Coaxial Polycaprolactone/Polyvinyl Alcohol Electrospun Nanofibers Enhance Implant Osseointegration in a Rat Tibial Pin Model

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Introduction: Total joint replacement (TJR) is successful and provides an attractive option for patients with disabling arthritis. Implant stability and long-term survival of TJR necessitates early incorporation of an implant by bone formation at the bone-implant surface, also referred to as osseointegration. Evidence has shown that defective osseointegration leads to implant instability, micromotion, osteolysis and loosening.

Electrospinning technology represents one of the promising new technologies to emulate the nanoscale extracellular matrix (ECM) of bone. We recently described the development of a novel coaxial electrospun polycaprolactone (PCL)/polyvinyl alcohol (PVA) core-sheath nanofiber (NF) blended with both hydroxyapatite (HA) and type I collagen (Col) (PCLCol/PVAHA), and found that these NFs bind firmly on the titanium rod surface, with no disruption or delamination during pullout testing. We also found that the PCLCol/PVAHA NFs can be used for the controlled release of pharmacologic agents and enhancing the adhesion and proliferation of murine pre-osteoblastic cells. This technique thus provides a promising source for enhancing implant osseointegration, while simultaneously allowing for local drug delivery at the implant-bone interface.

Erythromycin (EM), a 14-member lactone ring macrolide antibiotic, has received attention for its novel anti-inflammatory effects at sub-antimicrobial doses. We have previously published a review on the potential use of EM to inhibit wear debris-induced inflammation, osteoclastogenesis, and osteolysis (both in vitro and in vivo). Previous studies have also evaluated the use of strontium coatings on implants and its potential for enhancing osseointegration. However, the optimal vehicle for delivery of these compounds has not been elucidated. The aim of this continuation study was to determine the osseointegration efficiency of PCLCol/PVAHA NF as an implant coating in a rat tibia implantation model.

Methods: We evaluated coaxial electrospun PCL/PVA core-sheath NF blended with both HA and Col (PCLCol/PVAHA) coated on titanium pins with the addition of either strontium or erythromycin on a rat tibial pin model in order to assess for osseointegration. Tibial pins were surgically inserted into 13 week Sprague-Dawley rats forming four different groups with eight rats in each group: 1) Titanium pins alone (Ti); 2) Titanium pins with NFs (NF); 3) Titanium pins with NFs and strontium (NF+SR); 4) Titanium pins with NFs and erythromycin (NF+EM). Using micro computed tomography scanning performed in vivo at 0, 4 and 8-week time points and accompanying software, bone contact surface area was quantified and compared between groups to assess for effectiveness of osseointegration. Percent change in bone contact surface area between the implant and surrounding bone was analyzed between 4 and 8-week
time points. Mechanical testing was performed to assess the push in force required to displace a pin implant from the surrounding bone. This was done using a mini Instron with a loading rate of 2 mm/min. The static friction force was determined from the recorded load/displacement curves.

**Results:** There was a trend toward increased total bone contact surface area at 8 weeks in the NF and NF+SR groups when compared to the NF+ER and Ti pins alone groups, although this was not statistically significant (p>0.05). However, we found that there was a large increase from 4 weeks to 8 weeks in bone contact surface area in all of the nanofiber groups compared to the Titanium pins alone (p<0.05). Preliminary mechanical testing results, with 3 rats per group, showed the average force required to displace the implant was higher in the NF, NF+SR, and NF+EM groups compared to the Ti pin alone, but this difference was not significant (p>0.05).

**Discussion:** Our data suggest that the nanofiber coating improved bone contact surface area over time, thus suggesting enhanced osseointegration. This presents a promising technique in improving implant osseointegration, as well as the potential for local drug delivery at the bone-implant interface, thereby minimizing the potential for aseptic loosening, osteolysis, and implant failure.

**Significance:** PCLCol/PVAHA coaxial NFs could be applied as promising nanofabricated coatings with various biomolecules/drugs to promote early and efficient osseointegration, while simultaneously allowing for local drug delivery at the bone-implant interface, thus minimizing the potential for aseptic loosening, osteolysis, and ultimate implant failure.

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