-dose or fractionated low-dose light. Bioluminescence imaging (BLI) was used to quantify bioburden before and after treatment.

Results: Following high-energy fracture of the tibia, accompanied by soft-tissue trauma, 2 rats were given aPDT regimens. In rat #1, after 3 h of growth and incubation with 5-ALA, aPDT of 250 mW/cm2 caused an immediate 30% reduction in bioburden, followed by a steady reduction over 3.5 h of 98% overall reduction of MRSA. In rat #2, incubation with 5-ALA for 60 minutes was followed by a suboptimal dose of aPDT light (50 mW/cm² for 10 minutes), which resulted in a 25% reduction in bioburden that quickly rebounded. Another dose of 5-ALA was administered followed by another low-energy light dose and the bioburden slowly receded so that 3 h after the second treatment, bioburden had reduced by half. A third 5-ALA/low light dose treatment was given, which eliminated almost all the remaining microbes.

Conclusion: Both low-dose and high-dose aPDT regimens resulted in control of planktonic (and early biofilm forming) bacteria. This treatment has a potential adjuvant role in debridement and irrigation of contaminated fractures. Future studies will focus on long-term survival after treatment.





The FDA has stated that it is the responsibility of the physician to determine the FDA clearance status of each drug or medical device they wish to use in clinical practice.