Evaporative Assembly of Drug-Eluting Bioresorbable Nanocomposite Micropatterns

Yexin Gu, Andrew Ihnen, Joung-Hyun Lee, Woo Lee
Stevens Institute of Technology

Statement of Purpose: Hospital-acquired infection during implant surgery is the leading cause of orthopaedic implant failure. Infection occurs because a small number of bacteria adhere preferentially to abiotic implant surfaces and form biofilms. Consequently, infected implants must be surgically removed with tremendous patient trauma and additional healthcare burden of >$1B in the U.S. every year[1]. Bioresorbable, antibiotic-loaded coatings have been found to be effective in reducing biofilm formation on orthopaedic implant surfaces from in vitro, animal, and clinical studies[2,3] However, these coatings cover the entire surface of implants, significantly delaying and interfering with osteointegration until the coatings are degraded over several months. Thus, the goal of this project is to explore the possibility of creating drug-eluting, bioresorbable micropatterns that can be used to both promote bone tissue formation and prevent biofilm formation on orthopaedic implant surfaces.

Methods: An inkjet-based evaporative assembly method was developed to print nanocomposite micropatterns, consisting of biphasic calcium phosphate (BCP) and Rifampicin (RIF, model antibiotic) nanocrystals (~100 nm) dispersed in biodegradable poly(d,l-lactic-co-glycolic) acid (PLGA) matrix using a Materials Printer (DMP2800, FUJIFILM Dimatix) (Fig. 1). RIF/BCP/PLGA containing suspensions with various compositions were carefully prepared as inks and later printed on substrates for optical and electronic microscope visualization. ATR-FTIR was used to measure the RIF and BCP release rate of fabricated micropatterns[4,5]. Devices that integrating microfluidic channels and a Ti alloy substrate were utilized to *in vitro* monitor in real time the effects of our micropatterns on bacterial killing and osteoblast cell development and bone tissue-like structure[6,7].

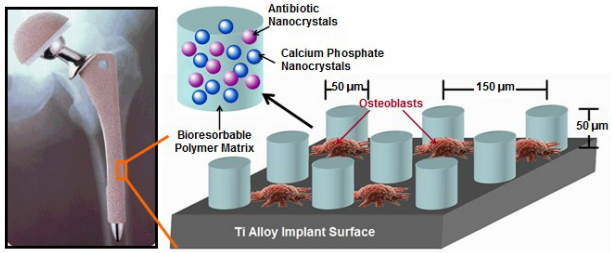

Fig. 1 Drug-eluting, bioresorbable nanocomposite micropattern

Results: A well-established RIF/BCP embedded PLGA micropattern can be observed under optical microscope (Fig. 2a). We have also observed that the addition of BCP to the ink significantly affect the morphology and uniformity of the initial micropatterns. Particularly, the addition of BCP nanocrystals was found to increase splashing behavior as evident from the formation of smaller islands between the patterned features. Furthermore, during the evaporative assembly process, the BCP nanocrystals become entrapped within the confine of the shrinking droplet, and become dispersed in the polymer matrix (Fig. 2b).

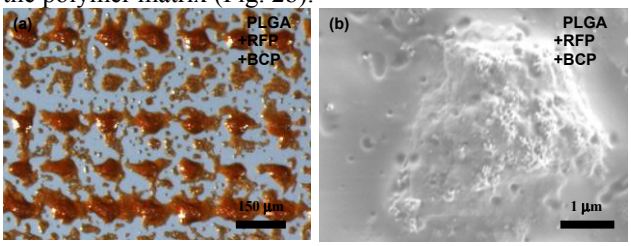

Fig. 2 (a) ~20µm thick PLGA+RFP+BCP micropattern, (b) surface SEM image of PLGA+RFP+BCP

Bacteria culture data show that biofilm colonies formed on the surface micropatterned with PLGA only (Fig. 3a) whereas a few bacteria remaining on the PLGA/RIF/BCP pattern surface were killed after 5 h culture (Fig. 3b). Cell culture data also show that osteoblasts cultured on the micropattern surface adhere, spread, and proliferate well in comparison to those on plain surface (Fig. 3c, d).

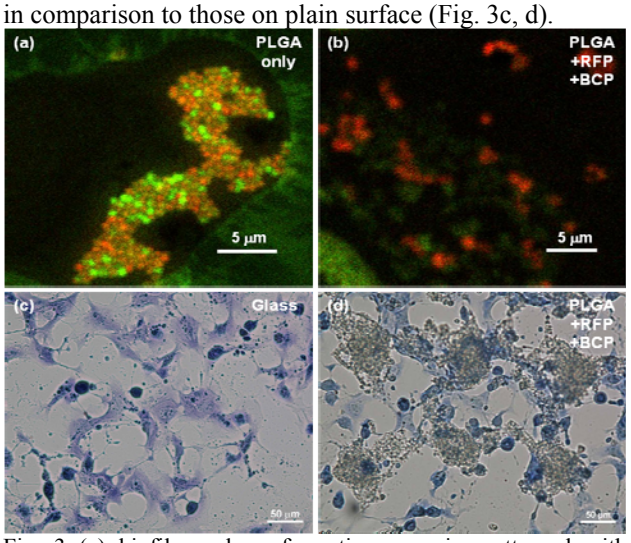

Fig. 3 (a) biofilm colony formation on micropatterned with PLGA only (green live cells) after 5h, (b) no biofilm formation with dead bacteria (red) on PLGA+RFP+BCP micropattern after 5h, (c) osteoblast on plain substrate after 24h, and (c) osteoblast on PLGA+RFP+BCP micropattern after 24h.

Conclusions: PLGA micropatterns embedded with RIF/BCP nanocrystals on Ti alloy surface were fabricated using evaporative assembly ink-jet printing method. Bacteria and osteoblast culture results show that those multifunctional micropatterns exhibit promising anti-infection and cell promotion features. However, for further improve the micropatterns both printing condition and ink formulation need to be optimized to minimize splashing and achieve steady RIF/BCP release

References:

1. Long. Stevens Ins. Tech. Feb. 4, 2009.
2. Price JS. J Biomed Mater Res. 1996;30:281-286.
3. Sánchez E. Eur J Pharm Biopharm. 2001;52:151-158.
4. Kharlampieva, E. Langmuir 2004;20:10712-10717.
5. Kharlampieva E. Langmuir 2007;23:175-181.
6. Lee JH. Biomed Microdevices. 2008;10:489-498.
7. Lee JH. Biomaterials 2009;submitted.