Is periodontal regeneration clinically predictable?

Gunilla Tynelius-Bratthall and Göran Söderholm

Under de senaste 10–15 åren har ett flertal intressanta metoder avsedda att återbilda förlorat tandfäste presenterats i både kort- och långtidsstudier. I denna översikt över möjligheter och svårigheter att åstadkomma kliniskt signifikant parodontal regeneration fokuserar författarna på dels egna studier, dels på sådana som genomförts av andra forskare. Särskilt intresse har riktats mot frågan huruvida hittills vunna resultat genom styrd vävnadsregeneration (GTR) demonstrerat sådan grad av klinisk signifikans att parodontal regeneration kan anses vara förutsägbar givet rätt teknik används.

The ultimate goal of periodontal treatment has been to achieve regeneration, i.e. new cementum, periodontal ligament and bone. Different regenerative techniques such as citric acid root conditioning and use of a variety of grafting materials have been suggested for this purpose. Furthermore, reports on growth factors, guided tissue regeneration (GTR) and enamel matrix derivatives have shown promising results (Table 1). Various combinations of these techniques have also been reported. Figures 1–3 illustrates examples of different regenerative procedures.

GTR and non-resorbable membranes

Guided tissue regeneration (GTR) means that by the use of a barrier, a membrane, epithelial downgrowth into the defect is prevented. Instead, cells from the periodontal ligament are stimulated to form a new connective tissue attachment.

The first report on GTR treatment in marginal periodontitis was presented by Nyman et al. in 1992 [1]. By using a membrane, they succeded in achieving a remarkable gain of clinical attachment. Histologically, they could demonstrate that a connective tissue attachment had been formed. Histological evidence of new connective tissue attachment after GTR treatment was further shown in animal studies [2] and human case reports [3–5]. Several studies using expanded polytetrafluoroethylene (e-PTFE) membranes, Gore-Tex® Periodontal Material (W.L. Gore & Associates, Flagstaff, AZ, USA), demonstrated that gain of probing attachment and bone regeneration may occur after treatment of infrabony defects [6, 7]. Few of these studies were fully controlled, however. For a study to be considered fully controlled, defects with similar anatomy in the same patient should be treated with and without membranes and the clinical outcome compared.

Authors

Gunilla Tynelius-Bratthall, LDS, Odont Dr, Associate Professor, Department of Periodontology, Faculty of Odontology, Lund University, Malmö.
Göran Söderholm, LDS, Odont Dr, Chief Dental Officer, Periodontology Clinic, Public Dental Service, Malmö, Sweden.

Key words

Periodontal regeneration; guided tissue regeneration

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Figure 1. An infrabony pocket of a maxillary first premolar **(a)** when the flap is raised, **(b)** when a bioactive ceramic is applied and **(c)** after suturing the flap.

Figure 2. **(a)** A deep infrabony pocket of a maxillary first molar, serving as abutment tooth, and a cantilever pontic in a bridge construction, **(b)** with a membrane adapted and **(c)** after 6 months of healing. The probing pocket depth is significantly reduced but a gingival retraction can be seen.

Figure 3. An infrabony defect at the distal surface of the mandibular right canine (note root furrow) **(a)** when the flap is raised, **(b)** when enamel matrix protein derivative is applied and **(c)** 4 weeks after surgery.

Own studies

In order to perform such a controlled study, individuals showing contralateral defects of maxillary premolars in x-rays were selected. Oral hygiene instructions, scaling and root planing of test and control teeth were performed 2 months before the baseline examination. Nine subjects with remaining probing pocket depth ≥5 mm in the defect areas were selected for the study. A split-mouth design was applied, with one premolar randomly chosen to be treated according to the GTR procedure and the contralateral with an open debridement procedure. The membrane had to be removed after 6 weeks in a second surgical procedure. No second surgery was performed in the control teeth, however. The outcome of the treatment was studied with clinical and radiographic parameters. In order to evaluate early changes in the x-rays, subtraction radiography was used. The clinical (Fig. 4) and radiographic results 6 months postoperatively did not show any statistically significant difference between test and control teeth [8].

In the present controlled study of infrabony pockets, a limited mean gain of attachment was demonstrated compared to the results of case reports presented earlier. Looking at the single subjects, the material demonstrated variations for both test and control teeth. In this report maxillary premolars were studied since these teeth – and especially the first premolar – often show severe periodontal problems. This is probably related to problems performing proper plaque control in these regions due to the root anatomy, i.e. root furrows and furcation involvements. The root anatomy may also aggravate tight adaptation of the membrane. Besides, in this study a couple of test sites showed partial necrosis of the flaps, due to limited flap thickness in this region.

Studies on e-PTFE membranes have indicated that gain or loss of clinical attachment is related to the presence of periodontal pathogens in the GTR-treated area [9] and that the use of antibiotics in GTR treatment may improve the gain of clinical attachment [10]. The risk of infection seems to be low, however, and the need for prophylactic antibiotic administration is not clearly shown [11]. Factors such as non-exposure of the membrane seem to be more important to prevent contamination. It is also important to stress that GTR treatment is not different from conventional periodontal surgery and should be performed in periodontally pretreated patients with good pre- and postoperative plaque control.

Table 1. Different regenerative procedures available in clinical practice

Citric acid/coronally positioned flap
Hydroxyapatite
Demineralised freeze-dried bone
Bioactive ceramics
Growth factors
Guided tissue regeneration
Enamel matrix derivatives

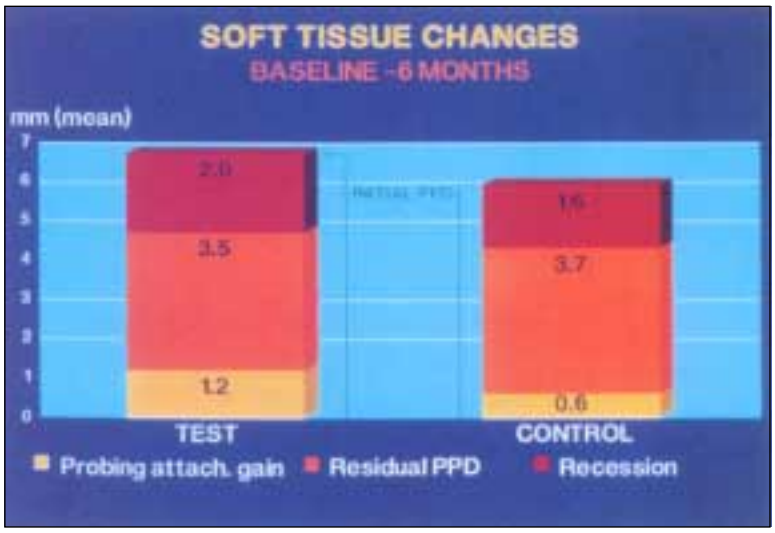

Figure 4. Graphic presentation of mean presurgery pocket depth and 6 months postsurgery residual pocket depth, attachment gain and gingival recession for test and control sites after GTR treatment. (PPD = probing pocket depth).

Resorbable versus non-resorbable membranes

When using an e-PTFE membrane, a second surgical procedure has to be performed in order to remove the barrier. With the use of resorbable membranes (Table 2), however, a second surgical procedure is not needed. In a dog study, Caffesse et al. in 1994 [12] compared the histological response to a bioresorbable membrane, Resolut® Regenerative Material (W.L. Gore & Associates, Flagstaff, AZ, USA) with that to an e-PTFE membrane in experimentally induced class II buccal furcation defects. The results of the study showed no histological differences between the two groups.

In a study in humans by Cortellini et al. in 1996 [12], the clinical outcome of non-resorbable and bioresorbable membranes was compared to that of modified Widman flap procedures. It was found that GTR treatment resulted in a sig-

Table 2. Different types of membranes, non-resorbable and resorbable

Non-resorbable:
Polytetrafluoroethylene (e-PTFE) membranes
Teflon membranes
Resorbable:
Polylactide and polyglycolide membranes
Guidor® Matrix Barrier
Resolut® Regenerative Material
Collagen membranes
Polyglactin 910 membranes
Vicryl® Periodontal Mesh

nificantly increased gain of probing attachment compared to modified Widman flap procedures. There was no statistically significant difference in gain of probing attachment between non-resorbable and bioresorbable membranes. In a study by Cafesse et al. in 1997 [13], the clinical results of GTR using a resorbable barrier, Resolut® Regenerative Material, were compared with those using a non-resorbable e-PTFE barrier. It was concluded that the resorbable barrier tested was as effective as the non-resorbable e-PTFE barrier for the treatment of class II furcations and intrabony defects. In the study by Cortellini et al. [12], test and control sites were not located in the same patient.

Own studies

In a study on resorbable membranes (Resolut® Regenerative Material) and infrabony defects [14], we decided to use a split mouth design in order to exclude the influence of patient-specific characteristics. Subjects with bilateral infrabony defects at single-rooted teeth were selected. Presurgical scaling of test and control sites was performed as well as use of systemic antibiotics in order to optimise the healing potential. A total of 22 teeth in 9 patients with probing pocket depth ≥5 mm 3 months after scaling were included.

At baseline clinical parameters were recorded and reproducible radiographs for computer-based marginal bone level measurements were taken. Bacterial samples were collected to investigate the presence of periodontitis-associated bacteria, for example *Porphyromonas-*, *Prevotella-* and *Fusobacterium*-like microorganisms, and to test the resistance to amoxicillin. Amoxicillin was chosen since it has an antimicrobial action against a large number of oral bacteria including gram-negative anaerobic rods. As expected, all types of microorganisms present in the samples were not susceptible to amoxicillin, and metronidazole was used in two patients. Antibiotics were prescribed for one week, starting one day before surgery.

At the test defects a bioresorbable membrane, Resolut®Regenerative Material, was used. Before the flaps were repositioned, the epithelium on the inner surface of the flap was removed and care was taken to cover the membranes completely before the flaps were sutured. Control defects received the same surgical protocol without a membrane. In most of the cases test and control sites were treated at the same time.

Clinical, radiographic and microbiological examinations were repeated 6 and 12 months postoperatively. Test and control sites demonstrated a statistically significant improvement of gingival conditions, reduction of pocket depths and gain of clinical attachment (Fig. 5). None of the clinical parameters yielded statistically significant differerence between test and control teeth, however. Computer-based marginal bone level measurements showed only small differences in the majority of both test and control sites. The differences were not significant. Periodontitis-associated bacteria were present at baseline, and did not demonstrate any unwanted change in the 6- and 12-month samples. This means that black-pigmented gram-negative rods or *Fusobacterium*-like bacteria, known to interfere with the healing after treatment with GTR [9], were found on levels similar to those in baseline samples.The findings of this study suggest that the clinical, radiographic and microbiological improvements were not significantly enhanced by the GTR therapy.

Is periodontal regeneration clinically predictable?

In the studies by Proestakis et al. [8] and Bratthall et al. [14] with test and control sites within the same patient, no statistically significant difference in gain of probing attachment was found between test and control teeth. Pritlove-Carson et al. [15], also treating paired periodontal defects, did not find any significantly different gain of probing attachment between membrane-treated and conventional flap-treated sites. In a controlled study by Eickholz et al. [16] on non-resorbable membranes, patients demonstrating both double and single intrabony defects were investigated. No statistically significant difference between test and control sites was found. Similar results were found by Nygaard-Østby et al. [17], also using non-

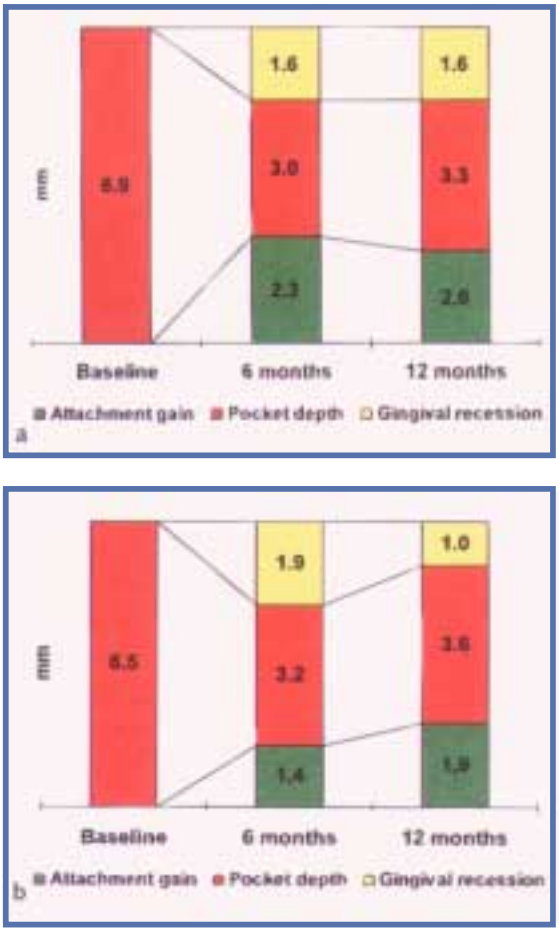

Figure 5. Graphic presentation of mean presurgery (baseline; Bl) pocket depth and postsurgery (6 and 12 months) residual pocket depth, attachment gain and gingival recession (**a**) for sites subjected to membrane procedures, GTR, and (**b**) for sites subjected to surgical procedures, control sites.

resorbable membranes, compared to healing after gingival flap surgery alone. In contrast to our studies, test and control sites were not located in the same patient. This was also the case in a recent clinical report by Mayfield et al. [18] showing no difference between test (resorbable membranes) and control sites. In contrast to the controlled studies mentioned above, Cortellini et al. [12], however, found that GTR treatment resulted in a significantly increased gain of attachment compared to modified Widman flap procedures.

The paper by Cortellini et al [12] was also included in a recent literature review [19] covering both case reports and controlled studies on different regenerative materials. In that review, data from studies of each treatment category were pooled for analysis. The pooled data showed an increased average attachment gain in the GTR reports compared with the open flap debridement studies. The authors conclude, however, that "there are surprisingly few comparative studies showing the benefits of GTR over open flap debridement procedures in the treatment of intrabony defects."

Table 3. Factors related to the clinical outcome of various GTR techniques

Host response
Smoking
Plaque index
Periodontitis-associated bacteria
Type of defect
Early membrane exposure

What factors might influence this difference or rather, what factors would influence the gain of clinical attachment when using GTR procedures? Analyses of factors related to the healing of GTR procedures (Table 3) have shown that an overall poor oral hygiene and cigarette smoking are negatively correlated to parameters of clinical outcome [20, 21]. The presence of periodontitis-associated bacteria would also interfere with the healing after treatment with GTR [9], as would early exposure of the membrane [20]. Host response factors other than those caused by smoking most probably influence the clinical outcome [21]. This might explain the difference between Cortellini et al. [12] and other controlled studies. Subjects with multiple vertical defects may have impaired host defence mechanisms compared to subjects with single defects.

The depth of the defect has also been mentioned as crucial for the outcome of the treatment. According to Laurell et al. [19], the intrabony defect has to be at least 4 mm deep to benefit from GTR procedures. This is in contrast to Mayfield et al. [18]. In this controlled study, subjects with interproximal intraosseous defects ≥ 4 mm identified radiographically were selected. The 4 mm depth was verified clinically at surgery. There were no significant differences between GTR-treated sites and flap surgery-treated sites. Smoking had a negative effect on healing in both test and control groups, however.

Assuming that regenerative techniques such as GTR will result in a new attachment as shown in histological studies, this can only be measured as gain of *clinical probing* attachment. When comparing mean values of probing attachment levels of test and control sites, most investigators can not demonstrate any statistically significant difference. Nor do radiographic examinations show any significant differences. It is obviously

important to select a patient with an optimal host response, low in plaque index and periodontitis-associated bacteria and with the right type of defect and root anatomy. This subject, however, will presumably respond well to any open debridement procedure.

The question *when* GTR will provide an increased attachment level compared to conventional surgery is still not answered. Also, it is still not clearly shown whether a GTR-induced attachment will be of better quality, i.e. more resistant to plaque bacteria, than clinical attachment achieved after conventional periodontal surgery. Ten years ago Thorkild Karring [22] asked: "Repair or regeneration, does it matter?" It seems that we are still not prepared to give a complete answer.

Summary

During the last 10–15 years several interesting methods of achieving new attachment, including GTR and enamel-derived protein, have been presented. This means that long and short-term clinical studies are now available. This paper focuses on controlled GTR studies both by our group and by others. Methods available to-day are discussed, in particular concerning the predictability of achieving periodontal regeneration.

References

1. Nyman S, Lindhe J, Karring T, Rylander H. New attachment following surgical treatment of human periodontal disease. J Clin Periodontol 1982; 9: 290–6.
2. Aukhil I, Petterson E, Suggs C. Guided tissue regeneration. An experimental procedure in beagle dogs. J Periodontol 1986; 57: 727–34.
3. Gottlow J, Nyman S, Lindhe J, Karring T, Wennström J. New attachment formation in the human periodontium by guided tissue regeneration. Case reports. J Clin Periodontol 1986; 13: 604–16.
4. Becker W, Becker B, Prichard J, Caffesse R, Rosenberg E, Gian Grasso J. Root isolation for new attachment procedures. A surgical and suturing method. Three case reports. J Periodontol 1987; 58: 819–26.
5. Stahl S, Froum S, Tarnow D. Human histologic responses to guided tissue regenerative techniques in intrabony lesions. Case reports on 9 sites. J Clin Periodontol 1990; 17: 191–8.
6. Becker W, Becker B, Berg L, Prichard J, Caffesse R, Rosenberg E. New attachment after treatment with root isolation procedures: Report for treated class III and class II furcations and vertical osseous defects. Int J Periodont Rest Dent 1988; 8(3): 9–23.
7. Cortellini P, Pini Prato G, Baldi C, Clauser C. Guided tissue regeneration with different materials. Int J Periodont Rest Dent 1990; 10: 137–51.
8. Proestakis G, Bratthall G, Söderholm G, Kullendorff B, Gröndahl K, Rohlin M, Attström R. Guided tissue regeneration in the treatment of infrabony defects on maxillary premolars. A pilot study. J Clin Periodontol 1992; 19: 766–73.
9. Nowzari H, Slots J. Microorganisms in polytetrafluoroethylene barrier membranes for guided tissue regeneration. J Clin Periodontol 1994; 21: 203–10.
10. Nowzari H, Matian H, Slots, J. Periodontal pathogens on polytetrafluoroethylene membrane for guided tissue regeneration inhibits healing. J Clin Periodontol 1995; 22: 469–74.
11. Dahlén G. Local and general antimicrobial prophylaxis in GTR treatment. In: Guided Periodontal Tissue Regeneration. Hugoson A, Lundgren D, Lindgren B, editors. Stockholm: Förlagshuset Gothia 1995: 114–26.
12. Cortellini P, Pini Prato G, Tonetti MS. Periodontal regeneration of human intrabony defects with bioresorbable membranes. A controlled clinical trial. J Periodontol 1996a; 67: 217–23.
13. Caffesse RG, Mota LF, Quiñones CR, Morrison EC. Clinical comparison of resorbable and non-resorbable barriers for guided periodontal tissue regeneration. J Clin Periodontol 1997; 24: 747–52.
14. Bratthall G, Söderholm G, Neiderud AM, Kullendorff B, Edwardsson S, Attström R. Guided tissue regeneration in the treatment of human infrabony defects. Clinical, radiographical and microbiological results: a pilot study. J Clin Periodontol 1998; 25: accepted for publication.
15. Pritlove-Carson S, Palmer RM, Floyd PD. Evaluation of guided tissue regeneration in the treatment of paired periodontal defects. Br Dent J 1995; 179: 388–94.
16. Eickholz P, Benn DK, Staehle HJ. Radiographic evaluation of bone regeneration following periodontal surgery with or without expanded polytetrafluoroethylene barriers. J Periodontol 1996; 67(4): 379–85.
17. Nygaard-Østby P, Tellefsen G, Sigurdsson TJ, Zimmerman GJ, Wikesjö UM. Periodontal healing following reconstructive surgery: effect of guided tissue regeneration. J Clin Periodontol 1996; 23: 1073–9.
18. Mayfield L, Söderholm G, Hallström H, Kullendorff B, Edwardsson S, Bratthall G, Brägger U, Attström R. Guided tissue regeneration for the treatment of intraosseous defects using a bioresorbable membrane. A controlled clinical study. J Clin Periodontol 1998; 25: 585–95.
19. Laurell L, Gottlow J, Zybutz M, Persson R. Treatment of intrabony defects by different surgical procedures. A literature review. J Periodontol 1998; 69: 303–13.
20. Cortellini P, Paolo G, Pini Prato G, Tonetti MS. Long-term stability of clinical attachment following guided tissue regeneration and conventional therapy. J Clin Periodontol 1996b; 23: 106–11.
21. Trombelli L. Retrospective analyses of factors related to clinical outcome of guided tissue regeneration procedures in intrabony defects. J Clin Periodontol 1997; 24: 366–71.
22. Karring T. Repair or regeneration, does it matter? In: Periodontology To-day. Guggenheim B, editor. Basel: Karger, 1988: 271–80.

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Address

Gunilla Tynelius-Bratthall, Department of Periodontology, Faculty of Odontology, Carl Gustafs väg 34, SE-214 21 Malmö, Sweden.