Human Histologic Evaluation of Bioactive Ceramic in the Treatment of Periodontal Osseous Defects

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This study examined the healing of intrabony defects around 5 teeth treated with bioactive glass ceramic (PerioGlas). Healing was evaluated by clinical measurements, radiographic observation, and histologic analysis. The protocol included a presurgical phase of scaling and root planing therapy, with measurements obtained immediately prior to the surgical procedures and after 6 months of healing. Following therapy, there was a mean of 2.7 mm of probing depth reduction, 2.2 mm of clinical attachment gain, and 0.5 mm of recession. The histologic analysis revealed healing by a long junctional epithelium with minimal new connective tissue attachment to the teeth, except in one case where the intrabony region demonstrated new cementum formation and new connective tissue attachment. Graft particles were found to be biocompatible, as evidenced by being embedded in a stroma of dense connective tissue with minimal inflammatory infiltrate. There was minimal new bone formation limited to the most apical borders of the defects. No signs of periodontal regeneration as defined by new cementum, periodontal ligament, and bone formation on a previously diseased root surface were observed. Although the clinical results are encouraging and radiographs evidenced radiopacities within the defects, histologic analysis revealed that as a periodontal grafting material, bioactive glass ceramic has only limited regenerative properties. (Int J Periodontics Restorative Dent 2000;20:459-467.)

Periodontal regeneration is defined as the reproduction or reconstitution of the lost periodontium as evidenced histologically in the form of new cementum, periodontal ligament, and alveolar bone connected via Sharpey's fibers to a previously diseased root surface.1-3 Surgical procedures incorporating autologous bone grafts, allografts, alloplasts, xenografts, and barrier membranes have been used to treat intrabony defects with the goal of attaining periodontal regeneration. It is now clear that neither radiographic nor clinical resolution of probing depth ensures that the desired biologic result has been achieved.4 Successful periodontal regeneration has been demonstrated histologically with autologous bone grafts and with bone allografts.5-9 Allografts have been advocated to reduce the morbidity associated with bone autografts and to obviate a secondary harvesting site. In addition, studies have demonstrated that there is minimal risk of disease transfer with demineralized freeze-dried bone allografts be-
cause of the virucidal agents used in the processing of this material. However, some patients are not amenable to the use of these materials. Therefore, other noninvasive treatment modalities have been investigated. Xenografts have been shown to have potential for periodontal grafting, with human histologic sections demonstrating new attachment with new cementum and connective tissue as well as significant new bone formation.

Alloplastic materials suggested to treat periodontal defects include reabsorbable materials such as hydroxyapatite, tricalcium phosphate, and calcium carbonate, and nonabsorbable materials such as dense hydroxyapatite, porous hydroxyapatite, and bioactive ceramics. According to the 1996 World Workshop in Periodontics, "On a histologic basis, however, [alloplasts] act almost exclusively as biologic fillers inducing little bone fill and very limited if any periodontal regeneration." Typically, the healing evidences a long junctional epithelium, graft material encapsulated within connective tissue, minimal bone formation, minimal reabsorption of the graft material, and minimal inflammation. Clinical results have been reported to be similar to results with other graft materials, with a defect fill of 60% to 70%.

PerioGlas (US Biomaterials) is a bioactive nonporous glass composed of silicon dioxide (45%), calcium oxide (24.5%), sodium oxide (24.5%), and phosphorous pentoxide (6%). Animal studies have shown potential for new attachment when periodontal defects are treated in nonhuman primates. Clinical case reports have demonstrated gains in clinical attachment, reduced probing depths, and radiographic fill of osseous defects. It is necessary to realize the biologic potential of a regenerative material in addition to observing clinical and radiographic results, as previous reports on alloplasts demonstrate the weakness in using clinical data alone to evaluate periodontal regeneration.

The aim of this study was to determine the type of healing that occurs in human intrabony defects following placement of a bioactive ceramic, PerioGlas, because the effect of bioactive ceramic on the healing of human periodontal defects has not been evaluated histologically. The primary objectives of the study were to: (1) histologically determine the type of healing that occurs following placement of a bioactive ceramic into human periodontal defects; (2) determine the biocompatibility of the material; (3) determine the osteoconductive potential of the material; and (4) evaluate the clinical and radiographic results of the regenerative procedures.

**Method and materials**

The study protocol was approved by the institutional review board at each study site. All patients gave informed consent prior to being enrolled in the study. Patients with severe periodontal disease and a hopeless dentition were recruited for this study. One tooth in each of 5 patients judged by a committee of clinicians to have a poor prognosis was selected for the study.

After the screening visit, all 4 quadrants were scaled and root planed with local anesthesia, and patients were instructed in oral hygiene techniques. The periodontal surgical study treatment was performed within 4 weeks of the debridement visit. Customized stents were fabricated for each patient to take standardized clinical and surgical measurements throughout the study. These measurements included relative attachment level (stent to base of pocket), relative recession (stent to gingival margin), and probing pocket depth (gingival margin to base of pocket). In addition, an individualized radiographic stent was fabricated to permit geometric standardization of images.

At the surgical visit, sulcular incisions were made extending at least one tooth mesial or distal to the osseous defect with vertical releasing incisions as indicated. Full-thickness mucoperiosteal flaps were elevated, and the intrabony defects were degranulated. The apical border of the defect was demarcated by using a 1/2 round carbide bur on the root surface or by aggressive root planing. The teeth were root planed with a combination of hand, ultrasonic, and rotary instruments. The cortical walls of
the osseous defect were perforated with a ⅛ round bur to obtain a bleeding bony surface prior to placing the graft material. The PerioGlas was reconstituted in sterile saline and then placed into the osseous defects according to the manufacturer's directions. Periodontal flaps were coronally positioned to cover the graft material and sutured with expanded polytetrafluoroethylene (e-PTFE) sutures. Patients were instructed in postoperative care and given prescriptions for an antibiotic, an analgesic, and a chlorhexidine diglucocone rinse.

Follow-up visits to monitor safety and healing were performed on days 2, 4, 7, 14, and 28 and then 2, 3, 4, 5, and 6 months following the surgery. The sutures were removed from all surgical sites on day 14. Oral hygiene assessment and supragingival scaling were performed on day 28 and then at 2, 3, 4, 5, and 6 months and continued at monthly intervals. Clinical measurements were repeated and radiographs were obtained at 6 months postoperative. Block biopsies were obtained at 7 months (cases 1 to 3) or 12 months (cases 4 and 5). Following local anesthesia, the region of the original osseous defect and adjacent tooth structure were removed. The marginal gingiva and osseous tissue to the base of the original periodontal defect were included, with a minimum of additional tissue. The biopsies were fixed in 10% buffered formalin, dehydrated in step gradients of alcohol, and infiltrated and embedded in methyl methacrylate. Serial sections were obtained in a mesiodistal plane. After block extraction, the residual defect was grafted with a bone autograft, allograft, or a combination as indicated, and barrier membranes were placed to reconstruct the region for future insertion of endosseous implants. Patients were then rehabilitated with dental implants and appropriate prostheses.

Results

All sites healed without complications. Presurgical and postsurgical clinical measurements are summarized in Table 1. There was a mean decrease in probing depth of 2.7 mm, a 2.2-mm mean gain of clinical attachment, and mean recession of 0.5 mm.

Case 1

Case 1 consisted of an intrabony defect on the distal surface of the mandibular right first molar (Fig 1). This 3-mm defect had a 2-walled morphology that circumscribed the tooth from the distobuccal line angle to the midlingual surface in the region of the lingual furcation. After 7 months, the attachment level increased by 2 mm and there was 1 mm of recession. The gingival tissues were pink and firm and did not bleed on probing. The 6-month postoperative radiograph indicated evidence of bone fill (Fig 1c).

Histologically, the graft material demonstrated biocompatibility, as there was minimal inflammatory cell infiltrate in the grafted defect. The PerioGlas was surrounded by dense connective tissue with little evidence of graft reabsorption. Minimal new bone formation was limited to the base of the osseous defect. There was new cementum on the root surface and a narrow zone of new connective tissue attachment. The attachment apparatus, as defined by new bone, periodontal ligament, and cementum, was not regenerated in this specimen (Figs 1d to 1f).

Table 1 Summary of clinical measurements (mm)

<table>
<thead>
<tr>
<th>Case</th>
<th>Probing pocket depth reduction</th>
<th>Relative attachment level gain</th>
<th>Recession loss/gain (–)</th>
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<tr>
<td>1</td>
<td>3</td>
<td>2</td>
<td>1</td>
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<td>2</td>
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<td>1</td>
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<td>3</td>
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<td>0</td>
<td>1</td>
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<tr>
<td>4</td>
<td>4.5</td>
<td>5</td>
<td>–0.5</td>
</tr>
<tr>
<td>5</td>
<td>3</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Total*</td>
<td>2.7 ± 1.3</td>
<td>2.2 ± 1.3</td>
<td>0.5 ± 1.3</td>
</tr>
</tbody>
</table>

*Mean ± standard deviation.
Fig 1a  Case 1 consists of an intrabony defect on the distal surface of the mandibular right first molar. Note that the second premolar and first molar demonstrate a large periapical radiolucency and received endodontic treatment prior to the surgical intervention.

Fig 1b  Lingual view demonstrates 3-mm intrabony defect extending from the distal to the lingual aspects of the first molar. The defect is debridged of all granulation tissue, the root surface is thoroughly scaled and planed, and the walls of the defect are penetrated with a 1/8 round bur prior to placing the bioactive ceramic graft material.

Fig 1c  In the 6-month postoperative radiograph, the defect is filled with the graft material, but there is poor trabeculation of the grafted site.

Fig 1d  Histologic section of the first molar 7 months after grafting. The distal root was extracted with the associated periodontal tissues for histologic evaluation. The attachment apparatus has not been completely regenerated, as there is no new periodontal ligament and only limited new bone formation. AJE = apical extent of junctional epithelium; NC = new cementum; RC = reference notch. (Original magnification × 2.5; toluidine blue and basic fuchsin stain.)

Fig 1e  Area grafted with bioactive ceramic is invaded by dense connective tissue. There are no signs of inflammation around the graft particles that show no signs of reabsorption. AJE = apical extent of junctional epithelium; NC = new cementum; BC = bioactive ceramic particles in connective tissue matrix; NB = new bone. (Original magnification × 4; toluidine blue and basic fuchsin stain.)

Fig 1f  Higher magnification of Fig 1e shows limited bone formation at the base of the defect toward the root surface. There is new cementum on the root surface. NB = new bone; BC = bioactive ceramic particle in connective tissue matrix; NC = new cementum. (Original magnification × 32; toluidine blue and basic fuchsin stain.)
Case 2

Case 2 consisted of a maxillary right canine with an intrabony defect on the mesial and palatal surfaces. The defect was debrided and the root surface meticulously root planed prior to placement of the graft material. The defect depth was 4 mm on the mesial surface. The postoperative radiograph showed a clear delineation between the host bone and the grafted material. There was no evidence of periodontal regeneration.

Case 3

Case 3 consisted of a deep and wide intrabony defect on the mesial surface of a mandibular left second molar. The defect was treated as described above, and the results were similar to the other cases. There were no signs of periodontal regeneration (Fig 2). The root surface was lined with a long junctional epithelium extending to the base of the defect. There was minimal new connective tissue attachment and no evidence of new bone formation or new cementum.

Case 4

Case 4 consisted of a one- and two-walled defect on the mesial and mesiobuccal surfaces of the maxillary left first premolar (Fig 3). Again, the defect was treated as described above, and the results for this case were similar to those of cases 2 and
Fig 4a  Case 5 is a maxillary right second premolar. This tooth has a circumferential intrabony defect that is deepest on the mesiopalatal surface. The defect has been debrided and is ready for the graft material. The intraosseous defect in the area of the first premolar extraction site has been degranulated and was also grafted with bioactive ceramic.

Fig 4b  Extraction site of the first premolar has a radiolucent area evidencing a residual osseous defect. The postoperative radiograph 7 months after the surgery appears to represent a positive result of the treatment. The periodontal defect appears to be resolved and the bony defect in the first premolar site is radiopaque and seems to be well trabeculated.

Fig 4c  Circumferential defect on the palatal surface of the second premolar is evident, as is the intraosseous defect where the first premolar was previously extracted.

3. There were residual graft particles within the defect surrounded by noninflamed, dense connective tissue. Minimal new bone formation was limited to the borders of the periodontal defect, and the root surface was lined by a long junctional epithelium. New connective tissue formation was minimal, and there did not appear to be new cementum on the root surface.

Case 5

Case 5 involved a circumferential intrabony defect on the palatal and mesial surfaces of the maxillary right second premolar (Fig 4). The previous extraction site of the first premolar had a radiolucency that proved clinically to be a bony defect. The periodontal and extraction defects were degranulated, the root surface was thoroughly scaled and planed, and the walls of the defect were penetrated to stimulate the
local blood supply. The bioactive ceramic was placed to fill the defect around the second premolar. The intraosseous defect in the area of the first premolar extraction site was debrided of all granulation tissue and was also grafted. The 7-month postoperative radiograph showed resolution of the defects. As with the other defects in this case series, the histologic findings contradict the radiographic results. Histologically, the periodontal defect healed with a long junctional epithelium. There was no new connective tissue attachment and only limited new bone formation around the most apical particles of the grafting material. The histologic evaluation of the bony defect from the non-healed extraction site showed no evidence of new bone formation. The graft material filling the defect was embedded in a stratum of dense connective tissue. The borders of the defect appeared to have sclerosed.
Discussion

Periodontal regeneration continues to be the ultimate goal of periodontics although it is interdependent on multiple factors, some of which are beyond the routine management and understanding of the clinician. The definition of regeneration is histologic. The issue is further confused by the emergence of products that claim osteoconduction, osteoinduction, or both. It is thus incumbent upon the clinician to determine which method and materials to use for specific treatments.

Two recent publications, from the World Workshops in Clinical Periodontics and the landmark Workshop on Periodontal Regeneration, similarly described periodontal regeneration as the replacement of cementum, periodontal ligament, and bone on a root surface previously exposed to bacterial plaque. The gold-standard grafting materials include intraoral and extraoral autogenous bone, demineralized freeze-dried bone allograft, and xenografts, whereas a number of reports demonstrated the efficacy of autogenous and allograft bone. The xenograft Bio-Oss (Osteohealth) has recently been studied with and without an adjunctive membrane. In that previous study, new cementum and Sharpey's fiber attachment along with significant new bone production were observed. Although there was significant bone regeneration, it did not completely fill the defect. Similar limitations are noted with barrier membranes alone, but with even less evidence of bone formation.

This study was designed to measure the effectiveness of a bioactive glass ceramic, PerioGlas, to produce periodontal regeneration in infrabony defects by observing the histologic results. Although there is some evidence of healing, significant apical proliferation of epithelium in most sections to a subosseous level approaching the original defect resulted in no periodontal regeneration. This eliminated the possibility of new connective tissue attachment. There was also only a limited amount of new cementum and connective tissue attachment at the most apical portion of the defects, with the exception of case 1, where there was evidence of new cementum and new connective tissue formation.

Some demonstration of osteoconduction was evidenced on the surface of isolated crystals and interconnecting 2 or more crystals as well as on the surface of bone at a distance from the tooth, but the lack of a positive osteoconductive response is not encouraging. Clinical parameters improved despite the lack of histologic evidence of periodontal regeneration. The attachment levels increased, probing depths decreased, the tissues were pink, and there was no bleeding on probing. The radiographic analysis is difficult to interpret because the material is radiopaque and fills the defect from insertion to time of retrieval. However, there is no question that the material is biocompatible, as the residual crystals are firmly embedded in a stroma of connective tissue with little evidence of an inflammatory infiltrate.

Previous investigations with PerioGlas have had varying results in the treatment of periodontitis. A histologic nonhuman primate study demonstrated no evidence of particle resorption after 2 months of healing. There was, however, significant new cementum regeneration. In human studies, clinical measurements and radiographs indicated an improvement of periodontal health. Comparing these studies with the present investigation indicates that there can be a discrepancy between data obtained by clinical probing versus radiographs versus histologic evaluation. One must be especially cautious when using radiographic data to interpret results from regenerative procedures performed with a radiopaque graft material. In such cases, even immediate postoperative radiographs can be misleading and be misinterpreted as a successful response only because the graft material can be visualized.

There is no question that many factors influence success or failure when treating infrabony defects by regenerative techniques. Some are within the control of the clinician and should be maximized. These include complete debridement of the root surface, absence of tooth mobility, appropriate flap design to protect the grafted material and/or barrier membrane, and the total exclusion of diseased granulation tissue. In addition, there should be realistic goals for the result of treatment depending on the containment of the osseous defect, defect selection, patient selection, and postoperative follow up.
Conclusions

Human periodontal defects were treated with bioactive glass ceramic and studied clinically and by radiographic and histologic analysis.

1. The histologic analysis of human periodontal defects treated with bioactive glass ceramic revealed healing by a long junctional epithelium with minimal new connective tissue attachment. The graft particles were embedded in a stroma of dense connective tissue with minimal inflammatory infiltrate. There was minimal new bone formation limited to the most apical borders of the defects.

2. The clinical results evidenced a mean of 2.7 mm of probing depth reduction, 2.2 mm of clinical attachment gain, and 0.5 mm of recession.

3. Radiographic evaluation is not conclusive for regenerative procedures using radiopaque grafting materials.

Acknowledgment

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References