



# Second Attempt of Guided Tissue Regeneration on a Previous Successfully Grafted Site with Periodontal Breakdown—A 5-Year Follow-up

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## Abstract

Guided tissue regeneration (GTR) has been proven to promote attachment and regeneration of periodontal tissue. However, there is a 20 to 40% incidence of attachment loss on regenerated attachments reported in the literature. To my knowledge, this is the first case report on a second attempt in GTR on a previous successful grafted site with clinical attachment loss. A healthy 17-year-old Chinese male patient had GTR performed with xenograft particles and bovine resorbable membrane on his root-canal treated, fused upper right lateral incisor and upper right canine (#12-#13) in 2007. Probing depth on the mid-palatal region of #12-#13 was reduced to 4 mm and maintained for the next 4 years. But in the fifth year, probing depth increased to 11 mm with no endodontic symptoms, and a second attempt of GTR using the same materials was carried out. The probing depth at the surgical site was reduced to 4 mm and successfully maintained for another 5 years. Irregular maintenance and the presence of plaque retentive factor could have caused the clinical attachment loss on #12-#13. This case shows it is possible to attempt GTR on a previous successfully grafted site. GTR did not increase tissue resistance against periodontal breakdown. Hence, proper maintenance planning for GTR sites is important to prevent periodontal breakdown.

## Keywords

- ▶ guided tissue regeneration
- ▶ periodontal breakdown
- ▶ periodontal maintenance
- ▶ risk factors

## Introduction

Guided tissue regeneration (GTR) has been proven to reduce periodontal pocket depth (PD) and improve clinical attachment level (CAL) in infrabony defects. In general, the success and stability of GTR are related to good plaque control, deep and narrow intrabony defect (>3 mm) and thick soft tissue (>1 mm), GTR protocol with good wound stability, and a good postoperative regime with an adequate healing period.<sup>1</sup> Although predictable surgical techniques and suitable indications for GTR have been well reported in the literature, information on planning maintenance for GTR sites

and management of CAL loss on the regenerated attachment remain scarce. Recurrence of CAL loss after GTR was reported to be about 1 to 4 mm in 20.8% (5/24) and 36.4% (4/11) of sites respectively in 5 years<sup>2,3</sup> and 26.7% (4/15) sites in 20 years.<sup>4</sup> To my knowledge, this is the first case report that demonstrates a second attempt at GTR on a previous successfully grafted site which experienced recurrent CAL loss and was thereafter successfully maintained the CAL gain for 5 years. In addition, recommendations pertaining to patient-related and local risk factors for clinicians to consider during maintenance planning of GTR cases are highlighted in this case report.

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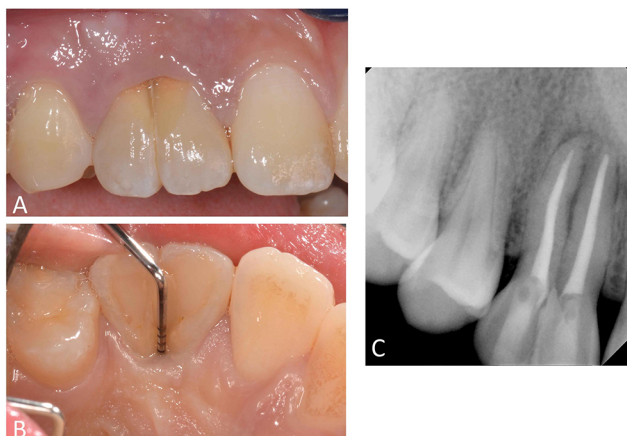
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## Case Presentation

A healthy, non-smoker 17-year-old Chinese boy presented in 2007 with necrotic pulp and asymptomatic apical periodontitis, perio-endo lesion, and PD of 6 mm at the mid-palatal region of a fused upper right lateral incisor and upper right canine (#12-#13) with two roots sharing a fused crown. Initial periodontal management and root canal treatment were performed on the fused tooth and obturated with Roth's Sealer (Roth International Ltd, Chicago, United States) and Gutta-percha. During an exploration surgery on #12-#13 in 2007, a buccal fenestration from the endodontic infection was found between the root of #12-#13 with a palatal 10-mm infrabony defect. Hemisection of the root could not be carried out due to the long root trunk. Separation of the crown was not feasible owing to the proximity of both root canals in #12-#13 at the cervical region (noticeable in ►Fig. 1C). Separating the crown and creating the contour at the cervical region for access to oral hygiene instruction might expose the gutta-percha and potentially causing root resorption in the future. The infrabony defect was grafted with bovine porous bone mineral granules (BioOss, Geistlich) and bioresorbable bovine collagen membrane (BioMend, Geistlich). Composite was applied on the fused crown of #12-#13. PD on the mid-palatal region of #12-#13 was reduced to 4 mm and periodontal maintenance was carried out on average every 4.85 months from 2007 to 2009 with a lapse in recall during 2009 to 2012. Another clinician (author) saw the patient in 2013 with a complaint of a foul smell from the fused tooth. Periodontal examination showed a fused #12-#13 (►Fig. 1A) with an increase of PD to 11 mm noted at the mid-palatal region of #12-#13 (►Fig. 1B) with normal mobility and occlusion. The periapical radiograph revealed normal bone level, adequate root-filled, and a slight widening of the periodontal ligament on #12-#13 (►Fig. 1C). Nonsurgical periodontal therapy was carried out to debride #12-#13 but the deep periodontal PD failed to resolve, leading to exploratory surgery in 2014. During the exploratory surgery, a full mucoperiosteal flap with a simplified papilla preservation technique was raised



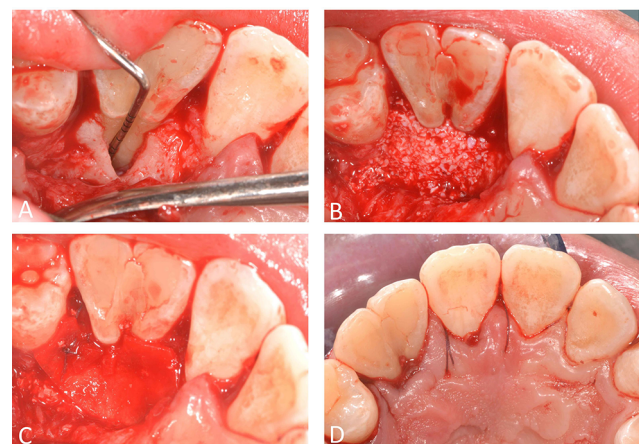
**Fig. 1** (A) Preoperative labial view of #12-#13. (B) Preoperative palatal view of #12-#13 with probing depth 11 mm. (C) Preoperative periapical radiograph on #12-#13

from #11 to #15. A V-shaped, three-walled intrabony defect about 4 mm in depth was found only on the palatal surface of #12-#13 (►Fig. 2A) with intact buccal bone and interdental bone around #12-#13. The patient opted to be grafted with the same material because of previous successful surgery; bovine porous bone mineral granules (Bio-Oss, Geistlich) were packed into the defect (►Fig. 2B). Subsequently, a bioresorbable bovine collagen membrane (BioMend, Geistlich) was trimmed and placed over the bone graft on palatal and extending into the distal part of interdental of #12-#13, subsequently stabilized with Vicryl 5/0 suture (Ethicon, Johnson & Johnson) (►Fig. 2C). The flap closure was completed with the same Vicryl 5/0 suture (►Fig. 2D). A composite was added to the palatal pit around the region of the fused roots and trimmed following the palatal surface to improve cleansability and reduce plaque retention. The patient was prescribed amoxicillin 500 mg every 8 hours for 5 days, ibuprofen 400 mg every 8 hours for 3 days, and 0.2% chlorhexidine gluconate mouthwash every 12 hours for 1 week.

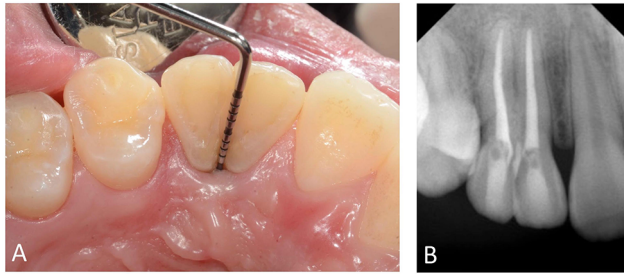
The healing of the surgical site was uneventful and the sutures were removed after 1 week. Six months after the second GTR, PD on the mid-palatal region of #12-#13 reduced to 4 mm, and no obvious recession was noted (►Fig. 3A). The CAL gain in total was 7 mm. A periapical radiograph that was taken at the 1-year review revealed normal bone level and periapex with no widening of periodontal ligament space (►Fig. 3B). The patient was seen three monthly for periodontal maintenance and a 4-mm PD has been maintained for the past 5 years (►Fig. 4). In addition, the patient denied any incidence of foul smell from the fused #12-#13 since the second GTR was done until the recent 5-year review.

## Discussion

Long-term maintenance regimens for periodontal surgery are not widely discussed and documented. The longest follow-up periods for GTR that have been reported were for over 10 years



**Fig. 2** (A) Intraoperative: Infrabony defect about 4 mm in depth. (B) Intraoperative: bovine porous bone mineral granules (Bio-Oss, Geistlich) filled the defect. (C) Intraoperative: bioresorbable bovine collagen membrane (BioMend, Geistlich) placed over the bone graft and stabilized with Vicryl 5/0 suture. (D) Postoperative palatal view of flap closure with Vicryl 5/0 suture.



**Fig. 3** (A) Probing depth reduced to 4 mm at 6 months postoperative review. (B) Periapical radiograph at 1-year postoperative review.



**Fig. 4** Probing depth remained at 4 mm at 5 years postoperative review.

(►Table 1).<sup>4,6</sup> The maintenance regime that was proposed by the Cortellini et al. and Sculean et al. studies was three monthly.<sup>4,5</sup> This case involved a patient who had 9 months to 1 year maintenance intervals between 2009 and 2012. Besides the local risk factor of the groove between the fused roots of #12-13 and plaque accumulation around the palatal pit, an irregular maintenance interval and presence of plaque retentive factor could have caused CAL loss after the first GTR. Hence, the second GTR was attempted to eliminate periodontal pocket and achieve attachment gain using bovine bone graft particles and bovine resorbable membrane, which has been shown with new cementum and periodontal ligament with osteogenesis in an 8-months review of histomorphometry analysis.<sup>7</sup> Plaque retention area on the palatal pit was eliminated by adding composite and the patient was placed on a 3-month periodontal maintenance protocol to prevent periodontal breakdown. This measure has positively led to a good outcome of maintaining a 4-mm PD at the mid-palatal region of #12-#13 over the last 5 years. The regenerated attachment has been shown to be no more susceptible to periodontal breakdown compared with normal attachment.<sup>8</sup> Hence we strongly propose that GTR sites be maintained every 3 months as advocated in long-term >10 years GTR studies with good CAL gain (►Table 1,  $2.8 \pm 1.2$  mm in Sculean et al.,<sup>5</sup>  $4.9 \pm 2.0$  mm in Cortellini et al.,<sup>4</sup> and  $3.8 \pm 2.7$  mm in Petsos et al.<sup>6</sup>), especially for patients with a high risk of CAL loss. Additional assessment during periodontal maintenance should include tooth mobility and ascertainment of any plaque retentive areas (►Table 2). Jiggling forces around the tooth can disrupt periodontal stability and hasten

periodontal breakdown in the presence of plaque and can be controlled via occlusal adjustment<sup>9</sup> or splinting.<sup>10</sup>

Periodontal breakdown after GTR can be observed over a few years after the procedure.<sup>2-4</sup> It is prudent for clinicians to formulate good maintenance planning to ensure the prevention of periodontal breakdown or relapse of disease at the previous successfully treated surgical site. Relevant factors for clinicians to consider during maintenance planning can be divided into two main categories: patient risk factors and localized risk factors. Patient risk factors include the patient's health status, plaque control, compliance with a recall program, and smoking habit. Diabetes mellitus, albeit lack in evidence in treated periodontitis patients, can presumably affect the recurrence of the disease.<sup>11</sup> Periodontitis is known for being the sixth most common complication for patients with diabetes mellitus.<sup>12</sup> Hyperglycemia can cause immune dysfunction with a reduction in complement and polymorphonuclear cells, as well as reduction in monocytes and T-lymphocytes. The disturbance in innate and cellular immune response inevitably leads to the progression of periodontitis in diabetic patients. Logically, it can be assumed that patients with poor diabetes control require close monitoring of their periodontal condition at shorter maintenance intervals. Patients with positive Interleukin-1 (IL-1) genotype experienced about 50% loss of first-year CAL gain after 3 years of GTR and about 10 times more likely to experience CAL loss >2mm compared with negative IL-1 genotype patients.<sup>18</sup> In bacteria-challenging environment, patients with positive IL-1 genotype can produce over 2-4 times of IL-1 cytokine levels in the gingival crevicular fluid leading to an increase in periodontal inflammation, tooth loss and susceptibility to severe periodontitis. Hence, patients with positive IL-1 genotype will require strict periodontal recall to monitor their periodontal condition. Smoking status is another major consideration in planning good maintenance intervals. Smoking is an important predictor of long-term outcomes of periodontal therapy.<sup>13</sup> In Cortellini and Tonetti's long-term prospective study on GTR, all six treated teeth which were lost during follow-up were from smokers (►Table 1).<sup>14</sup> In addition, smokers tend to be not compliant with scheduled periodontal maintenance visits.<sup>15</sup> Thus, the maintenance protocol that is planned for smokers should be even more stringent.

Patient compliance with periodontal maintenance is an important factor in maintaining the grafted site. Regular periodontal maintenance is crucial in preventing disease progression and leads to better prognosis.<sup>16,17</sup> Five out of the six teeth that were lost in the long-term follow-up after GTR were from subjects who failed to attend regular periodontal maintenance.<sup>14</sup> Further, noncompliant dental attenders for periodontal maintenance demonstrated an increase in attachment loss.<sup>16,17</sup> On the other hand, participation in a periodontal recall program decreased failure of GTR<sup>13,14</sup> and should thus be advocated for all GTR patients. Since microbe load in the patient's mouth is related to disease progression, the disruption of the biofilm during mechanical debridement in a periodontal maintenance visit can halt the ongoing destructive process in the periodontium (►Table 2). Therefore, clinicians need to educate patients about the importance of maintenance and compliance with the recall



**Table 1** Summary of literature review on periodontal maintenance after Guided Tissue Regeneration (GTR)

No.	Study	Number of subjects/sites	GTR method	Average SPT	Follow-up period (mean)	Outcomes
1	Gottlow et al 1992 <sup>19</sup> (non-randomized clinical trial).	39 subjects, 88 sites	PTFE membrane	Not reported	5 y	90.9% (80/88) of sites CAL gain >2 mm, and the 80 sites were included for follow-up. 75% (60/80) of sites CAL gain ≥ 3mm, 15% (12/80) of sites CAL loss ≥ 2mm in 3 y. No CAL loss of >2 mm at 4 and 5 y.
2	Cortellini et al 1996 <sup>17</sup> (non-randomized clinical trial).	44 subjects, 175/175 sites	Teflon membrane (Gore-tex periodontal membrane).	<ul style="list-style-type: none"> <li>• First year: monthly.</li> <li>• Thereafter SPT: every 3 mo.</li> </ul>	5 y	CAL gain was 4.0 ± 2.1 mm at 1 y, CAL loss was 1.2 ± 1.4 mm at 5 y.
3	Cortellini and Tonetti 2004 <sup>14</sup> (non-randomized clinical trial).	175 subjects, 175 sites	Nonabsorbable membrane (ePTFE), absorbable membrane (PLA), with or without alloplastic materials.	<ul style="list-style-type: none"> <li>• First year: monthly prophylaxis.</li> <li>• Thereafter SPT: every 3 mo (117/175 subjects assessed<sup>a</sup>).</li> </ul>	Longest 16 y, average 8 ± 3.4 y.	Six teeth lost (all smokers, 5 without SPT). Mean CAL gain 4.6 ± 2.0 mm at 1 y, 66.2% with no CAL loss of ≥2 mm over 16 y.
4	Sculean et al 2008 <sup>5</sup> (randomized controlled clinical trial).	19 subjects GTR: 10 sites, EMD+GTR: 9 sites.	GTR with or without EMD Emdogain, GTR using Resolut, Gore-Tex membrane.	<ul style="list-style-type: none"> <li>• 6 wk of chlorhexidine mouth rinse.</li> <li>• Fortnightly visit for the first 2 mo, monthly visit for the first year.</li> <li>• Subsequently, four visits per year (every 3 mo).</li> </ul>	10 y	GTR group: CAL gain of 3.2 ± 1.4 mm at 1 y and 2.8 ± 1.2 mm at 10 y. CAL loss of 0.4 ± 1.2 mm at 10 y. EMD+GTR group: CAL gain of 3.3 ± 1.1 mm at 1 y and 2.9 ± 1.2 mm at 10 y. CAL loss of 0.4 ± 1.2 mm at 10 y. Note: 5-y follow-up was reported by Sculean et al 2004. <sup>20</sup>
5	Stavropoulos and Karring 2005 <sup>3</sup> (case series).	11 subjects; 11 sites	Deproteinized bovine protein impregnated with 2 mg/mL gentamicin sulfate and PLA/PGA Resolut membrane.	<ul style="list-style-type: none"> <li>• Prophylaxis weekly for first 6 wk.</li> <li>• Monthly prophylaxis till 5 mo.</li> <li>• No further information on subsequent recalls.</li> </ul>	5 y	Two teeth lost. CAL gain of 3.8 ± 1.9 mm at 1 y and 4.1 ± 1.6 mm at 5 y. 36.4% (4/11) sites with CAL loss.
6	Slotte et al 2007 <sup>2</sup> (case series).	24 subjects; 24 sites	Deproteinized bovine protein (BioOss) bioresorbable membrane (Guidor/BioGide).	<ul style="list-style-type: none"> <li>• Fortnightly visit for the first 3 mo.</li> <li>• Once a month for the next 3 mo.</li> <li>• No details on subsequent recalls.</li> </ul>	5 y	Mean gain in CAL was 4.2 ± 2.1 mm at 1 y, 4.1 ± 1.8 mm at 3 y, and 4.3 ± 2.0 mm at 5 y examinations. 20.8% (5/24) of sites with CAL loss, two sites were from a smoker.
7	Cortellini et al 2017 <sup>4</sup> (randomized controlled clinical trial).	30 subjects; 30 sites	Titanium PTFE (n = 15), PTFE membrane (n = 15), with or without alloplastic materials.	<ul style="list-style-type: none"> <li>• First year: monthly.</li> <li>• Thereafter: every 3 mo.</li> </ul>	20 y	No tooth lost. Mean CAL gain of 4.9 ± 2.0 mm at 20 y for Titanium PTFE and 6.7 ± 2.0 mm for PTFE membrane. Mean CAL loss of 0.1 ± 0.3 mm at 20 y for Titanium PTFE and 0.5 ± 0.1 mm at 20 y for PTFE membrane. 26.7% (4/15) of sites with CAL loss.

(Continued)

**Table 1** (Continued)

No.	Study	Number of subjects/sites	GTR method	Average SPT	Follow-up period (mean)	Outcomes
8	Petsos et al 2019 <sup>6</sup> (randomized controlled clinical trial).	12 subjects; 25 sites	PLA membrane (Guidor). Split mouth ( $n = 10$ ), Parallel ( $n = 15$ )	<ul style="list-style-type: none"> <li>Recall at 3, 6, 12 mo.</li> <li>Subsequently, patients who came back at least once per year were considered compliant.</li> <li>Subsequent recalls not well described.</li> </ul>	20 y	4 GTR-treated teeth extracted due to prosthodontic reasons. CAL gain was $3.90 \pm 2.76$ mm at 10 y and $3.80 \pm 2.69$ mm at 20 y. CAL change was $0.78 \pm 1.93$ mm at 10 y, and $0.30 \pm 0.21$ mm (split mouth) and $0.93 \pm 0.66$ mm (parallel) at 20 y. 1 GTR-treated tooth with CAL loss $> 2$ mm at 10 yr, 2 GTR-treated teeth with CAL loss $> 2$ mm at 20 yr. Note: 10-y follow-up was reported by Nickles et al 2009. <sup>21</sup>

Abbreviations: CAL, clinical attachment level; EMD, enamel matrix derivatives; ePTFE, expanded polytetrafluoroethylene; GTR, guided tissue regeneration; PGA, polyglycolic acid; PLA, polylactic acid; PTFE, polytetrafluoroethylene; SPT, supportive periodontal therapy.

<sup>3</sup>Only subjects who were treatment compliant were analyzed

**Table 2** Considerations for planning periodontal maintenance after guided tissue regeneration (GTR)

Assessment in periodontal maintenance		Rationale and management
Plaque retentive factor		Promotes plaque accumulation, needs to be eliminated. <sup>22</sup>
Tooth mobility		Jiggling force disturbs periodontal stability, requires occlusal adjustment <sup>9</sup> or splinting. <sup>10</sup>
Periodontal maintenance planning factors		Rationale (Proposal for three monthly maintenance)
Patient related	Systemic condition	Diabetes <sup>11</sup> and IL-1 polymorphism positive <sup>18</sup> patients are associated with CAL loss.
	Smoking	Smoking affects GTR outcome <sup>23,24</sup> and disease progression. <sup>25</sup> Hazard ratio of 7.2 for regenerated CAL loss $\geq 2$ mm. <sup>14</sup>
	Compliance to periodontal maintenance	Mechanical disruption of biofilm during maintenance is important to halt disease progression. <sup>11,16</sup> Increase in CAL loss in noncompliant attenders. <sup>16,17</sup>
Local	Plaque control	Full mouth plaque score more than 10%. <sup>14</sup>
	Residual pockets	Residual pockets are a reservoir for periodontal pathogens. High-risk disease progression $\geq 8$ residual pockets, low risk $\leq 4$ residual pockets. <sup>11</sup>

Abbreviations: CAL, clinical attachment level; GTR, guided tissue regeneration.

system at the beginning of the treatment. Finally, local factors such as plaque control and residual pockets can affect the stability of attachment after regeneration. Patients with a plaque score  $> 10\%$ <sup>14</sup> and  $\geq 8$  residual pockets are at risk of loss of attachment at the regenerated site and should have a short periodontal recall interval.<sup>11</sup>

The limitation of this report is no clinical photo documentation from the previous operator during the first GTR attempt in 2007, hence we could not observe the bony defect at the first grafting procedure. The potential research focus for GTR in the future can include the investigation of the effect of different periodontal maintenance intervals after GTR; the prevalence and factors associated with periodontal breakdown after GTR; the success rate and changes in CAL after second GTR, and the resistance of regenerated attachment against periodontitis after second GTR.

## Conclusion

This case report showed that GTR can be performed on a previous successfully grafted site where there is a recurrence

of periodontal breakdown to achieve PD reduction and CAL gain. Good maintenance planning taking into consideration patient-related and local risk factors is crucial to prevent periodontal breakdown at the GTR site.

## Funding

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## Conflict of Interest

None declared.

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