Efficacy of Xenogeneic Bone Grafting With Guided Tissue Regeneration in the Management of Bone Defects After Surgical Endodontics

Silvio Taschieri, MD, DDS, Massimo Del Fabbro, BSc, PhD,† Tiziano Testori, MD, DDS,‡ and Roberto Weinstein, MD, DDS§*

Purpose: The purpose of this prospective clinical trial was to monitor the outcomes of periradicular surgery in large periapical lesions with or without guided tissue regeneration (GTR) and anorganic bovine bone.

Materials and Methods: All teeth in the study revealed a periradicular lesion measuring at least 10 mm. A total of 63 teeth in 44 patients were included according to specific selection criteria. In the test group, after root end filling was completed, the defect was filled with anorganic bovine bone and was covered with a resorbable collagen membrane. In the control group, neither graft nor membrane was used.

Results: A total of 59 teeth in 41 patients were evaluable at 1-year follow-up. Of these, 24 teeth belonged to the test group and 35 to the control group. Overall, 46 teeth (78%) had successfully healed, 10 (16.9%) demonstrated uncertain healing, and 3 exhibited treatment failure. Investigators found no statistically significant differences in outcome between test and control groups.

Conclusions: The present study showed that the use of GTR in association with anorganic bovine bone in the treatment of patients with large periradicular lesions of strictly endodontic origin has no beneficial effect on outcome.

J Oral Maxillofac Surg 65:1121-1127, 2007

Successful outcomes of endodontic surgery may be affected by a myriad of factors.[1,2] In 1991, Gutmann and Harrison[3] delineated the clinical factors that may influence the prognosis of endodontic surgery. Among questionable tooth-related factors were the amount and location of bone loss.[2-4] Two retrospective studies indicated that the prognosis was substantially worsened in teeth with total loss of buccal bone plate.[4,5] With the introduction of guided tissue regeneration (GTR) to oral and periodontal surgery, a new treatment option has become available for such defects. Placement of a mechanical barrier, such as a membrane, over an osseous defect can prevent quickly proliferating oral epithelium and gingival connective tissue from growing into the defect. More slowly proliferating cells with osteogenic potential can then repopulate the defect, resulting in more predictable bone repair.[6]

In 2001, von Arx and Cochran[7] proposed a classification of membrane application in endodontic surgery. Lesions in Class Ia showed compromised bony defects at the apex without marginal lesions, and Ib lesions included through-and-through bone defects. Few clinical studies have evaluated the efficacy of GTR in these types of lesions.[8-12]

This prospective clinical study investigated the success rate of endodontic surgery in patients with large periapical lesions with or without anorganic bovine bone associated with a resorbable membrane.

Materials and Methods

All patients who required endodontic surgical treatment were recruited during a period of 24 months at

Received from the Department of Odontology, Istituto Ortopedico Galeazzi I.R.C.C.S., University of Milan, Milan, Italy.

*Visiting Professor and Head, Section of Endodontics.

†Researcher and Head, Section of Oral Physiology.

‡Head, Section of Implant Dentistry and Oral Rehabilitation.

§Professor and Head, Department of Odontology

Address correspondence and reprint requests to Dr Del Fabbro: Department of Odontology, Galeazzi Institute, University of Milan, Via R. Galeazzi 4, 20161 Milan, Italy; e-mail: massimo.delfabbro@unimi.it

0278-2391/07/6506-0010$32.00/0
doi:10.1016/j.joms.2006.10.022

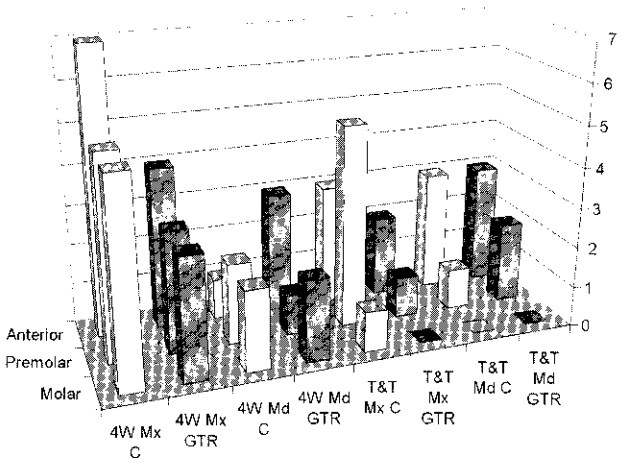

FIGURE 2. Distribution of teeth according to location and treatment group. 4W, four-wall defects; T&T, through-and-through lesions; Mx, maxilla; Md, mandible; C, control group (*white bars*); GTR, guided tissue regeneration group (*shaded bars*).

Taschieri et al. Xenogeneic Bone Grafting for Bone Defects After Endodontic Surgery. J Oral Maxillofac Surg 2007.

et al[14,15]: complete healing, incomplete healing, uncertain healing, or unsatisfactory outcome. These healing criteria are used to assess periapical healing and are validated for periradicular surgery in the absence of bone grafts. In this study, radiographic assessment must be cautiously interpreted, as was mentioned by Garrett et al.[12] In fact, as pointed out by these authors, a bone substitute like the one used in this study is radiopaque, and the pattern of resorption and progressive replacement with new bone under different clinical conditions remains a matter of controversy.[16-20]

Cases scored as complete healing were considered successful. Because of the radiopacity of the bone substitute, differentiation between uncertain and incomplete radiographic healing scores in those cases in which Bio-Oss was used was not always feasible. Therefore, we decided to pool together cases scored as uncertain or incomplete healing. These were considered doubtful and were scheduled to be re-evaluated 3 years later. Any unsatisfactory healing at 1-year follow-up was considered treatment failure.

Two blinded examiners (S.T., T.T.) independently evaluated all radiographs at 4.3× magnification with the use of surgical magnification loupes.

In cases of disagreement between the 2 evaluators, radiographs were re-evaluated jointly. At each scheduled clinical appointment, any evidence of signs or symptoms was recorded, in accordance with the guidelines of Gutmann and Harrison,[21] that is, clinical success, clinically questionable status, and clinical failure.

After clinical and radiographic assessment was performed at 12 months postsurgery, cases were grouped as follows:

1. Successful: radiographic classification of complete healing and absence of clinical signs/symptoms (clinical success).
2. Doubtful: radiographic classification of incomplete or uncertain healing and/or presence of clinical signs/symptoms (clinically questionable).
3. Failure: radiographic classification of unsatisfactory healing and the presence of any clinical signs/symptoms (clinical failure).

Statistical Analysis

Fisher's exact test was used to statistically assess differences between treatment groups. The tooth was regarded as the unit of analysis. A probability of $P = .05$ was assigned as the level of significance.

Results

A total of 63 teeth in 44 patients were treated with periradicular surgery. Two patients (3 teeth) failed to attend the final follow-up visit and were excluded from the study. One patient's tooth was extracted during the surgical procedure before root end resection because of a root perforation; this patient's extracted tooth was excluded from the study. Of the

Table 2. SUMMARY OF OUTCOMES ACCORDING TO TREATMENT GROUP AND TYPE OF DEFECT

	Treatment Group	Successful	Uncertain	Failure	Total	Success, %
4-Wall defects	Control	18	3	1	22	81.8
	GTR	14	2	0	16	87.5
	Subtotal	*32*	*5*	*1*	*38*	*84.2*
Through-and-through lesions	Control	8	4	1	13	61.5
	GTR	6	1	1	8	75.0
	Subtotal	*14*	*5*	*2*	*21*	*66.7*
	Total	46	10	3	59	78.0

Abbreviation: GTR, guided tissue regeneration.

Taschieri et al. Xenogeneic Bone Grafting for Bone Defects After Endodontic Surgery. J Oral Maxillofac Surg 2007.

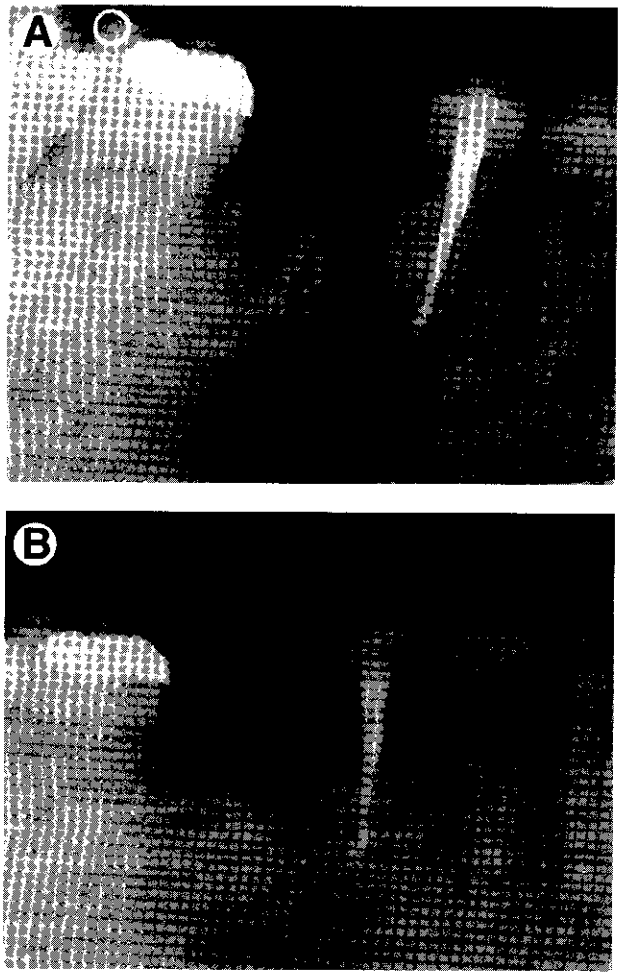

FIGURE 3. A large periapical lesion treated without guided tissue regeneration. *A*, Radiograph soon after surgery. *B*, The same lesion 1 year after surgery, classified as success. Radiographically, the bicuspid shows a periapical lesion that could appear to be contiguous with the lesion of the molar. However, during surgery and after molar removal, the 2 lesions appeared to be separate entities with no communication. The 2 areas of radiolucency were located on different planes. We assumed that bone healing of the bicuspid was not affected by molar removal and by the healing process that occurred at the level of the molar itself.

Taschieri et al. Xenogeneic Bone Grafting for Bone Defects After Endodontic Surgery. J Oral Maxillofac Surg 2007.

remaining 41 patients, 28 were women and 13 were men. Mean age was 36 years for women and 43 years for men. All patients returned at the scheduled follow-up time. Thus, a total of 59 teeth could be evaluated for up to 1 year. Forty of these were treated in center number 1 (S.T. was the surgeon), and 19 were treated in center number 2 (T.T.). Table 1 shows the distribution of cases among the 2 clinics and the relative success rate. No significant difference in outcome was found between the 2 clinics for each of the treatment groups considered.

Among the teeth evaluated at 1 year, 39 were located in the maxilla (16 anterior, 14 premolars, 9 molars) and 20 in the mandible (10 anterior, 6 premolars, 4 molars). Twenty-one cases involved through-and-through (buccal lingual) lesions. Figure 2 shows distribution of teeth according to location and treatment group. Table 2 presents treatment outcomes according to treatment group.

At 1-year follow-up, 46 teeth had successfully healed (78%), 10 exhibited doubtful healing, and 3 were classified as treatment failures, as reported in Table 2. Figure 3A shows a radiograph of a large periapical lesion treated without GTR; Figure 3B shows the same case that was classified as a success at 1-year follow-up. Cases classified as doubtful healing were scheduled for further follow-up 3 years later. Figure 4 shows a radiograph of a through-and-through lesion treated without GTR that was classified as doubtful healing at 1-year follow-up; the presence of scar tissue apical to the root end can be appreciated.

Investigators found no statistically significant differences in outcome between patients treated with GTR (83.3% success) and those in whom GTR was not used (74.3% success) ($P = .09$). Also, no difference was noted in terms of tooth location (maxilla vs mandible; $P = .07$). Conversely, the outcomes of the 4-wall defects (control plus GTR cases) were signifi-

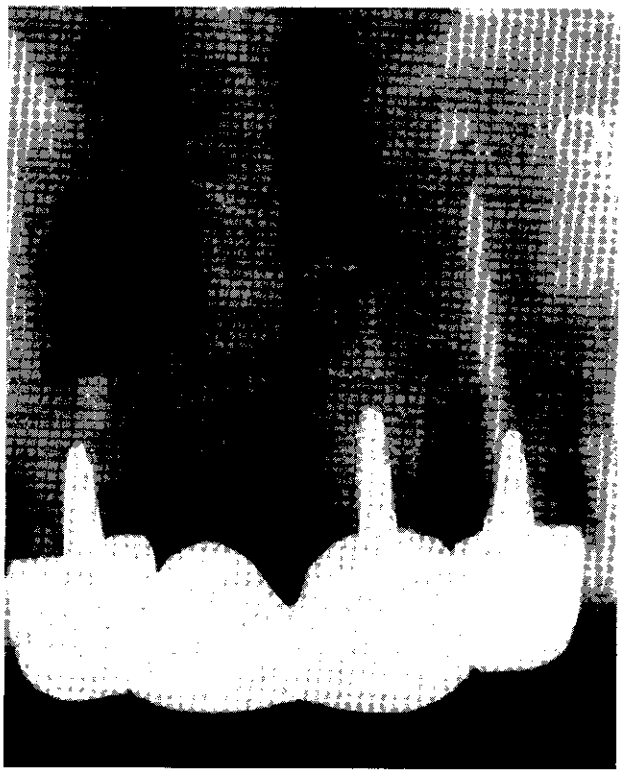

FIGURE 4. Through-and-through lesions without guided tissue regeneration. Isolated scar tissue surrounded by compact bone may be observed at a distance from the root end 1 year after surgery. This case was classified as doubtful healing.

Taschieri et al. Xenogeneic Bone Grafting for Bone Defects After Endodontic Surgery. J Oral Maxillofac Surg 2007.

cantly better than those of through-and-through (buccal lingual) lesions ($P = .03$).

Discussion

A number of clinical studies on periradicular surgery performed with the use of microsurgical endodontic instruments have been published. The overall success rate of such procedures is generally high. Nevertheless, many variables, such as surgical procedure, materials, radiographic and clinical outcome assessment, patients' systemic condition, type of tooth, quality of previous root canal treatment or retreatment, and quality of coronal restoration, may affect the prognosis of the surgical treatment. Furthermore, different criteria for the evaluation of success and failure of the treatment have been adopted.[22-24] When heterogeneity for clinical variables and success criteria is attained, a direct comparison among or between various studies is very difficult to perform.

Delays or alterations in healing have been reported when lesion size was greater than 5 mm.[2,25,26] Several authors showed that the prognosis for smaller lesions after periradicular surgery is better than the prognosis for larger ones.[4,5,27-29]

Hirsch et al[4] reported a success rate of only 27% among 33 teeth with total buccal bone loss, compared with a healing rate of 50% in teeth with intact buccal bone. Skoglund and Persson[5] described an initial success rate of 37% with total buccal bone loss; 33% were listed as uncertain, and 30% as unsuccessful. Over a 4-year evaluation process, the success rate was increased to only 38.5%. Data from the present study are in agreement with data generated by these 2 studies; investigators found that the 12-month outcome for through-and-through lesions was significantly worse with respect to lesions with intact bony plates, independent of the use of GTR.

Rubinstein and Kim[30] observed that small lesions (0 to 5 mm) and those of medium size (6 to 10 mm) healed within 7.25 months, and lesions larger than 10 mm healed within 11 months.

Some authors have suggested that the size of the preoperative lesion has no bearing on the ultimate resolution of the periradicular defect.[31,32] However, in 1972, Rud et al[2] observed that tooth location and extent of cortical bone loss may have a significant bearing on the healing pattern.

Several studies in humans and animals have evaluated the concept of GTR. This has led to the development of membranes or barriers that allow the cellular regrowth of periodontal defects caused by pathosis or surgical trauma.[33]

The use of a barrier in such lesions is an attempt to improve the self-regenerative healing process by excluding the undesired proliferation of gingival connective tissue or the migration of the oral epithelium into such defects, which can impair the formation of normal trabecular bone.[34]

In guided tissue regeneration, many authors have underlined the importance of maintaining proper space below the membrane.[35-37] To achieve more predictable regeneration, some authors have suggested the combined use of barrier membranes and graft materials that may act as space maintainers.[38-41]

In 1995, Pecora et al[8] showed that large periapical lesions healed more rapidly and with better quality bone when a membrane (expanded polytetrafluoroethylene [e-PTFE] Goretex) was used. In 2001, Pecora et al[10] conducted a clinical randomized study to evaluate the adjunctive effects of calcium sulphate grafts on the surgical treatment of patients with through-and-through periradicular lesions. Results of this study demonstrate that the addition of calcium sulphate as a bone graft during conventional surgical treatment improves clinical outcomes. Tobón et al[11] concluded that the use of nonabsorbable membrane or a combination of nonabsorbable membrane and resorbable hydroxyapatite improved the predictability of clinical, radiographic, and histologic healing over outcomes with conventional techniques. This study provided histologic results comparable with those gathered through experimental studies in animals.[42,43] Conversely, Garrett et al,[12] in a prospective controlled study, suggested that placement of a membrane over the bony opening created during a periradicular surgical procedure has no beneficial effect on the rate of healing, and that the added expense to the patient would not be warranted. In 1998, Santamaria et al[9] reported no statistical significance in density and residual volume with the use of a resorbable or a nonresorbable membrane. Some histomorphometric and histologic studies in animal models found no significant difference in bone regeneration whether or not GTR was used.[44,45]

Similar to the findings of the latter studies, we found no significant differences in outcome between the GTR and control groups in the treatment of patients with periapical lesions over 10 mm. von Arx in 2001 suggested that clinicians might hesitate to apply the GTR principle in endodontic surgery because good long-term results have been attained with surgical approaches that do not include membrane application.[7]

Finally, even if an apparent benefit of grafting is seen with through-and-through lesions (75% healing in grafted defects vs 61.5% in controls), the small number of cases studied does not allow statistical confirmation of findings.

The present study suggests that combined use of GTR and anorganic bovine bone in periapical lesions Class Ia and Ib has no beneficial effects on the rate of

healing 1 year postoperatively. Additional quantitative and histologic studies with larger sample sizes and longer recall rates are needed to confirm these results.

References

1. Hoen MM, Pink FE: Contemporary endodontic retreatments: An analysis based on clinical treatment findings. J Endod 28: 834, 2002
2. Rud J, Andreasen JO, Möller Jensen JE: A multivariate analysis of various factors upon healing after endodontic surgery. Int J Oral Surg 1:311, 1972
3. Gutmann JL, Harrison JW: Surgical Endodontics. Boston, MA, Blackwell Scientific Publications, 1991, p 355
4. Hirsch JM, Ahlstrom U, Henrikson PA, et al: Periapical surgery. Int J Oral Surg 8:173, 1979
5. Skoglund A, Persson G: A follow up study of apicoectomized teeth with total loss of the buccal bone plate. Oral Surg Oral Med Oral Pathol 59:78, 1985
6. Gottlow J, Nyman S: Barrier membranes in the treatment of periodontal defects. Curr Opin Periodontol 3:140, 1996
7. von Arx T, Cochran DL: Rationale for the application of the GTR principle using a barrier membrane in endodontic surgery: A proposal of classification and literature review. Int J Periodontics Restorative Dent 21:127, 2001
8. Pecora G, Kim S, Celletti R, et al: The guided tissue regeneration principle in endodontic surgery: One-year postoperative results of large periapical lesions. Int Endod J 28:41, 1995
9. Santamaria J, Garcia AM, de Vicente JC, et al: Bone regeneration after radicular cyst removal with and without guided bone regeneration. Int J Oral Maxillofac Surg 27:118, 1998
10. Pecora G, De Leonardis D, Ibrahim N, et al: The use of calcium sulphate in the surgical treatment of a through and through periradicular lesion. Int Endod J 34:189, 2001
11. Tobón SI, Arismendi JA, Marin ML, et al: Comparison between conventional and two bone regeneration techniques in periradicular surgery. Int Endod J 35:635, 2002
12. Garrett K, Kerr M, Hartwell G, et al: The effect of a bioresorbable matrix barrier in endodontic surgery on the rate of periapical healing: An in vitro study. J Endod 28:503, 2002
13. Young MPJ, Korachi M, Carter DH, et al: The effects of an immediately pre-surgical chlorhexidine oral rinse on the bacterial contaminants of bone debris collected during dental implant surgery. Clin Oral Implants Res 13:20, 2002
14. Molven O, Halse A, Grung B: Observer strategy and the radiographic classification of healing after endodontic surgery. Int J Oral Maxillofac Surg 16:432, 1987
15. Molven O, Halse A, Grung B: Incomplete healing (scar tissue) after periapical surgery: Radiographic findings 8-12 years after treatment. J Endod 22:264, 1996
16. Artzi Z, Tal H, Dayan D: Porous bovine bone mineral in healing of human extraction sockets. Part I: Histomorphometric evaluations at 9 months. J Periodontol 71:1015, 2000
17. Araújo MG, Carmagnola D, Berglundh T, et al: Orthodontic movement in bone defects augmented with Bio-Oss: An experimental study in dogs. J Clin Periodontol 28:73, 2001
18. Dies F, Etienne D, Abboud NB, et al: Bone regeneration in extraction sites after immediate placement of an e-PTFE membrane with or without a biomaterial: A report on 12 consecutive cases. Clin Oral Implants Res 7:277, 1996
19. McAllister BS, Margolin MD, Cogan AG, et al: Eighteen-month radiographic and histologic evaluation of sinus grafting with inorganic bovine bone in the chimpanzee. Int J Oral Maxillofac Implants 14:361, 1999
20. Piattelli M, Favero GA, Scarano A, et al: Bone reactions to inorganic bovine bone (Bio-Oss) used in sinus augmentation procedures: A histologic long-term report of 20 cases in humans. Int J Oral Maxillofac Implants 14:835, 1999
21. Gutmann JL, Harrison JW: Surgical Endodontics. Boston, MA, Blackwell Scientific Publications, 1991, p 338
22. Testori T, Capelli M, Milani S, et al: Success and failure in periradicular surgery: A longitudinal retrospective analysis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 87:493, 1999
23. Zuolo ML, Ferreira MOF, Gutmann JL: Prognosis in periradicular surgery: A clinical prospective study. Int Endod J 33:91, 2000
24. Friedman S, Mor C: The success of endodontic therapy—Healing and functionality. J Calif Dent Assoc 32:493, 2004
25. Tay WM, Gale KM, Harty FJ: The influence of periapical radiolucencies on the success or failure of apicectomies. J Br Endod Soc 11:3, 1978
26. Storms JL: Factors that influence the success of endodontic treatment. J Can Dent Assoc 35:83, 1969
27. Rud J, Andreasen JO: A study of failures after endodontic surgery by radiographic, histologic and stereomicroscopic methods. Int J Oral Surg 1:311, 1972
28. Finne K, Nord PG, Persson G: Retrograde root filling with amalgam and Cavit. Oral Surg 43:621, 1977
29. Nordenram A, Svardstrom G: Results of apicectomy: A clinical-radiological examination. Swed Dent J 63:593, 1970
30. Rubinstein RA, Kim S: Short-term observation of the results of endodontic surgery with the use of a surgical operation microscope and Super-EBA as root-end filling material. J Endod 25:43, 1999
31. Lehtinen R, Aitasalo K: Comparison of the clinical and roentgenological state at the re-examination of root resections. Proc Finn Dent Soc 68:209, 1972
32. Forssell H, Tammisalo T, Forssell K: A follow up study of apicectomized teeth. Proc Finn Dent Soc 84:85, 1988
33. Wang HL, MacNeil RL: Guided tissue regeneration: Absorbable barriers. Dent Clin North Am 42:505, 1998
34. Gottlow J, Nyman S, Karring T, et al: New attachment formation as the result of controlled tissue regeneration. J Clin Periodontol 11:494, 1984
35. Rankow HJ, Krasner PR: Endodontic applications of guided tissue regeneration in endodontic surgery. J Endod 22:34, 1996
36. Zitzmann NU, Naef R, Schärer P: Resorbable versus nonresorbable membranes in combination with Bio-Oss for guided bone regeneration. Int J Oral Maxillofac Implants 12:844, 1997
37. Tatakis D, Promsudthi A, Wikesjö UM: Devices for periodontal regeneration. Periodontology 2000 19:59, 1999
38. Schallhorn R, McClain P: Combined osseous composite grafting root conditioning and GTR. Int J Periodontics Restorative Dent 8:8, 1988
39. Lekovic V, Kenney EB, Carranza FA Jr, et al: Treatment of grade II forcation defects using porous HA in conjunction with a PTFE membrane. J Periodontol 61:575, 1990
40. Anderegg CR, Martin SJ, Grey JL, et al: Clinical evaluation of the use of DFDBA with guided tissue regeneration in the treatment of molar furcation invasios. J Periodontol 62:264, 1990
41. Dahlin C, Gottlow J, Linde A, et al: Healing of maxillary and mandibular bone defects using a membrane technique: An experimental study in monkey. Scand J Plast Reconstr Surg Hand Surg 24:13, 1990
42. Dahlin C, Linde A, Gottlow J, et al: Healing of bone defects by guided tissue regeneration. Plast Reconstr Surg 8:672, 1988
43. Nyman S: Bone regeneration using the principle of guided tissue regeneration. J Clin Periodontol 18:494, 1991
44. Maguire H, Torabinejad M, McKendry D, et al: Effect of resorbable membrane placement and human osteogenic protein-1 on hard tissues healing after periradicular surgery in cats. J Endod 24:720, 1998
45. Bohning BP, Davenport WD, Jeansonne BG: The effect of guided tissue regeneration on the healing of osseous defects in rat calvaria. J Endod 25:81, 1999