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Research Article

Assessment of Bone Regeneration Outcomes Using Bioactive and Standard Membranes in Dental Implant Procedures: A Clinical and Histomorphometric Study

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ABSTRACT

Adequate bone volume and quality are essential for successful dental implant therapy, and these are frequently repaired using barrier membrane-assisted guided bone regeneration (GBR). Beyond passive space maintenance, recent developments in bioactive membranes seek to stimulate osteogenesis; nevertheless, there is now little clinical and histomorphometric proof. In this study, the results of bone regeneration using a bioactive resorbable membrane and a conventional collagen membrane utilized in GBR procedures related to dental implant treatment were compared. 50 patients in need of localised ridge augmentation participated in a prospective, randomized, controlled, single-blind clinical investigation. A standardized particle graft was administered to each subject, and they were randomized to receive either a conventional collagen membrane or a bioactive collagen membrane. Histomorphometric, radiological (CBCT), and clinical data were gathered. The proportion of new bone in biopsy cores was the main outcome, whereas the residual graft percentage, volumetric bone growth, implant stability (ISQ), and complications were secondary outcomes. Both parametric and nonparametric tests were used in the statistical analyses, and $p < 0.05$ was used as the significance level. In comparison to controls, the bioactive membrane group had substantially larger volumetric and horizontal bone growth (310.6 ± 45.8 mm³ and 3.42 ± 0.82 mm), more new bone formation ($46.3 \pm 8.7\%$), and higher implant stability (ISQ 78.5 ± 3.6) ($p < 0.05$). There was no discernible variation in the rates of complications. When compared to conventional collagen membranes, bioactive membranes showed better clinical and histomorphometric results, improving implant stability and bone quality without raising problem. This supports the use of bioactive membranes as an improved GBR material for predictable bone regeneration.

Keywords: Guided Bone Regeneration, Bioactive Membranes, Dental Implants, Histomorphometric Analysis,Bone Regeneration Outcomes

INTRODUCTION

Dental implant therapy has become a predictable solution for the replacement of missing teeth, but successful osseointegration and long-term implant stability depend critically on adequate alveolar bone volume and quality[1]. When alveolar deficiencies or peri-implant defects exist, guided bone regeneration (GBR) techniques that combine osteoconductive graft materials with barrier membranes are widely used to re-establish ridge dimensions and create a stable environment for implant placement[2]. Barrier membranes function by excluding soft-tissue ingrowth, stabilizing the graft, and maintaining a secluded space for bone formation properties that directly influence both the quantity and quality of regenerated bone[3].

Historically, barrier membranes have been categorized as non-resorbable (e.g., e-PTFE, titanium-reinforced) and resorbable (principally collagen-based) types[4]. More recently, "bioactive" membranes membranes engineered to provide not only passive barrier function but also active physicochemical or biological cues (such as ion-release, osteoconductive coatings, growth-factor incorporation, or degradable metallic frameworks such as magnesium-based membranes) have been developed to enhance osteogenesis, modulate inflammation, and improve space maintenance without the need for a second-stage removal[5]. Advances in synthetic polymers, composite membranes, and mineral-doped or biologically functionalize membranes have expanded options for clinicians aiming to improve regenerative outcomes in complex defects[6].

Despite promising preclinical and early clinical data for several bioactive concepts, heterogeneity in membrane materials, study designs, defect types, and outcome measures has limited clear translation into evidence-based recommendations[7]. Clinical endpoints such as radiographic bone fill and implant survival are important, but histomorphometric analysis of biopsy specimens remains the gold standard for assessing the quality (new bone percentage, residual graft, and marrow/connective tissue proportions) and the maturation of regenerated tissues[8]. High-quality randomized clinical trials that combine clinical, radiographic, and histomorphometric outcomes comparing novel bioactive membranes directly against standard collagen membranes are still relatively few, and standardized reporting of histological outcomes is variable[9]. This evidence gap complicates selection of membranes for specific clinical scenarios and underscores the need for well-designed comparative studies[10].

Accordingly, the present clinical and histomorphometric study aims to compare bone regeneration outcomes achieved with a selected bioactive membrane versus a standard resorbable collagen membrane in dental implant-related GBR procedures[11]. Clinical and radiographic measurements of ridge diameters, implant stability, and complication rates are secondary goals; histomorphometric measurements of new bone formation and graft/residual material percentages at specified healing intervals are primary results [12]. This study aims to offer solid, translational data to guide membrane selection and enhance implant result prediction in damaged alveolar locations by combining clinical, radiographic, and microscopic objectives.[13].

LITERATURE REVIEW

Elgali I(2015):An in-depth analysis of the biological underpinnings of GBR, membrane classes (resorbable versus non-resorbable), and the effects of membrane characteristics (porosity, degradation, and space maintenance) on healing. The authors summarise preclinical and clinical data and point out that the type of membrane used affects the amount and calibre of bone that is regenerated. However, they also point out that outcome measures vary and that histology-based endpoints are necessary[14]. Rayyan F(2025): In a randomized rabbit calvarial model, magnesium-based resorbable membranes were compared to controls (no membrane) with histomorphometric evaluation at 8 weeks. Results showed favourable new bone formation and effective space maintenance for Mg membranes; authors discuss degradation behaviour and local tissue response[15]. Zhou L(2021):A clinical RCT comparing different combinations of bone substitutes and titanium meshes reported no significant differences in quantity and density of

regenerated bone between groups radiographically; the study included biopsies in a subset for histology but emphasized clinical and volumetric endpoints[16].

Kitson N(1994):An experimental study evaluated polypropylene membrane performance in critical defects, performing histomorphometry to quantify new bone and connective tissue. Findings supported barrier function but highlighted variations in tissue composition depending on membrane type and defect model[17]. Pesce P(2021):This clinical study analyzed biopsies from GBR procedures and found variable bone formation between maxillary and mandibular sites and questioned the additive benefit of covering titanium mesh with collagen membrane in all scenarios. Histomorphometric metrics (new bone %, residual graft) were central to conclusions[18]. Thoma DS(2016):A randomized controlled clinical trial comparing a novel PEG hydrogel membrane to a standard collagen membrane found comparable clinical outcomes for treatment of peri-implant dehiscence; histologic sampling showed similar bone healing patterns. Authors concluded the synthetic membrane was non-inferior in that indication[19].

Yang C(2022):Preclinical jaw-defect models tested a synthetic composite membrane (PCL/PEG with bioactive glass), reporting improved osteogenesis and favourable histology compared to controls. Histomorphometric outcomes supported the bioactive glass contribution to bone formation[20]. Park J(2016):This study evaluated a PLLA-coated magnesium-dysprosium alloy membrane in a rabbit calvarial GBR model, combining in vitro degradation/cytotoxicity tests with in vivo histology and histomorphometry; results suggested good biocompatibility and predictable degradation with bone formation beneath the membrane[19]. Annen BM(2011):A controlled preclinical study compared pre-mineralised ELR membranes to non-mineralized variants and reported superior new bone percentages and maturation with mineralised ELRs by histomorphometric analysis. Authors discuss tunable bioactivity and potential clinical translation[21]. Marino M(2024):A recent materials-focused review summarizing resorbable and non-resorbable membranes, advances in bioactive/functionalised membranes, and clinical evidence quality. The authors call for standardized clinical/histological outcome reporting and more RCTs comparing novel bioactive membranes to current collagen standards[22].

MATERIALS AND METHODS

Study design: This study is a prospective, randomized, controlled, single-blind (outcome assessor blinded), parallel-group clinical trial comparing a selected bioactive resorbable membrane (test) with a standard resorbable collagen membrane (control) used in guided bone regeneration (GBR) for localized alveolar defects associated with dental implant therapy. The trial registered on a recognized public registry and conducted after institutional ethics committee approval; all participants provided written informed consent. Primary endpoint: histomorphometric percentage of new bone in biopsy cores taken at implant placement. Secondary endpoints: residual graft percentage, marrow/connective tissue percentage, CBCT volumetric and linear ridge changes, implant primary stability (ISQ), and clinical complications. This integrated clinical radiographic histologic design follows current best practice for translational GBR trials.

Data collection: This study used a standardized and calibrated clinical and laboratory workflow as a data collection method to promote consistency and reproducibility of all the cases. The highly trained implant surgeons were involved in all the surgical procedures with a standardized operating procedure. Flap elevation, defect preparation was followed by the application of one particulate graft material of the same manufacturer and lot number, followed by randomly placing either bioactive or standard collagen membrane, which was attached with sutures or fixation pins to maintain space and close the primary wound. Standardization and documentation of postoperative management such as antibiotics, analgesic and oral hygiene instructions were done. Cone-beam computed tomography (CBCT) was done at preoperative, immediately after, and at regular healing times and the patient was in the same position with the

same imaging protocols. Linear and volume bone measurements were measured through a verified image analysis software and all radiography examination was made by an independent examiner who was blinded. Core biopsies were taken at grafted sites at the time of the implant placement using sterile trephine burs to enable the use of histologic and histomorphometric analysis. The samples were promptly continued in 10 percent neutral buffered formalin and dehydrated and embedded in polymethyl methacrylate (PMMA) resin to undergo undecalcified sectioning. The calibrated digital analysis was performed on quantitative analysis of images and the observers were not aware of the group allocation. Two trained examiners independently conducted all the histomorphometric measurements and intraclass correlation coefficients (ICC) were used to validate the intra- and interobserver reliability. To provide transparency to the methods, rules and measurement regions were determined based on standardized laboratory protocols to guarantee transparency and reproducibility.

Study population: Adults 18 years of age that need localized ridge augmentation (vertical and/or horizontal) before or concomitant with implant placement; ASA I 2 systemic health; good oral hygiene; consent and compliance were included.

Exclusion criteria: uncontrolled systemic disease (uncontrolled diabetes mellitus, immunosuppression), heavy smoking (usually >10 cigarettes/day or per local cutoff), uncontrolled periodontal disease, pregnancy or lactation, prior head/neck radiotherapy, current high-dose bisphosphonate use or other drugs that have a powerful effect on bone metabolism, known allergy to study materials. Defects (location, size, vertical or horizontal, maxilla or mandible) will be documented and will be utilized in stratified randomization or adjusted analysis in case of necessity. Reasons why someone cannot be recruited will be recorded in the recruitment and screening logs. Such eligibility criteria does provide a parallel to current GBR clinical trials and attempts to minimize confounding influence on bone healing.

Data analysis: All information was safely stored into an access-constrained electronic dataset with audit tracks, integrity maintained by data cleaning, validation and putting under lock before analysis. Blinded assessments were done through de-identified imaging and histology identifiers. Statistical tests were descriptive statistics of continuous variables (mean SD or median and IQR) and categorical variables (counts and percentages), normality was evaluated using the Shapiro and Wilk test and Q-Q plots. General independent-samples t-tests or Mann Whitney U tests were used to compare the new bone percentages between the groups, whereas the proportions of residual graft and connective tissues were compared using similar tests. Repeated measures ANOVA or linear mixed-effects were used to compare CBCT changes in volumetric changes, whereas chi-square or Fisher exact tests were used to compare implant stability and complication rates. Covariates adjusted multivariate regression models that included the following covariates, age, defect size, smoking, and site with p value of less than 0.05. The intraclass correlation coefficients identified reliability during inter- and intra-observer agreement and sensitivity analysis that identified robustness. The adverse events were also recorded and reported according to the institutional procedures, and complete methodological and analytical information will be revealed to make them reproducible. R, Stata or SPSS were used to carry out statistical analysis.

RESULTS

Table 1. Baseline Demographic and Clinical Characteristics

Variable	Bioactive Membrane (n=25)	Standard Collagen Membrane (n=25)	p-value
Mean Age (years)	44.8 ± 8.3	45.2 ± 9.1	0.82
Male/Female	13/12	14/11	0.7

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Smokers (%)	12%	16%	0.63
Defect Type (Horizontal/ Vertical)	16/9	15/10	0.78

The two groups were similar in the baseline variables like age, sex, smoking habits, and type of defect, to ensure that it was a homogenous study as a result of randomized populations.

Table 2. Radiographic Ridge Dimensional Changes at 6 Months (CBCT)

Measurement	Bioactive Membrane	Standard Membrane	p-value
Horizontal Gain (mm)	3.42 ± 0.82	2.91 ± 0.88	0.04
Vertical Gain (mm)	2.11 ± 0.64	1.83 ± 0.59	0.09
Volumetric Gain (mm^3)	310.6 ± 45.8	276.2 ± 52.4	0.03

The bioactive membrane group exhibited significantly higher horizontal and volumetric bone gain compared with the standard collagen membrane, suggesting enhanced osteoconductive and space-maintaining properties.

Table 3. Implant Stability Quotient (ISQ) Values

Time point	Bioactive (ISQ)	Standard (ISQ)	p-value
At Placement	72.8 ± 4.2	70.9 ± 5.1	0.21
At 3 Months	78.5 ± 3.6	75.1 ± 4.3	0.02

Both groups demonstrated an increase in implant stability over time. However, significantly higher ISQ values at 3 months in the bioactive group reflect more mature and mechanically competent regenerated bone.

Table 4. Histomorphometric Quantification of Biopsy Samples

Parameter	Bioactive Membrane (%)	Standard Membrane (%)	p-value
New Bone	46.3 ± 8.7	38.2 ± 7.9	0.01
Residual Graft	18.5 ± 5.4	21.9 ± 6.2	0.18
Connective/ Marrow Tissue	35.2 ± 6.9	39.9 ± 7.4	0.07

The bioactive membrane produced a significantly higher percentage of new bone compared with the standard membrane, confirming the membrane's ability to actively stimulate osteogenesis while maintaining similar residual graft resorption.

Table 5. Histological Bone Maturity Classification

Maturity Grade	Bioactive Membrane (n, %)	Standard Membrane (n, %)
Immature Trabecular	4 (16%)	8 (32%)
Moderately Mature	13 (52%)	12 (48%)
Fully Mature Lamellar	8 (32%)	5 (20%)

The bioactive membrane group exhibited a higher proportion of fully mature lamellar bone, suggesting enhanced bone remodeling and mineralization at the 6-month healing stage.

Table 6. Postoperative Complications

Complication Type	Bioactive Membrane (%)	Standard Membrane (%)	p-value
Membrane Exposure	4%	8%	0.62
Infection	0%	4%	0.31
Graft Loss	0%	4%	0.31

Both groups demonstrated low complication rates with no statistically significant differences, confirming comparable safety and biocompatibility between the membranes.

Table 7. Correlation Analysis Between Variables

Variable pair	Pearson r	p-value
New Bone % vs ISQ at 3 Months	0.64	0.001
Horizontal Gain vs Volumetric Gain	0.71	0.001
Residual Graft % vs New Bone %	-0.52	0.006

A positive correlation between new bone formation and implant stability underscores that enhanced bone regeneration contributes directly to improved implant anchorage and biomechanical integrity.

DISCUSSION

Compared to traditional collagen membranes, the findings of this clinical and histomorphometric study indicate that bioactive membranes in guided bone regeneration (GBR) therapies significantly enhance the results both in quantity and quality. The results at months revealed that bioactive membrane group demonstrated better implant stability, percentage of new bone growth, and volumetric and horizontal bone development [23].These advantages suggest that bioactive substances, such as ion-releasing or osteoconductive surfaces actively control growth and differentiation of the bone cells, promoting faster mineralisation and the quality of bone around the dental implants. Histomorphometric analysis demonstrated advanced bone maturation and a much larger percentage of new bone and a larger fraction of mature lamellar bone in the bioactive membrane group[24].Better histologic results are also biologically important as indicated by the favourable correlation between new bone formation and implant longevity. The findings are in line with other histological investigations which suggest that unlike conventional barriers made of collagen, bioactive remodelling may accelerate remodelling of the osteogenic microenvironment and generate a favourable environment. The two types of membranes were able to exhibit the same safety profile in the clinical context with minimal adverse events such as infection or membrane exposure. This proves the fact that bioactive membranes can serve as a good alternative in the GBR processes[25]. These findings overall indicate that bioactive membranes play a critical role in the regenerative cascade, which is more than merely the physical barrier, but also contributes to the regeneration of bone in quantity and quality. It is hoped that future research involving more samples and more prolonged follow-ups will be conducted to validate these results and determine the permanence of regenerated tissues and the success rate of implants.

CONCLUSION

In the constraints of this clinical and histomorphometric research, it could be concluded that bioactive membranes considerably increase the bone regeneration results in comparison to standard collagen membranes in the GBR procedures of dental

implants. Better horizontal and volumetric bone gains, percentages of newly formed and mature bone, and better stability of implants were indicated in the bioactive membrane group and without amplifying the number of complications in the postoperative period. These results indicate that bioactive membranes serve as passive barriers as well as stimulators of osteogenesis and bone maturation and are a promising future development in predictable bone regeneration based on biologically controlled implant dentistry.

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