Antibiotic-eluting scaffolds eradicate infection and facilitate bone regeneration in a rabbit model of osteomyelitis

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INTRODUCTION: Treatment for chronic osteomyelitis (OM) requires debridement of the infected bone followed by the administration of systemic antibiotics [1]. Despite this combined approach, reoccurrence of OM is high and current local antibiotic-delivery devices such as antibiotic-impregnated polymeric beads are not ideal as they require a second procedure for removal and are not conducive to bone healing [2]. We have previously utilized a collagen-hydroxyapatite scaffold with proven regenerative potential [3] to deliver an antibiotic in a dual-release manner, with an initial burst release of antibiotic to clear bacterial activity followed by a sustained, controlled release to prevent reoccurrence of infection [4]. Herein, we sought to compare the capacity of two antibiotic-eluting scaffolds (containing vancomycin or gentamicin) to eliminate infection and facilitate bone healing in a rabbit model of chronic OM.

METHODS: Antibiotic-eluting collagen-hydroxyapatite scaffolds containing either vancomycin (Vanc-scaff) or gentamicin (Gent-scaff) were fabricated by lyophilization. The radii of New Zealand White rabbits were inoculated with 8.5 x 10^5 CFUs of *Staphylococcus aureus* JAR. At 4 weeks, the infected area was debrided (6 mm) and either left empty, or treated with a commercially available gentamicin fleece (Septocoll E®), a Vanc-scaff or a Gent-scaff (n=9). Animals were euthanized at 12 weeks. All animals received systemic antibiotics (Cefazolin 25 mg/kg b.d. SC) between weeks 4 and 8. Quantitative bacteriology was performed to assess infection and computed tomography (CT) scans were carried out to assess bone healing. Statistical comparisons were performed using ANOVA. Significance was accepted at $p<0.05$.

RESULTS: Comparable levels of bacteria were found in tissues harvested from all groups at 4 weeks. At 12 weeks, 6/6 animals treated with the Gent-scaff were found to be infection-free, compared to 4/6 animals that were treated with the Vanc-scaff or Septocoll E, and 1/6 animals where defects were left empty (Fig 1A). CT evaluations demonstrated a significantly higher bone volume in both Vanc-scaff and Gent-scaff groups at 8 weeks compared to 4 weeks, and at 12 weeks compared to 8 weeks, highlighting the capacity of antibiotic-eluting scaffolds to facilitate bone healing in this model (Fig. 1B).

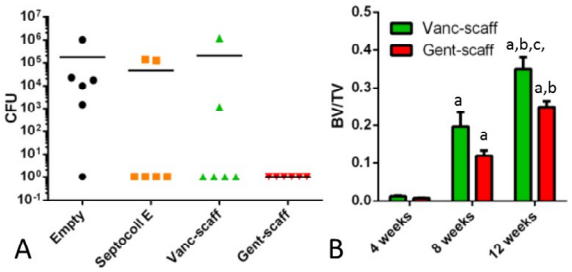

Fig. 1. A) Bacteriology at 12 weeks. B) Bone volume (BV)/ total volume (TV). Significance; a vs. 4 weeks, b vs 8 weeks, c vs Gent-scaff.

DISCUSSION & CONCLUSIONS: This work has demonstrated the capacity of an antibiotic-eluting scaffold to treat infection and facilitate bone tissue regeneration in a rabbit model of OM. These antibiotic-eluting scaffolds may prove to be a powerful tool in the fight against chronic OM, as they can be implanted into an infected bone defect left void following debridement to aid in bacterial clearance. Furthermore, since the scaffolds are biodegradable and facilitate bone healing, they do not require a second procedure for removal, thereby reducing hospital times and costs.

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REFERENCES: [1] Kavanagh N et al., Clin Microbiol Rev. 2018; 31:e00084-17. [2] Shah SR et al., Chinese Science Bulletin. 2013; 58:4342-4348. [3] Lyons F et al, Clin Orthop Rel Res. 2014; 471:1318-1328. [4] Sheehy EJ et al, ORS. 2018; Paper no. 0025.