Önder Solakoglu, Niusha Amiri, M. Oliver Ahlers

The use of Bone Allograft material and Enamel matrix derivates in the regenerative treatment of mandibular furcation class II defects in localised periodontitis with trauma from occlusion: a report of two cases and a narrative review of the literature

**Introduction:** Periodontitis can result in irreversible loss of connective tissue and supporting alveolar bone. Despite advances in regeneration therapy, treatment of periodontal furcation defects is still a challenge. This case report describes a combined regenerative approach in the treatment of grade II furcation defects in mandibular molars.

**Material and Methods:** In the present case study, 2 clinical cases with advanced localised periodontitis and an occlusal trauma as a cofactor were studied over 8 and 5 years, respectively. Following initial occlusal adjustment, the periodontal defects were treated successfully with guided tissue regeneration along with allogenic cancellous bone, enamel matrix proteins and endogenous growth factors.

**Results:** The treatment was effective in the regenerative therapy of destructive periodontal disease in both patients. Significant amount of bone fill was seen in clinical and radiographic re-evaluation and clinical results were maintained in the follow-up after 8 and 5 years.

**Conclusion:** Successful regeneration of periodontal tissues can be achieved using the combination of guided tissue regeneration (GTR), Allograft bone substitute, Emdogain and plasma rich in growth factor (PRGF). The combination therapy resulted in regeneration of tooth supporting tissue with improved clinical attachment levels and healthy gingiva.

**Keywords:** guided tissue regeneration; chronic periodontitis; Enamel matrix derivates; Allograft bone substitute; plasma rich in growth factor; occlusal trauma

Adjunct Associate Professor of the Prosthetic Department of the University Medical Center Hamburg-Eppendorf, Hamburg, Germany; Specialty Dental Practice limited to Periodontology and Implant Dentistry (FPI-Hamburg), Hamburg, Germany: Önder Solakoglu, Dr. med. dent., MCD, MSc, DDS

Associate Dentist, Specialty Dental Practice limited to Periodontology and Implant Dentistry (FPI-Hamburg), Hamburg, Germany: Niusha Amiri, DDS

Associate Professor of the Prosthetic Department of the University Medical Center Hamburg-Eppendorf, Hamburg, Germany; Specialty Dental Practice limited to Craniomandibular Dysfunction (CMD-Centrum Hamburg-Eppendorf), Hamburg, Germany: M. Oliver Ahlers, Priv-Doz. Dr. med. dent.

Citation: Solakoglu Ö, Amiri N, Ahlers MO: The use of Bone Allograft material and Enamel matrix derivates in the regenerative treatment of mandibular furcation class II defects in localised periodontitis with trauma from occlusion: a report of two cases and a narrative review of the literature. Dtsch Zahnärztl Z Int 2021; 3: 98–110 Peer-reviewed article: submitted: 20.12.2019, revised version accepted: 09.04.2020 DOI.org/10.3238/dzz-int.2021.0012



Figure 1 Initial periodontal measurement at baseline of case #1.

### Introduction

The prevalence of periodontal diseases in Germany is estimated to be about 90 % [41]. Many of these patients are unaware that inadequate oral hygiene is a risk factor for the emergence of periodontal diseases as well as of the fact that periodontitis interacts with various systemic diseases, notably diabetes, atherosclerosis, rheumatoid arthritis and pulmonary infections [56]. In spite of this, awareness is steadily increasing, even in the group of senior citizen patients, that they can contribute substantially to the health of their own teeth and these patients are prepared to invest time and resources into their dental health [34].

The onset of periodontal inflammation is usually associated with the accumulation of biofilm and calculus. Pathogenic microbiota in the subgingival biofilm start an immuneinflammatory response that leads to pocket formation. The host responses through innate and adaptive immunity attenuates the bone resorption and breakdown of connective tissue [27]. This pathogenic process can lead to tooth loss if left untreated.

In addition to the inflammatory processes, a variety of cofactors have been described in the literature, which may favour the progression of a periodontal lesion. In addition to general medical factors, such as incorrectly adjusted diabetes mellitus, autoimmune diseases, and nicotine consumption, local factors may also adversely affect the aetiology and progression of periodontal defects



Figure 2 Pre-operative radiograph of tooth #37 with grade II furcation lesion and an advanced infrabony defect at the mesial aspect.

[22]. These factors may be e.g. poorly adapted restorative margins, endodontic infections and occlusal trauma. Grinding and clenching of teeth due to sleep- and awake-bruxism is caused by muscle hyperactivity and can result in occlusal trauma of vulnerable teeth. Since 1965 it has been controversely discussed in the literature if occlusal trauma could act as a contributing factor in periodontal destruction, which may potentially cause degenerative changes in the periodontal ligament and the loss of supporting alveolar bone [25]. Waerhaug refused this theory suggesting that functional traumatic forces cannot act as a co-factor in the causation

of angular defects [59]. After the presentation of the co-destruction theory researchers started to examine the concept of multiple risk factors that resulted in the initiation and progression of periodontal diseases. As stated in a study by Ramfjord and Ash, uncorrected occlusal discrepancies have been shown to exacerbate periodontal disease, occlusal adjustments should be performed in the initial periodontal treatment phase in order to eliminate dysfunctional overloading of symptomatic teeth [48].

Periodontal Treatment Planning is a complex and multidisciplinary procedure that requires different



Figure 3 Initial periodontal measurement at baseline of case #2.



**Figure 4** Pre-operative radiograph of tooth #47 with a grade II furcation involvement and an advanced infrabony defect at the distal aspect.

therapeutic steps. One of the most important steps in the treatment of periodontal diseases is the diagnosis of co-factors and their elimination early in the course of periodontal therapy. Inflammation reduction is achieved through initial periodontal therapy, including supragingival and subgingival scaling, localised or generalised deep scaling and root planning in combination with the administration of antibacterial substances. According to the new S3 guideline for subgingival instrumentation and adjunctive antibiotics it is not recommended to use adjunctive antibiotics if the patients are over the age of 56 years and present with less than 35 % of periodontal pockets with a pocket probing depth

(PPD) exceeding 5 mm (S3 guideline DGZMK, AWMF no.: 083-029). During the phase of periodontal repair, the healing process leads to the formation of a long epithelial attachment. Long epithelial attachment is considered as non-functional scarring, since the periodontal tissue architecture is not restored. At the end of the initial periodontal treatment a re-evaluation indicates if further surgical procedures are necessary, or the elimination of inflammation has been achieved successfully and can be maintained through supportive periodontal therapy.

One of the most common dentoalveolar consequences of periodontitis in molar teeth is the involvement of the furcation of the infected tooth. The therapy of furcation defects has always been a challenge and different therapies have been proposed according to the anatomical situation, the degree of furcation involvement as well as other local and systemic factors [15]. In general, 2 significantly different treatment approaches should be distinguished, a resective or a regenerative approach.

In the following, the treatment objective was to achieve complete recovery of periodontal tissue through periodontal regeneration. Periodontal regeneration can be achieved by guided tissue regeneration (GTR), a periodontal surgical procedure that aims at the formation of new alveolar bone and new connective tissue attachment, functionally oriented on the newly formed cementum [3]. Regeneration of the involved furcation depends also on anatomic factors. The location of the furcation entrance has a great impact on a positive outcome of the procedure. A furcation entrance being located relatively far subgingivally due to a high root trunk increases the chances of success compared to a more coronally located furcation entrance, due to a low root trunk. Furthermore, the root divergence also plays a role. If the roots are relatively far apart, they can be cleaned more sufficiently due to a better access and therefore the prognosis for a more successful outcome of the regenerative procedure is better compared to a narrow root divergence [28]. It should also be noted that the vitality of the tooth must be evaluated initially. A non-vital tooth can be maintained through an endodontic treatment and could also be treated regeneratively, but a non-vital tooth that lacks endodontic treatment must not be treated with regenerative therapy [51].

Different techniques and materials have been described in the literature to achieve this goal [17]. In order to enhance the results of the treatment and restore periodontal new attachment with bone reconstruction, combined techniques have been advocated. The use of grafting materials with or without barrier membranes and osteopromotive agents, like enamel matrix derivates (Emdogain, Straumann AG, Basel, Switzerland), has been proposed to increase the percentage of cases with successful new attachment and periodontal reconstruction [7, 30, 42]. Emdogain is a mixture of enamel matrix derivatives (EMD) that contributes to periodontal ligament cells regeneration in a process mimicking natural root development [37]. Plasma rich in growth factors (PRGF, Biotechnology Institute [BTI], Vittoria, Spain) seems to be one of the most promising and novel methods used for tissue repair and regeneration [4]. The application of PRGF-Endoret technology provides proteins and growth factors that activate and accelerate the regeneration process. It is also capable of stimulating bone tissue regeneration by enhancing osteoblast proliferation, migration, chemotaxis, and the expression of a wide range of pivotal molecules involved in tissue regeneration [60]. Moreover, PRGF-Endoret provides a three-dimensional, biocompatible and biodegradable fibrin scaffold that retains and later releases growth factors; furthermore it also acts as a temporal nesting scaffold for the cells [6]. In this procedure the white blood cells are excluded so that proinflammatory activity which may act as a negative factor for tissue regeneration is also removed [43].

Although in theory this process appears straightforward, the implementation into daily practice is complicated and dependent on the respective practical skills of the periodontist. If dysfunctional cofactors



**Figure 5 A** Periodontal probing at the distal aspect of tooth #47 (case 2); **B** Periodontal probing at the mid-buccal furcation aspect of tooth #47 (case 2).

are involved the professional interaction with the referring dentist or a specialist in the diagnosis and treatment of craniomanidublar dysfunction (CMD) may be helpful [24].

The aim of this publication is to present 2 cases of localised periodontitis with mandibular furcation lesions grade II which were treated using allograft bone, bio-resorbable pericardium membrane (Jason Membrane, Botiss Company, Berlin, Germany) and Emdogain following the concept of guided tissue regeneration. In both cases the co-factor of localized occlusal trauma had to be controlled before the initiation of regenerative periodontal therapy. The case reports are followed by a literature review including the application of regenerative procedures in periodontics.

### **Case Reports**

Both cases presented in this article were treated in a private practice limited to Periodontology and Implant Dentistry by the same clinician (Dr. Ö. S., FPI-Hamburg, Germany). Both patients were referred to this office for the treatment of advanced periodontal disease. They were in good general health and indicated on the medical history forms not to smoke cigarettes and not to suffer from any other diseases and not to take any



**Figure 6 A** Intraoperative view following flap reflection and removal of the granulation tissue at tooth #37 (case 1); **B** Intraoperative view following application of EMD and the bone allograft material at tooth #37 (case 1); **C** Intraoperative view following primary wound closure using a circumferential suture (case 1).

medications. According to the new classification of periodontal diseases both patients presented with a stage III disease due to their furcation grade II defects, PPD exceeding 5 mm and the potential of tooth loss. Furthermore, they presented with a fast progression rate on the molar teeth with furcation grade II involvement due to the local cofactor of occlusal trauma, which resulted in a grading of III. The individual caries risk was low for case 1 and medium for case 2. Any operative, restaurative, or endodontic dental treatment was carried out by the referring dental offices.

Informed consent was obtained from patients prior to periodontal therapy. The initial treatment consisted of professional teeth cleaning with further oral hygiene instructions and aids for interproximal cleaning. The plaque index (PI) was monitored and recorded and periodontal treatment was initiated when the PI was below 10 %, indicating an efficient oral hygiene. Systematic periodontitis treatment including deep scaling and root planning was performed following the modified concept of full-mouth-disinfection. Sixteen weeks later the clinical situation was re-evaluated, and the patients were informed about the option of subsequent regenerative periodontal therapy. Except the co-factor of occlusal trauma the teeth scheduled for treatment were vital and no caries or other limiting factors like insufficient margins were detectable.

### Case 1

A 40-year-old healthy female presented in 2010 for treatment of localized advanced periodontitis.

The general (BOP) was at 9 % and most of the bleeding was provoked around the tooth scheduled for regenerative treatment. The PI was reduced to 8 %, which indicates efficiency of plaque control performed by the patient. Nevertheless, the initial examination of tooth 37 revealed a pocket probing depth (PD) of 8 mm and bleeding on probing on all the sites, except mid-buccal (Figure 1). On the obtained periapical radiograph, the furcation involvement with interradicular bone destruction is clearly visible (Fig. 2).

Diagnosis regarding occlusal trauma determined an occlusal dysfunction as a co-factor for the aetiology of this periodontal defect. Therefore, prior to periodontal treatment the referring dentist was asked to eliminate the overloading on the respective teeth from the suspected sleep bruxism habit by means of a night guard. This was followed by a final re-evaluation, which should be the basis for the later following regenerative periodontal procedure.

### Case 2

A healthy male patient, 56 years of age at the onset of treatment, was referred by a general practitioner to us in 2013 for treatment of advanced periodontal disease. The periodontal status is illustrated in Figure 3. Several advanced periodontal defects were detected throughout the patient's dentition, that were scheduled for non-surgical periodontal treatment. Suppuration was recorded at tooth #47. An advanced periodontal defect is visible on the radiograph indicating the influence of occlusal trauma as a cofactor by means of widened periodontal ligament spaces surrounding the mesial and distal roots of tooth #47 as well as at the distal root and the interradicular area of tooth #46. Additionally, a very mild vertical bony defect was visible at the distal aspect of tooth #46 as well as significant subgingival calculus. Gutta-percha points were inserted into the pocket before a periapical radiograph was taken. The distally inserted gutta-percha point shows the circumferential infrabony defect (Figure 4), the 6-point pocket depths measurements (Figure 5) indicated pocket depths of up to 12 mm and a vertical component of 6 mm (subgroup B), according to the classification of Tarnow and Fletcher [55] as well as a BOP of 33 %. Furthermore, the tooth #47 showed degree 1 mobility as well an enamel crack in occluso-gingival direction (type II) [53], which could also be interpreted as a result of occlusal trauma.

In interdisciplinary cooperation with the specialist for diagnosis



**Figure 7 A** Intraoperative view following flap reflection and removal of the granulation tissue at tooth #47 (case 2); **B** Intraoperative view following application of EMD and the bone allograft material at tooth #47 (case 2); **C** Intraoperative view following positioning of the pericardium membrane at tooth #47 (case 2); **D** Intraoperative view showing the autogenous fibrin membrane before application at tooth #47 (case 2); **E** Intraoperative view showing the autogenous fibrin membrane positioned on top of the pericardium membrane at tooth #47 (case 2); **F** Intraoperative view following primary wound closure using a circumferential suture (case 2).

and treatment of craniomandibular dysfunction (Priv.-Doz. Dr. M. O. A., CMD-Centrum Hamburg-Eppendorf), the patient received functional therapy involving occlusal adjustments aimed at the elimination of occlusal trauma as well as wearing an occlusal splint beforehand. The occlusal splint was constructed following the concept by Ramfjord using a maxillary ("Michigan") splint [49]. This maxillary occlusal stabilization splint covers all teeth, features a cuspid rise and freedom in centric in an area of 0.5-1.0 mm on the splint's occlusal plane [8]. In this bite plane, centric relation represents the therapeutic position that stabilizes the mandible in occlusal relations. Increasing the vertical dimension that is achieved by occlusal part results in relaxation of masticatory muscles.

## **Materials and Methods**

#### Materials

The surgical procedure followed the manufacturer's protocol in a step-bystep approach: Removal of the granulation tissue adhering to the infected root surface, smoothing of the root surface, application of EDTA Prefgel (Straumann AG, Basel, Switzerland) and subsequent rinsing with sterile saline was followed by the application of the EMD.

For the optimal precipitation of the enamel matrix proteins on the root surface, EMD was applied immediately after preparation with Pref-Gel and the root surface was free from blood and saliva.

Thirty-six ml venous blood was collected from the patients prior to surgery in 4 tubes each containing 0.5 cc concentrate of sodium citrate 3.8 % as anti-coagulant and centrifuged according to the manufacturer's specifications (Biotechnology Institute, Vitoria, Spain). After centrifugation, regularly the following layers are obtained:

- the yellowish top layer the plasma;
- the leukocyte layer or "buffy coat" below the plasma layer, about 5 mm in thickness;
- the bottom layer, which contains the red cells.

The plasma, in turn, is divided in 2 different fractions, which are characterized by different concentration of platelets:

- a bottom fraction, "fraction-2", which covers a layer of 2 ml thickness above the leukocyte layer or "buffy coat"; this fraction contains 2 to 3 times more platelets compared with the blood;
- the superficial fraction-1 (above the fraction-2) contains a similar number of platelets as the peripheral blood. This fraction forms a gelatinous fibrin membrane after activation with 10 % calciumchloride in a ratio of 1:2.

After it's formation the fibrin membrane was placed under the grid of the compression box and gently compressed with the lid of the box in order to obtain a standardized thickness. Puros allograft (Zimmer Dental GmbH, Munich, Germany) was first rehydrated in sterile saline solution and then immersed in the fraction-2 of the PRGF system. The tissue was first covered with a pericardium membrane and then covered with a PRGF fibrin membrane.

### **Surgical protocol**

Following the administration of local anaesthesia (Ultracain D-S forte 1:100.000, Sanofi-Aventis Deutschland GmbH, Frankfurt, Germany an intrasulcular incision was made and mucoperiosteal flaps were raised.

Cleaning, removal of the granulation tissue and smoothing of the root surface, especially in the furcation area was carried out with ultrasound hand instruments, fine rotating diamond instruments and a Piezosurgery device. The situation was precisely re-evaluated intraoperatively in order to rule out a grade III furcation defect, as regenerative treatment would not have been performed in the presence of a grade III furcation lesion. The finding of grade II furcation defects confirmed the evaluation of the diagnostic X-ray. The root surface was then conditioned with PrefGel and after 2 minutes, it was rinsed with a sterile saline solution and EMD was applied. Puros allograft was firstly rehydrated with normal saline and consecutively mixed with the fraction-2 containing platelet concentrate and then placed on the defect site.

In order to achieve accelerated wound healing, the Puros allograft was used in combination with the PRGF-Endoret fibrin membrane. The graft material was compacted into the infrabony defect, compressing against the surrounding bone, layer by layer, until the furcation defect was filled. The pericardium membrane was used to cover the bone graft and then the fibrin membrane, obtained from the fraction-1 of the PRGF system was used to cover the pericardium membrane before primary closure was achieved. The surgical procedures are illustrated in Figures 6 and 7.

Wound closure was performed by tension-free primary closure using non-resorbable PTFE sutures (Goretex company, Flagstaff, Arizona, USA). After the tissues were sutured, the incision line was inspected for any open areas or particles.

#### **Postoperative care**

The patients received postoperative instructions including rinsing with 0.2 % chlorhexidine (Glaxo Smith Kline, Brentford, UK) 3 times daily for 2 weeks as well as amoxicillin 1 g (3 times daily) for 1 week and ibuprofen 600 mg as needed [26]. They were advised to avoid brushing the area up to 2 weeks after surgery. The sutures were removed after 14 days. At follow-up appointments 2 months after the surgery the wound healing was monitored. For a period of 1 year after the regenerative treatment no subgingival debridement or probing was performed.

Supportive periodontal therapy was carried out regularly after the

treatment. Patients were advised to have their routine supportive periodontal care every 3 months by their general dentist – without any subgingival intervention. Additionally, the patients were seen in the periodontal practice for annual recall appointments in order to re-evaluate the treatment outcomes.

#### Results

After 12 months, 6-point pocket chart measurements demonstrated distinctive clinical improvements. Furthermore, patients were placed in an alternating 3-month recall during supportive periodontal therapy (SPT) and clinically and radiologically evaluated at 1 year, 3 years, and 5 years postoperatively. The results during 8-years of SPT in case 1 and 5 years of SPT in case 2 are presented in the following section.

### Case 1

During the follow-up period of 8 years there were no signs for inflammation detectable and the periodontal tissues appeared healthy (Figure 8). Radiographic examination 8 years after the surgery revealed almost 100 % defect fill; no furcation involvement was radiographically visible or clinically detectable (Figure 9). A significant reduction of the PPD from 8 mm initially to a maximum of 3 mm 1 year after the regenerative treatment was observed and this clinical condition remained stable without bleeding on probing throughout the subsequent follow-up period of 8 years (Figure 10). The occlusal condition was evaluated on a regular basis and the night guard was worn regularly by the patient and adjusted in order to ensure the elimination of dynamic interferences on the splint in the premolar- and molar-region while maintining equilibrated static occlusal contacts.

### Case 2

Five years after the regenerative surgery on tooth #47, probing pocket depths were recorded indicating probing depths ranging from 2 to 5 mm without any signs of gingival inflammation. In comparison, the initial PPD of 12 mm on deepest pocket before surgery and a residual

probing depth of 3 mm at the same location on the tooth 5 years after the procedure demonstrates a 9 mm gain in clinical attachment level and no furcation involvement or mobility was observed. Radiographic evaluation obtained 5 years after therapy showed an almost complete defect fill and an increased radiopacity in the furcation area, compared to the situation at baseline (Figures 11-12). Furthermore, the non-surgically treated molar teeth #26, #27 and #36, #37 presented without inflammation and increased PPD throughout the follow-up period, tooth #38 unfortunately developed an advanced periodontal pocket at the mesial aspect and will be scheduled for treatment in the near future. As described in the case 1 the occlusal situation of the teeth was evaluated annually as was the occlusion on the occlusal splint. The splint was worn by the patient every night.

# Discussion

### **Occlusal Trauma**

In the present case report, the combined regenerative therapy with GTR, allograft bone substitute and the application of EMD, a pericardium membrane, and PRGF is presented in 2 patients who suffered from severe localised periodontitis. Both patients were treated by the same periodontist and were followed up for 8 and 5 years, respectively.

The initial assessment of the general periodontal condition of the 2 patients presented in this report confirmed that at the beginning of the therapy both patients suffered from dental trauma from occlusion. The role of trauma from occlusion in periodontal diseases has been debated controversially in periodontal literature.

The evaluation of records from a private practice limited to periodontics strongly suggest an association between initial occlusal discrepancies and various clinical parameters indicative of periodontal disease [44]. In another study by the same authors, teeth with multiple types of occlusal contacts had shown significantly deeper initial probing depths and poorer prognosis compared to



Figure 8 Clinical view of tooth #37 after 8 years postoperatively.



Figure 9 Radiographic evaluation of tooth #37 after 8 years postoperatively.

teeth without occlusal discrepancies [29]. The results of a study, performed on a group of 31 individuals in Japan, suggested that involuntary masseter muscle activity caused by bruxism might be related to the severity of periodontitis [35]. Statistically significant correlations were found in between the total amount of secondary occlusal trauma per patient and the severity of periodontitis and attachment loss in a study with 288 cases [10].

A cross sectional study on 2,980 subjects has shown the association of non-working side contact

with deeper probing depth and more clinical attachment loss [9]. Recently, it has been demonstrated that traumatic occlusion can aggravate the symptoms of periodontitis [46]. According to Ramfjord and Ash, occlusal therapy may be required to enhance occlusal stability at any stage of periodontitis but is most often necessary in advanced periodontitis [48]. A literature review has concluded that untreated occlusal discrepancies can exacerbate periodontal disease; therefore, occlusal therapy should be an integral part of the periodontal treatment [40]. It has



also been stated that clinician's decision, whether or not to use occlusal adjustment as a component of periodontal therapy should be related to an evaluation of clinical factors involving patient comfort and function [50]. Burgett et al. evaluated the effect of occlusal adjustment combined with periodontal treatment on the level of connective tissue attachment, the depth of gingival pockets and tooth mobility [11]. The results of this study indicated a greater gain of attachment level when occlusal adjustments have been performed in the treatment of periodontitis. McGuire et al. postulated that patients are twice as likely to loose their teeth if there is increasing mobility, if they have a parafunctional habit and do not wear a bite guard [39]. The results of a 10- to 18-year follow up study in patients suffering from chronic generalized moderate to severe periodontitis revealed that patients affected with bruxism who did not wear a splint had an inferior periodontal prognosis compared to those who did wear a splint [45]. The results of a literature review performed by Sutthiboonyapan and Wang indicated that an occlusal splint appears to be a useful device to treat patients with parafunctional habit related symptoms and dentists should consider recommending occlusal splints as part of the comprehensive dental care for patients with bruxism [54]. In a recent narrative review Fan and Caton evaluated the

role of occlusal trauma and excessive occlusal forces and postulated that in animal and human studies some associations between occlusal trauma and occlusal discrepancies and the progression of periodontal disease exists. Therefore, occlusal trauma seems to be a very important potential co-factor for the progression of periodontal diseases and should be identified and controlled throughout interdisciplinary therapy [18]. Furthermore, the new classification of periodontal diseases also identifies occlusal trauma as an important factor for modifying the risk of disease progression (grading) [57].

According to these expert opinions and outcomes of scientific literature patients suffering from periodontal disease should be regularly screened for bruxism. The new Bruxism-Screening-Index of the German Society of Craniomandibular Function and Disorders in the DGZMK (www.DGFDT.de) was introduced recently in order to facilitate a simplified identification of the respective patients.<sup>1</sup>

Furthermore, in the light of the cited literature it appears reasonable to specifically check for occlusal trauma prior to periodontal therapy as described in this paper and – if applicable – to perform occlusal therapy before the initiation of periodontal regenerative procedures.

Guided Tissue Regeneration in advanced periodontal

# defects and mandibular class II furcation defects

In the present case reports we applied a combination of allograft bone substitute, EMD, a pericardium membrane, and PRGF for the regenerative therapy of advanced localized periodontal mandibular class II defects using the technique of GTR. As mentioned before, both patients were treated by the same periodontist and were followed up for 8 and 5 years, respectively.

The role of trauma from occlusion in periodontal diseases has been controversially discussed in the first part of the discussion. The following part of the discussion will discuss the rational and the evidence for the use of the before mentioned materials.

# The use of GTR combined with osseous grafts in mandibular class II furcation defects

Different therapeutic modalities have been proposed in guided tissue regeneration in order to achieve the regeneration of periodontal tissues. Among these, the use of different bone grafting materials, barrier membranes, enamel matrix derivates and growth factors has been described and investigated in the literature.

The effects of GTR combined with osseous grafts and GTR alone in the treatment of class II furcation defects was investigated in a metaanalysis of 20 randomized con-

<sup>&</sup>lt;sup>1</sup> Bruxismus-Screening-Index: https://www.dgfdt.de/documents/266840/3732097/Bruxismus-Screening+DGFDT/f52a44c1-6b03-4b7b-8dd0-c301be890e08

trolled clinical trials [14]. According to this investigation, in GTR combined with osseous grafts the closure rate of the furcation, the attachment level gain and the bone fill (vertical/ horizontal) were higher compared to conventional open flap debridement procedure and GTR alone [14]. The combination of resorbable membranes and bone replacement materials can improve the chances of recovery, although so far limited human clinical trials are available [51].

The use of allogeneic bone grafts with a resorbable pericardium membrane as described in the present case reports facilitated new bone formation by inhibiting connective tissue invasion as well as epithelial downgrowth [1]. There are many types of allografts available that are suitable to use in different types of defect. Puros allograft is available as particulate grafts or as a bone block. The allogeneic material offers a combination of preserved natural collagen, mineral crystals, and structural bony architecture that is percieved to be optimal. Furthermore, the material is produced through the validated Tutoplast Refinement Process [52].

This graft cleaning and preservation process includes a solvent dehydration that virtually eliminates the possibility of disease transmission and removes unwanted materials while preserving the natural collagen matrix. The Tutoplast process is well established after 40 years of experience. The manufacturer states the application in more than 5 million procedures. The matrix of puros aims to facilitate the regeneration and bone formation in greater quantities. Histological examinations in the sinus lift or the extraction sockets have shown that the material indeed is mostly converted into vital, endogenous bone within 4 to 7 months, resulting in a bone density similar to that of the original bone. Histomorphometric host evaluation of the bone has indicated between 5 % and 8 % residual content of augmentation material, which further demonstrates the resorption of this bone grafting material during healing [11, 39, 45].



Figure 11 Radiographic evaluation of tooth #47 after 5 years postoperatively.

The high volume stability of allograft bone can significantly reduce absorption of the buccal bone lamella in extraction sockets but it is not able to prevent it [19].

# The use of enamel matrix derivates (EMD)

For more than 2 decades, enamel matrix derivates have been used in the treatment of intrabony defects, furcation defects, and recession defects [38, 42]. The wound-healingpromoting effect of EMD and the lowering of systemic inflammatory factors have been investigated repeatedly [23, 61]. Recently, EMD has also been suggested as an adjunct to non-surgical periodontal treatment in deep inflamed periodontal pockets of 5–9 mm depth [2]. A large number of studies indicate that EMD may have the potential to trigger regenerative responses in periodontal ligament cells [31, 37].

# The use of enamel matrix derivates (EMD) combined with GTR in the treatment of mandibular furcation grade II defects

Clinical success in using GTR without EMD or in combination with EMD also depends on cofactors such as smoking, age, oral hygiene status. In a study from Dresden it was shown in 51 patients that the use of EMD led to a significant reduction of the inflamed gingival pocket depth, as compared to the exclusive GTR treatment alone [30]. The use of EMD with GTR for the treatment of mandibular molar grade II furcation defects has shown clinical improvements. In a 24-month prospective clinical study, however, a significant reduction in proximal furcation defects was found in a test group of 12 patients [13]. Nevertheless, a complete regeneration of the defect cannot always be expected.

## The use of enamel matrix derivates (EMD) combined with osseous grafts in mandibular furcation class II defects

Outcomes of regenerative periodontal surgery using a combination of an EMD and autogenous bone has shown higher soft and hard tissue improvements compared to the treatment with EMD alone [63]. The use of bovine-derived xenograft with EMD has shown to be effective in enhancing new bone and cementum formation in the treatment of intrabony defects [62]. In another study, EMD in combination with a bone



Figure 12 Periodontal measurement at 5 years postoperatively (case 2).

substitute graft has shown to improve the treatment of class II furcation defects in 41 patients, but with no significant improvement compared to bone substitute graft alone [47]. According to yet another study, EMD either alone or in combination with grafts can be effectively used to treat intra-osseous defects and the additional use of a graft seems to enhance the clinical outcomes [58].

# The use of enamel matrix derivates (EMD) combined with GTR and osseous grafts

The synergistic effects of using a resorbable membrane with an allograft bone substitute material as well as EMD were demonstrated in a case-control study performed on 30 patients with chronic periodontitis. It was shown that the combination of EMD and allograft and barrier membranes could significantly reduce the pocket depth as well as the vertical attachment level – compared to the treatment with allograft and barrier membranes alone [32].

# The use of platelet-rich-growth factors (PRGF)

Furthermore, platelet-rich-growth factors (PRGF) have been used to facilitate bone and tissue healing. It specifically stimulate angiogenesis and proliferation and migration of osteoblasts [6]. According to Döri et al., the use of PRGF enables the stimulation, the proliferation and the differentiation of periodontal ligament cells and osteoblasts [16]. Fibrin matrix releases growth factors and acts as a temporal nesting scaffold for the cells [5].

# The use of GTR and plateletrich-growth factors (PRGF)

A higher improvement trend was seen in grade II furcation lesions that were treated with PRGF/GTR compared to GTR alone [33] and fibrin membrane has shown to have the potential of improving GTR results in the management of intrabony defects [36]. The PRGF-Endoret technology was implicated with inorganic bone substituents in lateral sinus lift procedures and it has shown to increase the healing process and help to obtain a more reliable bone regeneration and also higher quality of bone [12].

In summery, the literature indicates that the combination of the EMD with the technique of Guided Tissue regeneration and osseous grafts with the application of plateletrich-growth factors (PRGF) may be superior to the application of individual materials and techniques and bears a synergistic effect in the regenerative treatment of furcation defects. The 2 case reports presented in this publication illustrate the practical procedures and the potential of this technique.

### Conclusion

Choosing the most suitable regenerative procedure is based on general and site specific conditions. Accurate assessment of the periodontal defect, appropriate selection of the therapeutic approach, management and long-term retention of teeth with periodontal defects, depends not only on the operator's skill and experience but also on the selection of the suitable regenerative materials and techniques. Osseous defect characteristics, the degree of furcation involvement and the tooth's endodontic status significantly influences the therapeutic success. Moreover, teeth that are treated as intensely as demonstrated in this report should be relieved from occlusal trauma in order to optimize the condition for successful regeneration.

Furthermore, the cost-benefit ratio for this treatment approach should be discussed with the patient beforehand. The scientific literature provides evidence for long-term stability of successfully periodontally regenerated teeth. This approach is much less invasive than for example the treatment option of a 3 unit bridge and has a superior long-term prognosis if good supportive periodontal care is provided. However, the treatment option with a dental implant needs also be addressed in the decision making process. The longterm prognosis of a dental implant is comparable to a periodontally regenerated tooth. The costs involved for the placement of a dental implant is at least in Germany much higher than for periodontal regeneration of a single tooth and exceeds including the prosthodontic rehabilitation at least 2.5 times the amount for regeneration. Furthermore, the treatment time and the number of surgical interventions is much higher for implant restaurations than for tooth maintenance.

In conclusion, it can be stated that the combination of allogeneic cancellous bone substitute, EMD, PRGF, fibrin membrane and a resorbable pericardium barrier membrane promises good clinical results in the regenerative treatment of furcation degree II defects in mandibular molars. Furthermore, teeth that are treated as intensely as demonstrated in this report should be relieved from occlusal trauma in order to optimize the condition for successful regeneration.

# **Conflicts of interest**

The authors declare that there is no conflict of interest within the meaning of the guidelines of the International Committee of Medical Journal Editors.

### References

1. Ahn YS, Kim SG, Kim CS, Oh JS, Lim SC: Effect of guided bone regeneration with or without pericardium bioabsorbable membrane on bone formation. Oral Surg Oral Med Oral Pathol Oral Radiol 2012; 114: 126–131

2. Aimetti M, Ferrarotti F, Mariani GM, Romano F: A novel flapless approach versus minimally invasive surgery in periodontal regeneration with enamel matrix derivative proteins: a 24-month randomized controlled clinical trial. Clin Oral Investig 2017; 21: 327–337

3. Alpiste Illueca FM, Buitrago Vera P, de Grado Cabanilles P, Fuenmayour Fernandez V, Gil Loscos FJ: Periodontal regeneration in clinical practice. Med Oral Patol Oral Cir Bucal 2006; 11: E382–392

4. Anitua E: The use of plasma-rich growth factors (PRGF) in oral surgery. Pract Proced Aesthet Dent 2001; 13: 487–493

5. Anitua E, Alkhraisat MH, Orive G: Perspectives and challenges in regenerative medicine using plasma rich in growth factors. J Control Release 2012; 157: 29–38

6. Anitua E, Tejero R, Zalduendo MM, Orive G: Plasma rich in growth factors promotes bone tissue regeneration by stimulating proliferation, migration, and autocrine secretion in primary human osteoblasts. J Periodontol 2013; 84: 1180–1190

7. Ausenda F, Rasperini G, Acunzo R, Gorbunkova A, Pagni G: New perspectives in the use of biomaterials for periodontal regeneration. Materials (Basel) 2019; 12 (13). pii: E2197. doi: 10.3390/ma12132197

8. Badel T, Simonić-Kocijan S, Lajnert V Dulčić N, Zadravec D: Michigan splint and treatment of temporomandibular joint. Medicina Fluminesis 2013; 49; 112–120

9. Bernhardt O, Gesch D, Look JO The influence of dynamic occlusal interferences on probing depth and attachment level: results of the Study of Health in Pomerania (SHIP). J Periodontol 2006; 77: 506–516

10. Branschofsky M, Beikler T, Schäfer R, Fleming TF, Lang H: Secondary trauma from occlusion and periodontitis. Quintessence Int 2011; 42: 515–522

11. Burgett FG, Ramfjord SP, Nissle RR, Morrison EC, Charbeneau TD, Caffesse RG: A randomized trial of occlusal adjustment in the treatment of periodontitis patients. J Clin Periodontol 1992; 19: 381–387

12. Călin DL, Mitrea M, Rusu A: External sinus lift using the technology PRGF endoret: A case report. Rev Română Anat funcțională și Clin macro- și Microsc și Antropol 2017; XVI: 80–86

13. Casarin RCV, Ribeiro EP, Nociti FH et al.: Enamel matrix derivative proteins for the treatment of proximal class II furcation involvements: A prospective 24-month randomized clinical trial. J Clin Periodontol 2010; 37: 1100–1109

14. Chen TH, Tu YK, Yen CC, Lu HK: A systematic review and meta-analysis of guided tissue regeneration/osseous grafting for the treatment of Class II furcation defects. J Dent Sci 2013; 8: 209–224

15. Chowdhary Z, Mohan R: Furcation involvement: Still a dilemma. Indian J Multidiscip Dent 2017; 7: 34–40

16. Döri F, Huszár T, Nikolidakis D et al.: Effect of platelet-rich plasma on the healing of intrabony defects treated with Beta tricalcium phosphate and expanded polytetrafluoroethylene membranes. J Periodontol 2008; 79: 660–669

17. Eickholz P, Pretzl B, Holle R Kim TS: Long-term results of guided tissue regeneration therapy with non-resorbable and bioabsorbable barriers. III. Class II furcations after 10 years. J Periodontol 2006; 77: 88–94

18. Fan J; Caton JG: Occlusal trauma and excessive occlusal forces: Narrative review, case definitions, and diagnostic considerations. JClin Perio 2018; 45 (Suppl 20): S199–206 19. Fotek PD, Neiva RF, Wang HL: Comparison of dermal matrix and polytetrafluoroethylene membrane for socket bone augmentation: a clinical and histologic study. J Periodontol 2009; 80: 776–785

20. Froum SJ, Wallace SS, Elian N, Cho SC, Tarnow DP: Comparison of mineralized cancellous bone allograft (Puros) and anorganic bovine bone matrix (Bio-Oss) for sinus augmentation: histomorphometry at 26 to 32 weeks after grafting. Int J Periodontics Restorative Dent 2006; 26: 543–551

21. Gapski R, Neiva R, Oh T-J, Wang HL: Histologic analyses of human mineralized bone grafting material in sinus elevation procedures: a case series. Int J Periodontics Restorative Dent 2006; 26: 59–69

22. Gaudilliere DK, Culos A, Djebali K et al.: Systemic immunologic consequences of chronic periodontitis. J Dent Res 2019; 98: 985–993

23. Gennai S, Petrini M, Tonelli M, Marianelli A, Nisi M; Graziani F: PD065: Acute phase response following non-surgical periodontal therapy with enamel matrix derivative. A randomized clinical trial. J Clin Periodontol 2018. doi.org/ 10.1111/jcpe.66\_12914

24. Gher ME: Changing concepts. The effects of occlusion on periodontitis. Dent Clin North Am 1998; 42: 285–299

25. Glickman I, Smulow JB: Effect of excessive occlusal forces upon the pathway of gingigval inflammation in humans. J Periodontol 1965; 36: 141–147

26. Goodson JM, Haffajee AD, Socransky SS et al: Control of periodontal infections: A randomized controlled trial I. The primary outcome attachment gain and pocket depth reduction at treated sites. J Clin Periodontol 2012; 39: 526–536

27. Graves D: Cytokines that promote periodontal tissue destruction. J Periodontol 2008; 79 (8 Suppl): 1585–1591

28. Hamp SE, Nyman S LJ: Periodontal treatment of multirooted teeth. Results after 5 years. J Clin Periodontol 1975; 2: 126–135

29. Harrel SK, Nunn ME: The association of occlusal contacts with the presence of increased periodontal probing depth. J Clin Periodontol 2009; 36: 1035–1042

30. Hoffmann T, Richter S, Meyle J et al: A randomized clinical multicentre trial comparing enamel matrix derivative and membrane treatment of buccal class II furcation involvement in mandibular molars. Part III: Patient factors and treatment outcome. J Clin Periodontol 2006; 33: 575–583

31. Iviglia G, Kargozar S, Baino F: Biomaterials, current strategies, and novel nano-technological approaches for periodontal regeneration. J Funct Biomater 2019; 10(1). pii: E3. doi: 10.3390/jfb10010003.

32. Jaiswal R, Deo V: Valuation of the effectiveness of enamel matrix derivative, bone grafts, and membrane in the treatment of mandibular Class II furcation defects. Int J Periodontics Restor Dent 2013; 33: e58–64

33. Jenabian N, Haghanifar S, Ehsani H, Zahedi E, Haghpanah M: Guided tissue regeneration and platelet rich growth factor for the treatment of Grade II furcation defects: A randomized doubleblinded clinical trial – A pilot study. Dent Res J (Isfahan); 2017; 14: 363–369

34. Jordan AR, Micheelis W: Fünfte Deutsche Mundgesundheitsstudie (DMS V) Deutscher Zahnärzteverlag, Köln 2016

35. Kato S, Ekuni D, Kawakami S, Mude HM, Morita M, Minagi S: Relationship between severity of periodontitis and masseter muscle activity during waking and sleeping hours. Arch Oral Biol 2018; 90: 13–18

36. Lei L, Yu Y, Han J et al.: Quantification of growth factors in advanced plateletrich fibrin and concentrated growth factors and their clinical efficiency as adjunctive to the GTR procedure in periodontal intrabony defects. J Periodontol 2020; 91: 462–472

37. Lyngstadaas SP, Lundberg E, Ekdahl H, Andersson C, Gestrelius S: Autocrine growth factors in human periodontal ligament cells cultured on enamel matrix derivative. J Clin Periodontol 2001; 28: 181–188

38. Masaeli R, Zandsalimi K, Lotfi Z, Tayebi L: Using enamel matrix derivative to improve treatment efficacy in periodontal furcation defects. J Prosthodont 2018; 27: 733–736

39. McGuire MK, Nunn ME: Prognosis versus actual outcome. III. The effectiveness of clinical parameters in accurately predicting tooth survival. J Periodontol 1996; 67: 666–674

40. Meredyk K, Kostrzewa-Janicka J, Nędzi-Góra M: The effect of occlusal loading on the periodontal tissues. A literature review. Part I – Occlusion and periodontitis. Dent Med Probl 2015; 52: 215–221

41. Micheelis W: Deutsche Mundgesundheitsstudie – DMS IV – ein kurzer Überblick. Deutscher Zahnärzte Verlag, Köln 2006, S. 1–10

42. Miron RJ, Sculean A, Cochran DL et al.: Twenty years of enamel matrix derivative: the past, the present and the future. J Clin Periodontol 2016; 43: 668–683 43. Nishiyama K, Okudera T, Watanabe T et al.: Basic characteristics of plasma rich in growth factors (PRGF): blood cell components and biological effects. Clin Exp Dent Res 2016; 2: 96–103

44. Nunn ME, Harrel SK: The effect of occlusal discrepancies on periodontitis. I. Relationship of initial occlusal discrepancies to initial clinical parameters. J Periodontol 2001; 72: 485–494

45. Nunn ME, Fan J, Su X, Levine RA, Lee HF, McGuire MK: Development of prognostic indicators using classification and regression trees for survival. Periodontol 2000 2012; 58: 134–142

46. Pan W, Yang L, Li J et al.: Traumatic occlusion aggravates bone loss during periodontitis and activates Hippo-YAP pathway. J Clin Periodontol 2019: 46: 438–447

47. Queiro LA, Santamari MP, Casati MZ, et al.: Enamel matrix protein derivative and/or synthetic bone substitute for the treatment of mandibular class II buccal furcation defects. A 12-month randomized clinical trial. Clin Oral Investig 2016; 20: 1597–1606

48. Ramfjord SP, Ash MM: Significance of occlusion in the etiology and treatment of early, moderate and advanced periodontitis. J Periodontol 1981; 52: 511–517

49. Ramfjord SP, ASH MM: Reflections on the Michigan occlusal splint. J Oral Rehabil 1994; 21: 491–500

50. Sanadi DRM, Chelani DLR, Bhakkand DSR, Sheth DJK: Role of trauma from occlusion in periodontal disease – A controversy. IOSR J Dent Med Sci 2016; 15: 118–122

51. Sanz M, Jepsen K, Eickholz P, Jepsen S: Clinical concepts for regenerative therapy in furcations. Periodontol 2000 2015; 68: 308–332

52. Schoepf C: The Tutoplast<sup>®</sup> process: A review of cfficacy. Int Mag Oral Implantol 2006; 1: 10–15

53. Segarra MS, Shimada Y, Sadr A, Sumi Y, Tagami J: Three-dimensional analysis of enamel crack behavior using optical coherence tomography. J Dent Res 2017; 96: 308–314

54. Sutthiboonyapan P, Wang HL: Occlusal splints and periodontal/implant therapy. J Int Acad Periodontol 2019; 31: 45–50

55. Tarnow D, Fletcher P: Classification of the vertical component of furcation involvement. J Periodontol 1984; 55: 283–284

56. Tonetti MS, Jepsen S, Jin L, Otomo-Corgel J: Impact of the global burden of periodontal diseases on health, nutrition and wellbeing of mankind: A call for global action. J Clin Periodontol 2017; 44: 456–462

57. Tonetti MS, Greenwell H; Kornman KS: Staging and grading of periodontitis: Framework and proposal of a new classification and case definition. J Clin Periodontol 2018; 45 (Suppl 20): S149–161

58. Trombelli L, Farina R: Clinical outcomes with bioactive agents alone or in combination with grafting or guided tissue regeneration. J Clin Periodontol 2008; 35: 117–135

59. Waerhaug J: The angular bone defect and its relationship to trauma from occlusion and downgrowth of subgingival plaque. J Clin Periodontol. 1979; 6: 61–82

60. Wang H-L, Pappert TD, Castelli WA, chiego DJ Jr., Shyr Y, Smith Ba: The effect of platelet-derived growth factor on the cellular response of the periodontium: an autoradiographic study on dogs. J Periodontol 1994; 65: 429–436

61. Wennström JL, Lindhe J: Some effects of enamel matrix proteins on wound healing in the dento-gingival region. J Clin Periodontol 2002; 29: 9–14

62. Yamamoto S, Masuda H, Shibukawa Y, Yamada S: Combination of bovinederived xenografts and enamel matrix derivative in the treatment of intrabony periodontal defects in dogs. Int J Periodontics Restorative Dent 2007; 27: 471–479

63. Yilmaz S, Cakar G, Yildirim B, Sculean A: Healing of two and three wall intrabony periodontal defects following treatment with an enamel matrix derivative combined with autogenous bone. J Clin Periodontol 2010; doi.org/10.1111/ j.1600–051X.2010.01567.x



(Photo: Önder Solakoglu)

ÖNDER SOLAKOGLU, DR. MED. DENT., MCD, MSC, DDS Prosthetic Department of the University Medical Center Hamburg-Eppendorf, Hamburg, Germany Martinistr. 52, 20251 Hamburg solakoglu@fpi-hamburg.de