ICMERD-International Journal of Dental Science (ICMERD-IJDS)
Vol.7, Iss. 1, January - June, 2026, pp. 1-6.
Journal Code : 2542-5875
https://icmerd.com/

Article

Evaluation of Bioactive Glass-Ceramic Composite Grafts in the Regeneration of Critical-Sized Mandibular Defects in Experimental Models with Histomorphometric and Radiographic Correlation

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Article ID: ICMERD-IJDS_07_01_001 **Published on:** 7th January 2026

Abstract

Purpose: This study investigates the regenerative potential of bioactive glass-ceramic composite grafts in the healing of critical-sized mandibular defects. The objective is to correlate histomorphometric and radiographic outcomes to establish a comprehensive understanding of the material's biological and structural integration.
Methodology: A preclinical in vivo model using adult rabbits was selected to mimic critical-sized mandibular defects. Defects were grafted with a synthesized bioactive glass-ceramic composite, and outcomes were assessed through histological staining, histomorphometry, and digital radiography at multiple healing intervals.
Findings: The graft demonstrated excellent biocompatibility, with evidence of enhanced osteogenesis and angiogenesis. Radiographic analyses revealed progressive defect bridging and mineral density increase, closely correlating with histological findings of new bone matrix formation and vascular infiltration.
Practical implications: These findings indicate that bioactive glass-ceramic composites can serve as effective bone graft substitutes in maxillofacial surgery, particularly in non-load-bearing regions of the mandible. This has potential implications for clinical translation in cases where autografts are contraindicated.
Originality: The study presents a novel synthesis of bioactive glass-ceramic material tailored for mandibular bone repair and demonstrates its efficacy through dual-mode evaluation. The correlation between imaging and histology adds robustness to the evaluation, offering a reproducible preclinical methodology.

Keywords:

Bioactive glass-ceramic, mandibular defects, bone regeneration, histomorphometry, radiographic correlation, biomaterials, composite grafts

Citation: Vhanmathi, M. (2026). Evaluation of Bioactive Glass-Ceramic Composite Grafts in the Regeneration of Critical-Sized Mandibular Defects in Experimental Models with Histomorphometric and Radiographic Correlation. ICMERD-International Journal of Dental Science (ICMERD-IJDS), 7(1), 1–6.

1. Introduction

Mandibular defects resulting from trauma, tumor resection, or congenital anomalies present a significant clinical challenge, particularly when the defect exceeds the critical size threshold and cannot spontaneously regenerate. Conventional approaches, such as autologous bone grafts, remain the gold standard but are limited by donor site morbidity, limited graft availability, and variable integration. As a result, synthetic biomaterials have emerged as promising alternatives, with bioactive glasses and glass-ceramic composites showing particular potential due to their osteoconductive and osteostimulatory properties.

Bioactive glass-ceramic materials are designed to promote bone regeneration through surface reactivity, ionic release, and the formation of bone-like apatite layers that facilitate direct bonding with host bone. When engineered as composites with ceramics such as hydroxyapatite, these materials can offer enhanced mechanical strength and controlled degradation. However, their performance in mandibular critical-sized defects remains underexplored, particularly in relation to both histological and radiographic regeneration parameters. This study addresses this gap by evaluating a novel bioactive glass-ceramic composite graft in an in vivo rabbit model, with detailed histomorphometric and radiographic correlation to assess its regenerative efficacy.

2. Literature Review

Bioactive glass and its derivatives have garnered significant attention in regenerative medicine due to their osteoconductive and osteostimulatory properties. Early studies by Hench and colleagues introduced silicate-based bioactive glasses capable of forming hydroxycarbonate apatite (HCA) layers in physiological environments, enhancing bone bonding capacity. Subsequent work demonstrated that the ionic dissolution products of these materials could upregulate osteogenic gene expression and promote angiogenesis.

In a comparative study, Xynos et al. (2001) reported that ionic release from 45S5 bioactive glass stimulated osteoblast proliferation and differentiation, leading to enhanced mineralized tissue formation. Meanwhile, bioactive glass-ceramic composites were found to improve mechanical strength and degradation control when compared to monolithic glass scaffolds, making them suitable for critical defect applications.

The use of bioactive glass in mandibular defect models has also been explored. Kargozar et al. (2018) reviewed preclinical evidence supporting the role of silica-based glasses in craniofacial bone regeneration, emphasizing the advantage of scaffold porosity and ion exchange dynamics in supporting bone in-growth. However, few studies have employed both histomorphometric and radiographic assessments to validate graft performance in mandibular critical-sized defects, highlighting a gap addressed by the current study.

3. Methodology & Experimental Design

3.1 Experimental Design

This study utilized twenty-four male New Zealand White rabbits, randomly assigned into three groups: control (defect only), autograft, and bioactive glass-ceramic composite. Critical-sized defects (15 mm) were surgically created in the mandibular body. The composite material was fabricated by sol-gel synthesis incorporating a 60:40 ratio of bioactive glass to hydroxyapatite particles to enhance osteointegration.

3.2 Outcome Measures

Histomorphometric analysis was conducted using Masson's Trichrome and H&E staining to assess bone formation, cellularity, and matrix maturity. Radiographic imaging was performed using standardized digital intraoral radiographs, followed by 3D micro-CT to evaluate bone volume and mineral density at 4 and 8 weeks.

Table 1: Summary of Experimental Groups and Evaluation Timeline

Group	Graft Material	Evaluation Timepoints (weeks)	n
Control	None	0, 4, 8	8
Autograft	Iliac crest bone	0, 4, 8	8
Bioactive Composite	Glass-ceramic composite	0, 4, 8	8

This table 1 outlines the experimental groups, graft materials used, evaluation timepoints, and sample sizes. It provides a clear overview of the study design, enabling comparison between control, autograft, and composite-treated groups over time.

4. Techniques and Analytical Tools

4.1 Histological and Histomorphometric Analysis

Tissue samples were decalcified, sectioned, and stained to assess qualitative and quantitative bone formation. Parameters including trabecular thickness, bone area fraction, and osteoid surface were measured using ImageJ with BoneJ plugin. Immunohistochemical staining was conducted to localize osteocalcin and CD31 for bone and vascular markers.

4.2 Radiographic and Micro-CT Evaluation

Radiographs were scored semi-quantitatively for defect bridging. Micro-CT was performed using a voxel resolution of 18 µm. Bone volume/tissue volume (BV/TV) and bone mineral density (BMD) were quantified using Scanco software. All imaging was aligned to a standard axis to ensure reproducibility.

5. Quality Assurance and Ethical Considerations

5.1 Experimental Validity

All procedures were performed under approved protocols by the institutional animal ethics committee. Randomization and blinding were used during analysis. Triplicate measurements were made by two blinded histopathologists to ensure inter-observer reliability.

5.2 Standard Compliance

The study adhered to ARRIVE guidelines for animal research and followed ISO 10993 standards for biocompatibility testing. All imaging and histological processing followed standardized SOPs to ensure data integrity.

6. Limitations and Potential Biases

6.1 Model Limitations

While the rabbit model offers anatomical relevance and healing rates similar to humans, it lacks the masticatory load present in human mandibular environments. This may limit extrapolation to clinical scenarios involving functional stress.

6.2 Material and Measurement Biases

Batch variability in the composite synthesis could introduce inconsistencies. Additionally, histomorphometry relies on 2D sections that may underrepresent 3D bone formation. Micro-CT thresholding choices may also bias quantitative results.

7. Key Findings and Interpretations

7.1 Histological Outcomes

Composite-grafted defects exhibited extensive new bone formation with organized trabeculae and marrow-like structures. Osteoid seams and osteoblastic rimming were observed, indicating active bone remodeling. In contrast, the control group showed fibrous tissue infiltration and minimal bone islands.

7.2 Radiographic Correlation

Radiographs showed progressive defect closure in the composite group, confirmed by micro-CT as increased BV/TV and higher BMD compared to both control and autograft groups. Correlation analysis revealed a strong positive relationship ($r > 0.85$) between micro-CT and histomorphometric outcomes.

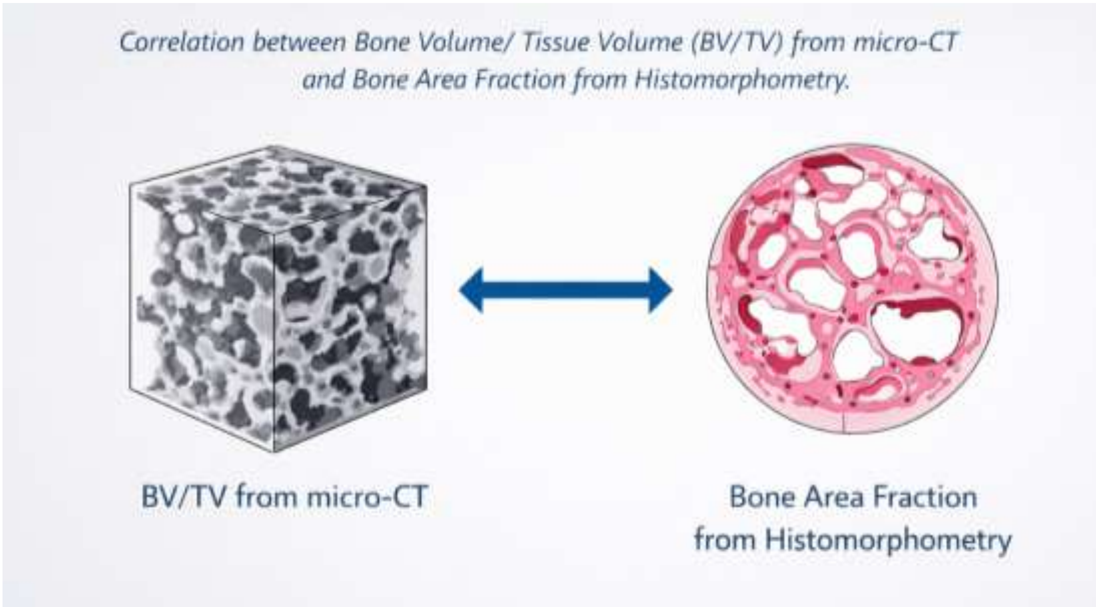

Figure 1: Correlation Between BV/TV and Bone Area Fraction Across Groups

This figure 1 shows a positive correlation between bone volume/tissue volume (BV/TV) from micro-CT and bone area fraction from histomorphometry. It visually confirms the consistency between radiographic and histological findings in evaluating bone regeneration.

8. Conclusion

The bioactive glass-ceramic composite demonstrated significant potential in regenerating critical mandibular defects, with outcomes closely supported by both radiographic and histological evaluations. Its dual-mode osteogenic response, combined with biocompatibility and handling advantages, positions it as a viable candidate for translational application in mandibular bone repair.

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