

## Article

# Intraoperative PBM Modulates Osteogenic Activity in Human Jawbone Explants: A Comparative Ex Vivo Translational Study

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## Abstract

**Background:** Surgical removal of jaw cysts may result in bone defects that compromise local structural integrity and delay spontaneous regeneration. Photobiomodulation (PBM) has been proposed as a minimally invasive intraoperative adjunct capable of modulating osteogenic activity; however, translational evidence derived from freshly harvested human jawbone tissue remains limited. **Objective:** This study evaluated the effects of an intraoperative 980 nm PBM protocol on early osteogenic activity, osteoblast-like cell abundance, morphometric outcomes, and cell viability in primary human jawbone explants obtained during cystectomy. **Materials and Methods:** A comparative translational ex vivo study was conducted using cortical bone explants harvested from 40 patients undergoing surgical treatment of medium- to large-sized maxillary or mandibular cystic lesions. For each patient, one explant was exposed immediately after harvesting to pulsed 980 nm laser irradiation (20 J total energy; 40 J/cm<sup>2</sup> fluence), whereas the paired explant served as an untreated control. Explants were cultured using a primary outgrowth technique and subjected to osteogenic induction for 14 days. Osteogenic activity was evaluated by immunofluorescence staining for alkaline phosphatase (ALPL) and osteocalcin (OCN), followed by confocal microscopy and quantitative morphometric analysis. Cell viability was assessed using a live/dead fluorescence assay. **Results:** Viable cultures were successfully established from 34 patients (85% experimental yield). PBM-treated explants exhibited significantly greater osteoblast-like cell counts than paired controls (median: 2820 vs. 1525 cells;  $p < 0.001$ ), together with greater cumulative osteoblastic area (median: 537,028 vs. 325,166 relative units;  $p < 0.001$ ) and higher osteoblastic area occupancy (median: 19.00% vs. 11.75%;  $p < 0.001$ ). Immunofluorescence analysis demonstrated qualitatively stronger ALPL and OCN expression in PBM-treated cultures. Cell viability did not differ significantly between paired PBM-treated and control cultures (Wilcoxon signed-rank test,  $p = 0.18$ ). **Conclusions:** In this comparative ex vivo model, intraoperative 980 nm PBM significantly enhanced early osteogenic activity and increased osteoblast-like cellular abundance in



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human jawbone explants while maintaining cellular viability. These findings provide translational support for further investigation of PBM as a biostimulatory adjunct to enhance bone regeneration following cyst surgery.

**Keywords:** photobiomodulation; jaw cysts; bone regeneration; osteogenic activity; confocal microscopy; ex vivo; oral and maxillofacial surgery

## 1. Introduction

Bone regeneration represents a critical aspect of contemporary oral and maxillofacial surgery, particularly following the treatment of cystic lesions of the jaws [1–3]. Although these lesions are generally benign, their progressive expansion and subsequent surgical removal may result in residual bone defects of variable size, potentially compromising local structural integrity, delaying functional rehabilitation, and affecting future implant-supported rehabilitation [4–6]. Consequently, the development of adjunctive therapeutic strategies capable of enhancing bone healing while minimizing surgical morbidity remains an important objective in regenerative oral surgery [7–9].

Autologous bone grafting remains the gold standard for reconstructing osseous defects because of its osteogenic, osteoinductive, and osteoconductive properties [1,10]. Nevertheless, donor-site morbidity, limited graft availability, and additional surgical interventions have stimulated interest in biological approaches that enhance endogenous regenerative processes [7,8,11–13]. Bone healing is a highly coordinated process involving interactions among resident progenitor cells, extracellular matrix components, vascular networks, and inflammatory mediators [14–16]. Therefore, modulation of early cellular events involved in osteogenesis represents a promising strategy to improve regenerative outcomes [16,17].

Mesenchymal stem cells and osteoprogenitor populations residing within bone tissue play a central role in skeletal regeneration through their capacity to proliferate, migrate, and differentiate into mature osteoblasts [15,17]. These cells contribute to the synthesis and mineralization of extracellular matrix, which ultimately determines the quality and quantity of newly formed bone [14,16,18]. Consequently, interventions that stimulate osteoblastic differentiation and activity have attracted considerable interest in bone tissue engineering and regenerative medicine [16,17].

Experimental models based on primary human bone explants provide a valuable translational platform for investigating osteogenic responses under controlled conditions [16,17]. Unlike immortalized cell lines, explant-derived cultures preserve native cell–matrix interactions and maintain important characteristics of the original tissue microenvironment [14,16]. Furthermore, they avoid interspecies biological differences inherent to animal models and may therefore provide findings that are more directly relevant to clinical practice [18]. The use of freshly harvested human bone tissue is particularly attractive in oral and maxillofacial surgery, where surgical procedures routinely generate biological material suitable for translational research.

PBM, formerly referred to as low-level laser therapy, has emerged as a promising non-invasive adjunctive modality in regenerative medicine and tissue engineering [19,20]. PBM utilizes non-thermal light energy to modulate cellular metabolism and biological signaling pathways, resulting in alterations in proliferation, differentiation, migration, and tissue repair processes [20,21]. Experimental studies have demonstrated that PBM may enhance mitochondrial respiratory activity, increase adenosine triphosphate production, and influence the expression of genes associated with osteogenesis and tissue regeneration [18,21–23]. In bone tissue, these biological effects have been associated with increased

osteoblastic activity, enhanced expression of osteogenic markers, and improved matrix formation and mineralization [20,22,23].

The biological effects of PBM are strongly dependent on irradiation parameters, including wavelength, power output, energy density, exposure time, and treatment protocol [22–25]. Among the wavelengths commonly used in PBM, near-infrared lasers offer greater tissue penetration than visible red-light systems and may therefore be particularly suitable for applications involving mineralized tissues [21,24]. The 980 nm wavelength has attracted increasing attention because of its ability to penetrate deeper tissue layers and interact with both mitochondrial chromophores and water molecules [21,25,26]. These interactions may influence cellular metabolism, inflammatory signaling pathways, and regenerative processes within bone tissue [21,27,28].

Within oral and maxillofacial surgery, PBM has been investigated as an adjunctive approach for promoting wound healing, reducing postoperative complications, and enhancing bone regeneration [20,23,28–30]. Nevertheless, the biological effects of PBM on freshly harvested human jawbone tissue remain insufficiently characterized. Most available evidence originates from studies using animal models, pre-osteoblastic cell lines, or immortalized osteoblast-like cultures such as MG-63 and SaOS-2 cells [31,32]. While these experimental systems have provided important mechanistic insights, they do not fully reproduce the biological complexity of native human bone tissue [17,18].

In the context of cystic jaw lesions, understanding how human bone tissue responds to PBM may have particular clinical relevance. Surgical treatment of medium- and large-sized cysts frequently results in defects that require prolonged healing periods and may benefit from regenerative stimulation [33–35]. Explant-based models offer a unique opportunity to investigate the direct effects of PBM on resident bone-derived cells under conditions that closely resemble the biological environment encountered during surgery [14,17,18]. Such translational approaches may contribute to the development of optimized protocols aimed at enhancing postoperative bone regeneration while preserving the minimally invasive nature of contemporary surgical management [34,36].

Therefore, the present study aimed to evaluate the effects of an intraoperative 980 nm PBM protocol on human jawbone explants harvested during surgical treatment of cystic lesions of the maxilla and mandible. Specifically, osteogenic activity was assessed using quantitative morphometric analysis, immunofluorescence staining for alkaline phosphatase (ALPL) and osteocalcin (OCN) expression, and cell viability assays [14,17]. By combining clinically derived human tissue with controlled laboratory analysis, this study sought to provide translational evidence regarding the influence of PBM on early osteogenic responses relevant to bone regeneration following cyst surgery [17,21,26].

## 2. Materials and Methods

### 2.1. Study Design

This study was designed as a comparative, exploratory translational *ex vivo* investigation evaluating the effects of an intraoperative PBM protocol on osteogenic behavior in human jawbone explants [16]. Because no previous human studies had characterized the variability of osteogenic outcomes in freshly harvested jawbone explants exposed to PBM, a formal *a priori* sample size calculation was not feasible. Sample size was therefore determined based on feasibility, expected explant viability reported in previous human bone culture studies, and the objective of obtaining at least 30 evaluable paired samples [17]. The final analytic cohort comprised 34 paired explants, providing sufficient precision for exploratory non-parametric analyses.

As an exploratory study, the primary objective was to estimate the magnitude and direction of the biological effects of PBM rather than to test a predefined hypothesis.

Accordingly, the findings should be regarded as hypothesis-generating and may serve to inform sample size calculations for future confirmatory investigations.

Each patient served as their own biological control by providing two morphologically comparable explants, one allocated to PBM and the other maintained as an untreated control, thereby minimizing inter-individual biological variability. The analytical hierarchy consisted of patient → paired explants → multiple microscopic fields. Five non-overlapping microscopic fields (three for viability assessment) were acquired for each explant and averaged to generate a single value per explant; these paired values constituted the statistical units for all inferential analyses.

The primary outcomes were early osteogenic differentiation, osteoblast-like cell count, cumulative osteoblastic area, and osteoblastic area occupancy under standardized in vitro culture conditions [16,18]. The term osteoblast-like refers to cells exhibiting morphological and immunophenotypic characteristics consistent with osteoblastic differentiation and does not imply definitive terminal lineage identification [16].

## 2.2. Study Population and Ethical Approval

Bone explants were harvested from 40 consecutive patients undergoing surgical treatment for cystic lesions of the maxilla or mandible measuring >10 mm in their greatest radiological dimension and classified as medium (10–20 mm) or large (>20 mm) [1,2,34–36]. Histopathological diagnoses included radicular cysts, dentigerous cysts, and keratocystic lesions [31,32]. Owing to the limited sample size, pathology-specific subgroup analyses were not performed. The study was conducted at the Department of Oral and Maxillofacial Surgery, Emergency County Clinical Hospital of Târgu Mureș, Romania, between January and December 2023.

Eligible participants presented with cystic lesions of sufficient size to allow safe harvesting of adjacent cortical bone through the routine surgical access window without modifying the standard operative procedure [34–36]. Exclusion criteria comprised previous radiotherapy or chemotherapy involving the head and neck region, osteonecrosis or osteoradionecrosis [29], active acute cystic infection or local suppuration [28], and systemic metabolic disorders or medications known to significantly affect bone metabolism [1,28].

The study protocol was approved by the Institutional Ethics Committee (Approval No. 13555/21 June 2022) and was conducted in accordance with the Declaration of Helsinki. Bone harvesting did not require any additional surgical procedures beyond routine clinical management, and all specimens were anonymized before laboratory processing. Because of the intrinsic variability of primary explant cultures, only paired samples demonstrating successful baseline cell outgrowth and osteogenic differentiation were included in the final analytic cohort. Accordingly, the study population represents a biologically responsive exploratory cohort rather than a population-based clinical sample [18,33].

## 2.3. Bone Explant Harvesting Procedure

Bone explants were collected during standard cystectomy procedures [1,2]. Following surgical exposure of the cystic cavity through a vestibular approach, small cortical bone fragments were harvested from the routine surgical access site without removing additional perilesional bone or altering the standard surgical procedure [34]. Only medium- and large-sized cystic lesions were included, as smaller lesions do not permit reliable or reproducible explant harvesting [33–36]. Immediately after collection, bone fragments were placed under sterile conditions in transport medium for subsequent laboratory processing.

For each patient, two morphologically comparable explants were obtained and randomly allocated before laboratory processing to either the PBM or untreated control group using a simple random allocation procedure. Cortical thickness and bone density were not

quantitatively assessed, and all explants were harvested from clinically accessible cortical bone adjacent to the cystic cavity. Although care was taken to select morphologically comparable specimens, intrinsic variability in bone microarchitecture may have influenced baseline osteogenic potential [18].

#### *2.4. Experimental Groups and PBM Protocol*

PBM was applied immediately after bone explant harvesting in the operating room, before transport to the laboratory [36]. Although irradiation was performed on explanted tissue, it was delivered during the same surgical session and therefore represented an intraoperative adjunct rather than a delayed laboratory intervention. For each patient, two morphologically comparable bone explants were obtained, with one randomly allocated to the PBM group and the other serving as an untreated control.

PBM was delivered using a 980 nm diode dental laser (Litemedics Prime; Litemedics, Cluj-Napoca, Romania) operating in pulsed mode with an output power of 1 W, pulse frequency of 20 kHz, duty cycle of 50%, average power of 0.5 W, peak power of 1 W, and the manufacturer's preset biostimulation mode. Laser energy was delivered through a 320 µm optical fiber positioned 50 mm from the tissue in non-contact mode for 40 s [21,26]. Real-time temperature monitoring was not performed; however, non-contact irradiation, pulsed emission, moderate average power, and a short exposure time were selected to minimize thermal accumulation [25,37,38].

At a working distance of 50 mm, the laser spot diameter was approximately 8 mm, corresponding to an irradiated area of approximately 0.50 cm<sup>2</sup>. With an average output power of 0.5 W applied for 40 s, each explant received a total energy of 20 J, equivalent to an energy density (fluence) of 40 J/cm<sup>2</sup> [22,33,36]. Based on the pulsed emission mode (peak power, 1 W; duty cycle, 50%), the theoretical peak energy density was approximately 80 J/cm<sup>2</sup>. All dosimetric calculations were standardized to the measured spot size at the specified working distance to ensure reproducibility of the irradiation protocol [19]. These parameters fall within the biostimulatory range reported for bone tissue and are consistent with the recommendations of the World Association for Photobiomodulation Therapy (WALT) [19].

#### *2.5. Transport and Laboratory Processing*

Bone explants were transported to the laboratory within 3 h of harvesting [35,36]. All subsequent experimental procedures were performed at the Department of Immunology, Center for Advanced Medical and Pharmaceutical Research (CCAMF), George Emil Palade University of Medicine, Pharmacy, Science and Technology of Târgu Mureş. Upon arrival, explants were processed under sterile conditions according to a standardized protocol applied uniformly to all specimens. Laboratory personnel responsible for routine cell culture procedures were aware of treatment allocation because laser irradiation had been completed before sample processing [39]. In contrast, all morphometric analyses and image quantification were performed by investigators blinded to treatment allocation.

#### *2.6. Explant Culture and Cell Isolation*

Bone fragments were rinsed with Dulbecco's phosphate-buffered saline (DPBS) to remove residual blood and transferred to culture flasks containing Dulbecco's Modified Eagle Medium (DMEM) supplemented with 10% fetal bovine serum and 1% antibiotic solution [37,38]. Explants were cultured using the explant outgrowth technique, allowing spontaneous migration of cells from the bone tissue [12,16,40,41]. Cultures were maintained at 37 °C in a humidified atmosphere containing 5% CO<sub>2</sub>, with regular medium replacement. Cellular outgrowth was monitored microscopically throughout the culture period. Once adequate cell confluence had been achieved, bone fragments were removed, and adherent

cells were detached by enzymatic dissociation for subsequent expansion or osteogenic differentiation assays [37].

For morphometric analyses, five randomly selected, non-overlapping microscopic fields were acquired from each culture using identical magnification and imaging parameters. Imaging locations were standardized by systematic scanning of the central culture region, and the mean value obtained from the five fields was used for statistical analysis of each explant.

### *2.7. Osteogenic Differentiation Protocol*

Cells derived from explant cultures were cultured under osteogenic conditions for 14 days before immunofluorescence and morphometric evaluation [14]. Osteogenic differentiation was induced using a standard osteogenic medium consisting of basal culture medium supplemented with  $\beta$ -glycerophosphate (10 mM), L-ascorbic acid (50  $\mu$ g/mL), and dexamethasone (100 nM) [16,17]. Cultures were maintained under controlled conditions with regular medium replacement throughout the differentiation period, allowing evaluation of early osteogenic differentiation using alkaline phosphatase (ALPL) and osteocalcin (OCN) expression [14].

### *2.8. Immunofluorescence Staining and Confocal Microscopy*

Osteogenic differentiation was evaluated by immunofluorescence staining for alkaline phosphatase (ALPL) and osteocalcin (OCN), established markers of osteoblastic differentiation and matrix maturation [14,42,43]. Cells were fixed, permeabilized, and incubated with primary antibodies against ALPL and OCN, followed by fluorochrome-conjugated secondary antibodies. Nuclei were counterstained with 4',6-diamidino-2-phenylindole (DAPI). Images were acquired using a Leica TCS SP8 confocal microscope (Leica Microsystems, Wetzlar, Germany). Identical acquisition settings, including magnification, laser power, detector gain, and field of view, were applied to all samples to ensure standardized qualitative and morphometric comparisons between PBM-treated and control cultures.

Morphometric analyses were performed using ImageJ software (version 1.54f; National Institutes of Health, Bethesda, MD, USA). Osteoblast-like structures were identified by manual and threshold-assisted segmentation based on fluorescence intensity, cell morphology, and ALPL/OCN positivity [37,38,44]. Uniform segmentation thresholds and analysis parameters were applied to all images. Quantitative image analysis was performed independently by two investigators, blinded to treatment allocation, using predefined morphological criteria, and the mean of the two measurements was used for statistical analysis. Inter-observer agreement was excellent (intraclass correlation coefficient > 0.90). Differences between cumulative osteoblastic area and cell counts reflect variations in individual cell size and clustering, as segmentation quantified contiguous fluorescent regions rather than individual cells.

### *2.9. Cell Viability Assessment and Statistical Analysis Framework*

Cell viability was evaluated using a live/dead fluorescence assay based on Calcein AM and Ethidium Homodimer III [37,39]. Viable cells exhibited green cytoplasmic fluorescence, whereas non-viable cells showed red nuclear fluorescence. Stained cultures were imaged immediately by confocal microscopy under standardized acquisition settings. Cell viability was quantified as the percentage of live cells relative to the total cell count in three standardized, non-overlapping microscopic fields per explant. Mean viability values were calculated for each explant and compared between PBM-treated and paired control cultures. Viability assessment served as a quality-control endpoint rather than a primary morphometric outcome. Images were acquired according to a predefined systematic scanning protocol to minimize selection bias.

Statistical analyses were performed using IBM SPSS Statistics version 29.0 (IBM Corp., Armonk, NY, USA). Because PBM-treated and untreated explants were paired within each patient, comparisons were performed using the Wilcoxon signed-rank test, an appropriate non-parametric method for paired data. Morphometric outcomes are presented as median (interquartile range [IQR]), whereas cell viability is reported as mean  $\pm$  standard deviation (SD). Statistical significance was defined as  $p < 0.05$ .

### 3. Results

#### 3.1. Study Cohort and Experimental Yield

Bone explants were harvested from 40 consecutive patients undergoing surgical treatment for cystic lesions of the maxilla or mandible and processed according to the standardized experimental protocol. Of the 40 enrolled patients, 34 generated viable osteogenic cultures suitable for comprehensive morphometric analysis and constituted the final analytic cohort (85% yield). Six paired explant samples were excluded because at least one explant failed to demonstrate adequate cellular outgrowth or baseline osteogenic differentiation [37]. Analysis of the excluded samples revealed no apparent clustering according to patient age or anatomical localization. Histopathological diagnosis and operative duration were not systematically recorded for the excluded specimens; therefore, it was not possible to determine whether lesion type or surgical complexity contributed to culture failure. These variables should be prospectively collected in future investigations. All subsequent analyses were performed on the final analytic cohort ( $n = 34$ ). A detailed comparison of cyst histopathology and surgical duration between included and excluded samples was not performed, as these variables were not systematically recorded; therefore, their potential influence on explant viability and osteogenic responsiveness cannot be completely excluded. The final analytic cohort included 23 males and 11 females with a mean age of  $41.8 \pm 11.6$  years. Explants were evenly distributed between the maxilla ( $n = 17$ ) and mandible ( $n = 17$ ).

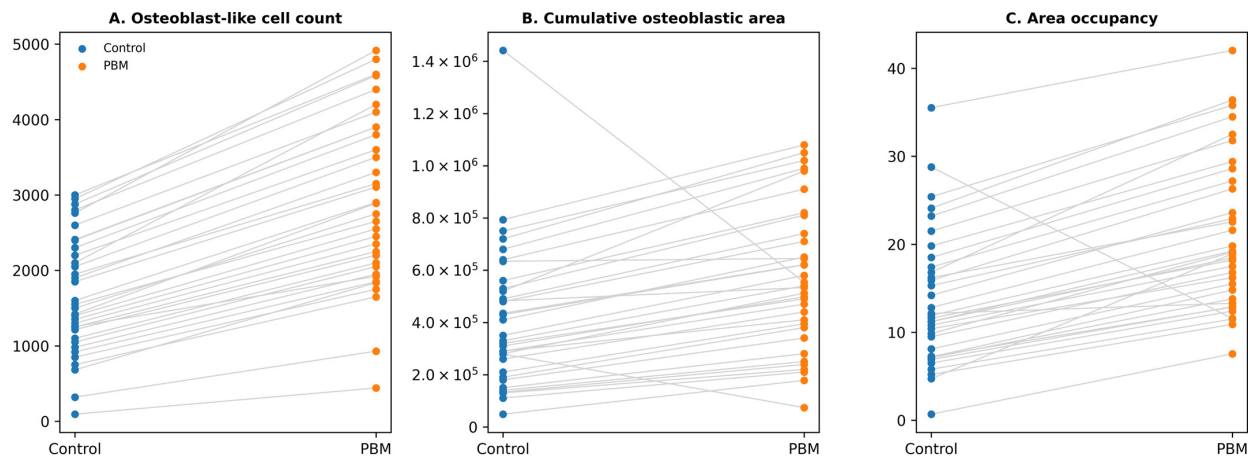
#### 3.2. Quantitative Morphometric Analysis

Quantitative morphometric analysis demonstrated significantly greater osteogenic activity and expansion of osteoblast-like cell populations in PBM-treated explants compared with paired untreated controls (Table 1; Figure 1). Osteoblast-like cell count increased from a median of 1525 (IQR 1100–2300) in controls to 2820 (IQR 2050–3900) following PBM (Wilcoxon signed-rank test,  $W = 0$ ,  $p < 0.001$ ). Similarly, cumulative osteoblastic area increased from 325,166 (IQR 190,551–530,111) to 537,028 (IQR 380,440–820,221) relative units ( $W = 53$ ,  $p < 0.001$ ), while osteoblastic area occupancy increased from 11.75% (IQR 7.10–18.50) to 19.00% (IQR 13.80–28.60) ( $W = 34$ ,  $p < 0.001$ ). Collectively, these findings indicate that PBM increased both the abundance and spatial distribution of osteoblast-like cellular structures in paired human jawbone explants.

**Table 1.** Quantitative morphometric comparison between paired untreated and PBM-treated human jawbone explants (Wilcoxon signed-rank test).

| Outcome                           | Control Median (IQR)      | PBM Median (IQR)          | Wilcoxon W | p-Value |
|-----------------------------------|---------------------------|---------------------------|------------|---------|
| Osteoblast-like cell count        | 1525 (1100–2300)          | 2820 (2050–3900)          | 0          | <0.001  |
| Cumulative osteoblastic area (RU) | 325,166 (190,551–530,111) | 537,028 (380,440–820,221) | 53         | <0.001  |
| Osteoblastic area occupancy (%)   | 11.75 (7.10–18.50)        | 19.00 (13.80–28.60)       | 34         | <0.001  |

Data are presented as median (interquartile range, IQR). Statistical comparisons were performed using the Wilcoxon signed-rank test because paired treated and untreated explants originated from the same patient.



**Figure 1.** Paired quantitative morphometric comparison of osteogenic outcomes in human jawbone explants following PBM.

Paired dot plots illustrating the three primary morphometric outcomes obtained from human jawbone explants cultured under osteogenic conditions for 14 days. Each pair of connected dots represents matched explants obtained from the same patient, with untreated control explants shown in blue and PBM-treated explants shown in red. Gray connecting lines indicate the paired experimental design. (A) Osteoblast-like cell count. (B) Cumulative osteoblastic area (relative units). (C) Osteoblastic area occupancy (%). Statistical comparisons were performed using the paired Wilcoxon signed-rank test. PBM treatment resulted in significantly greater osteoblast-like cell counts, cumulative osteoblastic area, and osteoblastic area occupancy than paired untreated controls ( $p < 0.001$  for all comparisons).

### 3.3. Immunofluorescence Assessment of Osteogenic Marker Expression

Immunofluorescence staining confirmed ALPL and OCN expression in both groups [43]. PBM-treated cultures exhibited qualitatively stronger and more extensive ALPL and OCN fluorescence than paired controls [14,44], consistent with enhanced osteogenic differentiation following PBM exposure [21]. Semi-quantitative fluorescence intensity measurements were not performed; therefore, morphometric quantification of osteoblast-like structures and surface occupancy served as indirect quantitative indicators of osteogenic activity.

### 3.4. Cell Viability Analysis

Live/dead fluorescence assays demonstrated high baseline cellular viability in both groups [37,42].

Quantitative analysis showed no significant difference in viability between paired PBM-treated and control cultures (Wilcoxon signed-rank test,  $p = 0.18$ ).

No increase in non-viable cells was observed following PBM exposure, suggesting that the applied irradiation parameters did not induce detectable cytotoxic effects [32,42].

## 4. Discussion

The present exploratory ex vivo study demonstrates that intraoperative PBM using a 980 nm diode laser significantly enhances early osteogenic activity in paired human jawbone explants obtained during cystectomy. Compared with untreated paired controls, PBM-treated explants exhibited significantly higher osteoblast-like cell counts, greater cumulative osteoblastic area, and greater osteoblastic surface occupancy, while maintaining high cellular viability. Because each treated explant was directly compared with its paired control from the same patient, analysis using the Wilcoxon signed-rank test appropriately

accounted for within-subject biological variability and strengthened the reliability of the observed treatment effects.

Bone regeneration following surgical removal of maxillary and mandibular cysts remains a clinically important challenge, particularly when medium- to large-sized defects require prolonged healing before complete structural restoration [3,34–36]. Although spontaneous regeneration frequently occurs, healing may be slow and unpredictable, prompting continued interest in minimally invasive adjunctive therapies capable of enhancing endogenous osteogenesis without increasing surgical morbidity [6,10,38]. Within this context, PBM has attracted considerable attention because of its reported ability to modulate cellular metabolism, proliferation, differentiation, and tissue repair [16,18].

The magnitude of the observed biological response was substantial. Relative to paired untreated controls, PBM increased the median osteoblast-like cell count by approximately 85%, the cumulative osteoblastic area by approximately 65%, and the osteoblastic area occupancy by approximately 62%. Although direct quantitative comparisons with previous human PBM studies remain challenging because of differences in irradiation protocols, wavelengths, biological models, and outcome measures, the magnitude and direction of these effects are consistent with the growing body of experimental evidence demonstrating stimulatory effects of PBM on osteogenic cells and mesenchymal stem cell differentiation [18,21,23,36].

The concurrent increase in cell number, cumulative cellular area, and spatial occupancy suggests that PBM may promote not only expansion of osteoblast-like cell populations but also a more organized distribution of osteogenic cells throughout the culture surface [37,44]. Such coordinated changes are biologically relevant because successful bone regeneration depends not only on the presence of osteogenic cells but also on their ability to populate the regenerative environment and initiate extracellular matrix deposition [15,38]. Nevertheless, because no functional mineralization assays were performed, these findings should be interpreted as evidence of enhanced early osteogenic differentiation rather than confirmed mineralized bone formation.

Qualitative immunofluorescence further supported this interpretation. PBM-treated cultures appeared to demonstrate stronger and more extensive ALPL and OCN immunofluorescence, two well-established markers of osteoblastic differentiation [14,43,44]. Although fluorescence intensity was not quantified and complementary assays such as alkaline phosphatase activity, Alizarin Red S staining, or von Kossa staining were not included, the concordance between immunofluorescence findings and quantitative morphometric outcomes provides consistent evidence supporting enhanced osteogenic activity following PBM exposure.

The biological mechanisms responsible for these observations cannot be directly established by the present study but are compatible with previously proposed mechanisms of PBM action. Experimental investigations have shown that near-infrared irradiation may enhance mitochondrial respiratory chain activity, increase adenosine triphosphate production, regulate reactive oxygen species, and activate intracellular signaling pathways involved in osteogenic differentiation [18,21,36]. Unlike many previous investigations that relied on immortalized osteoblast-like cell lines or animal models [31,32], the present study employed freshly harvested human jawbone explants, thereby preserving native cell–matrix interactions and providing a biologically relevant translational model that more closely reflects the tissue environment encountered during oral and maxillofacial surgery [17,37,43]. However, because molecular analyses were beyond the scope of this exploratory investigation, these mechanistic explanations remain hypothetical.

From a translational perspective, PBM should be considered a potential adjunct rather than an alternative to established regenerative strategies. Management of cystic jaw defects

currently ranges from spontaneous healing to the use of autogenous grafts, biomaterials, platelet-rich fibrin, and staged surgical approaches [4,6,8]. The present findings suggest that PBM may represent an attractive complementary intervention because it requires only a brief intraoperative application, introduces no additional donor-site morbidity, and integrates easily into routine surgical workflows [35,36]. Nevertheless, the absence of a positive control group, such as recombinant BMP-2 or another validated osteogenic stimulator, prevents direct comparison of PBM with established regenerative interventions. Future comparative studies are therefore needed to determine the relative biological efficacy of PBM within the broader spectrum of bone regeneration strategies.

Several methodological considerations should be acknowledged when interpreting these findings. First, this was an exploratory *ex vivo* study designed to investigate early biological responses rather than clinical healing outcomes. The analytic cohort consisted exclusively of explants demonstrating successful cellular outgrowth and osteogenic differentiation, representing a biologically responsive subset rather than a population-based sample [18]. Furthermore, the explant model preserves important native cell–matrix interactions [14] but cannot reproduce the complex biological environment present *in vivo*, where vascularization, inflammatory signaling, immune regulation, and biomechanical loading all contribute to bone regeneration [7,8,24,42]. Consequently, the observed effects should be interpreted as modulation of early osteogenic potential rather than direct evidence of accelerated clinical bone healing.

Second, several potentially influential variables could not be evaluated. Histopathological subtype, surgical duration, inflammatory status, smoking history, lesion size, and other patient-related characteristics were not systematically recorded, precluding subgroup analyses that might explain inter-individual variability in osteogenic responsiveness. Similarly, cortical thickness and bone density were not quantitatively assessed before culture. Future studies incorporating comprehensive baseline characterization may help identify clinical predictors of responsiveness to PBM and explain why some explants exhibit greater biological stimulation than others.

Third, although the selected irradiation parameters were chosen within established biostimulatory ranges [22,23], thermal monitoring was not performed during laser application. To minimize potential photothermal effects, irradiation was delivered in non-contact mode using pulsed emission, moderate average power, and a short exposure time [21,25]. These methodological precautions were intended to favor photobiomodulatory rather than thermal mechanisms; however, future investigations should include independent laser output calibration together with real-time temperature monitoring to further distinguish photobiological from photothermal effects.

Finally, osteogenic differentiation was evaluated at a single 14-day time point following a single PBM exposure. While this design permitted assessment of early differentiation markers, it could not characterize the temporal evolution of the cellular response. Earlier evaluations would help define proliferative effects, whereas longer culture periods combined with quantitative mineralization assays would determine whether the observed increase in osteogenic activity ultimately translates into enhanced matrix maturation and mineral deposition. Likewise, repeated PBM applications may produce different biological responses and deserve systematic investigation.

Despite these limitations, several methodological strengths support the validity of the present findings. The paired experimental design minimized inter-patient biological variability by allowing each patient to serve as their own control. Image acquisition and morphometric analyses were standardized, measurements were performed by blinded investigators with excellent inter-observer agreement, and all quantitative endpoints demonstrated a consistent direction of effect. Together, these observations provide coherent

evidence that intraoperative PBM favorably modulates early osteogenic behavior in freshly harvested human jawbone explants.

Overall, the present study contributes clinically relevant translational evidence supporting the biological potential of PBM as an intraoperative adjunct during cyst surgery. Although definitive conclusions regarding clinical efficacy cannot yet be drawn, the consistent enhancement of early osteogenic activity observed in this human ex vivo model provides a strong rationale for prospective clinical trials incorporating longitudinal imaging, quantitative mineralization assessment, and functional healing outcomes to determine whether these promising cellular effects translate into improved postoperative bone regeneration [35,36].

## 5. Conclusions

This exploratory translational ex vivo study suggests that photobiomodulation applied to human jawbone explants enhances early osteogenic activity, as reflected by an increased osteoblast-like cell count, cumulative osteoblastic area, and osteoblastic area occupancy. Compared with paired untreated controls, laser-treated explants exhibited significantly greater osteoblast-like cellular abundance and osteogenic tissue expansion across all quantitative morphometric endpoints.

These findings are limited to indirect cellular measures of osteogenic activity obtained from an exploratory ex vivo model and should therefore be regarded as hypothesis-generating. Prospective clinical studies incorporating quantitative mineralization assays, radiographic bone fill, and functional healing outcomes are warranted to determine whether these biological effects translate into improved clinical bone regeneration following cyst surgery.

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## References

1. Starch-Jensen, T.; Deluiz, D.; Deb, S.; Bruun, N.H.; Tinoco, E.M.B. Harvesting of autogenous bone graft from the ascending mandibular ramus compared with the chin region: A systematic review and meta-analysis focusing on complications and donor site morbidity. *J. Oral Maxillofac. Res.* **2020**, *11*, e1. [\[CrossRef\]](#) [\[PubMed\]](#)
2. Daoud, S.; Zoabi, A.; Kasem, A.; Totry, A.; Oren, D.; Redenski, I.; Srouji, S.; Kablan, F. Computer-assisted evaluation confirms spontaneous healing of donor site one year following bone block harvesting from mandibular retromolar region—A cohort study. *Diagnostics* **2024**, *14*, 504. [\[CrossRef\]](#) [\[PubMed\]](#)
3. Nyimi, B.F.; Zhao, Y.; Liu, B. The changing landscape in treatment of cystic lesions of the jaws. *J. Int. Soc. Prev. Community Dent.* **2019**, *9*, 328–337. [\[CrossRef\]](#) [\[PubMed\]](#)

4. Wang, J.; Yao, Q.Y.; Zhu, H.Y. Efficacy of bone grafts in jaw cystic lesions: A systematic review. *World J. Clin. Cases* **2022**, *10*, 2801–2810. [[CrossRef](#)] [[PubMed](#)]
5. Tas, A.; Celebi, E.; Çukurova Yilmaz, Z. Assessment of bone healing after surgical management of odontogenic cysts utilizing fractal analysis—A retrospective cross-sectional study. *PeerJ* **2025**, *13*, e19745. [[CrossRef](#)] [[PubMed](#)]
6. Li, Y.; He, L.; Tang, Z.; Shao, L.; Zhang, W.; Su, J. Long-term implant success after treatment of a giant mandibular dentigerous cyst: A case report. *Int. J. Surg. Case Rep.* **2025**, *135*, 111831. [[CrossRef](#)] [[PubMed](#)]
7. Sakdejyont, S.; Chobpenthai, T.; Suksirivecharuk, P.; Ninatkiattikul, I.F.; Poosiripinyo, T. A review on bone tumor management: Cutting-edge strategies in bone grafting, bone graft substitute, and growth factors for defect reconstruction. *Orthop. Res. Rev.* **2025**, *17*, 175–188. [[CrossRef](#)] [[PubMed](#)]
8. Nicolae, C.-L.; Pîrvulescu, D.-C.; Niculescu, A.-G.; Epistatu, D.; Mihaiescu, D.E.; Antohi, A.M.; Grumezescu, A.M.; Croitoru, G.-A. An Up-to-Date Review of Materials Science Advances in Bone Grafting for Oral and Maxillofacial Pathology. *Materials* **2024**, *17*, 4782. [[CrossRef](#)] [[PubMed](#)]
9. La Rosa, G.R.M.; Priolo, C.Y.; Abiad, R.S.; Romeo, V.R.; Ambu, E.; Pedullà, E. Assessment of bone regeneration after maxillary radicular cyst enucleation with or without bone grafting materials: A retrospective cohort study. *Clin. Oral Investig.* **2024**, *28*, 213. [[CrossRef](#)] [[PubMed](#)]
10. Elsalanty, M.E.; Genecov, D.G. Bone grafts in craniofacial surgery. *Craniofac. Trauma Reconstr.* **2009**, *2*, 125–134. [[CrossRef](#)] [[PubMed](#)]
11. Zhang, J.; Zhang, W.; Yue, W.; Qin, W.; Zhao, Y.; Xu, G. Research Progress of Bone Grafting: A Comprehensive Review. *Int. J. Nanomed.* **2025**, *20*, 4729–4757. [[CrossRef](#)] [[PubMed](#)]
12. Cao, H.; He, S.; Wu, M.; Hong, L.; Feng, X.; Gao, X.; Li, H.; Liu, M.; Lv, N. Cascaded controlled delivering growth factors to build vascularized and osteogenic microenvironment for bone regeneration. *Mater. Today Bio* **2024**, *25*, 101015. [[CrossRef](#)] [[PubMed](#)]
13. Wang, Y.; Zhang, X.; Li, X.; Cheng, M.; Cui, X. The vascular microenvironment and its stem cells regulate vascular homeostasis. *Front. Cell Dev. Biol.* **2025**, *13*, 1544129. [[CrossRef](#)] [[PubMed](#)]
14. Lin, X.; Patil, S.; Gao, Y.G.; Qian, A. The bone extracellular matrix in bone formation and regeneration. *Front. Pharmacol.* **2020**, *11*, 757. [[CrossRef](#)] [[PubMed](#)]
15. Huang, W.; Zhou, C.; Yu, Y.; Qin, S.; Chen, L.; Lin, H.; Zhang, S.; Xia, L.; Liang, W. Functionalized mesenchymal stem cells for enhanced bone regeneration: Advances and challenges. *Stem Cell Res. Ther.* **2025**, *16*, 600. [[CrossRef](#)] [[PubMed](#)]
16. Coccoluto, L.; Roberto, R.; Paola, P.; Francesca, R.; Raffaele, V. Osteoblastic differentiation and proliferation of human mesenchymal stem cells or osteoblast-like cells on bone scaffolds in oral and periodontal surgery: A systematic review of in vitro studies. *J. Adv. Oral Res.* **2025**, *16*, 121–139. [[CrossRef](#)]
17. Han, Y.; Li, X.; Zhang, Y.; Han, Y.; Chang, F.; Ding, J. Mesenchymal Stem Cells for Regenerative Medicine. *Cells* **2019**, *8*, 886. [[CrossRef](#)] [[PubMed](#)]
18. Collignon, A.M.; Lesieur, J.; Vacher, C.; Chaussain, C.; Rochefort, G.Y. Strategies Developed to Induce, Direct, and Potentiate Bone Healing. *Front. Physiol.* **2017**, *8*, 927. [[CrossRef](#)] [[PubMed](#)]
19. Hanna, R.; Chow, R.; Dalvi, S.; Arany, P.R.; Bensadoun, R.-J.; Santos-Silva, A.R.; Tunér, J.; Carroll, J.D.; Hamblin, M.R.; Anders, J.; et al. Photobiomodulation Therapy in the Management of Orofacial Neuropathic Pain—WALT Position Paper 2026. *J. Clin. Med.* **2026**, *15*, 1304. [[CrossRef](#)] [[PubMed](#)]
20. Moscatel, M.B.M.; Pagani, B.T.; Trazzi, B.F.d.M.; Reis, C.H.B.; Ribeiro, C.A.; Buchaim, D.V.; Buchaim, R.L. Effects of Photobiomodulation in Association with Biomaterials on the Process of Guided Bone Regeneration: An Integrative Review. *Ceramics* **2025**, *8*, 94. [[CrossRef](#)]
21. AlGhamdi, K.M.; Kumar, A.; Alfayez, M.; Mahmood, A. Influence of Low-Level Red Laser Irradiation on the Proliferation, Viability, and Differentiation of Human Embryonic Stem Cell-Derived Mesenchymal Stem Cells. *Life* **2025**, *15*, 1125. [[CrossRef](#)] [[PubMed](#)]
22. Della Coletta, B.B.; Jacob, T.B.; Moreira, L.A.d.C.; Pomini, K.T.; Buchaim, D.V.; Eleutério, R.G.; Pereira, E.d.S.B.M.; Roque, D.D.; Rosso, M.P.d.O.; Shindo, J.V.T.C.; et al. Photobiomodulation Therapy on the Guided Bone Regeneration Process in Defects Filled by Biphasic Calcium Phosphate Associated with Fibrin Biopolymer. *Molecules* **2021**, *26*, 847. [[CrossRef](#)] [[PubMed](#)]
23. Iaria, R.; Vescovi, P.; De Francesco, P.; Giovannacci, I. Laser Photobiomodulation: What Are the Ideal Parameters for Each Type of Laser Used in Dental Practice to Promote Fibroblast Proliferation and Differentiation? A Systematic Review. *Life* **2025**, *15*, 853. [[CrossRef](#)] [[PubMed](#)]
24. Alsarhan, J.; El Feghali, R.; Alkhudari, T.; Benedicenti, S. Non-Pharmacological Therapies for Management of Temporomandibular Myofascial Pain Syndrome: Laser Photobiomodulation or Dry Needling? Meta-Analyses of Human Clinical Trials. *Photonics* **2024**, *11*, 965. [[CrossRef](#)]
25. Amaroli, A.; Colombo, E.; Zekiy, A.; Aicardi, S.; Benedicenti, S.; De Angelis, N. Interaction between Laser Light and Osteoblasts: Photobiomodulation as a Trend in the Management of Socket Bone Preservation—A Review. *Biology* **2020**, *9*, 409. [[CrossRef](#)] [[PubMed](#)]

26. Na, S.; TruongVo, T.; Jiang, F.; Joll, J.E.; Guo, Y.; Utreja, A.; Chen, J. Dose analysis of photobiomodulation therapy on osteoblast, osteoclast, and osteocyte. *J. Biomed. Opt.* **2018**, *23*, 075008. [[CrossRef](#)] [[PubMed](#)]
27. Gao, X.; Xing, D. Molecular mechanisms of cell proliferation induced by low power laser irradiation. *J. Biomed. Sci.* **2009**, *16*, 4. [[CrossRef](#)] [[PubMed](#)]
28. Hosseinpour, S.; Tunér, J.; Fekrazad, R. Photobiomodulation in oral surgery: A review. *Photobiomodul. Photomed. Laser Surg.* **2019**, *37*, 814–825. [[CrossRef](#)] [[PubMed](#)]
29. Del Vecchio, A.; Tenore, G.; Pergolini, D.; Rocchetti, F.; Palaia, G.; Romeo, U. The Role of the Laser Photobiomodulation (PBM) in the Management of Patients at Risk or Affected by MRONJ. *Oral* **2022**, *2*, 7–15. [[CrossRef](#)]
30. Saki, M.; Tahamtan, S.; Shavakhi, M.; Grzech-Leśniak, K.; Fekrazad, R. The effectiveness of photobiomodulation therapy on bone regeneration of oral and craniofacial defects: A systematic review of animal and in vitro studies. *Lasers Med. Sci.* **2025**, *40*, 384. [[CrossRef](#)] [[PubMed](#)]
31. Mészáros, B.; Csoti, A.; Szanto, T.G.; Telek, A.; Kovács, K.; Toth, A.; Volkó, J.; Panyi, G. The hEag1 K<sup>+</sup> Channel Inhibitor Astemizole Stimulates Ca<sup>2+</sup> Deposition in SaOS-2 and MG-63 Osteosarcoma Cultures. *Int. J. Mol. Sci.* **2022**, *23*, 10533. [[CrossRef](#)] [[PubMed](#)]
32. Deana, A.M.; de Souza, A.M.; Teixeira, V.P.; Mesquita-Ferrari, R.A.; Bussadori, S.K.; Fernandes, K.P.S. The impact of photobiomodulation on osteoblast-like cell: A review. *Lasers Med. Sci.* **2018**, *33*, 1147–1158. [[CrossRef](#)] [[PubMed](#)]
33. Vigliar, M.F.R.; Marega, L.F.; Duarte, M.A.H.; Alcalde, M.P.; Rosso, M.P.d.O.; Ferreira Junior, R.S.; Barraviera, B.; Reis, C.H.B.; Buchaim, D.V.; Buchaim, R.L. Photobiomodulation therapy improves repair of bone defects filled by inorganic bone matrix and fibrin heterologous biopolymer. *Bioengineering* **2024**, *11*, 78. [[CrossRef](#)] [[PubMed](#)]
34. Irimia, A.; Moraru, L.; Ciubotaru, D.A.; Caruntu, C.; Farcasiu, A.-T.; Caruntu, A. Minimally Invasive Two-Staged Surgery in the Treatment of Large Cystic Lesions of the Jaw. *Healthcare* **2021**, *9*, 1531. [[CrossRef](#)] [[PubMed](#)]
35. Shah, N.; Logani, A.; Kumar, V. A minimally invasive surgical approach for large cyst-like periapical lesions: A case series. *Gen. Dent.* **2014**, *62*, e1–e5. [[PubMed](#)]
36. Abdellatife, T.A.; Zaki, M.H. Impact of photobiomodulation on postoperative pain and bone healing following cystic enucleation: A randomized clinical trial. *Egypt. J. Oral Maxillofac. Surg.* **2025**, *16*, 60–66. [[CrossRef](#)]
37. Lazăr, L.; Manu, D.R.; Dako, T.; Mârțu, M.-A.; Suci, M.; Ormenișan, A.; Păcurar, M.; Lazăr, A.-P. Effects of Laser Application on Alveolar Bone Mesenchymal Stem Cells and Osteoblasts: An In Vitro Study. *Diagnostics* **2022**, *12*, 2358. [[CrossRef](#)] [[PubMed](#)]
38. Pagin, M.T.; de Oliveira, F.A.; Oliveira, R.C.; Sant’Ana, A.C.P.; de Rezende, M.L.R.; Greggi, S.L.A.; Damante, C.A. Laser and light-emitting diode effects on pre-osteoblast growth and differentiation. *Lasers Med. Sci.* **2014**, *29*, 55–59. [[CrossRef](#)] [[PubMed](#)]
39. Song, L.; Schwinn, L.-S.; Barthel, J.; Ketter, V.; Lechler, P.; Linne, U.; Rastan, A.J.; Vogt, S.; Ruchholtz, S.; Paletta, J.R.J.; et al. Implant-Derived *S. aureus* Isolates Drive Strain-Specific Invasion Dynamics and Bioenergetic Alterations in Osteoblasts. *Antibiotics* **2025**, *14*, 119. [[CrossRef](#)] [[PubMed](#)]
40. McLean, A.C.; Vargas, P.A. Cystic lesions of the jaws: The top 10 differential diagnoses to ponder. *Head Neck Pathol.* **2023**, *17*, 85–98. [[CrossRef](#)] [[PubMed](#)]
41. Prajapati, A.; Gulia, A.; Gundavda, K.; Botchu, R.; Janu, A. Cystic bone lesions: Diagnostic pitfalls and therapeutic considerations. *J. Clin. Orthop. Trauma* **2025**, *67*, 103046. [[CrossRef](#)] [[PubMed](#)]
42. Paim, E.D.; Branchini, G.; Lamers, M.; Diel, L.; Bonassi, J.R.; Macagnan, F.E. Effect of photobiomodulation on viability and proliferation of squamous cell carcinoma in vitro. *Lasers Med. Sci.* **2025**, *40*, 462. [[CrossRef](#)] [[PubMed](#)]
43. Sacher, C.; Holzinger, D.; Grogger, P.; Wagner, F.; Sperl, G.; Seemann, R. Calculation of postoperative bone healing of cystic lesions of the jaw—A retrospective study. *Clin. Oral Investig.* **2019**, *23*, 3951–3957. [[CrossRef](#)] [[PubMed](#)]
44. Lu, P.; Peng, J.; Liu, J.; Chen, L. The role of photobiomodulation in accelerating bone repair. *Prog. Biophys. Mol. Biol.* **2024**, *188*, 55–67. [[CrossRef](#)] [[PubMed](#)]

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