Clinical Application of Unigraft®
In the Treatment Of Human Periodontal Defects

Kung C. Wang, DMD, Stan S. Yang, Ph.D.

Abstract

Background: This study evaluated the use of Unigraft®, a resorbable bioactive glass, for repairing human periodontal intrabony defects. Thirteen healthy patients (8 males, 5 females, mean age 44) with moderate to advanced periodontitis participated in the study. A total of 30 sites were followed for a minimum of 6 months. Five of the 13 patients (14 sites) were followed for 12 months.

Methods: All patients underwent initial therapy, including scaling, root planing, and oral hygiene instruction. This was followed by a re-evaluation 4 to 6 weeks later. Baseline measurements included recession, probing depth, clinical attachment level, mobility, gingival index and plaque index. Comparison between baseline and post-operative data was performed by using the paired Student's *t* test.

Results: The 6- and 12-month groups resulted in 3.50±1.46 mm ($P < 0.0001$) and 3.10±1.44 mm ($P < 0.0001$) reduction in mean pocket depth, respectively, and a gain in clinical attachment of 3.00±1.68 mm ($P < 0.0001$) and 2.79 ±1.72 mm ($P < 0.0001$), respectively. A mean recession of 0.50±1.20 mm ($P=0.030$) and 0.21±1.37 mm ($P=0.57$) was obtained from the 6- and 12-month groups, respectively. No statistical difference in probing measurements between the 6- and 12-month determinations was found from the 12-month group.

Conclusions: This study indicates that the use of bioactive glass to repair periodontal infrabony defects produces significant improvements in pocket depth and clinical attachment with minimal effects on recession when compared to the baseline.

Key words

Periodontitis surgery; periodontitis therapy; grafts; bone; glass; bioactive glass

Introduction

Several therapeutic techniques, including bone graft, guided tissue regeneration and a combination of these two procedures have been used to repair intrabony defects[1]. Demineralized freeze-dried bone allografts (DFDBA) are frequently used as graft material because of its osteo-inductive capacity[2-6]. Nevertheless, there are certain concerns about the risk of disease transmission and inconsistent osteo-inductive properties[7,8]. A variety of alloplast materials, including hydroxyapatite (HA), tri-calcium phosphate (B-TCP) and bioactive glass, have been demonstrated to repair periodontal defects and to produce bone fill in the defect[9-21]. Alloplasts offer the advantages of consistent quality, unlimited supply and no risk of disease transmission. More recently, bioactive glass has been shown to generate more new attachment and bone fill to osseous defects than was seen with B-TCP and dense HA[22]. Histological analysis revealed a significant improvement in the bone growth pattern of the defects treated with bioactive glass compared with sites treated with HA or B-TCP[22,23]. No significant difference in soft and hard tissue measurements were observed between DFDBA and bioactive glass grafted sites[24]. As a graft material, bioactive glass was found to be hemostatic, easy to pack and remained in the defect site even with adjacent suctioning[24-28]. Bioactive glass has also been found to exhibit an anti-bacterial effect against sub-gingival and supra-gingival oral bacteria and may reduce implant-centered infections[29].

Bioactive glass is a unique material. Upon implantation, the material immediately interacts with the patient's body fluid and elicits a series of reactions that include leaching, dissolution and precipitation, to form a silica- and calcium-rich surface gel,

which traps cellular and non-cellular materials within the gel matrix. Within the matrix, hydroxycarbonate-apatite nucleates crystallize and interpose with mucopolysaccharides, glycoproteins, collagen and osteo-cellular materials. With time, the "living" matrix is transformed, remodeled and replaced by newly formed osseous tissue[31-33].

The objective of this study is to evaluate a bioactive glass particulate, Unigraft®, in the treatment of periodontal defects and to compare the clinical results with available literature data of other bioactive glass products.

Materials and Methods

Fifteen patients (10 male, 5 female), 30-52 years of age were recruited for the study. These patients were admitted to one of the author's clinics for the treatment of routine moderate to advanced chronic periodontitis. Each patient had at least one periodontal defect in the anterior or posterior segments, with probing depths of at least 4mm and radiographic evidence of intrabony defects. All defect sites exhibited a two-wall or two-to-three wall pocket. Teeth with furcation involvement and subjects who had a medical condition or therapeutic regimen that might affect the probability of soft tissue and bone healing were excluded from this investigation. Unigraft® bioactive glass was supplied by Unicare Biomedical, Inc. The graft material was used alone to correct periodontal defects.

Pre-surgical procedures

Initial therapy, including a thorough examination, full-mouth scaling and root planing using hand and ultrasonic instruments, and an occlusal adjustment when indicated, was performed on each patient. Each participant was then given detailed instructions in maintaining daily oral hygiene. Re-evaluation occurred within 4 to 6 weeks. During this examination, periodontal charting was repeated to assess the tissue response to the initial therapy and to review the criteria for surgery with respect to mobility, probing depth and attachment level. If the patient's probing depth was greater than 4mm and the tissue response and the plaque bleeding scores were satisfactory, the proposed nature of the study was explained and a written consent was obtained.

Probing measurements were recorded on the day of surgery and at every 3-month post-operative appointment. Cemento-enamel junction (CEJ) was used as a reference for the probing measurements, including recession, probing depth and clinical attachment level. Pocket depth was recorded using an EN 15 probe (Dentsply, Weybridge, UK) with a tip diameter of 0.5 mm. Probing depth was measured from the free gingival margin to the base of the periodontal pocket. Recession was determined by assessing the distance between CEJ and the free gingival margin. The attachment level was measured from the CEJ to the apical depth of the pocket.

Figure 1A. Debrided site reveals a two-wall defect on the mesial and facial aspects of a maxillary central incisor.

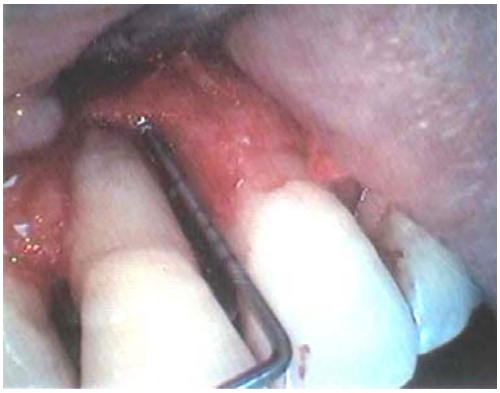


Figure 1B. Defect is filled with bioactive glass.

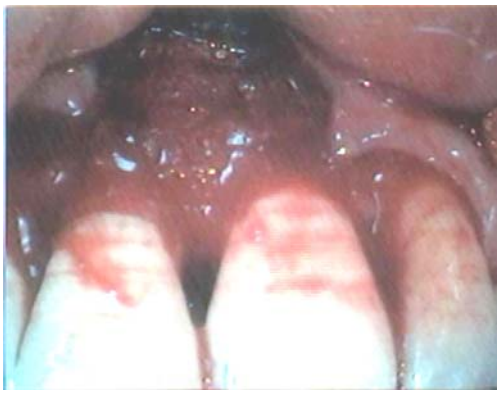
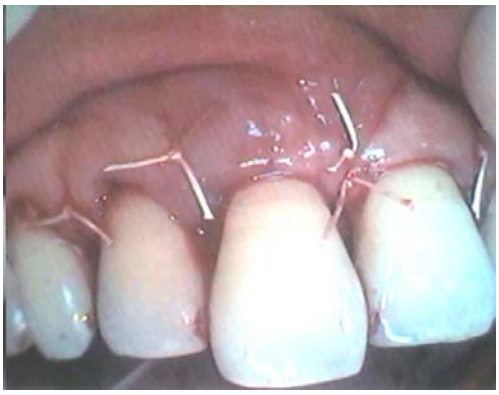


Figure 1C. Primary closure with 4-0 interrupted sutures.



Surgical procedures

All of the surgical procedures were performed under local infiltration anesthesia. Consequently intra-sulcular incisions were made and full-thickness mucoperiosteal flaps were raised. The interdental papillary tissue was retained as far as possible. The exposed root surfaces were carefully debrided and root planed using both hand and ultrasonic instruments. All granulation tissue was removed.

One vial (0.37 gram) of Unigraft® bioactive glass was emptied into a sterile dappen dish and 3 to 5 drops of the patient's blood were added according to the manufacturer's instructions. Excess blood fluid was removed by moist gauze. The graft was incrementally added to the defect and compacted with a spatula and moist gauze until the defect was completely filled. Care was taken not to overfill the defect. The mucoperiosteal flaps were repositioned and secured in place using interrupted 4-0 sutures. Every attempt was made to achieve primary closure. The surgical site was covered with periodontal dressing. Postoperatively, the patient was instructed to take Amoxicillin 500 mg, 4 times daily and 0.1% Chlorohexidine mouth rinse daily for 2 weeks. The patient was advised to refrain from tooth brushing, flossing and interdental cleaning in the treated area for 4 weeks after surgery.

Postsurgical procedures

Dressing, sutures and any plaque present in the surgical site were removed during the first post-operative visit. All participants were reviewed weekly thereafter for the first month for additional follow-up and plaque control. During the review session, supra-gingiva was gently cleaned and the oral hygiene instructions were repeated. Recall appointments were then made every month up to three months and then every three months for the remaining period of the study. Plaque, bleeding index, probing pocket depth, attachment level and recession were recorded at 3-, 6- and 12-month following surgery. Radiographs were taken immediately post-operation and at 6- and 12-month post-surgery.

Data Analysis

Probing measurements obtained at 6- and 12-month post-surgery were compared to baseline (pre-surgery) data. Means were calculated for each clinical parameter. Comparisons of baseline vs. post-surgical measurements, and 6-month vs. 12-month measurements were performed using the paired Student's *t* test for significance. Probabilities less than .01 were considered statistically significant.

Results

A total of 15 patients were enrolled in this study. 2 patients failed to return for the 6-month recall. As a result only 13 patients, 8 males, 5 females, all non-smokers, 30-52 years of age (mean age 44) completed the study and a total of 30 sites were evaluated for a 6-month period. Of these, 5 patients (14 sites) were followed up for 12 months. Their data are grouped separately for comparison.

The manipulation of the bioactive glass was easy during application. After dampened with the patient's blood, the graft material forms a cohesive mass that is transferred to the wound site with a dental spatula. In each case, primary closure was achieved and patients did not complain of particle loss.

Figure 1D. 3-month post-operative view shows well-healed soft tissue and minimal recession.

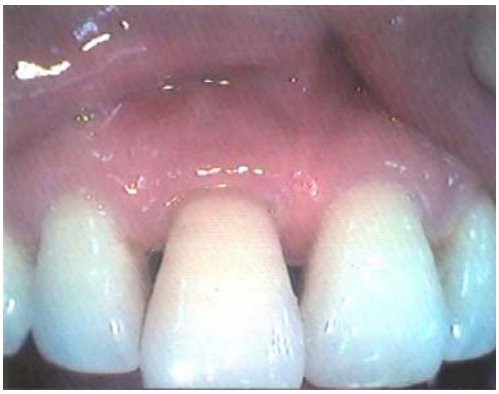
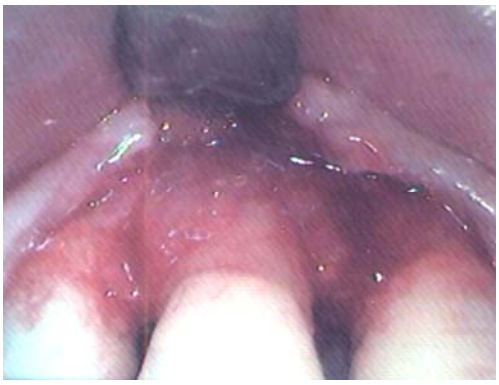


Figure 1E. Re-entry at 6-month post-operation reveals that the defect is filled with osseous tissue.



The sutures were removed during the first post-operative appointment. In general, the overlying mucoperiosteal flaps were very healthy in appearance. No apparent flap necrosis was observed and no adverse soft-tissue response was noted at subsequent postoperative appointments (Figures 1A-1D). Immediately after implantation, the bioactive glass particulate was partially radiolucent and could be differentiated from the surrounding

alveolar bone. Over time, the bioactive glass granules were gradually resorbed and transformed into osseous tissue as evidenced by the progressive appearance of trabecula pattern in the post-operative radiographs (Figures 2A-2D). No post-operative or other complications occurred in any of the patients treated. In one case, re-entry was necessary to clean out plaque that developed at a treated site during the 6-month revisit. When the flaps were raised, approximately 63% bone fill (CEJ-BP) was found in the previous defect grafted with bioactive glass (Figure 1E).

All grafted sites show overall improvements in probing depth and attachment level from baseline (Table 1). The 6-month and 12-month groups resulted in 3.50$\pm$1.46 mm ($P < 0.0001$) and 3.10$\pm$1.44 mm ($P < 0.0001$) reduction in mean pocket depth, respectively (Table 2). Attachment was measured from the CEJ to the apical depth of the pocket. A gain in clinical attachment of 3.00$\pm$1.68 mm ($P < 0.0001$), and 2.79 $\pm$1.72 mm ($P < 0.0001$) were obtained from the 6- and 12-month groups, respectively. Recession was determined from the CEJ to the free gingival margin. Though statistically insignificant, the 6- and 12-month subjects showed a slight increase of 0.50$\pm$1.20 mm ($P=0.030$) and 0.21$\pm$1.37 mm ($P=0.57$) in recession, respectively. For the 12-month group, there was no significant difference between the 6- and 12-month measurements in recession, attachment level and probing pocket depth.

Discussion

In general, the results of this study support recently published literature[24-31], in which intrabony defects were grafted with bioactive glass (Table 3). In 1998, Lovelace and coworkers[24] reported a 3.1mm (43%) reduction in pocket depth and a 2.3 mm gain in attachment on sites treated with bioactive glass. The present study generated an improvement of 3.1mm (52%) reduction in pocket depth and a 2.8 mm gain in attachment. In 1997, Low and coworkers[28] found a mean probing depth reduction of 3.3mm (43%) and a mean attachment gain of 1.9mm. Zamet and coworkers[27] demonstrated a pocket depth reduction of 3.7 mm (46%) and an attachment gain of 2.7mm on the

Figure 2A. Pre-surgical radiograph of a 11mm, 2-wall defect on the mesial and facial aspects of a mandibular first molar.

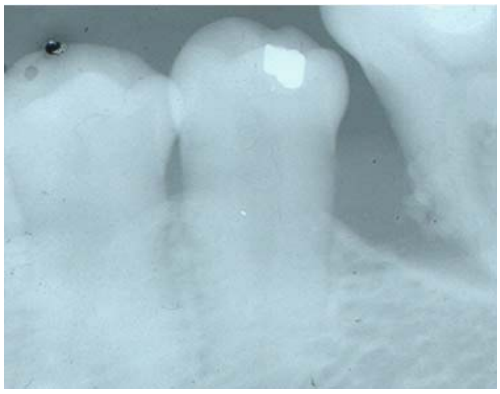


Figure 2B. Immediate post-operative radiograph reveals that the defect is filled with graft material.

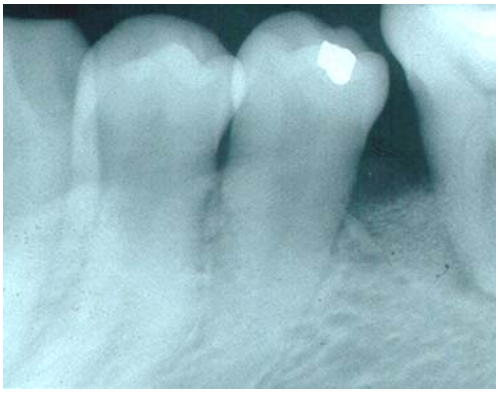


Figure 2C. 6-month post-operative radiograph shows lessened radio-opacity of the graft material.

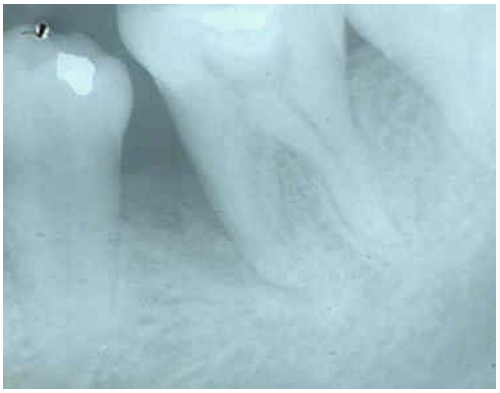
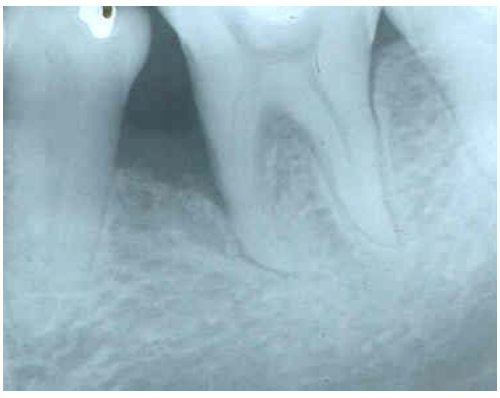


Figure 2D. 12-month post-operative radiograph demonstrates trabecula pattern emerging from the base of defect.



bioactive glass treated sites. Shapoff and coworkers[26] communicated a greater improvement in reduction of pocket depth, 5.3 mm (53%), and a 5.3mm gain in attachment. Nonetheless, their study had deeper initial pockets. Since a deeper pocket has a potential to produce greater improvement in pocket depth reduction, a more rational comparison is to judge the performance by percent pocket depth reduction. Recession data were rarely reported in the literature. Lovelace[24] and coworkers reported a recession gain of 0.8mm. This study produced a recession gain of 0.50mm and 0.21mm in the 6- and 12-month studies, respectively.

Statistically, 3-, 6-(data not included), and 12- month post-operative measurements in pocket depth, recession and attachment level were equivalent. In vivo conversion of bioactive glass into osseous tissue was theorized to take place in several steps, involving leaching of ions from bioactive glass surface, formation of silica- and calcium-rich surface gel and nucleation of hydroxy-carbonate-apatite matrix[32-34]. The cycle is accompanied by resorption of bioactive glass and remodeling of newly formed osseous tissue into trabeculae. Radiographs obtained from this study showed that the transformation of bioactive glass into osseous tissue continued over time within the 12-month period and might extend further as evidenced by the progressive changes in the radiographic pattern of the grafted site. The phenomena on revealed in this and other studies[26-31] indicate that the trabecula pattern first emerges from the base of the osseous defect and then gradually extends upward. In the case that required a re-entry procedure, about 63% bone fill was estimated after flap elevation. This single datum is also in line with the published values[24]. Furthermore, since all the literature data are derived from studies using bioactive glass with a broad distribution of particle size (90-710um), the present study appears to indicate that bioactive glass with a narrower particle size distribution (200-400um) performs favorably or equally well when compared with bioactive glass with a broad particle size distribution. Clinical measurements of bioactive glass with the smallest particle size distribution (300-350um) are not available for comparison[30,31].
Overall, results of this study are comparable to, and after excluding the outlier (Shapoff's data[26]) compare favorably with data reported in the literature.

Table 1. Periodontal Defects Treated With Bioactive Glass; 12-Month Post-Op Measurements (mm)

	Probing Depth (FGM-BP)			Recession (CEJ-FGM)			Attachment Level (CEJ-BP)		
Site	Base-line	12 month	PDR	Base-line	12 month	Reces-sion	Base-line	12 month	CAG
1	7	2	5	3	4	1	10	6	4
2	7	1	6	4	4	0	11	5	6
3	5	2	3	3	5	2	8	7	1
4	5	2	3	3	5	2	8	7	1
5	7	2	5	2	4	2	9	6	3
6	5	3	2	2	3	1	7	7	0
7	7	5	2	2	1	-1	9	6	3
8	7	5	2	2	0	-2	9	5	4
9	5	3	2	3	4	1	8	7	1
10	7	4	3	3	4	1	10	8	2
11	4	3	1	2	1	-1	6	4	2
12	7	3	4	5	4	-1	12	7	5
13	5	3	2	6	5	-1	11	8	3
14	5	2	3	5	4	-1	10	6	4
Mean	5.93	2.86	3.07	3.21	3.43	0.21	9.14	6.36	2.79
S.D. (±)	1.14	1.17	1.44	1.31	1.60	1.37	1.66	1.15	1.72

FGM: free gingival margin. BP: base of pocket. PDR: probing depth reduction.
CAG: clinical attachment gain.

Table 2. Summary of 6-Month and 12-Month Measurements (mm)

	Probing Depth		Recession		Attachment level	
	6-month	12-month	6-month	12-month	6-month	12-month
baseline	6.23±1.10	5.93±1.14	1.9±1.65	3.21±1.31	8.13±1.70	9.14±1.66
Post-op	2.73±1.26	2.86±1.17	2.4±1.48	3.43±1.60	5.13±1.43	6.36±1.15
Change	3.5±1.46	3.07±1.44	0.5±1.20	0.21±1.37	3.0 ± 1.68	2.79±1.72
% Change	56	52	26	7	37	31

Table 3. Clinical Measurements On The Use Of Bioactive Glass In The Repair Of Periodontal Defects

	Zamet[27]	Shapoff[26]	Lovelace[24]	Low[28]	Wang*
Material	PG	PG	PG	PG	UG
Duration (mo)	12	6	6	24	12
Study center	Univ	Univ/Pri	Univ/Pri	Univ/Pri	Pri
No. of sites	22	13	15	8	14
Pre-op PD (mm)	8.14	9.9	7.07	7.71	5.93
PDR (mm)	3.73	5.30	3.07	3.33	3.07
PDR (%)	46	53	43	43	52
CAG (mm)	2.7	5.3	2.3	1.9	2.8
Recession (mm)			0.8		0.21

PG: Perioglas. UG: Unigraft. Univ: University. Pri: Private practice. *: This study.

Conclusion

This study indicates that the use of bioactive glass to repair periodontal defects will produce significant improvement in pocket depth and attachment level, with minimal deterioration in recession when compared to the baseline.

References

1. Cortellini P. Bowers G. Periodontal regeneration of intrabony defects: An evidence-based treatment approach. *Int J Periodontics Restorative Dent* 1995;15:128-145.
2. Mellonig J. Bowers G. Bailey R. Comparison of bone graft materials. Part I. New bone formation with autografts and allografts determined by Strontium-85. *J Periodontol* 1981;52:291-296.
3. Mellonig JT. Decalcified freeze-dried bone allograft as an implant material in human periodontal defects. *Int J Periodontics Restorative Dent* 1984;4:40-55.
4. Bowers G. Granet M. Stevens M, et al. Histologic evaluation of new-attachment in humans. A preliminary report. *J Periodontol* 1985;56: 381-396.
5. Bowers G, Chadroff B, Carnevalc R, et al. Histologic evaluation of new attachment apparatus formation in humans: Part II. *J Periodontol* 1989;60:675-682.
6. Bowers G, Chadroff B. Carnevale R, et al. Histologic evaluation of new attachment apparatus formation in humans' Part 111. *J Periodontol* 1989;60:683-693.
7. Becker W, Urist MR, Tucker LM, Becker BE, Ochsenbein C. Human demineralized freeze-dried bone: inadequate induced bone formation in athymic mice: A preliminary report. *J Periodontol* 1995;66:822-828.
8. Becker W, Becker BE, & Caffesse R. A comparison of demineralized freeze-dried bone and autogenous bone to induce bone formation in human extraction sockets. *J Periodontol* 1994; 65:1128-1133.
9. Baldock W. Hutchens L, McFaIl W. Simpson D. An evaluation of tricalcium phosphate implants in human periodontal osseous defects of two patients. *J Periodontol* 1985;56:1-7.
10. Bowen J, Mellonig J, Gray J. Towle H. Comparison of decalcified freeze-dried bone allograft and porous hydroxyapatite in human periodontal osseous defects. *J Periodontol* 1989;60:647-654.
11. Froum S. Kushner L, Scopp I, Stahl S. Human clinical and histologic responses to durapatite implants in intraosseous lesions. Case reports. *J Periodontol* 1982;53:719-725.

12. Hoexter D. The use of tricalcium phosphate (Synthograft). Part I. Its use in extensive periodontal defects. *J Oral Implantol* 1983;10: 599-610.
13. Kenney E, Lekovic V. Han T Carranza F Jr.. Dimitrijevic B. The use of porous hydroxylapatite implants in periodontal defects. I. Clinical results after six months. *J Periodontol* 1985;56:82-88.
14. Meffert R, Thomas J, Hamilton K, Brownstein C. Hydroxylapatite as an alloplastic graft in the treatment of human periodontal osseous defects. *J Periodontol* 1985;56:63-73.
15. Oreamuno S, Lekovic V, Kenney E, Carranza F Jr, Takei H. Prokic B. Comparative clinical study of porous hydroxyapatite and decalcified freeze-dried bone in human periodontal defects. *J Periodontol* 1990;61:399-404.
16. Snyder A, Levin M. Cutright D. Alloplastic implants of tricalcium phosphate ceramic in human periodontal osseous defects. *J Periodontol* 1984;5 5:273-277.
17. Stahl S, Froum S. Histologic and clinical responses to porous hydroxylapatite implants in human periodontal defects. Three to twelve months postimplantation. J *Periodontol* 1987;58:689-695.
18. Stahl S, Froum S. Tamow D. Human clinical and histological responses to the placement of HTR polymer particles in 11 intrabony lesions. *J Periodontol* 1990;61:269-274.
19. Yukna R. HTR polymer grafts in human periodontal osseous defects I. 6-month clinical results. *J Periodontol* 1990;61:633-642.
20. Yukna R. Clinical evaluation of coralline calcium carbonate as a bone replacement graft material in human periodontal osseous defects. *J Periodontol* 1994;65:177-185.
21. Yukna R. Mayer E, Amos S. 5-year evaluation of durapatite ceramic alloplastic implants in periodontal osseous defects. *J Periodontol* 1989;60:544-551.
22. Fetner A, Hartigan M. Low S. Periodontal repair using Perioglas in nonhuman primates: Clinical and histologic observations. *Compendium Continuing Educ Dent* 1994;15:932-938.
23. Karatzas S, Zavras A, Greenspan D, Amar S. Histologic observations of periodontal wound healing after treatment with Perioglas in nonhuman primates. *Int J Periodontics Restorative Dent* 1999;19:489-499.
24. Lovelace TB, Mellonig JT, Meffert RM, et al. Clinical evaluation of bioactive glass in the treatment of periodontal osseous defects in humans. *J Periodontol* 1998; 69:1027-1035.
25. Hench L. Ceramic implants for humans. *Adv Ceramic Mater* 1986;1:306-324.
26. Shapoff CA. Alexander DC, Dark AE. Clinical use of a bioactive glass particulate in the treatment of human osseous defects. *Compendium* 1997;18:352-363.
27. Zamet JS. Darbar UR, Griffiths GS, et al. Particulate bioglass as a grafting material in the treatment of periodontal intrabony defects. *J Clin Periodontol* 1997;24:410-418.
28. Low SB, King CJ, Krieger J. An Evaluation of bioactive Ceramic in the treatment of periodontal osseous defects. *Int J Periodontics Restorative Dent* 1997;17:359-367.
29. Allan I, Newman H, Wilson M. Anti-bacteria effects of particulate biogalss against sub-and supra-gingival bacteria, *Biomaterials*, 2001, 22: 1683-1687
30. Schepers EJG, Ducheyne P, Bioactive glass particles of narrow size range for the treatment of oral bone defects. *J Oral Rehabilitation* 1997;24:171-181.
31. Schepers E, Ducheyne P, Barbier L, Long term clinical evaluation of bioactive glass particles of narrow size range. *Bioceramics* 1996; 9: 99-102.
32. Hench LL. Bioactive materials: The potential for tissue regeneration. *J Biomed Mater Res* 1998;41:511-518.
33. Hench LL. Bioactive ceramics: Theory and clinical applications. *Bioceramics* 1994;7: 3-14.
34. Hench LL, West JK. Biological applications of bioactive glasses. *Life Chem Rep* 1996;13: 187-241.