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Deproteinized bovine bone in association with guided tissue regeneration or enamel matrix derivatives procedures in aggressive periodontitis patients: a 1-year retrospective study

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Abstract

Objectives: To retrospectively evaluate and compare two regenerative periodontal procedures in young individuals with aggressive periodontitis (AgP).

Methods: Thirty-two patients aged 14–25 years (mean ± SD 19.3 ± 5.7) were diagnosed as having AgP with multiple intra-bony defects (IBDs) and treated by one of two regenerative modalities of periodontal therapy: guided tissue regeneration (GTR) using deproteinized bone xenograft (DBX) particles and a resorbable membrane (the GTR group), or an application of enamel matrix derivatives (EMD) combined with DBX (the EMD/DBX group). Periodic monitoring of treated sites included recording of probing depth (PD), clinical attachment level (CAL) and gingival recession. Pre-treatment and 1-year post-operative findings were statistically analysed within and between groups.

Results: The PD and CAL values decreased significantly with time, but not those between study groups. The mean pre-treatment and 1-year post-treatment PDs of the IBDs of the GTR group (n = 16; sites = 67) were 8.93 ± 1.14 mm and 3.58 ± 0.50 mm, respectively, and the mean CALs were 9.03 ± 1.03 mm and 4.16 ± 0.53 mm respectively. The mean PDs of the EMD/DBX group (n = 16; sites = 73) were 8.77 ± 1.04 mm and 3.61 ± 0.36 mm, respectively, and the mean CALS were 8.79 ± 1.04 mm and 3.77 ± 0.22 mm respectively ($p < 0.001$ for all).

Conclusion: Surgical treatment of AgP patients by either GTR or by application of EMD/DBX yielded similarly successful clinical results at 1-year post-treatment.

Key words: Aggressive periodontitis; deproteinized bovine bone (Bio-Oss®); enamel matrix derivatives (Emdogain®); guided tissue regeneration; periodontal regeneration

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Conflict of interest and source of funding statement
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Aggressive periodontitis (AgP) is characterized by a rapid loss of periodontal tissue. It presents with several distinctive features, such as early age at onset, involvement of multiple teeth and a relatively rapid progression (Baer 1971, Armitage 1999). The two distinguishable patterns are comprised of a localized form, which involves the first molars, the incisors and up to two additional teeth, and a more generalized form, which

involves extensive destruction (Baer & Socransky 1979, Hørmand & Frandsen 1979, Armitage 1999).

It is believed that the main contributing factors are quantitatively and qualitatively related to alterations in the immune response (Khocht & Albandar 2014), intra-host genes and host–environment interactions (Albandar 2014, Vieira & Albandar 2014). AgP is more common in certain ethnic populations and certain geographical regions (Albandar 2014, Susin et al. 2014).

The goals of AgP therapy are to completely arrest the disease progression, to regenerate lost or deprived periodontium, and to maintain health, similarly to the goals of chronic adult periodontitis (ChP) (Armitage 1999). Systematic reviews (Deas and Mealey 2010; Nibali et al. 2013) have also claimed that the efficacy of mechanical therapy may be comparable in both conditions.

Regenerative periodontal therapy may be accomplished mainly by two different approaches: one is selective cell population using tissue barriers, commonly referred to as guided tissue regeneration (GTR) (Gottlow et al. 1986), and the other is the application of tissue morphogenic factors, such as enamel matrix derivatives (EMD), for promoting tissue growth (Hammarström 1997, Heijl et al. 1997).

The combination of EMD with deproteinized bone xenograft (DBX) has been tested in a few trials in the belief that it may have the qualities of a bioactive bone graft (Lekovic et al. 2000, 2001a, Camargo et al. 2001, Scheyer et al. 2002, Sculean et al. 2002, 2003a, 2005, 2008a, Velasquez-Plata et al. 2002, Zucchelli et al. 2003, Döri et al. 2005, Yamamoto et al. 2007, Farina et al. 2014, Iorio-Siciliano et al. 2014). On the other hand, a number of studies (Donos et al. 2004, 2005, 2006) that used critical size defects in rats failed to support those claims. Moreover, two meta-analyses (Tu et al. 2010, Verardi 2012) could not demonstrate a significant contribution of this combination. However, Miron et al. (2012) showed that EMD enhanced osteoblast and periodontal ligament cell proliferation, differentiation and attachment to DBX particles in vitro. Recent in vivo (Miron et al. 2014) data have shown that EMD has the ability to enhance the speed of new bone formation when combined with DBX particles in rat osseous defects.

Encouraging results of regeneration have emerged from many randomized trials of periodontal therapy in ChP patients, but there are only a few reports that claim clinical success when treating AgP patients with either the GTR technique (Sirirat et al. 1996, Buchmann et al. 2002, Zucchelli et al. 2002a) or EMD application (Bonta et al. 2003, Kiernicka et al. 2003, Miliauskaite et al. 2007, Kaner et al. 2009). Furthermore, most of those reports, particularly those related to the latter, are based on small series of patients without clinical standardization and/or strict follow-up protocols.

The aim of this retrospective cohort study was to evaluate and compare the clinical outcome of periodontal regeneration procedures using either a GTR technique or the EMD approach in patients with localized or generalized AgP.

Material and Methods

The study was approved by the Tel Aviv University Ethics Committee. Cases that were diagnosed with AgP were selected for this retrospective study. The inclusion criteria comprised the following: (i) no systemic medical compromising conditions. (ii) not smoking or history of smoking; (iii) being treated periodontally through a surgical tissue regeneration approach either by a GTR technique or EMD application with DBX as the grafted biomaterial; (iv) having completed the active treatment phase followed by making all the frequent recall visits required by the maintenance regimen.

All the study patients were treated in the Department of Periodontology and Dental Implantology with full supervision of all steps by one of the senior staff members (ZA and AK). Treatment allocation was not randomized, but left to the operator's discretion. To determine the reproducibility of the measurements and the coefficient of variation for each parameter, randomly selected patients were checked for periodontal chart data and over 95% were found to be matched for verifying highly reproducible and accurate measurements.

The files of 32 consecutively treated patients (14 males, 18 females) who were diagnosed with localized or generalized AgP were available for the study. Their ages ranged between 14 and 25 years (mean 19.3 $\pm$ 5.7). A thorough family history, i.e. family tree, was searched for the occurrence of familial aggregation.

The patient's initial visit included extra- and intra-oral examinations, a thorough periodontal chart, full-mouth periapical radiographs and study models. Probing depth (PD), clinical attachment level (CAL) and height of exposed roots (recession – Rec) were recorded in all periodontal sites with evidence of destruction. The deepest PD at each periodontally involved inter-proximal/inter-radicular intra-bony site was recorded. The mean PD and CAL values (Tables 1–4) represent the average measurements of all sites of each treated intra-bony defect (IBD) in each patient. For example the mean PD in a given inter-proximal IBD was calculated as the average of the two inter-proximal sites of the tooth aspect in relation to the intra-osseous defect, excluding the other two aspects in relation to the adjacent tooth. The horizontal furcation involvement was assessed in the inter-radicular areas (Hamp et al. 1975). Bleeding on probing (BOP, Saxer & Mühlemann 1975) and plaque score index (PI, Turesky et al. 1970) were monitored carefully at each re-evaluation visit. All the study patients underwent a similar meticulous non-surgical periodontal treatment phase, including oral hygiene instructions and training, full-mouth scaling and root debridement in conjunction with systemic antibiotics of amoxicillin 500 mg + metronidazole 250 mg (TID) for 1 week (van Winkelhoff et al. 1989, Herrera et al. 2002, Guerrero et al. 2005). The patients were re-evaluated at 3 months, periodontal indices were re-recorded and a periodontal regenerative surgical procedure treatment plan was assigned for sites presenting vertical intra-bony defects with a PD equal to or greater than 6 mm. No regeneration procedure was planned for the rare sites where there was through-and-through furcation involvement (i.e. grade 3), The patients underwent one of the following regenerative procedures: (i) a

Table 1. Clinical mean (*) pre- and post-op periodontal probing depth (PD) in the GTR group

Patients	No. of IBD sites	ID sites	Pre PD*	Post PD*	PDR*
1	4	16/17†, 26/27†, 36/37, 46/47	6.5‡, 7.5, 6.5, 8 (7.1*)	4, 3.5, 3.5, 4.5 (4)	3.1
2	4	14/15†, 26/27†, 35/36†, 36/37	10.5, 9.5, 10.5, 7.5 (9.5)	5, 4, 4, 3 (4)	5.5
3	3	13/14, 31/41, 45/46	8.5, 9, 8 (8.5)	3, 3, 3 (3)	5.5
4	5	15/16†, 16/17†, 25/26†, 36/37, 46/47†	10, 9, 12, 11, 11 (10.6)	4, 4, 4.5, 4, 4 (4.1)	6.5
5	4	14/15, 16/17†, 25/26†, 36/37†	10, 9, 12.5, 10 (10.4)	4, 4.5, 4.5, 4 (4.3)	6.1
6	5	15/16†, 25/26†, 36/37, 45/46, 46/47†	8, 7.5, 7, 7, 7 (7.3)	4, 3.5, 4.5, 4.5, 4 (4.1)	3.2
7	4	15/16†, 25/26†, 35/36, 46/47†	10.5, 9, 10,10 (9.9)	4, 4, 4, 4 (4)	5.9
8	4	15/16†, 21/22, 25/26†, 45/46	9, 8, 9,8 (8.5)	3, 2.5, 3, 3 (2.9)	5.6
9	4	15/16†, 25/26†, 45/46, 46/47†	8, 7, 10, 10 (8.8)	3.5, 3.5, 3, 3 (3.3)	5.5
10	4	16/17†, 25/26†, 36/37†, 46/47†	11.5, 10, 10.5, 10.5 (10.6)	4, 4, 4, 4 (4)	6.6
11	4	14/15, 15/16†, 25/26†, 36/37	8.5, 9, 9, 9 (8.9)	2.5, 3, 3, 3 (2.9)	6
12	4	15/16†, 25/26†, 35/36†, 46/47†	9, 8, 9, 9 (8.8)	3.5, 3.5, 3.5, 3.5 (3.5)	5.3
13	4	15/16†, 16/17†, 26/27†, 46/47†	8, 7, 9.5, 9.5 (8.5)	4, 3.5, 3.5, 3.5 (3.6)	4.9
14	6	14/15, 15/16, 25/26†, 26/27†,36/37, 45/46	7, 7.5, 7, 7.5, 7, 8 (7.3)	3.5, 3, 4, 4.5, 4,3.5 (3.8)	3.5
15	4	16/17†, 11/12, 35/36†, 46/47†	10.5, 9, 10, 10 (9.9)	3.5, 3, 3, 4 (3.4)	6.5
16	4	14/15, 15/16†, 35/36, 36/37†	8, 8.5, 8, 8 (8.1)	2.5, 2.5, 3, 3 (2.8)	5.3

IBD, Intra-bony defect; PDR, Probing depth reduction.
*The average calculation of all sites of a given patient.
†Furcation involvement.
‡The average of the two inter-proximal sites of the tooth aspect related to the intra-osseous defect of each given IBD site.

Table 2. Pre and post-op mean (*) clinical attachment level (CAL) and recession (Rec) in the GTR group

Patients	No. of IBD sites	Pre CAL* GTR	Post Cal*	CAL* gain	Pre Rec	Post Rec
1	4	7.5‡, 7.5, 6.5, 8 (7.4*)	5, 4.5, 3.5, 4.5 (4.4*)	3	1,0,0,0	1,1,0,0
2	4	9.5, 9.5, 11.5, 7.5 (9.5)	4, 4, 6, 3 (4.3)	5.2	m1,0,1,0	m1,0,2,0
3	3	8.5, 9, 8 (8.5)	2, 3, 4 (3)	5.5	0,0,0	0,3,1
4	5	10, 9, 12, 11, 10 (10.4)	5, 5, 5.5, 4, 5 (4.9)	5.5	0,0,0,0, m1	1,1,1,0,1
5	4	10, 9, 12.5, 10 (10.4)	4.5, 5.5, 5, 4 (4.8)	5.6	0,0,0,0	0.5,1,0.5,0
6	5	8, 8.5, 8, 7, 7 (7.7)	4, 4.5, 4.5, 4.5, 4 (4.3)	3.4	0,1,1,0,0	0,1,1,0,0
7	4	10.5, 9, 10,10 (9.9)	5, 4, 4.5, 5 (4.6)	5.3	0,0,0,0	1,0,0.5,1
8	4	9, 8, 9,8 (8.5)	4, 3.5, 4, 4 (3.9)	4.6	0,0,0,0	1,1,1,1
9	4	8, 7, 10, 10 (8.8)	4, 3.5, 4, 4 (3.9)	4.9	0,0,0,0	0.5,0,1,1
10	4	11.5, 10.5, 11, 10.5 (10.9)	5, 4.5, 4.5, 5 (4.8)	6.1	0,0.5,0.5,0	1,1,1,1
11	4	8.5, 9, 9, 9.5 (9)	3.5, 4, 4, 3.5 (3.8)	5.2	0,0,0,0.5	1,1,1,1
12	4	9, 8, 9, 9 (8.8)	4.5, 4.5, 4.5, 4 (4.4)	4.4	0,0,0,0	1,1,1,0.5
13	4	8, 7, 9.5, 9.5 (8.5)	4, 3.5, 4, 4 (3.9)	4.6	0,0,0,0	0,0,0.5,0.5
14	6	7.5, 8, 7.5, 7.5, 7.5, 8 (7.7)	4, 3.5, 4.5, 5.5, 4.5,3.5 (4.3)	3.4	0.5,0.5,0.5,0,0.5,0	1,1,1,1,1,0
15	4	10.5, 9, 10, 10 (9.9)	4.5, 4, 4, 5 (4.4)	5.5	0,0,0,0	1,1,1,1
16	4	8.5, 8.5, 8.5, 9 (8.6)	3, 3.5, 3.5, 3 (3.2)	5.4	0.5,0,0.5,1	1,1,1,1

IBD, Intra-bony defect; Rec, Recession (m-minus i.e. coronal to the CEJ).
*The average calculation of all sites of a given patient.
‡The average of the two inter-proximal sites of the tooth aspect related to the intra-osseous defect of each given IBD site.

GTR procedure that included the usage of a bilayer porcine collagen resorbable membrane (Mem, Bio-Gide®; Geistlich Biomaterials, Wolhusen, Switzerland) as a biological tissue barrier and DBX particles (Bio-Oss®; Geistlich Biomaterials, Wolhusen, Switzerland) as a supporting biomaterial, or (ii) application of amelogenin extracts of enamel matrix derivatives (EMD, Emdogain®; Straumann AG, Basel, Switzerland) followed by DBX particles soaked in EMD.

Surgical procedure

Before surgery, the patients rinsed their mouths with 0.2% chlorhexidine (Corsodyl®; GlaxoSmithKline, Middlesex, UK) after which 2% lidocaine hydrochloride with norepinephrine (1:100,000) was administered by buccal and lingual infiltration as a local anaesthesia. Mucoperiosteal flaps were reflected for wide exposure of the defects, while still preserving the inter-proximal soft tissue using the papillary preservation technique (PPT) described by Takei et al. (1985, 1989) and Cortellini et al. (1995).The horizontal inter-proximal incision was performed on the opposite side (buccal or lingual) with respect to the site with the deepest PD value. Soft tissue debridement followed by thorough root planing was conducted to smooth the exposed root surface. A dummy matrix was trimmed to prepare a customized fitted resorbable collagen membrane in the GTR cases (Figs 1–2, Figs S1–S4, case #4). DBX particles (500–1000 μ) were placed to fill the intra-bony defect, followed by cover-

Table 3. Clinical mean (*) pre- and post-op periodontal probing depth (PD) in the EMD/DBX group

Patient numbers	No. of IBD sites	ID sites	Pre PD*	Post PD*	PDR*
1	4	16/17†, 22/23, 26/27†, 35/36	8.5‡, 10, 10, 10 (9.6*)	3, 2, 3, 3 (2.8)	6.8
2	4	15/16†, 36/37, 45/46, 46/47	10.5, 9.5, 9, 8.5 (9.4)	4, 3.5, 3.5, 3 (3.5)	5.9
3	3	15/16, 16/17†, 25/26	8, 8, 6 (7.3)	4,4,3 (3.7)	3.6
4	5	14/15, 16/17†, 25/26†, 26/27†, 36/37	8.5, 9, 9.5, 9, 10 (9.2)	4, 3.5, 4, 4, 4 (3.9)	5.3
5	5	14/15, 15/16†, 25/26†, 26/27†, 31/32	9.5, 10, 10, 9.5, 9 (9.6)	3.5, 3, 3.5, 3, 3.5 (3.3)	6.6
6	6	14/15, 15/16†, 25/26†, 26/27†,32/33, 45/46	9, 11, 9.5, 9, 8.5, 9.5 (9.4)	3, 4, 4, 3.5, 3.5, 4 (3.7)	5.7
7	4	14/15, 15/16†, 25/26†, 36/37	8.5, 6.5, 7, 8 (7.5)	3.5, 3.5, 4, 4.5 (3.9)	3.6
8	4	14/15, 15/16†, 35/36†, 46/47	8,7, 8, 6 (7.3)	4, 4, 4, 4 (4)	3.3
9	4	14/15, 15/16†, 21/22, 36/37†	9.5, 10, 9, 11 (9.9)	3, 3, 3, 3 (3)	6.9
10	4	15/16†, 26/27†, 35/36†, 31/32	10, 9, 9.5, 9 (9.4)	4, 4, 4, 3.5 (3.9)	5.5
11	4	25/26†, 26/27†, 36/37†, 42/43	7.5, 7, 7.5, 7 (7.3)	4, 4, 4, 3.5 (3.9)	3.4
12	6	15/16†, 11/21, 24/25, 26/27†,31/41, 45/46†	9, 8, 9, 9, 8, 9 (8.7)	4, 3.5, 4, 4, 3, 3.5 (3.7)	5
13	5	15/16†, 24/25, 25/26†, 26/27†, 36/37†	10, 10, 9, 10, 10 (9.8)	3.5, 3, 3.5, 3, 3 (3.2)	6.6
14	6	15/16†, 16/17†, 12/13, 26/27†, 35/36†, 45/46	10, 10.5, 9, 9.5, 9, 9.5 (9.6)	4, 3.5, 4, 3.5, 3.5, 3.5 (3.7)	5.9
15	4	21/22, 26/27†, 35/36, 45/46†	8, 7, 7, 7 (7.3)	4, 4, 3.5, 4 (3.9)	3.4
16	4	15/16†, 11/12, 36/37†, 46/47†	10, 8.5, 9, 9.5 (9.3)	4, 3, 3.5, 4 (3.6)	5.7

IBD, Intra-bony defect; PDR, Probing depth reduction.
*The average calculation of all sites of a given patient.
†Furcation involvement.
‡The average of the two inter-proximal sites of the tooth aspect related to the intra-osseous defect of each given IBD site.

Table 4. Pre and post-op mean(*) clinical attachment level(CAL) and recession (Rec) in the EMD/DBX group

Patient numbers	No. of IBD sites	Pre CAL*	Post Cal*	CAL* gain	Pre Rec	Post Rec
1	4	9‡,10, 10, 10 (9.8*)	4.5, 2, 3, 3.5 (3.3)	6.5	0.5,0,0,0	1.5,0,0,0.5
2	4	10.5, 9.5, 9, 8.5 (9.4)	4, 3.5, 3.5, 3 (3.5)	5.9	0,0,0,0	0,0,0,0
3	3	8, 8, 6 (7.3)	4.5, 4, 3 (3.8)	3.5	0,0,0	0.5,0,0
4	5	8.5, 9, 9.5, 9, 10 (9.2)	4, 3.5, 4, 4, 4 (3.9)	5.3	0,0,0,0,0	0,0,0,0,0
5	5	9.5, 10, 10, 9.5, 9 (9.6)	3.5, 3, 3.5, 3, 4.5 (3.5)	6.1	0,0,0,0,0	0,0,0,0,1
6	6	9, 11, 9.5, 9, 8.5, 9.5 (9.4)	3, 4, 4, 3.5, 3.5, 4 (3.7)	5.7	0,0,0,0,0,0	0,0,0,0,0,0
7	4	8.5, 6.5, 7, 8 (7.5)	3.5, 3.5, 4, 5 (4)	3.5	0,0,0,0	0,0,0,0.5
8	4	8,7, 8, 6 (7.3)	4, 4, 4, 4.5 (4.1)	3.2	0,0,0,0	0,0,0,0.5
9	4	9.5, 10.5, 9, 11 (10)	3.5, 4, 3.5, 4 (3.8)	6.2	0,0.5,0,0	0.5,1,0.5,1
10	4	10, 9, 9.5, 9 (9.4)	4, 4, 4, 3.5 (3.9)	5.5	0,0,0,0	0,0,0,0
11	4	7.5, 7, 7.5, 7 (7.3)	4, 4, 4.5, 3.5 (4)	3.3	0,0,0,0	0,0,0.5,0
12	6	9, 8, 9, 9, 8.5, 9 (8.8)	4, 3.5, 4, 4, 4, 3.5 (3.8)	5	0,0,0,0,0.5,0	0,0,0,0,1,0
13	5	10, 10, 9, 10, 10 (9.8)	3.5, 4, 3.5, 4, 3.5 (3.7)	6.1	0,0,0,0,0	0,1,0,1,0.5
14	6	10, 10.5, 9, 9.5, 9, 9.5 (9.6)	4, 3.5, 4, 3.5, 3.5, 3.5 (3.7)	5.9	0,0,0,0,0,0	0,0,0,0,0,0
15	4	8.5, 7, 7, 7 (7.4)	4.5, 4, 3.5, 4 (4)	3.4	0.5,0,0,0	0.5,0,0,0
16	4	10, 8.5, 9, 9.5 (9.3)	4, 3.5, 3.5, 4 (3.8)	5.5	0,0,0,0	0,0.5,0,0

IBD, Intra-bony defect; Rec, Recession.
*The average calculation of all sites of a given patient.
‡The average of the two inter-proximal sites of the tooth aspect related to the intra-osseous defect of each given IBD site.

age with the trimmed membrane. Primary soft tissue closure was achieved by releasing the flaps and stabilizing it using 5–0 resorbable coated polyglactin 910 (Vicryl®; Ethicon, Somerville, NJ 08876, USA) or a 5–0 polyamide monofilament non-absorbable suture (Ethicon), executed as interrupted internal mattress sutures to achieve complete closure in the inter-proximal areas (Cortellini et al. 2001). EMD/DBX-treated cases (Figs 1–2 and S5–S7, Case #2) were sham-operated except for conditioning of the exposed roots with 24% EDTA for 2 min., followed by liberal saline rinsing and then by application of EMD gel (Emdogain®) over the exposed root surface. Every effort was made to avoid bleeding in these sites. DBX particles soaked in EMD gel were then added to fill the defect, and the surgical site was similarly closed. The patients in both groups received meticulous post-operative instructions. Sutures were removed after 2 weeks. The patients were instructed to gently swab the surgical site with gauze soaked in CHX solution. During the maintenance phase, they were monitored weekly for the first month, followed by monthly visits for 6 months, and once every 3 months thereafter. Follow-up visits focused on reinforcement of oral hygiene instructions and supragingival prophylactic cleaning. The PD, clinical attachment level and Rec height were recorded at 6 and 12 months post surgery. Periapical and bite-wing radiographs were taken at the initial examination and after 6 and 12 months. However, only an observational evaluation was

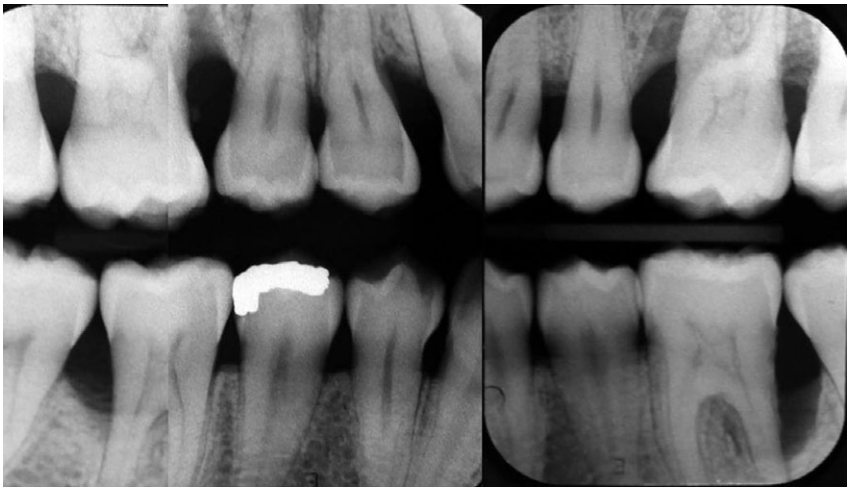

Fig. 1. Pre-operative bite-wing admission radiographs of a 21-year-old female (Case # 4 of the GTR group) with aggressive periodontitis. Note the intra-bony defects, particularly of the first molars.

conducted as an ortho-radial approach had been used and there had been no verification of standardized location and angulation of the periapical/bite-wing films.

Statistical analysis was by paired *t*-tests (for changes within study groups) and independent *t*-tests (for comparing study groups) – GTR; EMD). Probability values of $p < 0.05$ were accepted as significant.

Results

Patient compliance was very satisfactory, especially considering the strict oral hygiene maintenance regimen that was required. No adverse effects were noted throughout the administration of either mode of treatment.

A distinctive familial inheritance could be traced along the family tree of three patients, but it did not affect their response to treatment.

Upon re-evaluation of the non-surgical phase, periodontal indices were re-measured and provided evidence of a clinical improvement. Tureskey's modification in Quigley & Hein PI decreased drastically to 1.0 and below. Similarly, the average Saxer & Muhlemann BOP indices decreased to 0.4 and below. PD and CAL improved by 0–2 mm, primarily at the mild to moderate sites. However, the IBD sites persisted in showing a limited to no PD reduction (0–1 mm). A careful post-operative follow-up program was observed. The attached gingiva maintained a healthy appearance throughout the frequent visits, with no signs of oedema. Tables 1–4 show PD reduction and CAL gain at 1 year after the completion of the surgical phase. As there was no significant improvement of the PD and CAL indices at the extensive IBD sites, the baseline clinical and 1-year post-surgical phase recordings of the PD, CAL and Rec are listed in the Tables.

At 1 year, the mean PD in the GTR group ($n = 16$; sites = 67) decreased from 8.93 mm (±1.14, SD) to 3.58 (±0.50). The mean PD reduction was 5.35 mm (±1.10) ($p < 0.001$). The mean CAL in the GTR group decreased from 9.03 mm (±1.03) to 4.16 mm (±0.53), which was expressed by a mean CAL gain of 4.87 mm (± 0.91) ($p < 0.001$).

In the EMD group ($n = 16$; sites = 73), the mean PD decreased from 8.77 mm (±1.04) to 3.61 mm (±0.36), with a mean reduction of 5.15 mm (±1.28) ($p < 0.001$). The mean CAL decreased from 8.79 mm (±1.04) to 3.77 mm (±0.22), expressed by a mean CAL gain of 5.02 mm (±1.21) ($p < 0.001$). PD reduction and CAL gain values during the first year were highly significant in each group. However, assessments of the between-subject (GTR and EMD) effects showed no

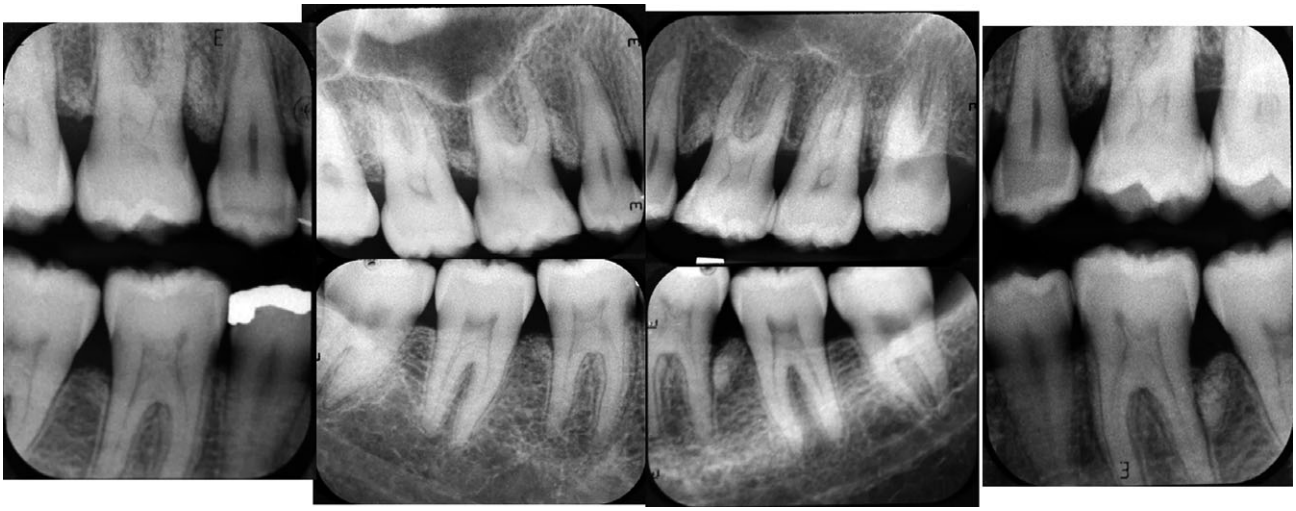

Fig. 2. At 1-year post-active therapy, the periapical and bite-wing radiographs demonstrate immaculate defect filling and healing.

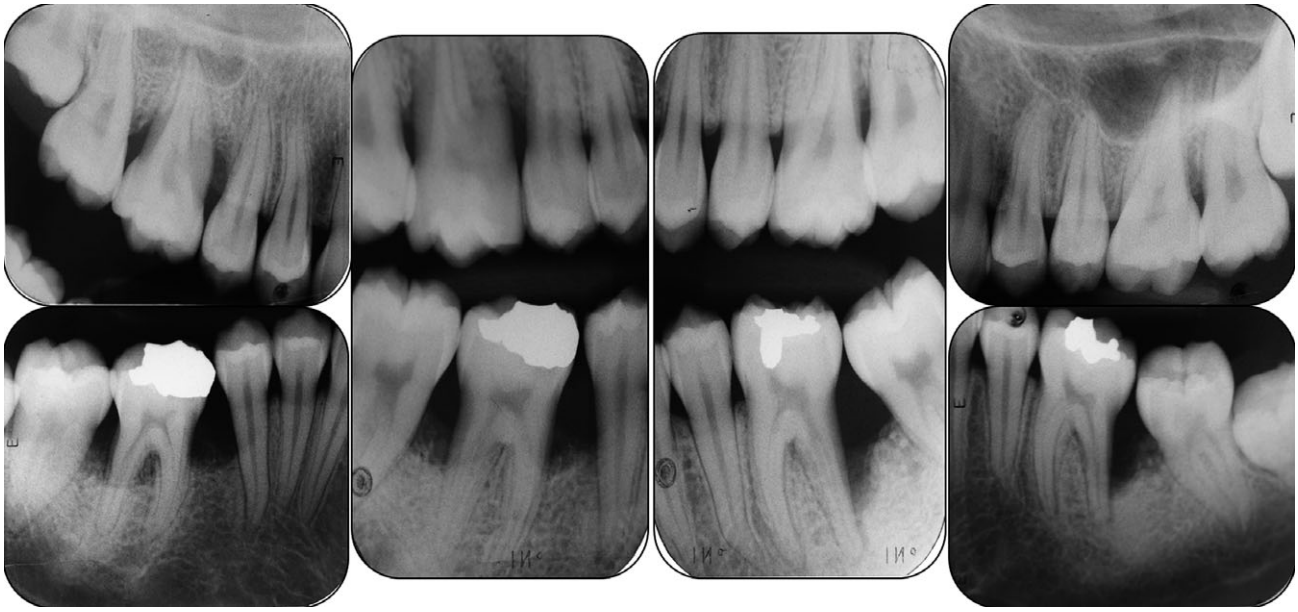

Fig. 3. Preoperative periapical and bite-wing radiographs of a 17-year-old female (Case # 2 of the EMD group) with aggressive periodontitis. Except for #26, there is severe periodontal breakdown in all first molars.

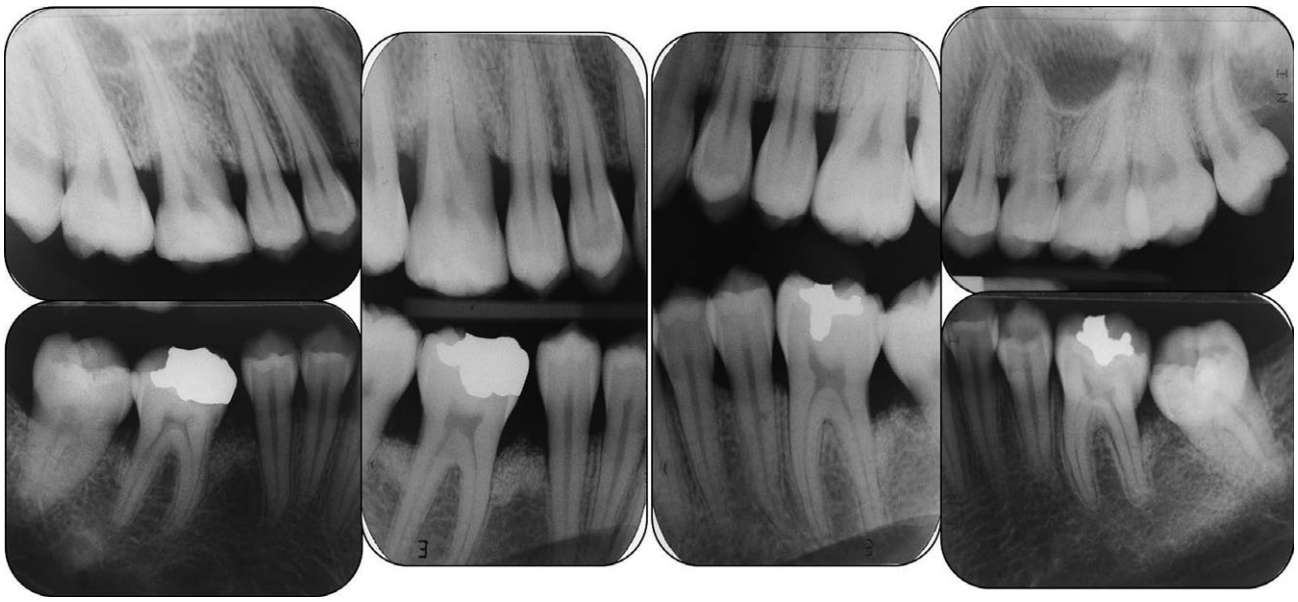

Fig. 4. The 1-year post-treatment periapical and bite-wing radiographs of Case # 2 of the EMD group show periodontal bone fill and healing.

statistical difference in either PD ($p = 0.65$) or CAL ($p = 0.69$).

All sites with furcation involvement that had been surgically accessed were grade 2 (Hamp et al. 1975) and they are listed in Tables 1 and 3. However, this important anatomical landmark was not inspected separately in this study, and is therefore not as identified as a distinct IBD in the statistical analysis. As for the Rec outcome, only a few sites showed mild recession (no greater than 1 mm) (Tables 2 and 4).

The post-operative radiographs disclosed a notable defect bone fill by both techniques.

Discussion

Guided tissue regeneration and amelogenin-derived protein applications are two ways to support periodontal regeneration via different biological pathways. In view of the differences between the two procedures and the different biological processes associated with these techniques, the similar results achieved in AgP patients after 1 year are of utmost importance.

In this study, GTR-treated sites showed PD reduction and CAL gain

of 61.1% and 54.5% respectively. EMD sites responded similarly, with PD reduction and CAL gain of 61.6% and 59.3% respectively.

Clinically, the sites in which there was evidence of furcation involvement responded well to both surgical procedures, primarily in their vertical components as reflected by the PD outcomes.

The follow-up radiographs which supported the clinical measurements were also not included in the study as the radiographic data did not meet the strict criteria of this research. Specifically, not all radiographs were taken and developed in a standardized fashion, and it could not be ensured that all were taken at identical angles and doses. We therefore felt that the radiographs could not provide a data base suitable for comparison. However, careful examination of the radiographs further supported our findings and conclusions by showing consistent hard tissue regeneration and re-formation of the lamina dura and periodontal ligament spaces (Figs S2 and S7).

Another shortcoming of the study design could stem from the fact that different IBD configurations were not considered as a variable factor in the interpretation of the outcome as they should have been. It is well known that the IBD morphology has a determinant effect on the regeneration capacity. Further inspection would be beneficial in determining a possible correlation between the amount of IBD resolution and the type of regenerative application that needs to be applied.

Successful healing of most periodontal surgical procedures requires wound stability, revascularization and the establishment of complete soft tissue closure. These requirements are crucial for successful results in the setting of regeneration treatment. It has also been shown that flap management via PPT enhances the outcome of regenerative procedures (Cortellini et al. 2001, Zucchelli et al. 2002b). For these reasons, we carefully adopted those clinical measures for both of our study groups.

In addition to flap design and management, meticulous surgical execution, patient compliance and a strict maintenance regimen appear to be key factors, regardless of the surgical mode of operation.

AgP is a rapidly progressing inflammatory disease. However, meticulous care may result in rather predictable long-term success (Buchmann et al. 2002, Bäumer et al. 2011, Nibali et al. 2013, Teughels et al. 2014).

ChP and AgP have shown distinctively different aetiological/contributing factors, the latter being more aggressive, rapid and severe (Albandar 2014). It is therefore encouraging that the effectiveness of regenerative periodontal treatment of intra-bony defects in AgP produces successful and maintainable periodontal status.

GTR and EMD have been reported to result in periodontal restitution in severe ChP (Gottlow et al. 1986, Sculean et al. 1999a,b,c, 2000a,b, 2001a,b, 2002, 2003a,b, 2004a,b, 2005, 2006, 2007, 2008a,b, Tonetti et al. 2002, Trombelli et al. 2002, Windisch et al. 2002, Zucchelli et al. 2002b, 2003, Sanz et al. 2004, Cortellini & Tonetti 2005, Palmer et al. 2008, Esposito et al. 2009, Koop et al. 2012, Tu et al. 2012, Döri et al. 2013). Surprisingly, there are only few data regarding AgP and they are not always encouraging (DiBattista et al. 1995, Vandana et al. 2004). On the other hand, there are individual studies that claim successful results using either GTR procedures (Sirirat et al. 1996) or EMD application (Zucchelli et al. 2002a). The properties and the characterization of the enamel matrix proteins as shown in IBD in cases of ChP appear to support wound healing and new periodontal tissue formation in IBD sites in cases of AgP as well.

Our results supported a recent report using the same surgical modalities (Iorio-Siciliano et al. 2014) in which non-contained intrabony defects showed significant CAL improvement that was calculated as being 60% and 50% for EMD/DBX and GTR/DBX respectively. Furthermore, that group's report also claimed no statistical significant difference between the two.

Although consensus reports (Palmer 2008) as well as systematic reviews (Esposito et al. 2009) did not differentiate between IBD treatment modalities of patients diagnosed as having AgP and/or ChP, it may be assumed that these sites healed successfully and that the favourable outcome was maintained.

Our findings are quite consistent if we relate them to the results of laboratory research. Recent reports on the immunological composition in severe defects of ChP and AgP sites (Rescala et al. 2010) showed no statistically significant differences in immunological and microbial parameters between subjects with ChP and AgP. One population study showed a comparable clinical outcome after treating ChP and AgP patients by a non-surgical approach (Rosalem et al. 2011). In another review, Deas & Mealey (2010) discussed the treatment outcome in ChP and Agp and agreed that the long-term outcome could be comparable with blurred boundaries.

Only a few reports examined the efficacy of regenerative procedures using either the GTR techniques in AgP patients (DiBattista et al. 1995, Sirirat et al. 1996, Buchmann et al. 2002, Zucchelli et al. 2002a, Sant'Ana et al. 2009, Lu et al. 2012) or EMD applications (Manor 2000, Bonta et al. 2003, Vandana et al. 2004, Miliauskaite et al. 2007, Kaner et al. 2009).However, no consensus was reached among them.

The combinations of GTR and a biomaterial grafting material (Trombelli et al. 2002, Stavropoulos & Karring 2005, Iorio-Siciliano et al. 2014) or EMD and a biomaterial (Lekovic et al. 2000, 2001a,b, Camargo et al. 2001, Scheyer et al. 2002, Velasquez-Plata et al. 2002, Sculean et al. 2002, 2003a, 2005, 2008a, Döri et al. 2005; Zucchelli et al. 2003, Iorio-Siciliano et al. 2014) have been extensively investigated. The results showed that the addition of a xenograft, such as DBX, resulted in encouraging results in IBD in ChP. However, this could be related to the excellent biocompatible and conductive properties of the biomaterial rather than to the unproven induction, as had been shown earlier (Donos et al. 2004, 2005, 2006).

In a Cochrane systematic review, Esposito et al. (2009) stated that there was no evidence of clinically significant differences between GTR and EMD in periodontal intra-bony lesions. However, these authors found that using bone substitute materials procedures were associated with less soft tissue marginal reces-

sion compared with the application of EMD alone.

For practical purposes, the significance of adding a biomaterial (DBX), whether in GTR and/or EMD techniques, is to provide a means of maintaining the volume of the filled defect (Lindhe et al. 2014) and thereby enhance the clinical outcome. As there is no selective barrier in EMD, the added biomaterial particles might give mechanical support to the soft tissue over-lay during the healing phase.

The findings of the current work demonstrated that both therapeutic modalities achieved a comparable clinical outcome, i.e. stability of the soft tissue position, minimal recession and ease in the ability to control plaque.

In conclusion, and within the limitations of this study, it appears that a successful regenerative therapeutic approach can be achieved in a predictable manner in AgP patients. The key seems to be the application of a meticulous treatment mode for both techniques followed by a strict supportive periodontal maintenance regimen.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Fig. S1. The upper right sextant of Case # 4 of the GTR group. The buccal (a) and palatal (b) aspects of the crestal bone topography. BBM particles were inserted to fill the defects (c) followed by overlay resorbable collagen membranes (d).

Fig. S2. The upper left sextant of Case # 4 of the GTR group. The periodontal probe showed a 2-wall intra-bony component of 7 mm (a), which was filled by BBM particles (b) and covered by a collagen membrane (c, d)

Fig. S3. The lower left sextant of Case # 4 of the GTR group. The periapical radiograph (a) shows extensive periodontal destruction along with furcation involvement of the first molar. The 6 mm intra-bony defect (a) was filled with BBM particles (c) followed by collagen membrane coverage (d).

Fig. S4. The lower right sextant of Case # 4 of the GTR group. The same description as in Fig. S3.

Fig. S5. The upper right first molar of Case # 2 of the EMD group. Buccal (a) and palatal (b) views of the debrided roots. EMD gel was applied along the exposed roots (c) followed by BBM particles as a biomaterial filler (d). The buccal (e) and palatal (f) views upon suturing.

Fig. S6. The lower left first molar of Case # 2 of the EMD group. The PPT flap elevation technique (a, b) was performed to exposed the periodontal defect (c). EMD gel was applied followed by BBM particles (d). The flaps were sutured to obtain full soft tissue closure (e). Immaculate healing was evident at 1 month, (f).

Fig. S7. The lower right first molar of Case # 2 of the EMD group. The same description as in Fig. S6. Note the preservation of the inter-proximal col tissue (b) to achieve full closure.

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Clinical Relevance

Scientific rationale for the study: Establishing the efficacy of two different surgical regenerative approaches in intra-bony defects in aggressive periodontitis patients.

Principal findings: A guided tissue regeneration technique and the application of enamel matrix derivatives, both in conjunction with bovine bone mineral particles, achieve a comparable clinical outcome.

Practical implications: Successful regenerative treatment can be achieved in a predictable manner in aggressive periodontitis patients. The key for both approaches seems to be the observation of a meticulous treatment mode, followed by a strict supportive periodontal maintenance regimen.