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Journal
The Journal of bone and joint surgery. American volume, 98(14)

ISSN
0021-9355

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Publication Date
2016-07-01

DOI
10.2106/jbjs.15.01273

Peer reviewed

J Bone Joint Surg Am
2016 Jul 20;98(14):1183-9.
doi: 10.2106/JBJS.15.01273.

In Vivo Efficacy of a "Smart" Antimicrobial Implant Coating

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- PMID: 27440566
- PMCID: PMC4994856
- DOI: 10.2106/JBJS.15.01273

Abstract

Background: Postoperative infection is a devastating complication following arthroplasty. The goals of this study were to introduce a "smart" implant coating that combines passive elution of antibiotic with an active-release mechanism that "targets" bacteria, and to use an established in vivo mouse model of post-arthroplasty infection to longitudinally evaluate the efficacy of this polymer implant coating in decreasing bacterial burden.

Methods: A novel, biodegradable coating using branched poly(ethylene glycol)-poly(propylene sulfide) (PEG-PPS) polymer was designed to deliver antibiotics both passively and actively. In vitro-release kinetics were studied using high-performance liquid chromatography (HPLC) quantification in conditions representing both the physiologic environment and the more oxidative, hyperinflammatory environment of periprosthetic infection. The in vivo efficacy of the PEG-PPS coating delivering vancomycin and tigecycline was tested using an established mouse model of post-arthroplasty infection. Noninvasive bioluminescence imaging was used to quantify the bacterial burden; radiography, to assess osseointegration and bone resorption; and implant sonication, for colony counts.

Results: In vitro-release kinetics confirmed passive elution above the minimum inhibitory concentration (MIC). A rapid release of antibiotic was noted when challenged with an oxidative environment ($p < 0.05$), confirming a "smart" active-release mechanism. The PEG-PPS coating with tigecycline significantly lowered the infection burden on all days, whereas PEG-PPS-vancomycin decreased infection on postoperative day (POD) 1, 3, 5, and 7 ($p < 0.05$). A mean of 0, 9, and 2.6 × 10(2) colony-forming units (CFUs) grew on culture from the implants treated with tigecycline, vancomycin, and PEG-PPS alone, respectively, and a mean of 1.2 × 10(2), 4.3 × 10(3), and 5.9 × 10(4) CFUs, respectively, on culture of the surrounding tissue ($p < 0.05$).

Conclusions: The PEG-PPS coating provides a promising approach to preventing periprosthetic infection. This polymer is novel in that it combines both passive and active antibiotic-release mechanisms. The tigecycline-based coating outperformed the vancomycin-based coating in this study.

Clinical relevance: PEG-PPS polymer provides a controlled, "smart" local delivery of antibiotics that could be used to prevent postoperative implant-related infections.

Figures

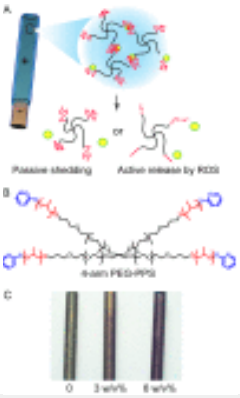

Fig. 1

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Schematics of the 4-armed PEG-PPS…

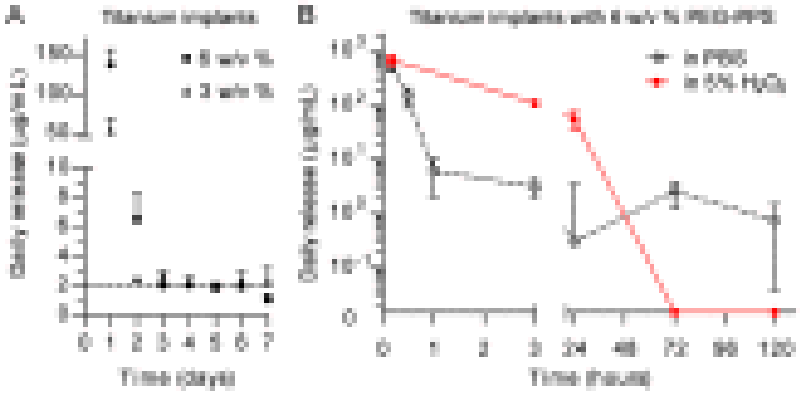

Fig. 2

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Figs. 2-A and 2-B In…

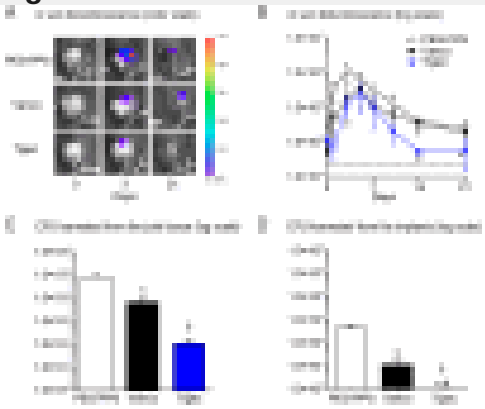

Fig. 3

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Figs. 3-A through 3-D In…

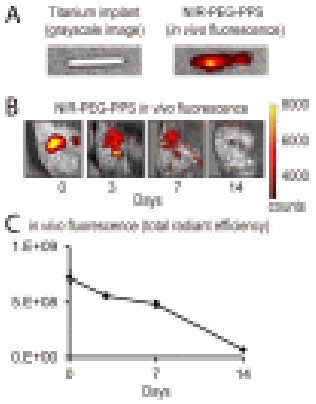

Fig. 4

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Figs. 4-A, 4-B, and 4-C…

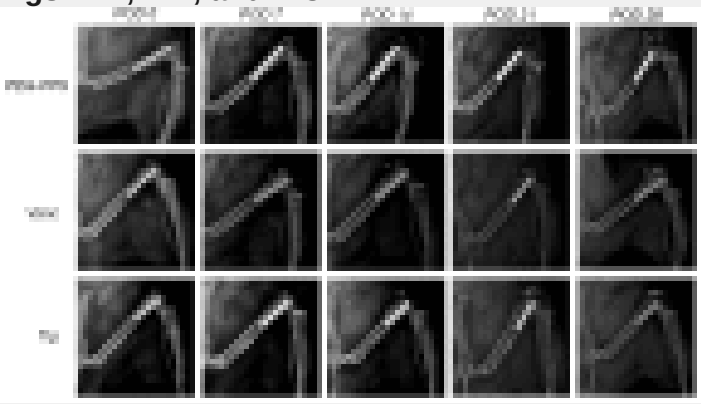

Fig. 5

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Representative radiographs from the PEG-PPS,…