# Use of an *ex vivo* human bone organ culture model to compare wound irrigation solutions

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**Introduction:**

It is estimated that by 2030 the total number of joint arthroplasties will reach 3.5 million. As this number grows, the number of revisions increase with some estimates being as high as 12%. There are several mechanisms of failure with infection being the leading factor (29.3%). Use of intra-operative irrigation solutions which balance antimicrobial efficacy and host cell toxicity can be an effective strategy in reducing infection but there are many formulations from which surgeons are to choose. Evaluation of irrigation solutions are largely done using *in vitro* methods; however, environmental conditions at the surgical site affect both bacterial metabolism and the antimicrobials themselves. In this study, we employ an ex vivo methodology that uses viable human bone cores with lipids and marrow still present to evaluate the antibacterial efficacy of irrigation fluids and their effect on host cells. The solutions evaluated use an array of technologies and antimicrobial agents including ethanol and acetic acid, chlorhexidine gluconate (CHG), polyhexamethylene biguanide (PHMB), hypochlorous acid (HOCl), citric acid, and povidone iodine (PVI).

**Methods:**

Viable human femoral heads (18 male, 24 female) were collected during total hip arthroplasty from which 168 bone cores were harvested (Figure 1a). The cores were inoculated with *Staph. aureus* in media best replicating human serum. Half of the cores were treated with irrigation solutions and the remaining patient matched cores were exposed to saline. Surviving bacteria counts were compared both acutely and 24hrs after treatment. An additional 126 cores were exposed to each irrigation fluid and incubated in a dynamic bioreactor system (Figure 1b). These specimens were metabolically and histologically compared to saline controls from the same patient both acutely and two-weeks after exposure.

**Results:**

Antibacterial efficacy tended to group according to formulation both acutely and 24hrs after exposure (Figure 2). Ethanol/acetic acid and PHMB containing solutions showed acute reductions greater than 3-log and 6-log 24hrs after exposure. This was a significantly larger reduction when compared to CHG, PVI, HOCl, and citric acid ($p<0.001$ – $p=0.02$) but not when compared to each other ($p=0.083$ – $p=0.574$). All fluids tested decreased host cell metabolic activity but only the ethanol/acetic acid treated samples were significantly different than the saline controls acutely ($p<0.001$). Significant metabolic differences were also seen between ethanol/acetic acid ($p<0.001$) and one PHMB formulation ($p=0.01$) two-weeks after exposure to the irrigation fluids.

**Conclusions:**

Using this methodology, ethanol/acetic acid and PHMB formulations tended to show greater reductions in surviving *S. aureus*. However, the acetic acid formulation also had the greatest impact on host cells.

**Clinical Significance:**

While standard *in vitro* cell culture has a place, use of more complex *ex vivo* models can provide additional insight as the biochemical environment of the surgical site impacts both bacteria and antimicrobial agents.

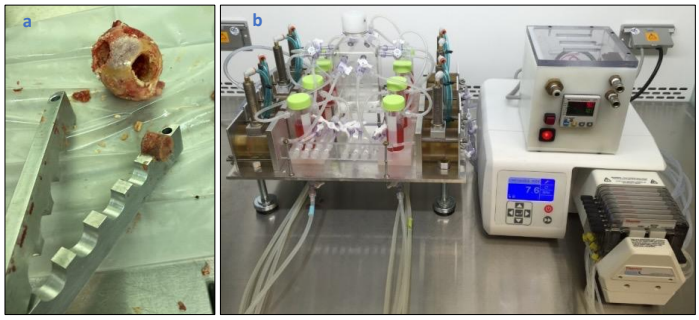


Figure1. a) Viable cancellous bone core harvest from a human femoral head. b) Bioreactor system with independent media circulation and pneumatic mechanical loading.

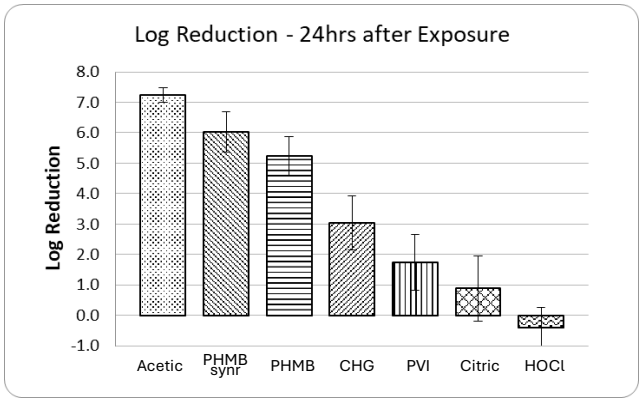


Figure 2. Chart showing log reductions of each irrigation fluid 24 hours after treatment.