Biomechanical Properties and Elution Profiles of Zoledronic Acid versus Denosumab-Laden Bone Cement for Musculoskeletal Tumor Applications: A Comparative Analysis

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INTRODUCTION: Zoledronic acid (ZA) and Denosumab (DMAB) are widely recognized for their potent anti-osteoclastic activity, making them valuable in the management of bone tumors and metastatic skeletal lesions. However, their incorporation into polymethylmethacrylate (PMMA) bone cement—a common strategy for localized drug delivery—may alter the material's structural integrity and release kinetics. Despite their clinical relevance, systematic comparisons of the biomechanical and elution properties of ZA- and DMAB-laden bone cement remain limited. This study aims to comprehensively evaluate the mechanical performance and drug release profiles of ZA- and DMAB-loaded PMMA cement in comparison to plain (Control) cement, providing critical insights for musculoskeletal tumor applications.

METHODS:

Standardized PMMA cement specimens (Simplex P) were prepared in three experimental groups: Control (unmodified cement), ZA-loaded cement, and DMAB-loaded cement. The Control group served as the baseline for comparison, while the ZA- and DMAB-loaded groups were formulated by incorporating therapeutic doses of each drug into the cement matrix prior to polymerization. Biomechanical testing was performed in accordance with ASTM standards to evaluate critical structural properties, including compressive strength, stiffness, Young's modulus, yield stress, and energy to yield. A servo-hydraulic testing system was utilized to apply controlled axial compression, and load-displacement curves were analyzed to derive mechanical parameters. Elution kinetics were assessed by submerging cylindrical cement specimens in phosphate-buffered saline (PBS) maintained at 37°C to simulate physiological conditions. The elution medium was sampled at 24-hour intervals over a 10-day period to quantify drug concentrations, allowing for the characterization of release profiles. Statistical analysis was conducted using one-way ANOVA with Tukey's post-hoc test to compare differences among the three experimental groups. A significance threshold of $p < 0.05$ was applied to determine whether observed variations in biomechanical properties and elution profiles were statistically meaningful.

RESULTS: Biomechanical testing revealed significant differences among the groups. The Control cement exhibited superior mechanical properties, requiring a significantly higher force (2873.2 ± 231.1 N) to achieve 50% displacement compared to ZA-loaded (2277.1 ± 145.1 N) and DMAB-loaded (2406.9 ± 130.3 N; $p < 0.001$) cements. Further analysis demonstrated that the Control group was stiffer ($p < 0.001$), had a higher Young's Modulus ($p < 0.001$), and exhibited greater Yield Load ($p < 0.001$), Yield Stress ($p < 0.001$), and Energy to Yield ($p < 0.05$) than both drug-loaded groups. However, no significant differences were observed in Displacement at Yield ($p = 0.342$) or Strain at Yield ($p = 0.342$), suggesting that while drug incorporation reduces stiffness and strength, it does not significantly affect deformation characteristics. Elution studies demonstrated sustained release of ZA over the 10-day period, whereas DMAB exhibited minimal release, likely due to its proteinaceous nature and larger molecular size, which may hinder diffusion through the PMMA matrix.

DISCUSSION AND CONCLUSION:

This study highlights that while the incorporation of ZA or DMAB into PMMA cement reduces its mechanical properties, the resulting material remains within an acceptable range for clinical use in musculoskeletal tumor management. The prolonged elution of ZA suggests its potential superiority for localized drug delivery, whereas the limited release of DMAB raises concerns regarding its efficacy in this delivery system. However, further in vivo and clinical studies are necessary to evaluate the trade-offs between biomechanical integrity and therapeutic effectiveness in tumor treatment. These findings provide a foundation for optimizing drug-loaded bone cement formulations in orthopedic oncology.

Table 1:

Biomechanical Parameters				
	Control Cement	*ZA-Loaded Cement*	*DMAB-Loaded Cement*	*p-value*
Stiffness [N/mm] (mean ± SD)	4943.5 ± 145.3	3508.6 ± 96.3	3349.0 ± 351.0	<0.001
Young's Modulus (N/mm2) (mean ± SD)	2099.1 ± 61.7	1489.8 ± 40.9	1422.1 ± 149.1	<0.001
Yield Load (N) (mean ± SD)	2094.7922 ± 147.4	1456.47 ± 78.1	1465.39 ± 146.6	<0.001
Yield Stress (N/mm2) (mean ± SD)	74.1 ± 5.2	51.5 ± 2.8	51.8 ± 5.2	<0.001
Displacement at Yield (mm) (mean ± SD)	0.44 ± 0.02	0.45 ± 0.028	0.5 ± 0.11	0.335
Strain at Yield (mm/mm) (mean ± SD)	0.037 ± 0.001	0.037 ± 0.002	0.042 ± 0.01	0.342
Energy to Yield (N*mm/mm) (mean ± SD)	38.7 ± 4.9	26.4 ± 2.2	29.1 ± 7.5	0.006
Energy to Yield (J) (mean ± SD)	465.57 ± 58.5	317.9 ± 26.6	350.05 ± 90.6	0.005