

Cement Brand, Viscosity, and Mixing Sequence Determine High-Dose Vancomycin Elution from Polymethylmethacrylate

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INTRODUCTION: High-dose vancomycin is routinely incorporated into polymethylmethacrylate (PMMA) spacers for chronic periprosthetic joint infection (PJI), but elution remains variable. While prior work explored PMMA brand and additive strategies, the effect of mixing sequence (polymer-first vs. monomer-first) has not been defined. The objective of this study was to characterize how PMMA brand, viscosity, pre-mixed aminoglycoside, and mixing sequence influence vancomycin elution, antimicrobial activity, and PMMA porosity.

METHODS: Ninety PMMA discs were prepared (five formulations: Simplex P, Palacos MV, Palacos R, Palacos MV+gentamicin, Palacos R+gentamicin) and loaded with 4 g vancomycin per 40 g cement, reflecting clinical spacer dosing. Two mixing techniques were compared: polymer-first (vancomycin + polymer powder, then monomer) and monomer-first (vancomycin + liquid monomer, then polymer). Discs (n=9 per group) were immersed in PBS, with eluates collected through 28 days. Vancomycin concentrations were measured colorimetrically, and antimicrobial activity was tested against methicillin-sensitive *Staphylococcus aureus* (MSSA, Xen36). MicroCT scanning assessed porosity at baseline and 28 days. Holm-corrected t-tests compared elution outcomes.

RESULTS: Vancomycin retained bactericidal activity against MSSA across all formulations. Brand strongly influenced elution: Palacos yielded 59% greater cumulative elution than Simplex ($2,633 \pm 268 \mu\text{g}$ vs. $1,657 \pm 323 \mu\text{g}$, $p < 0.01$). Mixing sequence was critical: monomer-first Palacos MV produced the highest cumulative elution ($2,888 \pm 191 \mu\text{g}$), 57% greater than high-viscosity Palacos R ($p < 0.001$), while polymer-first Simplex P produced the largest initial burst release at 1 hour ($415 \pm 25 \mu\text{g}$). Premixed gentamicin increased vancomycin elution in high-viscosity formulations but not in medium-viscosity Palacos. MicroCT detected no porosity increases $\geq 10\%$ across groups, indicating preserved mechanical integrity.

DISCUSSION: Cement brand, viscosity, and mixing order significantly alter high-dose vancomycin elution. Palacos MV mixed monomer-first maximized sustained elution, while polymer-first Simplex P produced the strongest initial burst. Dual-antibiotic formulations augmented release in select conditions, without compromising porosity. These findings confirm that elution behavior reflects both cement chemistry and mixing method, not simply antibiotic dose.

SIGNIFICANCE / CLINICAL RELEVANCE: Clinicians should consider cement brand, viscosity, and mixing sequence when preparing high-dose vancomycin PMMA spacers. Optimizing these variables may enhance local antibiotic delivery, improve infection eradication, and minimize systemic toxicity risks during revision arthroplasty.

