INTRODUCTION:
Infection of orthopaedic implants is a devastating complication that frequently requires prolonged management and multiple additional surgeries. Orthopaedic implants increase the risk of infection since bacteria can adhere to the implant surfaces and form biofilms. Farnesol is an antifungal agent, which also showed antimicrobial activities against Staphylococcus aureus (S. aureus) and Streptococcus mutans. However, the effects of farnesol on bacterial biofilm formation on orthopaedic materials and on osteoblasts have not been investigated, and are, therefore, the focus of this study.

METHODS:
Biofilms of S. aureus Seattle 1945 GFPuvr that express Green Fluorescent Protein were grown on titanium alloy discs. The effect of farnesol on biofilm formation with or without gentamicin was examined by fluorescence microscopy and quantitative cultures. In selected experiments, farnesol solution was dried on titanium discs prior to the addition of bacterial suspensions. The effect of farnesol on MC3T3-E1 pre-osteoblastic cells cultured on titanium alloy discs was also investigated following staining with Texas Red Phalloidin and DAPI.

RESULTS:
Soluble farnesol (30 mM) reduced the number of viable bacteria by $10^4$-fold and completely inhibited biofilm formation (Fig. 1A, 1B). Low concentrations of soluble farnesol (0.03 – 3 mM) did not inhibit biofilm formation (Fig. 1A, 1B) and did not potentiate the effect of a sub-maximal concentration of gentamicin (solid bars in Fig. 2). Dried farnesol on titanium alloy discs reduced the number of viable bacteria by 50-fold (Fig. 3). The effects of soluble and dried farnesol on bacterial biofilm formation lasted for at least 3 days (Fig. 3). Soluble farnesol added after the bacteria had attached (open bars in Fig. 4) or after the biofilm had formed (solid bars in Fig. 4) reduced the final number of viable bacteria by 210-fold or 56-fold, respectively. 3 and 30 mM soluble farnesol inhibited spreading of the MC3T3-E1 pre-osteoblastic cells on the titanium discs (Fig. 5).

DISCUSSION:
A high concentration of farnesol showed antibiotic properties against bacterial biofilms; however, it also had a negative effect on osteoblasts. Since the primary goal of treating orthopaedic infections is to eliminate all of the infectious foci, farnesol may be a useful adjunct to current clinical practices even if it has a temporary negative effect on the pre-osteoblasts. Application of farnesol clinically by coating implants, mixing with bone cement, or adding to irrigation fluid are therefore possibilities that should be studied further.