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1. [Pre-clinical \(*in vitro* & *in vivo*\) studies \(p. 2 – p. 8\)](#)
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Pre-clinical (*in vitro* & *in vivo*) studies

1. Magneto-sensitive decellularized bone matrix with or without low frequency-pulsed electromagnetic field exposure for the healing of a critical-size bone defect

Parmaksiz M, Lalegül-Ülker Ö, Vurat MT, Elçin AE, Elçin YM. *Mater Sci Eng C Mater Biol Appl.* 2021 May;124:112065. doi: 10.1016/j.msec.2021.112065.

<https://pubmed.ncbi.nlm.nih.gov/33947558/>

Bioactive ECM-based materials mimic the complex composition and structure of natural tissues. Decellularized cancellous bone matrix (DBM) has potential for guiding new bone formation and accelerating the regeneration process. On the other hand, low frequency-pulsed electromagnetic field (LF-PEMF) has been shown to enhance the regeneration capacity of bone defects. The present study sought to explore the feasibility of using DBM and DBM/MNP, and LF-PEMF for treating critical-size bone defects. Firstly, decellularization protocol was optimized to obtain a bioactive DBM, then MNPs were incorporated. Later, the physical, chemical and biological properties of DBM and DBM/MNP were assessed *in vitro*. MNPs homogeneously distributed into the DBM were not found to be toxic to human osteoblast cultures. Finally, an *in vivo* study was carried out with DBM and DBM/MNP composites in a bilateral critical-size rat cranial defect model (n = 48) with or without LF-PEMF exposure for 45 and 90 days. The histomorphometric and radiographic evaluations revealed that, while the collagen (positive control) and Sham (negative control) groups showed high incidence of fibrous connective tissue together with low level of osteogenic activity, both the DBM and DBM/MNP-grafted groups significantly promoted new bone tissue formation and angiogenesis, by the appropriate use of LF-PEMF for 90 days.

2. Application of a collagen scaffold saturated with platelet-rich plasma in prevention of bisphosphonate-related osteonecrosis of the jaw in the rat animal model

Razmara F, Bayat M, Shirian S, Shabankare G, Mohamadnia A, Mortazavi M, Alijani MR, Bahrami N. *Heliyon.* 2021 May;7(5):e06930. doi: 10.1016/j.heliyon.2021.e06930.

<https://pubmed.ncbi.nlm.nih.gov/34007929/>

Background: Among the myriad adverse events of drugs in the oral cavity, Bisphosphonate-related osteonecrosis of the jaw (BRONJ) is one of the most detrimental drug reactions that have ever been known. **Objective:** This study was aimed to investigate the success of applying collagen scaffold alone and platelet-rich plasma (PRP)+collagen scaffold in prevention of zoledronic acid-induced BRONJ in the

rat. **Methods:** A total of 17 male Wistar-rats were treated with 4 weekly doses of zoledronic acid. All rats were undergone bilateral tooth extraction of mandibular first molars and divided into three groups of scaffold + PRP + suture, scaffold + suture, and suture only. All rats were scarified and clinical, radiological, histological and histomorphomerial evaluations were made on week 8 post-treatment. The soft tissue healing, bone mineralized density (BMD), number of osteoclasts and osteoblasts, necrotic bone (NB), intensity of inflammation and new bone formation (NBF) were analyzed. **Results:** BMD, number of osteoblasts and NBF variables proved to be statistically were higher in the treatment groups than the control group. In addition, the PRP + scaffold group showed the better results in terms of BMD, number of osteoblasts and NBF than that of the scaffold alone group. Number of osteoclasts, inflammation intensity and osteonecrosis were also significantly different in the PRP + scaffold group compared to the scaffold alone and the control groups. **Conclusion:** Application of a PRP-enriched collagen scaffold appeared to be a successful preventive treatment for BRONJ by effecting of the number of osteoblasts and osteoclasts, BMD, NBF, inflammation, and osteonecrosis.

3. Prevention of coronal discoloration induced by regenerative endodontic treatment in an ex vivo model.

Shokouhinejad N, Khoshkhounejad M, Alikhasi M, Bagheri P, Camilleri J. 2018. Clin Oral Investig.; 22(4):1725-1731. [Epub 2017].

<https://www.ncbi.nlm.nih.gov/pubmed/29090391>

OBJECTIVES: The aim of this study was to assess the effect of sealing the pulp chamber walls with a dentin-bonding agent (DBA) on prevention of discoloration induced by regenerative endodontic procedures (REPs) in an ex vivo model. **MATERIALS AND METHODS:** Ninety-six bovine incisors were prepared and randomly divided into two groups. In one group, the pulp chamber walls were sealed with DBA before placement of triple antibiotic paste (TAP) containing minocycline inside the root canals, but in the other group, DBA was not applied. After 4 weeks, the root canals were filled with human blood a blood clot was allowed to form. After that, a collagen sponge (fleece) was placed over the blood clot and each group was then randomly divided into four subgroups (n = 12) according to the endodontic cements placed over the blood clot (ProRoot MTA, OrthoMTA, RetroMTA, or Biodentine). The color changes (ΔE) were measured at different steps. The data were analyzed using t test and two-way ANOVA. **RESULTS:** The specimens in which dentinal walls of pulp chamber were sealed with DBA showed significantly less coronal discoloration at each step of regenerative treatment ($p < 0.001$). However, application of DBA did not completely prevent the clinically perceptible coronal color change. Sealing the blood clot with different endodontic cements did not result in significant difference in coronal discoloration ($p > 0.05$). **CONCLUSIONS:** Sealing the pulp chamber walls before insertion of TAP decreased coronal discoloration following REP using different endodontic cements but did not prevent it. **CLINICAL RELEVANCE:** Discoloration of teeth undergoing REPs is an unfavorable outcome. Considering the significant contribution of TAP containing minocycline to the coronal tooth discoloration even after sealing the pulp chamber walls, the revision of current guidelines in relation to the use of TAP with minocycline might need to be revised.

* Study refers to Bone Protect fleece (Dentegris), which is a private label of Jason® fleece.

4. Healing of two-wall intra-bony defects treated with a novel EMD-liquid-A pre-clinical study in monkeys.

Shirakata Y, Miron RJ, Shinohara Y, Nakamura T, Sena K, Horai N, Bosshardt DD, Noguchi K, Sculean A. 2017. *J Clin Periodontol.*; 44(12):1264-1273.

<https://www.ncbi.nlm.nih.gov/pubmed/28965367>

Investigation of the effect of a novel enamel matrix derivative formulation (EMD-liquid or Osteogain) combined with an absorbable collagen sponge (ACS – collacone®) on periodontal wound healing in intra-bony defects in monkeys. **MATERIALS AND METHODS:** Chronic two-wall intra-bony defects were created at the distal aspect of eight teeth in three monkeys (*Macaca fascicularis*). The 24 defects were randomly assigned to one of the following treatments: (i) open flap debridement (OFD) + ACS alone, (ii) OFD + Emdogain® + ACS (Emdogain®/ACS), (iii) OFD + Osteogain + ACS (Osteogain/ACS) or (iv) OFD alone. At 4 months, the animals were euthanized for histologic evaluation. **RESULTS:** Osteogain/ACS resulted in more consistent formation of cementum, periodontal ligament and bone with limited epithelial proliferation compared to OFD alone, Emdogain®/ACS and OFD + ACS. Among the four treatment groups, the Osteogain/ACS group demonstrated the highest amount of regenerated tissues. However, complete periodontal regeneration was not observed in any of the defects in the four groups. **CONCLUSIONS:** The present findings indicate that in two-wall intra-bony defects, reconstructive surgery with Osteogain/ACS appears to be a promising novel approach for facilitating periodontal wound healing/regeneration, thus warranting further clinical testing.

5. Absorbable collagen sponges loaded with recombinant bone morphogenetic protein 9 induces greater osteoblast differentiation when compared to bone morphogenetic protein 2.

Fujioka-Kobayashi M, Schaller B, Saulacic N, Pippenger BE, Zhang Y, Miron RJ. 2017. *Clin Exp Dent Res.*; 3:32–40.

<http://onlinelibrary.wiley.com/doi/10.1002/cre2.55/pdf>

The aim of the present *in vitro* study was to evaluate the regenerative potential of an absorbable collagen sponge (ACS – collacone®) specifically designed for extraction socket healing loaded with rhBMP9 when compared to rhBMP2. The adsorption and release kinetics of rhBMP2 and rhBMP9 were first investigated by enzyme-linked immunosorbent assay quantification. Then, the cellular effects of stromal cell line (ST2) preosteoblasts were investigated utilizing four groups including rhBMP2 and rhBMP9 at both low (10 ng/ml) and high (100 ng/ml) concentrations loaded onto ACS. Cellular attachment (8 hours) and proliferation (one, 3, and 5 days) as well as osteoblast differentiation were investigated by real-time polymerase chain reaction (PCR) at 3 and 14 days, alkaline phosphatase (ALP) activity at 7 days, and alizarin red staining at 14 days. ACS fully adsorbed both rhBMP2 and rhBMP9 that were slowly released up to 10 days. Although neither rhBMP2 nor rhBMP9 had any effects on cell attachment or proliferation, pronounced effects were observed on osteoblast differentiation. ALP

activity was increased seven-fold with rhBMP2-high, whereas a marked 10-fold and 20-fold increase was observed with rhBMP9-low and high loaded to ACS, respectively. Furthermore, mRNA levels of collagen1, ALP, bone sialoprotein, and osteocalcin were all significantly higher for rhBMP9 when compared to control or rhBMP2 groups. Alizarin red staining further confirmed that rhBMP9-low and high demonstrated marked increases in mineralization potential when compared to rhBMP2-high. The results demonstrate the marked effect of rhBMP9 on osteoblast differentiation when combined with ACS in comparison to rhBMP2 at doses as much as 10 times lower. Further *in vivo* studies are necessary to investigate whether the regenerative potential is equally as potent.

6. Effects of EMD-liquid (Osteogain) on periodontal healing in class III furcation defects in monkeys.

Shirakata Y, Miron RJ, Nakamura T, Sena K, Shinohara Y, Horai N, Bosshardt DD, Noguchi K, Sculean A. 2017. *J Clin Periodontol.*; 44(3):298-307.

<https://www.ncbi.nlm.nih.gov/pubmed/27978604>

Evaluation of the effect of a novel liquid carrier system of enamel matrix derivative (Osteogain) soaked on an absorbable collagen sponge (ACS - collacone®) upon periodontal wound healing/regeneration in furcation defects in monkeys. **MATERIALS AND METHODS:** The stability of the conventional enamel matrix derivative (Emdogain®) and Osteogain adsorbed onto ACS was evaluated by ELISA. Chronic class III furcation defects were created at teeth 36, 37, 46, 47 in three monkeys (*Macaca fascicularis*). The 12 defects were assigned to one of the following treatments: (1) open flap debridement (OFD) + ACS, (2) OFD + Emdogain®/ACS, (3) OFD + Osteogain/ACS, and (4) OFD alone. At 16 weeks following reconstructive surgery, the animals were killed for histological evaluation. **RESULTS:** A 20-60% significantly higher amount of total adsorbed amelogenin was found for ACS-loaded Osteogain when compared to Emdogain®. The histomorphometric analysis revealed that both approaches (OFD + Emdogain®/ACS and OFD + Osteogain/ACS) resulted in higher amounts of connective tissue attachment and bone formation compared to treatment with OFD + ACS and OFD alone. Furthermore, OFD + Osteogain/ACS group showed higher new attachment formation, cementum, and new bone area. **CONCLUSIONS:** Within their limits, the present data indicate that Osteogain possesses favourable physicochemical properties facilitating adsorption of amelogenin on ACS and may additionally enhance periodontal wound healing/regeneration when compared to Emdogain®.

7. Osteogain® loaded onto an absorbable collagen sponge induces attachment and osteoblast differentiation of ST2 cells *in vitro*.

Miron RJ, Fujioka-Kobayashi M, Zhang Y, Sculean A, Pippenger B, Shirakata Y, Kandalam U, Hernandez M. 2017. *Clin Oral Investig.*; 21(7):2265-2272. [Epub 2016].

<https://www.ncbi.nlm.nih.gov/pubmed/27909893>

The aim of the present *in vitro* study was to investigate the regenerative potential of Osteogain®, a new liquid carrier system of enamel matrix derivative (EMD) in combination with an absorbable collagen

sponge (ACS – collacone®) specifically designed for extraction socket healing. **MATERIALS AND METHODS:** The potential of ACS was first investigated using ELISA to quantify total amelogenin adsorption and release from 0 to 10 days. Thereafter, the cellular effects of ST2 pre-osteoblasts were investigated for cellular attachment at 8 h and cell proliferation at 1, 3, and 5 days as well as osteoblast differentiation by real-time PCR and alizarin red staining for cells seeded on (1) tissue culture plastic, (2) ACS alone, and (3) ACS + Osteogain®. **RESULTS:** ACS efficiently loaded nearly 100% of the amelogenin proteins found in Osteogain®, which were gradually released up to a 10-day period. Osteogain® also significantly induced a 1.5-fold increase in cell attachment and resulted in a 2-6-fold increase in mRNA levels of osteoblast differentiation markers including runt-related transcription factor 2 (Runx2), collagen1a2, alkaline phosphatase, and bone sialoprotein as well as induced alizarin red staining when combined with ACS. **CONCLUSIONS:** In summary, these findings suggest that Osteogain® is capable of inducing osteoblast attachment and differentiation when combined with ACS. Future animal studies and randomized human clinical trials are necessary to further support these findings. **CLINICAL RELEVANCE:** The use of Osteogain® in combination with ACS may provide a valuable means to limit dimensional changes following tooth extraction.

8. Porcine dermis and pericardium-based, non-cross-linked materials induce multinucleated giant cells after their *in vivo* implantation: A physiological reaction?

Barbeck M, Lorenz J, Holthaus MG, Raetscho N, Kubesch A, Booms P, Sader R, Kirkpatrick CJ, Ghanaati S. *J Oral Implantol.* 2015; 41(6):e267-81. Epub 2014.

<https://www.ncbi.nlm.nih.gov/pubmed/25386662>

The present study analyzed the tissue reaction to two novel porcine-derived collagen materials: pericardium (Jason® membrane versus dermis Jason® fleece). By means of the subcutaneous implantation model in mice, the tissue reactions were investigated at 5 time points: 3, 10, 15, 30, and 60 days after implantation. Histologic, histochemical, immunohistological, and histomorphometric analysis methodologies were applied. The dermis-derived material underwent an early degradation while inducing mononuclear cells together with some multinucleated giant cells and mild vascularization. The pericardium-derived membrane induced two different cellular tissue reactions. The compact surface induced mononuclear cells and multinucleated giant cells, and underwent a complete degradation until day 30. The spongy surface of the membrane induced mainly mononuclear cells, and served as a stable barrier membrane for up to 60 days. No transmembranous vascularization was observed within the spongy material surface layer. The present data demonstrate the diversity of the cellular tissue reaction toward collagen-based materials from different tissues. Furthermore, it became obvious that the presence of multinucleated giant cells was associated with the material breakdown/degradation and vascularization. Further clinical data are necessary to assess extent to which the presence of multinucleated giant cells observed here will influence the materials stability, integration, and, correspondingly, tissue regeneration within human tissue.

9. Influence of Biphasic β -TCP with and without the use of collagen membranes on bone healing of surgically critical size defects. A radiological, histological, and histomorphometric study.

Calvo-Guirado JL, Ramirez-Fernandez MP, Degaldo-Ruiz RA. 2014. Clin Oral Implants Res.; 25(11):1228-38. [Epub 2013].

<http://www.ncbi.nlm.nih.gov/pubmed/24025159>

The aim of this study was to investigate, by means of radiological and histomorphometric analysis, the effect of resorbable collagen membranes on critical size defects (CSD) in rabbit tibiae filled with biphasic calcium phosphate. **MATERIALS AND METHODS:** Three CSD of 6 mm diameter were created in both tibiae of 20 New Zealand rabbits and divided into three groups according to the filling material: Group A (Ossceram), Group B (Ossceram plus Alveoprotect membrane), and Group C (unfilled control group). Five animals from each group were sacrificed after 15, 30, 45, and 60 days. Anteroposterior and lateral radiographs were taken. Samples were processed for observation under light microscopy. **RESULTS:** At the end of treatment, radiological analysis found that cortical defect closure was greater in Group B than Group A, and radiopacity was clearly lower and more heterogeneous in the Group A cortical defects than in Group B. There was no cortical defect closure in Group C. Histomorphometric evaluation showed significant differences in newly formed bone and cortical closure in Group B compared with Groups A and C, with the presence of higher density newly formed bone in cortical and medullar zones. There was no cortical defect closure or medullar bone formation in Group C. **CONCLUSIONS:** Biphasic calcium phosphate functioned well as a scaffolding material allowing mineralized tissue formation. Furthermore, the addition of absorbable collagen membranes enhanced bone gain compared with non-membrane-treated sites.

*Study refers to Alveoprotect (Bredent), which was a former private label of Jason® fleece.

10. Elution kinetics, antimicrobial efficacy, and degradation and microvasculature of a new gentamicin-loaded collagen fleece.

Kilian O., Hossain H., Flesch I., Sommer U., Nolting H., Chakraborty T., Schnettler R.; 2009. J Biomed Mater Res B Appl Biomater.; 90(1):210-22.

<http://www.ncbi.nlm.nih.gov/pubmed/19090489>

Conventional gentamicin-containing collagen fleeces currently in use are strongly acidic and exhibit limited biocompatibility thereby adversely affecting wound healing. To improve the antibiotic delivery system, a new phosphate-buffered, gentamicin-loaded fleece with pH-neutral properties has been developed (Jason® fleece G). This study aimed at comparing the elution kinetics of gentamicin release and the antimicrobial efficacy of conventional fleeces with the newly developed fleece *in vitro*. In addition, degradation and microvasculature of implanted fleeces were examined in a rat model and assessed using histology, as well as detection of ED-1 and PECAM-expression using immunohistochemistry. **METHODS:** We show that the phosphate-buffered fleeces have reduced



release ($p < 0.05$) of the integrated gentamicin. However, all of the fleeces tested had a significant antimicrobial effect on the growth of *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa* strains ($p < 0.01$). **RESULTS:** Among the fleeces tested, the new Jason G fleece had the weakest but nevertheless sufficient antimicrobial effectiveness. Evaluation of the antibiotic effect in the prevention of an infection showed no differences between the applied fleeces. Following surgical implantation of fleece in the backs of Wistar rats we observed, on day 5 after implantation, an increase in cell infiltration and microvascularization with the phosphate-buffered fleece as compared with conventional fleeces, which show necrotic cells on their surface. Unlike the acidic fleeces, on day 15 after implantation the pH-neutral fleece was resorbed widely.

CONCLUSIONS: Here, we show that the new, pH-neutral, gentamicin-containing fleece Jason G exhibits good overall antimicrobial effectiveness against both gram-positive and gram-negative bacteria *in vitro* with improved degradation properties and microvasculature formation *in vivo*.

Clinical studies and case series

11. Endodontic pulp revitalization in traumatized necrotic immature permanent incisors: Early failures and long-term outcomes—A longitudinal cohort study

Wikström A, Brundin M, Romani Vestman N, Rakhimova O, Tsilingaridis G. *Int. Endod. J.* 2022 Mar;00:1–16. doi: 10.1111/iej.13735.

<https://onlinelibrary.wiley.com/doi/full/10.1111/iej.13735>

Aim: This prospective cohort study evaluates clinical and radiographical outcomes of endodontic pulp revitalization (PR) of traumatized necrotic incisors. **Methodology:** Pulp revitalization was performed in 75 traumatized necrotic immature incisors from 71 patients. The radiographic outcome measures were continued root formation (width and length), root resorption, apex closure, periapical index, and root development stage. The clinical outcome measures were percussion pain, palpation pain, pathological tooth mobility, swelling, sinus tract, ankylosis, crown discolouration, response to pulp sensitivity test, and subjective pain. Treatment outcomes were categorized as a success based on the absence of clinical symptoms and when radiographic evidence was present for apical healing and continued root development. The performed statistical tests were repeated measures anova, pairwise comparisons of interactions (t-test), McNemar's test, and linear regression model. **Results:** In 45 of 75 teeth (60%), PR was successful with the resolution of clinical and radiographic signs and continued root development. PR failed due to the absence of bleeding (n = 19) and persistent infection (n = 11). PR showed statistically significant increases in root length (11%), and dentinal wall thickness (30%), root maturation (pre-operative 3.38 [CI 1.88; 4.88]; post-operative 4.04, [CI 2.56; 5.52]) apical closure (71.4%), healing of pre-operative apical periodontitis (100%), and healing of pre-operative inflammatory root resorptions (100%). Three predictive variables for continued root maturation were identified – root development stage at entry ($p = .0001$, β 0.649), [CI 0.431; 0.867], trauma to the soft tissues ($p = .026$, β -0.012), [CI -0.0225; -0.015], and pre-operative dentinal wall thickness ($p = .009$, β -0.001); [CI -0.001; 0.0001]. **Conclusions:** Our findings indicate that PR provides satisfactory clinical and radiographical outcomes in traumatized necrotic incisors. The failed cases were related to lack of bleeding and persistent infections, indicating that new techniques are needed to improve the predictability of PR.

12. A Simplified Procedure for Biologically-oriented Alveolar Ridge Preservation: Clinical and Histological Findings From a Case Report

Pramstraller M, Farina R, Simonelli A, Götz W, Trombelli L. *Clin Adv Periodontics.* 2021 Dec;11(4):189-194. doi: 10.1002/cap.10120.

<https://pubmed.ncbi.nlm.nih.gov/32945629/>

A recent systematic review failed to identify one approach for alveolar ridge preservation (ARP) with superior outcomes compared with the others. **The present case report presents a novel, simplified technique for ARP, namely the Biologically-oriented Alveolar Ridge Preservation (BARP), based on socket grafting and sealing.** **Case presentation:** After extraction of tooth #19, the socket was filled with a collagen sponge (Jason® fleece up to 4-5 mm from the most coronal extension of the bone crest (deep collagen layer). A bovine-derived xenograft (cerabone®) was placed on top of Jason® fleece to fill the coronal part of the socket (graft layer). Socket sealing was then performed by placing a Jason® fleece over the exposed portion of the graft (superficial collagen layer), and the wound healed by secondary intention. At implant insertion (4 months after ARP), limited reduction in bone width and no vertical change in ridge height were observed. Histological analysis of a biopsy specimen retrieved during implant site preparation showed a gradient ranging from interconnected trabeculae of mature, lamellar bone in the apical portion to cancellous bone incorporating a modest number of remodeled graft granules in the central portion. In the coronal portion, non-mineralized tissue with sparse isles of newly formed cancellous bone and residual graft granules was found. **Conclusion:** The present case report indicates that BARP might provide ideal conditions for preserving the pre-existing alveolar ridge dimensions following tooth extraction while restricting any potential interference of the graft biomaterial with bone healing dynamics to the coronal part of the socket.

13. A customized allogenic bone block for alveolar reconstruction quantitated by a 3D matching technique: A case report

Blume O, Back M, Martin K, Windisch P. *Clin Case Rep.* 2021 Sep;9(9):e04771. doi: 10.1002/ccr3.4771.

<https://pubmed.ncbi.nlm.nih.gov/34532047/>

After initial resorption, the bone volume showed long-term stability following loading of the implant. Furthermore, 3D matching was a suitable quantification method to analyze the volume development of bone augmentation.

14. Ridge preservation using Collacone compared with an empty socket: a pilot study

Anderud J, Lennholm C, Wälivaara DÅ *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2021 Aug;132(2):e55-e61. doi: 10.1016/j.oooo.2021.01.012.

<https://pubmed.ncbi.nlm.nih.gov/33741284/>

Objectives: The objective of this study was to evaluate the dimensional changes in alveolar bone and soft tissue after dental extraction/postextraction in alveoli filled/grafted with collagen (Collacone) compared with those left empty/ungrafted. **Study design:** Twenty-three patients with a single maxillary

incisor to be extracted were included in the study. The patients were randomized into either the treatment group, receiving a collagen sponge, or into the control group with an empty alveolus. All participants were examined and followed with cone beam computed tomography and 3-dimensional soft tissue scanning procedures during the healing process. The outcomes were statistically evaluated with Mann-Whitney U tests. **Results:** Seventeen patients were available for follow-up. The radiographic outcome showed an average loss of bone in the bucco-palatal width of 1.15 mm (range, 0.2-2.2) in the test group and 0.57 mm (range, 0-1.6) among the controls. There was no significant difference between the 2 groups ($P = .092$). The soft tissue topography height measurements revealed an average decrease of 1.737 mm (range, 0.118-2.872) in the test group and 1.899 mm (range, 0.454-3.014) in the control group. The difference was not significant ($P = .847$). **Conclusion:** The use of a Collacone collagen sponge does not enhance the bone and soft tissue healing outcome after extraction of an incisor in the maxilla compared with leaving the alveolus empty.

15. Clinical and radiographic evaluation of jumping distance management using a collagen matrix in flapless immediate implant placement

Kadkhodazadeh M, Amid R, Moscowchi A, Khoshkam V. *Dent Med Probl.* 2021 Apr-Jun;58(2):173-178. doi: [10.17219/dmp/130057](https://doi.org/10.17219/dmp/130057).

<https://pubmed.ncbi.nlm.nih.gov/33974751/>

Background: Improvement in implant design has made implant dentistry a challenging treatment modality worldwide. **Objectives:** This study aimed to investigate the efficacy of a xenogeneic collagen matrix in managing 3-4-millimeter gaps in flapless immediate implant placement. **Material and methods:** Twenty-two patients received 39 immediate implants via the flapless approach. Patients with intact bony walls, buccal bone thickness ≥ 2 mm and a jumping distance of 3-4 mm were included in this study. The gap between the implant and the socket walls was filled with a xenogeneic collagen matrix (Collacone®). The final clinical and radiographic evaluations were performed at least 24 months following functional loading. **Results:** There was no early or late failure, and the implants showed a 100% survival rate. The mean mesial (0.28 ± 0.39 mm) and distal (0.28 ± 0.39 mm) marginal bone loss (MBL) at the site of incisors was not significantly different from the values at the site of premolars and molars (0.30 ± 0.42 mm and 0.34 ± 0.48 mm, respectively). The evaluation of the implant success index (ISI) score revealed no difference between the mandible and the maxilla ($p = 0.700$), or incisors compared with premolars and molars ($p = 0.420$). The only significant difference was in terms of distal MBL, which was higher in the maxilla (0.39 ± 0.49 mm) than in the mandible (0.12 ± 0.23 mm) ($p = 0.040$). **Conclusions:** Within the limitations of this study, it seems that the application of a xenogeneic collagen matrix to manage 3-4-millimeter gaps in carefully selected cases may bring promising outcomes.

16. Modified Free Gingival Graft Technique for Root Coverage at Mandibular Incisors: A Case Series.

Carcuac O, Derks J. *Int J Periodont Restor Dent.* 2021 Mar-Apr;41(2):e37-e44. DOI: [10.11607/prd.5398](https://doi.org/10.11607/prd.5398).

<https://europepmc.org/article/med/33819324>

Numerous surgical techniques for root coverage have been suggested with different degrees of success, as assessed by the proportion of complete root coverage. Mandibular incisors, teeth with a high frequency of gingival recession defects (GRDs), were associated with the least favorable outcomes due to unfavorable anatomical conditions. In the present series of three cases, a modified version of the free gingival graft technique for the purpose of root coverage at mandibular incisors is illustrated. The purpose of the modification of the original technique was to achieve improved blood supply from the recipient site to the graft, with the ultimate aim of enhancing predictability and outcomes of the procedure. In all included cases, complete or almost complete root coverage was achieved at challenging GRDs in the mandibular incisor area.

17. Histomorphometric and Clinical Analysis of Ridge Preservation Procedures in Extraction Sockets with Buccal Bone Defects (>5mm) Using an In Situ Hardening Biphasic Calcium Phosphate (HA/ β -TCP) Graft and a Bioresorbable Matrix: A Human Study at 6 Months

Alfonsi F, Baldi N, Romeggio S, Tonelli P, Iezzi G, Velasco-Ortega E, Barone A. Appl Sciences. 2020 Apr; 10(9):3034. doi: 10.3390/app10093034.

<https://www.mdpi.com/2076-3417/10/9/3034>

Many biomaterials have been proposed for ridge preservation techniques to counteract fresh extraction socket resorption. The primary aim of this prospective single cohort study was to evaluate the histomorphometric outcomes of a synthetic biphasic calcium phosphate (60% HA/40% β -TCP) and a synthetic poly-lactic acid membrane, used to graft fresh extraction socket sites with a full or partial (>5mm) resorption of the buccal bone plate. Patients recruited were treated at one esthetic site with a ridge preservation procedure to receive an implant-supported prosthesis. After 6 months of healing, a bone biopsy was harvested. Outcome evaluations were: biological complications, histomorphometrical analysis, and alveolar horizontal and vertical bone loss (Δ AHB, Δ AVB). Thirteen subjects were included in this study. Two cases of biological complication were recorded. All 13 patients received implant insertion. From histomorphometric analysis, a mean of $48.9 \pm 11.9\%$, $29.0 \pm 9.3\%$, and $22.0 \pm 9.7\%$ was recorded for soft tissues, new bone, and residual graft particles, respectively. From clinical analysis, a mean of 0.5 ± 1.0 mm (p-value < 0.05) and 0.9 ± 1.3 mm (p-value < 0.05) was recorded for alveolar horizontal and vertical bone loss, respectively. In conclusion, this prospective cohort study showed encouraging results in preserving alveolar ridge dimension. A moderate percentage of new bone and an acceptable alveolar ridge loss were achieved at a 6 month follow-up.

18. Outcome of revascularization therapy in traumatized immature incisors

Mittmann, C. W., Kostka, E., Ballout, H., Preus, M., Preissner, R., Karaman, M., & Preissner, S. BMC Oral Health. 2020 Jul;20(1), 1-10. doi: 10.1186/s12903-020-01193-5.

<https://link.springer.com/article/10.1186/s12903-020-01193-5#citeas>

Background: The aim of this retrospective analysis was to evaluate the clinical and radiological outcome of revascularization therapy in traumatized permanent incisors to determine whether this approach could be implemented into clinical routine. **Methods:** A total of 16 traumatized incisors (either avulsion or severe luxation/intrusion) with open apices (> 1 mm) that underwent revascularization following a standardized protocol were analyzed with a mean follow-up of 22 months. Radiographs and clinical parameters (such as root length, pulp space, dentin wall width, apical foramen, alveolar bone loss, ankylosis/mobility, supra-/infraposition, discoloration, probing depth) were compared pre- and postoperatively and statistically analyzed. **Results:** Over the follow-up period, 81.3% of the teeth survived revascularization and regained sensitivity, while 18.7% failed, as they had to be extracted due to serious root resorption. Regarding radiographic outcomes a significant difference could only be found in the decrease of apical foramina ($p = 0.04$). The other parameters showed no significant difference between pre- and postoperative measurements. More than half of the teeth (56.3%) developed root resorptions and 31.3% displayed signs of ankylosis and 92.9% developed discolorations during follow-up. However, 85.7% of the teeth maintained the bone level and outcomes of mobility showed a significant solidification. **Conclusions:** Revascularization is a promising approach for the treatment of immature incisors to regain sensitivity and to enhance apical closure and at least to maintain alveolar bone in terms of a socket preservation. Further studies have to be performed to determine ideal conditions (type of trauma, age, width of apical foramen) for a revascularization.

19. Flapless immediate implant placement and provisionalization in periodontal patients: A retrospective consecutive case-series study of single-tooth sites with dehiscence-type osseous defects

Sicilia-Felechosa A, Pereira-Fernández A, García-Lareu J, Bernardo-González J, Sicilia-Blanco P, Cuesta-Fernández I. Clin Oral Implants Res. 2020 Mar;31(3):229-238. doi: 10.1111/clr.13559.

<https://pubmed.ncbi.nlm.nih.gov/31755601/>

Objective: To assess the clinical outcomes of flapless, immediate implant placement with simultaneous augmentation of dehiscence defects and immediate provisional restoration. **Materials and methods:** Retrospective evaluation of 40 periodontal patients who received a flapless immediate implant for single-tooth replacement with simultaneous augmentation of dehiscence defects and immediate provisional restoration, at follow-up periods ranging from 1 year minimum to 7 years maximum. Dehiscence defects were augmented using autogenous bone grafts and/or deproteinized bovine bone mineral, and autogenous or allogeneic connective tissue grafts. The following aspects were evaluated: clinical success (Clinical Oral Implants Research, 8, 1997, 161), crestal bone loss (calibrated digital periapical X-rays) and aesthetics (Pink Esthetic Score, PES). Additionally, a questionnaire was devised

to obtain patient's subjective evaluation. **Results:** A 98.3% (95% CI: 91%-99%) success rate was observed. At 8 weeks, mean bone loss was 0.47 mm (n = 39); between 8 weeks and 1 year, this value attained 0.24 mm and between years 1 and 5 years 0.06 mm (n = 9). The evaluated PES in 37 single-tooth implants was 12.4, with PES = 7 (aesthetic failures) in two cases, and aesthetic outcomes were excellent (PES ≥ 12) in 29 cases (78.4%). When compared with the contralateral tooth, a recession under 1 mm was observed in 78% of cases. The patient's subjective satisfaction value ranged from 98% to 100%. **Conclusion:** This type of minimally invasive treatment of alveoli with buccal plate deficiencies delivers, in the hands of an experienced clinician, a high clinical and aesthetic success percentage being rated by patients as satisfactory. Clinicians should be aware that 1-2 mm comparative recession could be observed.

20. Reconstruction of a Huge Residual Palatal Cleft.

Sancak K, Naifoğlu E, Yurttutan ME, Tuzuner AM. *J Craniofac Surg.* 2020 Jan/Feb;31(1):e50-e53.

<https://www.ncbi.nlm.nih.gov/pubmed/31609945>

Closure of large oronasal fistula (ONF) in cleft patients is a challenge for patients and surgeons. The extent of functional impairment has psychologic, social, and developmental consequences. The ONF affects the feeding and speech of patients. Keys to repairing fistulas in this region are a 2-layer, tension-free closure, and an attentive suturing technique. [In this article, the details and effectiveness of 2-flap palatoplasty are presented using also a collagen fleece \(Jason® fleece, botiss dental, Germany\) between the nasal and oral mucosa.](#)

21. Maintenance of Alveolar Ridge Dimensions Utilizing an Extracted Tooth Dentin Particulate Autograft and Platelet Rich Fibrin: A Retrospective Radiographic ConeBeam Computed Tomography Study

Pohl S, Binderman I, Tomac J. *Materials (Basel).* 2020 Feb;13(5):1083. doi: 10.3390/ma13051083.

<https://pubmed.ncbi.nlm.nih.gov/32121381/>

This study utilized radiographic comparative analysis in order to evaluate dimensional ridge changes four months after tooth extraction and immediate grafting with mineralized dentin particulate autograft and chopped platelet rich fibrin. Fiftyeight extraction sockets with up to 2 mm of missing buccal bone in the coronal aspect compared to the lingual bone were included. Graft material was covered with either a platelet rich fibrin membrane or collagen sponge with no effort to achieve primary closure. The dimensional changes of the ridge were assessed on conebeam computed tomography (CBCT) images acquired prior to extraction and four months later. The reduction in the buccal bone plate thickness 1 mm, 3 mm, and 5 mm below the buccal crest was -0.87 ± 0.84 mm, -0.60 ± 0.70 mm, and -0.41 ± 0.55 mm, respectively. The mean ridge width changes 1 mm, 3 mm, and 5 mm below the crest were -1.38 ± 1.24 mm, -0.82 ± 1.13 mm, and -0.43 ± 0.89 mm, respectively. The average midbuccal

bone height gain was +1.1%, while the midlingual height gain was 5.6%. A mineralized dentin autograft with platelet-rich fibrin is effective in preserving postextraction alveolar ridge dimensions.

22. Evaluation of new bone formation in sinus floor augmentation with injectable platelet-rich-fibrin-soaked collagen plug: a pilot study

Gülsen U and Dereci Ö. 2019. *Implant Dent*; 28:220-225

<https://www.ncbi.nlm.nih.gov/pubmed/30932921>

Aim: Evaluation of new bone formation after sinus floor augmentation with collagen plugs used as carriers for injectable platelet-rich fibrin (i-PRF). **MATERIALS AND METHODS:** Postoperative immediate and postoperative 6th month panoramic radiographies of patients treated between January 1, 2015, and February 1, 2018, with sinus floor augmentation using i-PRF-soaked collagen plugs were retrieved from the archives, and subantral bone heights of distal and mesial regions of simultaneously inserted implants were measured with a software program. Statistical analysis was performed to understand whether there is a significant change in new bone formation at 6th month follow-up control. **RESULTS:** A total of 18 implants were inserted in 12 patients. There was significant new bone formation at 6th month follow-up radiography at mesial and distal regions of inserted implants. **CONCLUSION:** New bone was regenerated with i-PRF carried by collagen plugs in sinus floor augmentation.

23. Time Analysis of Alveolar ridge preservation using a combination of mineralized bone-plug and dense-polytetrafluoroethylene membrane: a histomorphometric study.

Wen SC, Barootchi S, Huang WX and Wang HL. 2020. *J Periodontol.*; 91(2):215-222.

<https://www.ncbi.nlm.nih.gov/pubmed/31378923>

Histological evaluation and comparison of vital bone formation, residual graft particles, and fraction of connective tissue (CT)/other tissues between three different time points at 2-month intervals after alveolar ridge preservation with a cancellous allograft and dense-polytetrafluoroethylene (d-PTFE) membrane. **METHODS:** Ridge preservation with a cancellous allograft, covered with collacone® and d-PTFE membrane on top at 49 extraction sockets (one per patient). Volunteers were assigned to implant placement at three different time points of 2, 4, and 6 months, at which time core biopsies were obtained. Histomorphometric analysis was performed to determine the percentages of vital bone, residual graft particles, and connective tissue/other non-bone components, and subjected to statistical analyses. **RESULTS:** There was a statistically significant difference in the amount of vital bone at every time point. The percentage of residual graft particles showing statistical significance from 4 to 6 months, and 2 to 6 months, while there were no significant differences for the amount of CT/other tissue among the different time points. **CONCLUSIONS:** This study provided the first

histologic comparison of alveolar ridge preservation using a cancellous allograft and d-PTFE membrane at three different time points. Extraction sockets that healed for 6 months produced the highest amount of vital bone in combination with the least percentage of residual graft particles, while similar results were observed for the fraction of CT/other tissues between the three time points.

24. Comprehensive Treatment of Severe Periodontal and Periimplant Bone Destruction Caused by Iatrogenic Factors.

Zafiropoulos GG, Parashis A, Abdullah T, Sotiropoulos E, John G. 2018. Case Rep Dent.:7174608. Ecollection 2018.

<https://www.ncbi.nlm.nih.gov/pubmed/29666713>

Dental implant success requires placement after periodontal therapy, with adequate bone volume, plaque control, primary stability, control of risk factors, and use of well-designed prostheses. [This report describes the surgical and prosthetic management of a patient with severe iatrogenic periodontal/periimplant bone destruction.](#) **METHODS:** A 55-year-old female smoker with fixed partial dentures (FPDs) supported on teeth and implants presented with oral pain, swelling, bleeding, and a 10-year history of multiple implant placements and implants/prosthesis failures/replacements. Radiographs showed severe bone loss, subgingival caries, and periapical lesions. All implants and teeth were removed except implants #4 and #10, which served to retain an interim maxillary restoration. Extraction sockets and periimplant bone defects were cleaned and Jason® fleece G inserted and covered with non-resorbable dPTFE membranes. In the mandible, three new implants were placed and loaded immediately with a bar retained temporary denture. **RESULTS:** Seven months postoperatively, the bone defects were regenerated, and three additional mandibular implants were placed. All mandibular implants were splinted and loaded with a removable overdenture. **CONCLUSIONS:** In this case, periimplant infection and tissue destruction resulted from the lack of periodontal treatment/maintenance and failure to use evidence-based surgical and loading protocols. Combination therapy resolved the disease and the patient's severe discomfort while providing immediate function and an aesthetic solution.

25. Alveolar Ridge Preservation Using a Novel Synthetic Grafting Material: A Case with Two-Year Follow-Up.

Fairbairn P, Leventis M, Mangham C, Horowitz R. 2018. Case Rep Dent.:6412806.

<https://www.ncbi.nlm.nih.gov/pubmed/29487751>

[This case report highlights the use of a novel in situ hardening synthetic \(alloplastic\), resorbable, bone grafting material composed of beta tricalcium phosphate and calcium sulfate, for alveolar ridge preservation.](#) A 35-year-old female patient was referred by her general dentist for extraction of the mandibular right first molar and rehabilitation of the site with a dental implant. The non-restorable tooth was "atraumatically" extracted without raising a flap, and the socket was immediately grafted

with the synthetic biomaterial and covered with a hemostatic fleece (Jason® fleece). No membrane was used, and the site was left uncovered without obtaining primary closure, in order to heal by secondary intention. After 12 weeks, the architecture of the ridge was preserved, and clinical observation revealed excellent soft tissue healing without loss of attached gingiva. At reentry for placement of the implant, a bone core biopsy was obtained, and primary implant stability was measured by final seating torque and resonance frequency analysis. Histological analysis revealed pronounced bone regeneration while high levels of primary implant stability were recorded. The implant was successfully loaded 12 weeks after placement. Clinical and radiological follow-up examination at two years revealed stable and successful results regarding biological, functional, and esthetic parameters.

26. Immediate One-Time Low-Profile Abutment to Enhance Peri-implant Soft and Hard Tissue Stability in the Esthetic Zone.

Pelekanos S and Pozidi G. 2017. *Int J Periodontics Restorative Dent.*; 37(5):729-735.

<https://www.ncbi.nlm.nih.gov/pubmed/28817139>

Reductions in peri-implant bone height have been acknowledged as a normal consequence of implant therapy. Various restorative factors contribute to this phenomenon. One is repeated abutment retightening, which causes a mechanical disruption at the implant-abutment interface, leading to soft tissue recession. Several investigators proposed placement of the definitive abutment after implant placement as a solution to the problem. The definitive use of an intermediate abutment after implant placement seems to positively affect the soft tissue response. [This article aims to present a prosthetic sequence for achieving peri-implant tissue stability in the esthetic zone by presentation of two clinical cases.](#) In case two, collacone® was placed after extraction of the right central incisor followed by implant placement after 3 months and bone augmentation using cerabone® and Jason® membrane.

27. Prevention of post-operative bleeding in hemostatic compromised patients using native porcine collagen fleeces-retrospective study of a consecutive case series.

Zirk M, Fienitz T, Edel R, Kreppel M, Dreiseidler T, Rothamel D. 2016. *Oral Maxillofac Surg.* 20(3):249-54.

<https://www.ncbi.nlm.nih.gov/pubmed/27139018>

[The purpose of this retrospective study was to determine if post-operative bleeding can be prevented by suturing native collagen fleeces into extraction wounds immediately after teeth removal, regardless what anticoagulant regime is performed.](#) **METHODS:** A total of 741 extraction units were removed from 200 consecutive in-ward patients with or without alternation of different anticoagulant therapy regimes. Anti-vitamin K agents were the most prescribed drugs (n = 104, 52 %), followed by Acetylsalicylate (ASS) (n = 78, 39 %). Nineteen (9.5 %) patients received a dual anti-platelet therapy. Out of 104 patients receiving an anti-vitamin K agent (phenprocoumon), 84 patients were bridged, 20 patients continued to their anticoagulant therapy without alterations. Following careful tooth

extraction, extraction sockets were filled using a native type I and III porcine collagen sponge (collacone®, Botiss Biomaterials, Berlin), supported by single and mattress sutures for local hemostasis. Post-operative bleeding events were rated according to their clinical relevance.

RESULTS: In the post-operative phase, 8 out of 200 consecutively treated patients experienced a post-operative bleeding event. All of them had been designated for a long-term anti-vitamin K therapy ($p \leq 0.05$), and extractions were performed under a heparin bridging regime ($n = 6$) or an uninterrupted anti-vitamin K agent therapy ($n = 2$). No bleeding events occurred in patients with ASS 100 therapy or low-dose LMWH therapy ($p \leq 0.05$), or in patients with dual anti-platelet therapy (0 out of 24). None of the bleeding events put patients' health at risk or required systemic intervention.

CONCLUSIONS: Sufficiently performed local hemostatic measures, like the application of collagen fleeces in combination with atraumatic surgery, bears a great potential for preventing heavy bleeding events in hemostatic compromised patients, regardless of their anticoagulant therapy.

28. Minimally Invasive Alveolar Ridge Preservation Utilizing an In Situ Hardening β -Tricalcium Phosphate Bone Substitute: A Multicenter Case Series.

Leventis MD, Fairbairn P, Kakar A, Leventis AD, Margaritis V, Lückerrath W, Horowitz RA, Rao BH, Lindner A, Nagursky H. 2016. *Int J Dent.*:5406736.

<https://www.ncbi.nlm.nih.gov/pubmed/27190516>

In a case series of 10 patients requiring single extraction, in situ hardening beta-tricalcium phosphate (β -TCP) granules coated with poly(lactic-co-glycolic acid) (PLGA) were utilized as a grafting material and covered with a hemostatic dressing (Jason® fleece). All sites were left uncovered to heal by secondary intention. After 4 months, clinical observations revealed excellent soft tissue healing without loss of attached gingiva in all cases. At reentry for implant placement, bone core biopsies were obtained and primary implant stability was measured by final seating torque and resonance frequency analysis. Histological and histomorphometrical analysis revealed pronounced bone regeneration ($24.4 \pm 7.9\%$ new bone) in parallel to the resorption of the grafting material ($12.9 \pm 7.7\%$ graft material) while high levels of primary implant stability were recorded. Within the limits of this case series, the results suggest that β -TCP coated with polylactide can support new bone formation at postextraction sockets, while the properties of the material improve the handling and produce a stable and porous bone substitute scaffold in situ, facilitating the application of noninvasive surgical techniques.

29. Diode laser for harvesting de-epithelialized palatal graft in the treatment of gingival recession defects: A randomized clinical trial.

Ozcelik O, Seydaoglu G, Haytac CM. 2016. *J Clin Periodontol.*; 43(1):63-71.

<http://www.ncbi.nlm.nih.gov/pubmed/26660000>

The aim of present randomized controlled clinical study was to evaluate the effects of the use of diode laser for graft harvesting and palatal wound irradiation on post-operative morbidity and root coverage

outcomes after a coronally advanced flap (CAF) with de-epithelialized gingival grafts (DGG). **METHODS:** Fifty-two patients with isolated recessions were treated. The CTG resulted from the de-epithelialization of a free gingival graft (FGG) with blade (control group: DGG-B) or diode laser (DL) (test group: DGG-L). The DL was used to de-epithelialize the outer part of the FGG and photo-biostimulate the palatal wound area. The palatal wound was protected with a collagen fleece (Jason® fleece). Post-operative morbidity was evaluated by using Oral Health related Quality of Life (OHQoL) and Visual Analogue Scale-discomfort (VAS). Root coverage outcomes were also evaluated 6 months after operation. **RESULTS:** Statistically significant differences were found for OHQoL ($p=0.0001$) and VAS ($p=0.0001$) at the 7th day post-operatively favoring test sites. Root coverage results did not show a statistically significant difference. **CONCLUSIONS:** While both techniques were effective in regard to root coverage at 6-months, the DGG-L technique decreased post-operative morbidity associated with palatal donor-site surgery.

30. Efficacy and Biocompatibility of Jason® Collagen Fleece for Haemostasis after Iliac Crest Harvesting of Autologous Cancellous Bone – An Observational Clinical Study.

Fleege C., Schmidt J., Schmidt I., Zukowski D. and. Rauschmann M, Touch Medical Media 2012.

http://www4.asklepios.com/asklepiosCMS/webpageUpload/746501148_2012_Europ_Musc_Res_Jason.pdf

The objective of the observation study was to assess the efficacy, local tolerability, overall safety, and handling properties of the Jason haemostatic fleece used after iliac crest harvesting of autologous bone in comparison with the established reference device Lyostypt® and Hemocol®. **METHODS/DESIGN:** This was an observational, two-centre, prospective clinical study. Results: The bleeding scores and wound healing scores were all distributed near the most beneficial value of 1 and did not significantly differ between the two study arms. In contrast, the manageability scores and applicability scores were significantly lower in the Jason® group than in the reference group. **CONCLUSION:** Jason® fleece is equally effective and safe as Lyostypt and Hemocol, and offers significantly better handling comfort.