

## Vancomycin-Soaked Bone Allograft: Effective Concentration For Prophylactic And Therapeutic Indication

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### INTRODUCTION:

Antibiotics can be incorporated into bone grafts through soaking, creating antibiotic-impregnated bone grafts (AIBG) for local antibiotic delivery and bone formation stimulation.[1] Despite AIBG's introduction in 1947, consensus on the optimal antibiotic concentration remains vague.[1] Insufficient elution can lead to antibiotic resistance, while high local concentrations may induce osteoblast toxicity and systemic complications.[1] Hence, determining the ideal antibiotic amount and concentration for bone grafts is imperative to balance effectiveness and avoid potential drawbacks.

### MATERIALS and METHODS:

Gamma-irradiated cancellous femoral head bone allografts were morselized and soaked in vancomycin solutions of increasing concentrations from 0 mg/ml to 100 mg/ml for 30 minutes. Concentration of vancomycin elution was determined qualitatively with agar diffusion test and quantitatively with high performance liquid chromatography.

### RESULTS:

This study identified an optimal soaking ratio of 1:1, bone graft (g) to antibiotic volume (ml). The minimal inhibitory concentration (MIC) of *Staphylococcus* sp. for vancomycin is 2 mg/L. Increasing vancomycin concentration increased local elution concentration. Elution decreased in a negative exponential curve pattern with time. Vancomycin-soaked bone allograft (VSBA) prepared with 10 mg/ml to 100 mg/ml vancomycin concentration release 326 mg/L to 1920 mg/L. For therapeutic dose, with a minimal biofilm eradication concentration exceeding 1024 mg/L[2], the vancomycin concentration for VSBA was determined at 60 mg/ml, through a receiver operating curve analysis.

Table 1 shows the result of local vancomycin elution by soaking in increasing vancomycin concentration from 0-100 mg/ml. (ZOI – Zone of Inhibition)

Vancomycin Concentration (mg/ml)	Peak Eluted Vancomycin Concentration (mg/L)	Duration above MIC (Day)	Peak Eluted Vancomycin Concentration > 1024 mg/L	Day 1 ZOI measured (mm)	Duration of ZOI present (Day)
0	0.00	0	No	0	0
10	326.45	14	No	8.25	8
20	370.20	14	No	8.95	11
30	479.11	14	No	9.56	11
40	682.60	14	No	10.20	12
50	881.10	15	No	10.72	13
60	1043.40	15	Yes	10.71	13
70	1283.71	15	Yes	10.87	13
80	1378.38	15	Yes	11.18	13
90	1430.65	15	Yes	11.15	13
100	1920.01	15	Yes	11.97	13

### DISCUSSIONS:

Soaking ratio 1:1 allow thorough antibiotic incorporation. Bone allograft soaked in a 10 mg/ml vancomycin concentration can elute antibiotics 150 times higher than the MIC for up to 14 days, preventing bacterial colonization effectively. Biofilm-embedded pathogens require concentrations 1000 times above MIC for eradication. Local vancomycin concentration of 1,400 mg/L doesn't induce nephrotoxicity, and osteoblasts remain unaffected up to 2,000 mg/L for 14 days.[1] The ideal therapeutic concentration for bone graft soaking is 60 mg/ml, resulting in an elution of 1043 mg/L.

### CONCLUSION:

Establishing optimal vancomycin concentrations for prophylactic and therapeutic purposes allows non-excessive use of antibiotic application and avoid any potential toxicity.

### REFERENCES:

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2. Kostenko, V., H. Ceri, and R.J. Martinuzzi, *Increased tolerance of Staphylococcus aureus to vancomycin in viscous media*. FEMS Immunology & Medical Microbiology, 2007. **51**(2): p. 277-288.