Biodegradable antibiotic-releasing implant coatings to prevent orthopaedic implant infections

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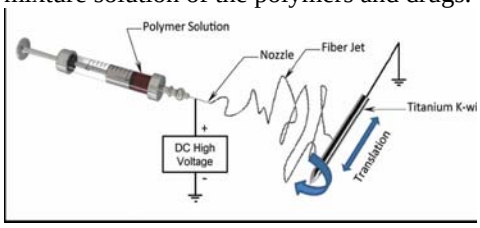
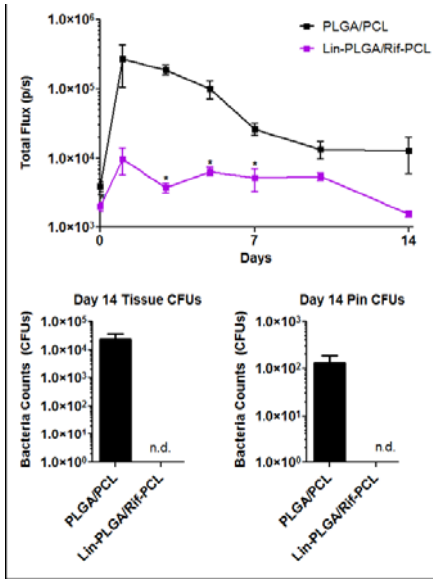
Introduction: Prosthetic joint infections (PJIs) represent one of the most devastating complications of total knee and hip replacement surgery. The current standard of care in preventing these infections is perioperative prophylactic systemic antibiotics. Despite this effort, the rate of deep infection after total joint arthroplasty is between 1-4%, which corresponds to nearly 20,000 post-arthroplasty infections in the US each year. Evidence indicates that bacteria form biofilm that block the penetration of immune cells and antibiotics, creating a chronic and persistent infection. Implant coating is one of the strategies to prevent biofilm formation on implant surfaces. Antimicrobial substances can be sustained release from the coating, thereby maintain local antibiotics concentration. In this study, we develop biodegradable coatings consist of biodegradable polymers, polycaprolactone (PCL) and poly(lactic-co-glycolic acid) (PLGA), to deliver a combination of antibiotics to adjacent tissue. The polymers' composition and antibiotics' dosage can be altered individually to provide optimal drug release kinetics to prevent biofilm formation.

Methods: A thin film of PCL, combined with PLGA coatings was applied to the implant using electrospinning technique followed by thermal treatment. Drug loaded polymer coatings were prepared by electrospining the mixture solution of the polymers and drugs.



The drug release profile was characterized in vitro in PBS by spectrophotometry. Using an established in vivo mouse model of PJI, in which a titanium Kirschner-wire (K-wire) implant was placed into the femur with the end extending into the knee joint and knee was inoculated with a bioluminescent S. aureus strain prior to closure. In vivo efficacy of coatings on titanium K-wire implants was measured by in vivo bioluminescence as well as in CFU isolated from the homogenized bone/joint tissue and isolated by sonication of the implants on day 14 after infection.

Results: The electrospinning method provided smooth, uniform coatings and ultimately improved the release profile. We evaluated drug release in vitro and in vivo (model drug) from coatings on titanium Kirschner-wire (K-wire) implants. Titanium K-wire implants coated with linezolid-PLGA and rifampin-PCL in a dual coating (Lin-PLGA/Rif-PCL) provide *in vitro* release above the MIC of *S. aureus.* for 21 and 8 days, respectively. In the combined coating (Lin-PLGA/Rif-PCL), there was a substantial reduction of bacterial burden as measured by in vivo bioluminescence as well as in CFU isolated from the homogenized bone/joint tissue and isolated by sonication of the implants on day 14 after infection (Figures shown below).



Conclusions: In vivo studies showed that antibiotic-loaded PCL/PLGA biodegradable implant coatings had efficacy in reducing the bacterial burden in our in vivo mouse model of orthopaedic implant infection. In optimized conditions, rifampin/linezolid-loaded coatings were capable of fully eradicating the infection. In this model, the Lin-PLGA/Rif-PCL coating was highly efficacious in reducing bacterial burden as measured by the bacterial *in vivo* bioluminescent signals and the CFU in the bone/tissue and on the implants.