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Surgical therapy of peri-implantitis with adjunctive hydroxyapatite and enamel matrix derivative

A one-year retrospective case series

KEYWORDS

Enamel derivative
Regenerative peri-implantitis therapy
GBR

SUMMARY

This case series retrospectively investigated the one-year surgical outcome of regenerative peri-implantitis therapy using a hydroxyapatite (HA) bone substitute material in combination with enamel matrix derivative (EMD) and collagen membrane for guided bone regeneration (GBR). Data-sheets of patients were screened to detect patients who received identical regenerative peri-implantitis therapy with surface decontamination and GBR applying HA, EMD and a collagen membrane under broad-spectrum antibiotic regime. For inclusion, information on pre- and postoperative clinical and radiographic parameters (probing pocket depth [PPD], bleeding on probing [BOP], suppuration [SUPP] and the radiological bone level [RBL]) had to be available for statistical analysis. Data of a total of 11 patients

(20 implants) were extracted out of 202 (336). All implants were still in function after one year. Bone defects decreased by an average of 1.3 mm mesially and 0.9 mm distally, respectively. Mean PPD was reduced from 4.9 mm to 2.7 mm. BOP decreased from 90% to 20%. SUPP decreased from 65% to 0%. Based on the success criteria applied, 15 of the 20 (75%) implants included were considered as successfully treated after one year. Regenerative peri-implantitis therapy according to the presented concept showed promising clinical and radiographic outcomes after one year. To estimate the beneficial effects of the combined use of HA, EMD and collagen membranes, further long-term investigations with a control group are needed.

Introduction

In implant dentistry, the majority of biological complications are caused by biofilm-related infectious inflammatory processes, leading to peri-implant diseases classified as peri-implant mucositis or peri-implantitis (BERGLUNDH ET AL. 2018). Peri-implant mucositis has been defined as an inflammatory process restricted to the peri-implant mucosa with clinical signs such as redness, swelling, bleeding on probing, suppuration and pathologic pocket formation (HEITZ-MAYFIELD & SALVI 2018).

Studies show that this condition is reversible and full restitution can be achieved by the removal of contributory (risk) factors and the introduction of adequate biofilm control (MEYER ET AL. 2017; SALVI ET AL. 2012).

When clinical signs are associated with progressive peri-implant bone loss, the disease is defined as peri-implantitis. Frequently detect morphology is characterized by crater-like defects (BERGLUNDH ET AL. 2018). Without treatment, bone loss continues, eventually leading to loss of osseointegration and ultimately implant failure. Depending on the case definition and the thresholds applied for probing pocket depth (PPD) and bone loss, the reported prevalence of peri-implantitis varies from 1% to 47% (DERKS & TOMASI 2015).

Similarities in bacterial etiology and host response have been documented between gingivitis and peri-implant mucositis as well as of periodontitis and peri-implantitis (BERGLUNDH ET AL. 2004; GUALINI & BERGLUNDH 2003). As a result of reduced vascularization and parallel orientation of the collagen fiber, peri-implant tissues are generally more prone to inflammatory breakdown than periodontal tissue (BELIBASAKIS 2014). Thus, peri-implantitis shows quicker progression with more pronounced bone loss than periodontitis (BERGLUNDH ET AL. 2011). Derks et al. claim that the majority of peri-implantitis cases progress in a non-linear accelerating pattern and are diagnosed within two to three years of function (DERKS ET AL. 2016). If assessed well, peri-implantitis can also be diagnosed before.

In view of the common features in the pathogenesis of peri-odontal and peri-implant diseases, similar diagnostic measures (gingival index, probing pocket depth, bleeding on probing) and treatment approaches (non-surgical, resective, regenerative) are used (RAMANAUSKAITE & JUODZBALYS 2016). The main goal of peri-implantitis treatment is to establish healthy peri-implant conditions, to eliminate all biofilm-retentive factors and to prevent any further disease progression (HEITZ-MAYFIELD & MOMBELLI 2014). While periodontitis treatment focuses on debridement of the contaminated root surface, peri-implantitis treatment concentrates on decontamination of the implant surface (KELEKIS-CHOLAKIS ET AL. 2018).

In an attempt to regain lost soft and hard tissues, several regenerative therapeutic approaches for guided tissue regeneration (GTR) and/or guided bone regeneration (GBR) with various materials are currently suggested (DAUGELA ET AL. 2016). While autogenous bone is described as the gold standard, allogenic, xenogenic and alloplastic materials are widely applied (JAMJOOM & COHEN 2015; THRIVIKRAMAN ET AL. 2017). Due to the limited availability of autogenous bone and the risk of disease transmissions of allografts and xenografts, there is an increasing interest in the use of alloplastic grafting materials (DEWI & ANA 2018).

Enamel matrix derivatives (EMD) have been successfully used in periodontology for over 20 years. EMD is able to induce proliferation of various cell types and cellular processes that are of critical importance to the healing of oral tissues (HOANG ET AL. 2000; MAYMON-GIL ET AL. 2016; ZELDICH ET AL. 2007A, 2007B). Re-

garding application of EMD to intraoral sites, several effects have been documented, including accelerated early wound closure (VILLA ET AL. 2015), soft tissue build-up (AL-HEZAIMI ET AL. 2012; TONETTI ET AL. 2004), significant improvement in keratinization (PILLONI ET AL. 2006; SHIN ET AL. 2007), decreased inflammation (OKUDA ET AL. 2001; VILLA ET AL. 2015), improved postsurgical re-vascularization (ASPRIELLO ET AL. 2011; GUIMARÃES ET AL. 2017) and antimicrobial and antiseptic effects (ARWEILER ET AL. 2002; WALTER ET AL. 2006). Similarities in pathogenesis and therapeutic goals between peri-implantitis and periodontitis prompted the application of EMD in peri-implantitis treatment (MERCADO ET AL. 2018; QU ET AL. 2011), on the assumption that EMD would also have beneficial effects in the regenerative treatment of peri-implantitis. Recently documented attempts at using EMD in the surgical treatment of peri-implantitis showed promising results (ISEHED ET AL. 2018).

The purpose of this study was to validate the surgical outcome of regenerative peri-implantitis therapy based on a GBR technique involving hydroxyapatite (HA) bone substitute material, EMD and a collagen membrane.

Materials and Methods

The study design was approved by the institutional review board (Northwest and Central Switzerland Ethics Committee [EKNZ], project ID 2017-02334).

Study population

Records of all patients who received regenerative peri-implantitis treatment at the department of Oral Surgery at the University Center of Dental Medicine (UZB) between 2000 and 2017 were retrospectively screened and analyzed with the aim to obtain a comparable protocol for regenerative peri-implantitis therapy (identical flap design, implant surface decontamination, applied substitute material, EMD and membrane for GBR and antibiotic use). Information on bleeding on probing (BOP), suppuration (SUPP) and probing pocket depth (PPD) scored on four sites per implant needed to be present.

The data of study individuals were included if they met the following criteria: (i) at least one implant with at least one PPD ≥ 6 mm in combination with BOP or SUPP and a marginal bone loss ≥ 3 mm identified on periapical radiographs, (ii) regenerative surgical peri-implantitis treatment according to the treatment modalities mentioned below, (iii) pre- and one-year postoperative data for PPD, BOP, SUPP and radiographic parameters if still in situ, (iv) data on implant survival. Study individuals were excluded if (i) any of the four criteria was missing, (ii) heavy smoking (>10 cigarettes per day), (iii) antiresorptive therapy and (iv) uncontrolled diabetes.

Included surgical treatment procedure (Fig. 1 and 2):

Presurgical treatment contained repeated pocket decontamination using rinsing with Betadine (11 mg povidone-iodine/ml, Mundipharma Company, Basel, Switzerland). The regenerative surgery contained an open-flap procedure following local anesthesia using Rudocain 1:200,000, intrasulcular incision and vertical releasing incisions, curettage of the peri-implant inflammatory soft tissue; implant surface decontamination with an airflow device (Airflow Powder Plus, Perioflow, EMS Dental, Switzerland) and site decontamination using rinsing with Betadine (11 mg povidone-iodine/ml, Mundipharma Company, Basel, Switzerland), the application of GBR with a mixture of bone graft material (SIC nature graft, SIC-Invent, Shanghai, China) and EMD (Straumann Emdogain, Straumann Group, Basel,

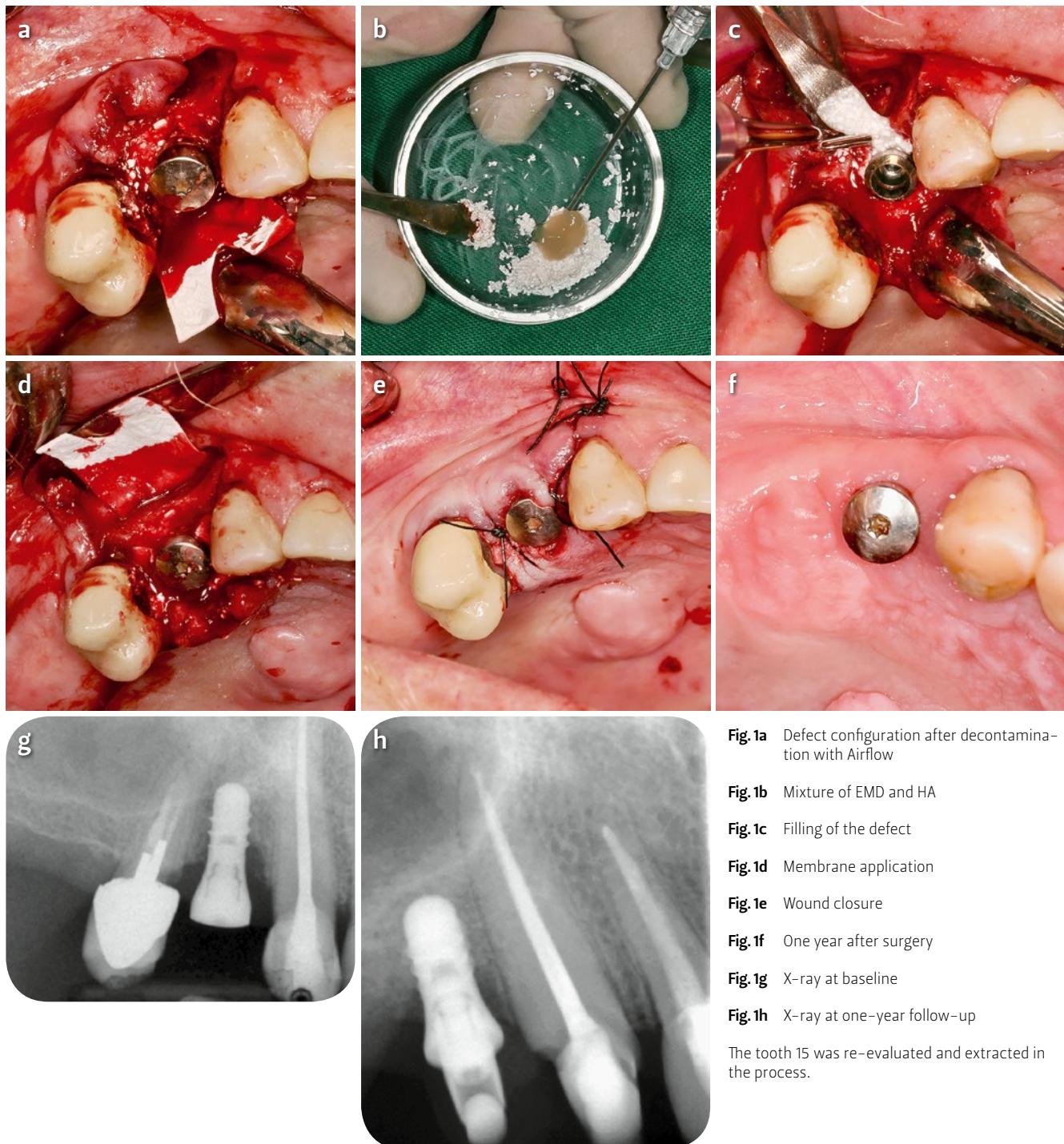


Fig. 1a Defect configuration after decontamination with Airflow

Fig. 1b Mixture of EMD and HA

Fig. 1c Filling of the defect

Fig. 1d Membrane application

Fig. 1e Wound closure

Fig. 1f One year after surgery

Fig. 1g X-ray at baseline

Fig. 1h X-ray at one-year follow-up

The tooth 15 was re-evaluated and extracted in the process.

Switzerland) covered by a resorbable collagen membrane (BioGide, Geistlich AG, Wolhusen, Switzerland) and finally wound closure using a non-absorbable, synthetic, monofilament suture (Dafilon 3–0, Braun, Melsungen, Germany).

All surgical treatments and follow-ups were performed by the same experienced oral surgeon (SK) at the university dental clinic (Universitäres Zentrum für Zahnmedizin Basel, UZB) in Basel, Switzerland. All patients received an eight-day antibiotic therapy using the van Winkelhoff cocktail (375 mg Amoxicillin and 250 mg Metronidazol 3×/day) starting one day before the surgical treatment. Postoperative check-ups were performed 1, 3 and 7 days after the surgical treatment. Follow-ups remeasuring PPD, BOP, SUPP on four sites per implant using a periodontal probe PCP12 (Hu-Friedy, Chicago, United States) were performed after 6 and 12 months. New intraoral radiographs were taken after 12 months and patients were registered in a supportive peri-implantitis recall system at the UZB or at their general dentists practice.

Clinical and radiographic data collection
After identification of all potential study individuals, preoperative and one-year postoperative data regarding PPD, BOP and SUPP were extracted from the patients' records. Pre- and one-year postoperative periapical radiographs from the affected implant site were collected to investigate the marginal bone level. Bone loss was defined as the linear vertical distance between

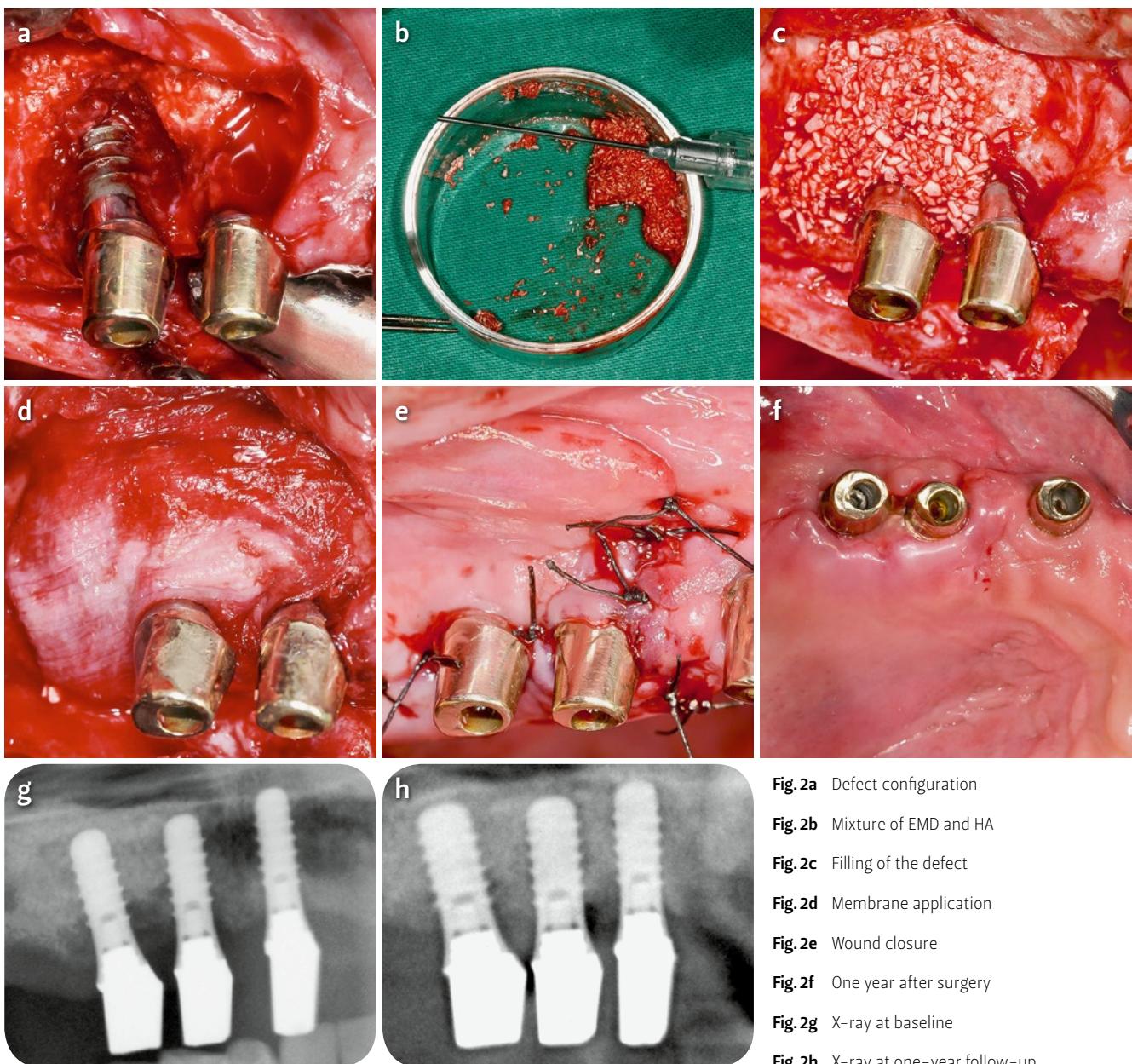


Fig. 2a Defect configuration

Fig. 2b Mixture of EMD and HA

Fig. 2c Filling of the defect

Fig. 2d Membrane application

Fig. 2e Wound closure

Fig. 2f One year after surgery

Fig. 2g X-ray at baseline

Fig. 2h X-ray at one-year follow-up

the to-be-osseointegrated surface of the implant and the most coronal level of bone in contact with the implant. Measurements were taken mesial and distal of the implant using a measurement tool from the DIGORA for Windows® software (Version 2.8, KaVo Dental GmbH, Biberach, Germany). The actual individual implant length was taken as the reference for calculating bone loss in millimeter. To ensure the reliability of the collected radiographic data, bone level measurements were conducted by two calibrated clinicians (DP, MJ) not involved in the treatment or follow-up of the patients.

Successful treatment outcome criteria (STOC)

To evaluate the success of the surgical treatment of the peri-implantitis cases, the criteria suggested by Heitz-Mayfield and Mombelli (HEITZ-MAYFIELD & MOMBELLI 2014) were used on all surfaces circumferentially:

1. PPD < 5 mm
2. No further bone loss
3. No BOP or SUPP

Statistical analysis

All collected clinical data were anonymized and evaluated descriptively and exploratively with the level of significance set at $\alpha = 0.05$, using IBM® SPSS® Statistics, version 26.0 (IBM Corp., Armonk NY, United States). Regarding the collected data, the t-test for paired samples (continuous data) or the McNemar test (dichotomous data) was applied. Implants were chosen as statistical unit for the analysis.

Results

Study population

Detailed demographic data on the study population are provided in Table I. The patient screening process resulted in 11 eligible individuals (out of 202) with a total of 20 implants (out of 336) inserted (6 Straumann Standard, 6 Straumann Standard Plus Roxolid®, 6 Straumann Bone Level Roxolid®, 2 Frialit-2). Among the study participants, 5 were female and 6 were male with a mean age of 52.4 years (SD 11.7, age range 32–67 years). A smoking habit was identified in 5 of the 11 individuals (10 im-

Tab.I Clinical demographic characteristics of the study population

Characteristics	Total patients n = 11	Total implants n = 20
Average age (years)	52.4	52.4
Sex		
Female	5	10
Male	6	10
Smoking		
Yes	5	10
No	6	10
General disease		
Rheumatism	2	5
Diabetes	1	2
Hormone disorder	1	1
No	7	12
Implant manufacturer		
Straumann	10	18
Friadent	1	2
Implant type		
Standard	3	6
Standard Plus	4	6
Bone Level RC	3	6
Frialite-2	1	2
Implant level		
Tissue	7	12
Bone	4	8

Tab.III Treatment success according to STOC at one-year follow-up

Implant	PPD <5 mm	RBL	BOP (-)	SUPP (-)	STOC
1	+	+	+	+	+
2	+	+	+	+	+
3	+	+	+	+	+
4	+	+	+	+	+
5	+	+	+	+	+
6	+	+	+	+	+
7	+	+	+	+	+
8	+	+	+	+	+
9	+	+	+	+	+
10	+	+	+	+	+
11	+	+	-	+	-
12	+	+	-	+	-
13	-	+	+	+	-
14	+	+	+	+	+
15	+	+	+	+	+
16	+	+	+	+	+
17	+	+	+	+	+
18	+	+	-	+	-
19	+	+	-	+	-
20	+	+	+	+	+

PPD: probing pocket depth; RBL: radiological bone level; BOP: bleeding on probing; SUPP: suppuration; STOC: successful treatment outcome criteria, illustrating the successfully treated implants (light background), according to the STOC (HEITZ-MAYFIELD & MOMBELLI 2014) at one-year follow-up.

Tab.II Clinical and radiographic parameters at baseline and at one-year follow-up

Clinical parameter	Baseline n = 20	SD	One-year follow-up n = 20	SD	SS
PPD	4.9 mm	1.35	2.7 mm	0.66	p < 0.001
BOP	18 (90%)		4 (20%)		p < 0.001
SUPP	13 (65%)		0 (0%)		p < 0.001
RBL					
Mesial	6 mm	2.12	4.7 mm	1.67	p < 0.001
Distal	4.9 mm	1.83	4.0 mm	1.36	p < 0.001

PPD: mean probing pocket depth on four implant sites; BOP: bleeding on probing on four implant sites; SUPP: suppuration on four implant sites; RBL: radiological bone level on two implant sites

plants). Two patients (5 implants) were suffering from rheumatic diseases, one (2 implants) from diabetes.

Clinical and radiographic outcome

Data on clinical and radiographic parameters at baseline and at one-year postoperative are provided in Table II. The mean PPD on the day of intervention was 4.9 mm (SD 1.35). This value decreased after one year to a mean PPD of 2.7 mm (SD 0.66, $p < 0.001$).

At baseline, 18 (90.0%) of the 20 implants were diagnosed with BOP, and 13 (65%) implants with pus. One year after intervention, 4 (20%) implants exhibited BOP ($p < 0.001$), while SUPP was no longer detected ($p < 0.001$).

Marginal bone loss on the day of intervention was measured at a mean of 6.0 mm at the mesial and 4.9 mm at the distal site. Measurements taken one year after surgery showed on average of 4.7 mm on the mesial and 4.0 mm on the distal implant aspect, indicating improved bone levels. Differences between baseline and one-year postoperative follow-up exhibited a statistically significant difference for both sites ($p < 0.001$).

Survival and success of implants treated

At the one-year follow-up, all implants treated were still in function, resulting in no implant loss (Tab. III). Out of the 20 implants included, 15 (75%) fulfilled all success criteria and were therefore considered successfully treated. Five implants (25%) failed to achieve all three success criteria, including four with remaining BOP, one with a PPD > 5 mm, while continuing suppuration or further bone loss was not observed. Complete resolution of the peri-implant defect with full bone regeneration and normalization of PPD (≤ 3 mm) was not found in any of the 20 cases included.

Discussion

The aim of this retrospective case series study was to investigate the success of surgical regenerative peri-implantitis therapy involving a combination of inorganic HA bone substitute, EMD and a resorbable collagen membrane. To the best of our knowledge, this is the first study to investigate the outcome of regenerative peri-implantitis therapy involving a GBR technique consisting of a mixture of HA-based graft material, EMD and a bioresorbable collagen membrane under systemic antibiotic regime. At the one-year follow-up, favorable results for the primary outcomes of implant survival and bone regeneration as well as for the secondary parameters PPD, BOP and SUPP were documented, resulting in a survival rate of 100% and a success rate of 75%.

Due to their slow resorption, HA bone grafting materials provide ideal long-term stability, supporting the host in the process of remodeling and replacing the graft by autogenous bone (DEWI & ANA 2018). The approach of adding EMD to graft material for a GBR-based regenerative treatment of peri-implantitis is a concept that has been used for more than 20 years at the UZB. Over the course of those two decades, however, a wide variety of different substitute materials, membrane types and implant surface decontamination methods have been applied. From the initial pool of peri-implantitis cases available (> 300), a homogeneous group was selected in which an identical treatment approach was adopted. Therefore, the number of implants included is relatively small, and the follow-up time is limited to one year. Considering that the used substitute material is non- or extremely slow resorbable, the radiographic and clinical examination does not give any information on the remodeling e.g.

bone formation but rather documents the presence of the substitute material particle. On the other hand, the inclusion criteria were very strict, which makes the data more reliable.

Since there is no established gold standard treatment protocol for surgical regenerative peri-implantitis therapy described in literature, another limitation of the present study is the lack of a control group, to compare our results with.

However, the surgical protocol adopted did prove the potential to reduce peri-implant inflammatory processes and prevent further soft and hard tissue destruction at least one year after surgery. Studies demonstrated that EMD improved postsurgical revascularization (OKUDA ET AL. 2001; VILLA ET AL. 2015), and induced cell migration and proliferation of growth factors, which ultimately promoted wound healing (ALMQVIST ET AL. 2011; PARKAR & TONETTI 2004). In addition, studies suggested that EMD has antimicrobial and antiseptic effects (ARWEILER ET AL. 2002). A previous study using EMD to treat peri-implantitis noted a higher postsurgical implant survival rate in the EMD group than in the control group (ISEHED ET AL. 2018).

Adjunctive use of antibiotics seems to be effective in preventing postoperative infections. Given the antimicrobial resistance problem, a mindful use of antibiotics is uninventable. We therefore performed a patient specific risk assessment before prescribing antibiotics. In the present study no postsurgical infections were observed despite the fact that a non-submerged transgingival healing approach was used. In the GBR treatment of peri-implantitis, EMD-induced accelerated wound closure (ISEHED ET AL. 2016) potentially reduced bacterial contamination of the graft, which in turn leads to improved regenerative outcomes. These distinct properties might give an additional boost to regenerative capacity and might improve overall regeneration. However, the study population included in this study received a combination of Metronidazole and Aminopenicillin as adjuvant anti-infective treatment. The so-called van Winkelhoff cocktail was state of the art in the past for the treatment of aggressive periodontitis. However, recent publications doubt the effectiveness of Metronidazole since an increased resistance could be observed for some anaerobic bacteria such as Prevotella and Gram-positive anaerobic cocci (VELOO & VAN WINKELHOFF 2015). Considering that the combination of Metronidazole with Aminopenicillin can cause severe side effects, the use of this van Winkelhoff cocktail needs justification in terms of resistance testing before application in order to identify the patients who will rather take benefit from this combination.

At the one-year follow-up visit, 100% of the implants showed a stabilized or improved RBL. The mean RBL exhibited a defect reduction of 1.3 mm (mesial) and 0.9 mm (distal). A current meta-analysis comparing the treatment outcomes of ten studies using GBR and a follow-up period of one to ten years reported a mean RBL regain of 1.86 mm (DAUGELA ET AL. 2016). The mean RBL reduction in the current study was slightly lower. However, the reviewed studies vary largely in sample size, surface decontamination techniques, bone substitute materials used, membrane types, prescribed antibiotics as well as follow-up times. Baseline bone defect configuration also impacts the therapy outcome and was not considered in this study (SCHWARZ ET AL. 2010). Differences in the mean RBL could be due to any of these parameters, which complicates direct comparison of the results with the literature.

As remodeling of the bone substitute material applied is still in process after 12 months, the radiographic improvement presented in this study partly reflects the substitute material and

only partly regenerated bone resulting in new osseointegration. However, the reduction in PPD achieved is an important step in successful regeneration, as observable in regenerative peri-odontal and peri-implant disease therapies.

Different criteria are used to define a successful treatment outcome, which makes comparison of success rates relatively challenging. Based on the STOC used in the present study, 75% of the implants were considered successfully treated at the one-year follow-up visit. For the remaining 25% of the implants, treatment failure was mainly due to persisting BOP and PPD measurements of > 5 mm. BOP around dental implants has proved to be a valuable diagnostic parameter for measuring peri-implant tissue health (RAMANAUSKAITE & JUODZBALYS 2016). Luterbacher et al. demonstrated a high risk of disease progression in the presence of BOP (LUTERBACHER ET AL. 2000). In the present study, 90% of the implants showed BOP at baseline, and one year after treatment only 20% were positive for BOP. These results highlight a reduction of the inflammatory process in 80% and an overall improvement of peri-implant tissue health.

Despite the promising findings of this study, a one-year follow-up is rather short. Therapy effects such as pocket depth reduction, infection control and bone graft substitute induced bone regeneration are still in process and cannot be fully validated. An extended follow-up of 3 to 5 years would provide more insights on the long-term treatment outcome. Patients' behavior such as oral hygiene and smoking can influence treatment outcome. Strict monitoring and frequent follow-ups to optimize patients' habits are recommended. Another important issue is to be seen in the treated defect morphologies. It is well known, that intrabony defects show better results in regenerative approaches than lateral defects. Unfortunately, the defect morphologies were not recorded in the present data which represents an additional important flaw.

Though this retrospective case series study has several limitations, the current data demonstrated promising treatment outcomes for the initial one-year phase after surgery, using a protocol involving the application of a hydroxyapatite (HA) bone substitute material, EMD, broad-spectrum antibiotics and a collagen membrane. However, controlled and sufficiently powered clinical trials with control groups are required to validate the present findings.

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Zusammenfassung

Einleitung

Ziel dieser retrospektiven Fallstudie war die Untersuchung des 1-Jahres-Erfolges einer chirurgischen regenerativen Periimplantitistherapie. Es wurde dabei erstmals die unter systemischer Gabe von Breitbandantibiotika geführte Knochenregeneration (GBR) mit einem Gemisch aus Hydroxyapatit-Knochenersatzmaterial (HA) und Schmelzmatrixproteinen (EMD) in Kombination mit einer Kollagenmembran untersucht.

Material und Methode

Für diese Studie wurde aus dem Patientenpool der Klinik für Oralchirurgie am Universitären Zentrum für Zahnmedizin Basel

(UZB) eine homogene Patientengruppe identifiziert, die eine identische regenerative Periimplantitistherapie unter Anwendung von Antibiotika, HA, EMD sowie einer Kollagenmembran erhalten hat. Aus den Patientenakten wurden prä- sowie 1-Jahr-postoperative Daten zu Bluten auf Sondierung (BOP), Sondierungstiefen (PPD), Pus (SUPP) sowie Röntgenbilder gesammelt. Die Daten wurden im Anschluss digitalisiert und statistisch ausgewertet. Das Fehlen eines der Messparameter führte zum Studienausschluss eines Patienten. Um den Erfolg der Therapie zu messen, wurden die Erfolgskriterien (successful treatment outcome criteria, STOC) nach Heitz-Mayfield und Mombelli angewendet.

Resultate

In der Klinik für Oralchirurgie am Universitären Zentrum für Zahnmedizin Basel (UZB) wurden im Zeitraum von 2000 bis 2017 über 200 Patienten mit einer Periimplantitis behandelt. Davon konnten 11 Patienten (5 Frauen, 6 Männer) mit insgesamt 20 Implantaten identifiziert werden, welche die Einschlusskriterien für diese Studie erfüllten.

Die statistischen Daten zeigen, dass sich ein Jahr nach der regenerativen Periimplantitistherapie noch alle 20 Implantate in Funktion befanden. Dabei haben sich die Knochendefekte im Mittel um 1,3 mm (mesial) und 0,9 mm (distal) regeneriert. Gleichzeitig haben im Mittel die Sondierungstiefen von 4,9 mm auf 2,7 mm abgenommen. Anfänglich wiesen rund 18 Implantate (90%) ein positives BOP und 13 Implantate (65%) Pus auf. Nach einem Jahr zeigten noch 4 Implantate (20%) ein positives BOP, Pus wurde bei keinem Implantat mehr detektiert. Gemessen an den STOC-Erfolgskriterien von Heitz-Mayfield und Mombelli konnten ein Jahr nach therapeutischer Intervention 15 Implantate (75%) als erfolgreich therapiert angesehen werden.

Diskussion

Die vorgestellte retrospektive Fallstudie zeigt vielversprechende Ergebnisse in der regenerativen Periimplantitistherapie mittels der beschriebenen GBR-Technik.

Ein Jahr nach chirurgischer Intervention konnte eine 100%-Überlebensrate und eine 75%-Erfolgsrate der behandelten Implantate gemessen werden. Weiter zeigten die Untersuchungen einen Rückgang von BOP um rund 78% und eine 100%-Elimination von Pus. Der periimplantäre Knochenabbau ist bei allen behandelten Implantaten stagniert, und eine beginnende Knochenregeneration zeichnet sich ab. Das verwendete HA-Knochenersatzmaterial resorbiert langsam und wirkt somit über längere Zeit als volumenstabiles Medium. Ein entscheidender Grund für die positiven Ergebnisse dieser Studie könnte in der Zugabe von Schmelzmatrixproteinen zum Knochenersatzmaterial liegen. Frühere Studien belegen bereits, dass Schmelzmatrixproteine eine antiseptische sowie antibakterielle Wirkung besitzen und die Wundheilung fördern. In Kombination mit der verordneten Antibiotikatherapie (Van-Winkelhoff-Cocktail) konnten bei allen Implantaten eine postoperative Infektion vermieden werden. In der aktuellen Literatur werden diverse regenerative GBR-Konzepte zur Therapie der Periimplantitis beschrieben. Aufgrund der unterschiedlichen Studienkonzepte, Materialien und Beobachtungszeiträume ist ein direkter Vergleich sehr schwierig. Eine prospektive klinische Studie mit einer grösseren Patientengruppe sowie einer Kontrollgruppe ist empfohlen, um die Ergebnisse dieser Studie weiter zu untersuchen.

Résumé

Introduction

Le but de cette étude rétrospective était l'examen du taux de réussite après une année suite à un traitement chirurgical régénératif dans le cas de péri-implantites. Pour une première fois, on a examiné la régénération osseuse guidée (GBR) avec un mélange de substitut osseux d'hydroxyapatite (HA) et de protéines de la matrice amélaire (EMD) en combinaison avec une membrane de collagène et des antibiotiques.

Matériel et méthode

Pour cette étude, un groupe de patients homogène a été identifié dans la patientèle de la clinique de chirurgie orale du centre pour la médecine dentaire de Bâle (UZB), ces derniers ont tous obtenu le même traitement utilisant l'HA, l'EMD ainsi que la membrane de collagène. À partir des dossiers des patients, les données suivantes ont été collectées avant l'intervention ainsi qu'une année après l'intervention : saignement au sondage (BOP), mesures de poches, suppuration et radiographies. Les données collectées ont été digitalisées et une analyse statistique a été établie. Le manque d'un des paramètres d'évaluation avait pour conséquence l'exclusion du patient. Afin de mesurer le succès du traitement, les critères de réussite (Successful treatment outcome criteria, STOC) d'après Heiz-Mayfield et Mombelli ont été appliqués.

Résultats

Plus de 200 patients ont été traités pour cause de péri-implantites entre les années 2000 et 2017 à la clinique de chirurgie orale du centre pour la médecine dentaire de Bâle (UZB). Parmi ces derniers, 11 patients (5 femmes et 6 hommes) avec en tout 20 implants qui remplissaient les critères d'inclusion pour cette étude ont pu être identifiés.

Les données statistiques montrent qu'une année après le traitement régénératif de péri-implantite tous les 20 implants ont persisté dans leur fonction. Les défauts osseux se sont régénérés en moyenne de 1,3 mm (mésial) et de 0,9 mm (distal). En paral-

lèle, les profondeurs de poches ont diminué en moyenne de 4,9 mm à 2,7 mm de profondeur. Au début, 18 des 20 implants (90 %) présentaient des saignements au sondage et 13 implants (65 %) suppuraient.

Après une année, plus que quatre implants (20 %) présentaient des saignements au sondage et plus aucun implant ne suppuraient. Mesurés selon les critères de réussite STOC de Heitz-Mayfield et Mombelli, 15 implants (75 %) ont été traités avec succès une année après l'intervention thérapeutique.

Discussion

L'étude de cas rétrospective présentée montre des résultats prometteurs dans le traitement régénératif de péri-implantite avec la technique GBR décrite.

Une année après l'intervention chirurgicale, on a pu mesurer un taux de survie de 100 % et un taux de réussite de 75 % des implants traités. De plus, les examens ont pu montrer une réduction de saignements au sondage de 78 % et une élimination de suppuration de 100 %.

La perte osseuse péri-implantaire a stagné chez tous les implants traités et une régénération osseuse commençait à se dessiner. Le substitut osseux à base de HA utilisé résorbe lentement et peut ainsi garantir plus longtemps la stabilité du volume. Un point décisif pour les résultats positifs de cette étude pourrait être l'addition de protéine de la matrice amélaire au substitut osseux. Des études plus anciennes démontrent que les protéines de la matrice amélaire ont un effet antiseptique et antibactérien et promeuvent la cicatrisation. En combinaison avec le traitement antibiotique prescrit (van-Winkelhoff-Cocktail), une infection postopératoire des implants a pu être évitée. Dans la littérature actuelle, divers concepts régénératifs GBR pour le traitement de péri-implantite sont décrits. En raison de différents modèles d'études, matériaux et périodes d'observations, une comparaison directe reste très difficile. Une étude clinique prospective avec un groupe de patients plus nombreux ainsi qu'un groupe de contrôle est recommandée afin d'examiner en profondeur les résultats de cette étude.

References

- AL-HEZAIMI K, AL-FAHAD H, O'NEILL R, SHUMAN L, GRIFFIN T: The Effect of Enamel Matrix Protein on Gingival Tissue Thickness in Vivo. *Odontology* 100 (1): 61–66 (2012)
- ALMQVIST S, KLEINMAN H K, WERTHÉN M, THOMSEN P, ÅGREN M S: Effects of Amelogenins on Angiogenesis-Associated Processes of Endothelial Cells. *J Wound Care* 20 (2): 68–75 (2011)
- ARWEILER N B, AUSCHILL T M, DONOS N, SCULEAN A: Antibacterial Effect of an Enamel Matrix Protein Derivative on *in Vivo* Dental Biofilm Vitality. *Clin Oral Investig* 6 (4): 205–209 (2002)
- ASPRIELLO S D, ZIZI A, SPAZZAFUMO L, RUBINI C, LORENZI T, MARZIONI D, BULLON P, PIEMONTESE M: Effects of Enamel Matrix Derivative on Vascular Endothelial Growth Factor Expression and Microvessel Density in Gingival Tissues of Peri-odontal Pocket: A Comparative Study. *J Periodontol* 82 (4): 606–612 (2011)
- BELIBASAKIS G N: Microbiological and Immuno-Pathological Aspects of Peri-Implant Diseases. *Arch Oral Biol* 59 (1): 66–72 (2014)
- BERGLUNDH T, ARMITAGE G, ARAUJO M G, AVILA-ORTIZ G, BLANCO J, CAMARGO P M, CHEN S ET AL.: Peri-Implant Diseases and Conditions: Consensus Report of Workgroup 4 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *J Clin Periodontol* 45 (June): S286–S291 (2018)
- BERGLUNDH T, GISLASON O, LEKHOLM U, SENNERBY L, LINDEH J: Histopathological Observations of Human Periimplantitis Lesions. *J Clin Periodontol* 31 (5): 341–347 (2004)
- BERGLUNDH T, ZITZMANN N U, DONATI M: Are Peri-Implantitis Lesions Different from Periodontitis Lesions? *J Clin Periodontol* 38 Suppl 11: 188–202 (2011)
- DAUGELA P, CICCIÙ M, SAULACI N: Surgical Regenerative Treatments for Peri-Implantitis: Meta-Analysis of Recent Findings in a Systematic Literature Review. *J Oral Maxillofac Res* 7 (3): e15 (2016)
- DERKS J, SCHALLER D, HÄKANSSON J, WENNSTRÖM J L, TOMASI C, BERGLUNDH T: Peri-Implantitis – Onset and Pattern of Progression. *J Clin Periodontol* 43 (4): 383–388 (2016)
- DERKS J, TOMASI C: Peri-Implant Health and Disease. A Systematic Review of Current Epidemiology. *J Clin Periodontol* 42 Suppl 16: S158–171 (2015)
- DEWI A H, ANA I D: The Use of Hydroxyapatite Bone Substitute Grafting for Alveolar Ridge Preservation, Sinus Augmentation, and Periodontal Bone Defect: A Systematic Review. *Heliyon* 4 (10): e00884 (2018)
- GUALINI F, BERGLUNDH T: Immunohistochemical Characteristics of Inflammatory Lesions at Implants. *J Clin Periodontol* 30 (1): 14–18 (2003)
- GUIMARÃES G F, DE ARAÚJO V C, NERY J C, PERUZZO D C, SOARES A B: Microvessel Density Evaluation of the Effect of Enamel Matrix Derivative on Soft Tissue After Implant Placement: A Preliminary Study. *Int J Periodontics Restorative Dent* 35 (5): 733–738 (2017)
- HEITZ-MAYFIELD L J A, SALVI G E: Peri-Implant Mucoitis. *J Clin Periodontol* 45 Suppl 20: S237–S245 (2018)
- HEITZ-MAYFIELD L J A, MOMBELLI A: The Therapy of Peri-Implantitis: A Systematic Review. *Int J Oral Maxillofac Implants* 29 Suppl: 325–345 (2014)

- HOANG A M, OATES T W, COCHRAN D L:** In Vitro Wound Healing Responses to Enamel Matrix Derivative. *J Periodontol* 71 (8): 1270–1277 (2000)
- ISEHED C, HOLMLUND A, RENVERT S, SVENSON B, JOHANSSON I, LUNDBERG P:** Effectiveness of Enamel Matrix Derivative on the Clinical and Microbiological Outcomes Following Surgical Regenerative Treatment of Peri-implantitis. A Randomized Controlled Trial. *J Clin Periodontol* 43 (10): 863–873 (2016)
- ISEHED C, SVENSON B, LUNDBERG P, HOLMLUND A:** Surgical Treatment of Peri-Implantitis Using Enamel Matrix Derivative, an RCT: 3- and 5-Year Follow-Up. *J Clin Periodontol* 45 (6): 744–753 (2018)
- JAMJOOM A, COHEN R E:** Grafts for Ridge Preservation. *J Funct Biomater* 6 (3): 833–848 (2015)
- KELEKIS-CHOLAKIS A, ATOUT R, HAMDAN N, TSOURNAKIS I:** Peri-Implant Complications. 1st edn, Springer International Publishing, Cham (2018)
- LUTERBACHER S, MAYFIELD L, BRAGGER U, LANG N P:** Diagnostic Characteristics of Clinical and Microbiological Tests for Monitoring Periodontal and Peri-Implant Mucosal Tissue Conditions during Supportive Periodontal Therapy (SPT). *Clin Oral Implants Res* 11 (6): 521–529 (2000)
- MAYMON-GIL T, WEINBERG E, NEMCOVSKY C, WEINREB M:** Enamel Matrix Derivative Promotes Healing of a Surgical Wound in the Rat Oral Mucosa. *J Periodontol* 87 (5): 601–609 (2016)
- MERCADO F, HAMLET S, IVANOVSKI S:** Regenerative Surgical Therapy for Peri-Implantitis Using Deproteinized Bovine Bone Mineral with 10% Collagen, Enamel Matrix Derivative and Doxycycline – A Prospective 3-Year Cohort Study. *Clin Oral Implants Res* 29 (6): 583–591 (2018)
- MEYER S, GIANNOPOLOU C, COURVOISIER D, SCHIMMEL M, MÜLLER F, MOMBELLI A:** Experimental Mucositis and Experimental Gingivitis in Persons Aged 70 or over. Clinical and Biological Responses. *Clin Oral Implants Res* 28 (8): 1005–1012 (2017)
- OKUDA K, MIYAZAKI A, MOMOSE M, MURATA M, NOMURA T, KUBOTA T, WOLFF L F, YOSHIE H:** Levels of Tissue Inhibitor of Metalloproteinases-1 and Matrix Metalloproteinases-1 and -8 in Gingival Crevicular Fluid Following Treatment with Enamel Matrix Derivative (EMDOGAINR). *J Periodontal Res* 36 (5): 309–316 (2001)
- PARKAR M H, TONETTI M:** Gene Expression Profiles of Periodontal Ligament Cells Treated With Enamel Matrix Proteins In Vitro: Analysis Using CDNA Arrays. *J Periodontol* 75 (11): 1539–1546 (2004)
- PILLONI A, PAOLANTONIO M, CAMARGO P M:** Root Coverage With a Coronally Positioned Flap Used in Combination With Enamel Matrix Derivative: 18-Month Clinical Evaluation. *J Periodontol* 77 (12): 2031–2039 (2006)
- QU Z, ANDRUKHOV O, LAKY M, ULM C, MATEJKA M, DARD M, RAUSCH-FAN X:** Effect of Enamel Matrix Derivative on Proliferation and Differentiation of Osteoblast Cells Grown on the Titanium Implant Surface. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 111 (4): 517–522 (2011)
- RAMANAUSKAITE A, JUODZBALYS G:** Diagnostic Principles of Peri-Implantitis: A Systematic Review and Guidelines for Peri-Implantitis Diagnosis Proposal. *J Oral Maxillofac Res* 7 (3): e8 (2016)
- SALVI G E, AGLIETTA M, EICK S, SCULEAN A, LANG N P, RAMSEIER C A:** Reversibility of Experimental Peri-Implant Mucositis Compared with Experimental Gingivitis in Humans. *Clin Oral Implants Res* 23 (2): 182–190 (2012)
- SCHWARZ F, SAHM N, SCHWARZ K, BECKER J:** Impact of Defect Configuration on the Clinical Outcome Following Surgical Regenerative Therapy of Peri-Implantitis. *J Clin Periodontol* 37 (5): 449–455 (2010)
- SHIN S H, CUEVA M A, KERNS D G, HALLMON W W, RIVERA-HIDALGO F, NUNN M E:** A Comparative Study of Root Coverage Using Acellular Dermal Matrix With and Without Enamel Matrix Derivative. *J Periodontol* 78 (3): 411–421 (2007)
- THRIVIKRAMAN G, ATHIRASALA A, TWOHIG C, BODA S K, BERTASSONI L E:** Biomaterials for Craniofacial Bone Regeneration. *Dent Clin North Am* 61 (4): 835–856 (2017)
- TONETTI M S, FOURMOUSIS I, SUVAN J, CORTELLINI P, BRAGGER U, LANG N P:** Healing, Post-Operative Morbidity and Patient Perception of Outcomes Following Regenerative Therapy of Deep Intrabony Defects. *J Clin Periodontol* 31 (12): 1092–1098 (2004)
- VELOO A C M, VAN WINKELHOFF A J:** Antibiotic Susceptibility Profiles of Anaerobic Pathogens in The Netherlands. *Anaerobe* 31: 19–24 (2015)
- VILLA O, WOHLFAHRT J C, MDLA I, PETZOLD C, RESENDAN J E, SNEAD M L, AND STAALE P LYNGSTADAAS:** Proline-Rich Peptide Mimics Effects of Enamel Matrix Derivative on Rat Oral Mucosa Incisional Wound Healing. *Journal of Periodontology* 86 (12): 1386–1395 (2015)
- WALTER C, JAVOR P, BERNIMOULIN J P, HÄGEWALD S:** Moderate Effect of Enamel Matrix Derivative (Emdogain® Gel) on Porphyromonas Gingivalis Growth in Vitro. *Arch Oral Biol* 51 (3): 171–176 (2006)
- ZELDICH E, KOREN R, DARD M, NEMCOVSKY C, M WEINREB:** Enamel Matrix Derivative Protects Human Gingival Fibroblasts from TNF-Induced Apoptosis by Inhibiting Caspase Activation. *J Cell Physiol* 213 (3): 750–758 (2007a)
- ZELDICH E, KOREN R, NEMCOVSKY C, WEINREB M:** Enamel Matrix Derivative Stimulates Human Gingival Fibroblast Proliferation via ERK. *J Dent Res* 86 (1): 41–46 (2007b)