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EFP Postgraduate Symposium provided showcase for top-level research

The strength of the EFP's postgraduate programme in periodontology, now taught at 17 universities in 12 countries, was on display at the 8th EFP Postgraduate Symposium, held in September in Sweden. Research presentations covered topics including bone augmentation, the relationship between periodontal risk and nutrition, and the use of magnetic resonance frequency analysis as a diagnostic tool. Perio Insight highlights a selection of these presentations together with the opening lecture by symposium chair Ingemar Abrahamsson.

The EFP Postgraduate Symposium takes place every two years and provides an opportunity for students, programme directors, and course co-ordinators from the EFP-accredited programmes to share research and learning. The eighth symposium, held from September 5 to 7, was hosted by the Sahlgrenska Academy at the University of Gothenburg.

Prof Ingemar Abrahamsson, chair of the symposium and programme director at the Sahlgrenska Academy, gave the opening lecture on "Peri-implantitis: Learning from pre-clinical models".

He said that, in patients with dental implants, peri-implantitis is common. The onset of the disease may occur early, but it is not possible to predict who will be affected. Therefore, pre-clinical *in vivo* models are necessary in peri-implantitis research.

His lecture outlined the experimental peri-implantitis model, explained how researchers at the university had used it in studies with dogs, and presented several *in vivo* studies on the progression of peri-implantitis and its treatment.

Explaining the benefits of the dog model for this kind of research, Prof Abrahamsson highlighted that dogs have a natural susceptibility to periodontitis similar to that of humans and the model is well documented and has been used successfully in research on periodontal diseases. The jaw size of certain breeds is comparable to the size of a human jaw, which means that implants of a normal size and shape can be used. Moreover, the oral environments in dogs and in humans is in many aspects similar and proper oral hygiene can be performed easily on a daily basis.

Prof Abrahamsson presented several examples of successful research using the dog model, covering ligature-induced breakdown, the spontaneous progression of peri-implantitis at different types of implant and at implants with different surface characteristics, and showing how surface characteristics influence the outcome of peri-implantitis treatment.

In conclusion, he said that pre-clinical *in vivo* models are "useful for studies on short-term effects of different implant types on peri-implant tissues" and are "important for the understanding of disease progression and for the development of new treatment concepts."

Research presentations

The symposium featured eight research presentations from students at universities in Belgium, France, Ireland, Israel, Netherlands, and Switzerland.

1. The use of MRFA as an adjunct to conventional clinical examination following peri-implantitis treatment: a 12-month follow-up

(**Ed Madeley**, *Trinity College, University of Dublin, Ireland).*

This study investigated the impact of peri-implant treatment on periodontal clinical parameters and implant-stability quotient values. It sought to ascertain if magnetic resonance frequency analysis (MRFA) can be used as a diagnostic tool to demonstrate post-operative healing following peri-implantitis treatment and to identify the most appropriate time for re-evaluation of implant stability.

Patients were sampled from a cohort of patients with peri-implantitis referred to or presenting at Dublin Dental University Hospital. Prostheses of diseased implants were dismantled at baseline and periodontal parameters – periodontal pocket depth (PPD), clinical attachment loss (CAL), bleeding on probing (BoP), and plaque score – were taken. Baseline MRFA levels were taken and baseline radiographs carried out before any treatment.

Patients were treated according to the severity of their disease, all patients received non-surgical therapy following baseline examination, and surgical and regenerative therapy was provided were suitable.

After baseline therapy, patients were reassessed at three, six, and 12 months and all clinical

parameters repeated in addition to MRFA measurements (except probing at three months where regenerative surgery had been carried out). Radiographs were repeated at 12 months.

Nineteen patients were enrolled in the study with 57 implants treated for peri-implantitis. All the tested mean clinical periodontal diagnostic parameters showed a statistically significant improvement in the 12 months after initial therapy. There was a statistically significant correlation between changes in all parameters and changes in ISQ levels over 12 months, apart from plaque and bleeding scores which showed no significant correlation. There was a trend for increasing mean implant stability quotient (ISQ) levels over 12 months, but it was not significant.

Conclusions: In the short to medium term, all treatments were successful in managing peri-implantitis. Implants treated surgically with guided tissue regeneration (GTR) or guided bone regeneration (GBR) achieved better clinical results (shown by periodontal disease reduction and bone gain) and showed more frequent correlations with MRFA readings. MRFA technology (the Osstell device) can be used as a complement to traditional periodontal tools for evaluating post-operative implant stability following the treatment of peri-implantitis.

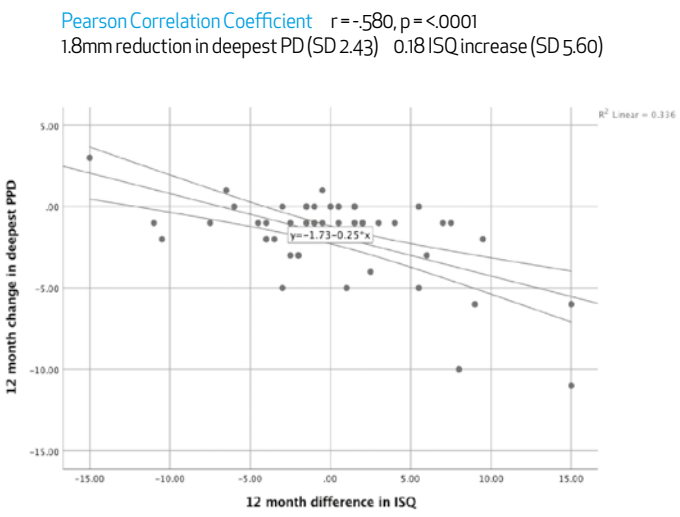

Figure 1. Correlation between changes in probing depth over 12 months and changes in ISQ (Osstel)

2. Leucocyte- and platelet-rich fibrin block for bone-augmentation procedure: a proof-of-concept study

(**Simone Cortellini**, *Catholic University of Leuven, Belgium).*

Numerous techniques have been described for reconstructing deficient alveolar ridges. Bone augmentation with autologous bone is often associated with increased morbidity and postoperative complications. A tissue-engineering approach with an L-PRF block may reduce these disadvantages and enhance bone regeneration. The use of L-PRF to create a graft with a high concentration of growth factors, platelets, and leucocytes may enhance the development of mature lamellar bone.

The objective of this proof-of-concept study was to evaluate the use of the L-PRF block for horizontal ridge augmentation and to investigate the effects of a new GBR technique with a tissue-engineering approach.

This single-cohort observational study evaluated the outcome of the L-PRF block for horizontal bone augmentation in the maxilla.

The L-PRF block is prepared by mixing a particulated biomaterial with chopped L-PRF membranes at a 50:50 ratio and adding liquid fibrinogen to glue everything together. Horizontal augmentation was assessed linearly and volumetrically immediately after surgery and between five and eight months later by matching consecutive cone-beam computed tomography (CBCT) scans.

Ten patients, mean age of 50.7 years (±17.2), representing 15 sites with horizontal alveolar deficiencies were included. Superimposition of pre-operative and post-healing CBCT scans showed an average linear horizontal bone gain of 4.6mm (±2.3), 5.3mm (±1.2) and 4.4mm (±2.3), measured at 2.0, 6.0, and 10mm from the alveolar crest, respectively. The volumetric gain was 1.05cm^3 (±0.7) on average. The resorption rate after five to eight months was 15.6 % (±6.7) on average.

Conclusions: L-PRF block may be a suitable technique to augment deficient alveolar ridges. L-PRF block appears a realistic alternative for horizontal augmentation of deficient alveolar ridges. This procedure is safe, predictable, with a high feasibility and a low morbidity.

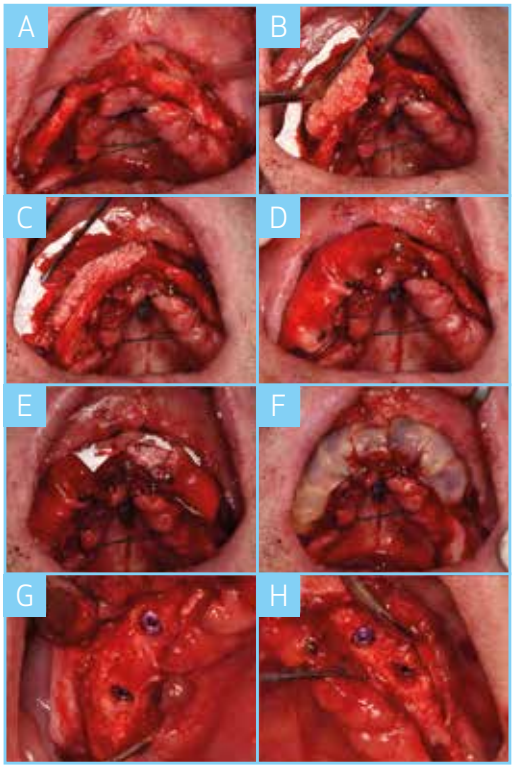

Figure 2. Application of L-PRF block for horizontal bone augmentation in the upper jaw in a patient with bilateral augmentation. A: knife-edge alveolar ridge. B&C: after buccal fixation of a collagen membrane, the L-PRF block is placed on the recipient site in the right upper jaw. D: palatal fixation of the collagen membrane to stabilise the graft. E: same procedure applied to the left upper jaw. F: coverage of the collagen membrane with L-PRF membranes. G&H: augmented sites at re-entry after nine months, for implant placement.

3. Relationship between periodontal risk and nutrition: a population-based study

(**Laurent Detzen**, *University of Paris, France).*

Periodontitis is a common inflammatory disease of the tooth-supporting tissues (bone, cement, periodontal ligament, and gingiva) caused by a microbial dysbiosis in the oral cavity. Poor-quality diet is one of many risk factors for periodontitis and recent evidence has suggested that nutritional habits might influence the development and severity of periodontitis.

It has been shown that diets with a high level of refined sugar can lead to an inflammatory state via oxidative stress, that unsaturated fats (omega 3) and anti-oxidative nutrients such as vitamin C may have a positive effect on periodontal health, and that a low-sugar diet is associated with a better periodontal status.

This study, which sought to evaluate the association between dietary intakes and the risk of periodontitis in a French adult population, included 35,390 subjects from the Nutrinet-Santé

e-cohort study, who completed a questionnaire about oral health between 2011 and 2012.

The risk of periodontitis was assessed by calculating the Periodontal Screening Score (PESS) on four selected questions, age, and smoking with a score ≥5 indicating a high risk of having severe periodontitis. Dietary data were obtained from at least three self-administered 24-hour records completed online. Association between PESS and diet was evaluated by univariate and multivariate analyses.

The study population had a mean age of 49.04±13.94 years and was composed mainly of women (75.8%). Overall, 20.5% of the population presented with a high risk of severe periodontitis. After adjustment for potential confounders (e.g. age, gender, BMI, socioeconomic status), those with high-risk PESS had significantly lower consumption of milk and dairy products (2.49 versus 2.57 portions/day; p=0.007) and water (1.24 versus 1.31 litres/day; p<0.0001) and had significantly higher consumption of added sugar (7.79% versus 7.74% of energy intake) compared to those with low-risk PESS. The consumption of fruits and vegetables was similar between the two groups after adjustment for possible confounders (6.17 vs. 5.59 portions per day; p=0.520). Concerning the micronutrients, high-risk-PESS individuals had a significantly lower intake of calcium (934.6 versus 957.9 mg/day; p=0.019).

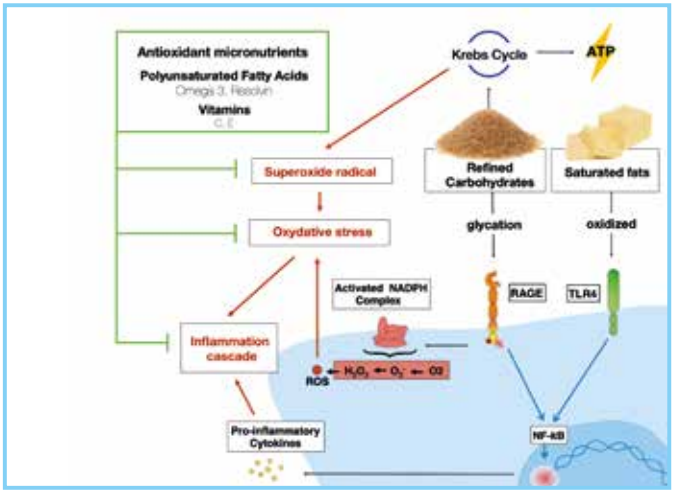

Figure 3. Pathways associated with refined carbohydrates, saturated fats or antioxidant intake.

Conclusion: The research supports an association between dietary habits and risk of periodontitis particularly related to intakes of calcium and refined carbohydrates. Further research is needed to elucidate the role of nutrition on both the prevention and treatment of periodontitis.

4. The use of autogenous particulate dentin as an appropriate bone substitute in socket-site preservation procedures: clinical, radiographical, and histological evaluations

(**Erez Netanely**, *Tel Aviv University, Israel*).

The efficacy of using an autogenous particulated dentin (P-Den) as a bone graft in socket-preservation procedures was examined, with P-Den – prepared by the Smart Dentin Grinder (SDG) device – applied as a biomaterial filler in 15 fresh human socket sites. Cylindrical hard-tissue specimens followed by implant placement took place six months after socket preservation. Clinical and radiographical findings showed immaculate healing, optimal ridge augmentation followed by successful implant reconstructive procedures.

Histological interpretation demonstrated newly formed bone around the grafted P-Den in direct contact, establishing bridging of a hard-tissue scaffold in the augmented area. It appears that P-Den can serve as a suitable alternative to autologous bone graft to preserve alveolar-ridge volume in oral reconstructive procedures.

The chemical composition of dentin is similar to that of bone. It is composed of hydroxyapatite (HA) deposited on type-I collagen matrix and non-collagenous glycoproteins such as bone sialoprotein (BSP) and matrix metalloproteinases (MMPs).

This study sought to evaluate – clinically, histopathologically, and histomorphometrically – the efficacy of using P-Den as a suitable bone-substitute alternative in human socket-preservation procedures.

Fifteen patients were scheduled for a single implant-placement procedure in a pathological, periodontally involved socket site. Extracted teeth were cleaned and prepared according to the SDG protocol to produce P-Den of 250-1200µm particle size. P-Den were then grafted into the socket up to the crestal level followed by a resorbable membrane coverage. Primary soft-tissue closure via a rotated pedicle flap was obtained. At six months, biopsies were harvested at the time of implant placement. Histological and histomorphometry analyses were performed using hematoxylin and eosin (H&E) and Paragon staining followed by a software Image-J application to calculate direct bone-dentin contact, newly formed bone (NFB), and P-Den area fractions.

All cases healed uneventfully. Computed tomography (CT) scans showed that P-Den kept the three-dimensional volume of the socket sites. *De novo* bone formation was shown to fill the entire grafted area previously occupied by the roots. Histologically, NFB was observed in the entire grafted area, particularly around the grafted P-Den. Most particles were surrounded, with direct contact with newly formed osseous tissue enriched by osteocytes. The non-decalcified processing specimens demonstrated high bone-titanium surface contact whereas P-Den was fully embedded and surrounded by NFB. Histomorphometry in a designated region of interest (ROI) showed an average of 25% NFB, while an average of 30% is captured by P-Den. Direct P-Den to NFB showed a range of 30-80%.

Conclusions: Particulate dentin is proven to be a fully biocompatible and excellent osteoconductive biomaterial that can be used to preserve socket-site volume in the immediate post-extraction phase. NFB ankylosed to P-Den becomes a solid matrix that enables implant anchorage and preserves the ridge dimension. P-Den could serve as a suitable alternative to an autologous bone graft to augment alveolar-ridge volume for subsequent implant-placement procedures.

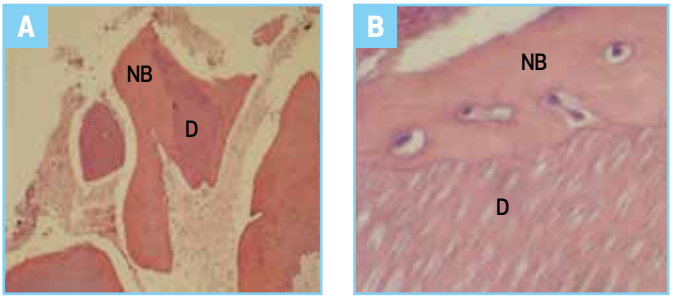

Figure 4.
A - Newly formed bone surrounded the grafted P-Den.
B - Direct enriched osteocyte lacunae NFB deposition onto a dentin particle is evident.

5. Influence of periodontal status on peri-implant tissues in a periodontally treated population: a cross-sectional study

(**Ioanna Papalou**, *University of Strasbourg, France*).

The prevalence of biological complications with implants presents a wide range in the literature, of between 1% and 47% depending on definitions. A history of periodontal disease has been proven to be an important risk factor for peri-implant disease. However, the evidence is not that strong regarding the influence of current periodontal status.

This study sought to evaluate the prevalence of peri-implantitis using different definitions and the relationship between the periodontal and peri-implant status for patients previously treated for periodontitis.

Patients with an implant placed at least three years ago, who had been treated for periodontitis, and who have been followed at the University of Strasbourg were included in this study. The demographic, periodontal, and implant data were collected and compared at the time of the examination and by reviewing the patients' files for past information. Different peri-implantitis definitions were evaluated (Karoussis, COIR, 2004; Berglund, JCP 2018).

Seventy-three patients with 246 implants were studied, of which 45% presented with a severe form of periodontitis at the intake. After a mean follow-up of 10 years the survival rate of implants was 96.4%; 13 years following initial periodontal treatment and 10 years following implant placement, the plaque score (29% vs 18%), bleeding on probing (BoP) (15% vs 24%), and the mean pocket depth (2.5mm vs 2.9mm) between teeth and implants were statistically different. Peri-implantitis defined as in Karoussis 2004 (PD≥5 mm + BOP + radiographic signs of bone loss>0.2mm/year) affected 8% of implants and 23% of patients, while peri-implantitis defined as in Berglundh 2018 (PD≥6 mm + BOP and/or radiographic signs of bone loss ≥3mm) affected 8% of implants and 19% of patients. The plaque score, BoP, and pocket depth around implants were correlated with that of natural teeth. The bone level around implants was mostly influenced by the characteristics of the prosthetic treatment.

Conclusion: The results of this study showed that the periodontal status of surrounding teeth influences peri-implant conditions in a periodontitis-treated population. This confirms and highlights the necessity of maintaining healthy conditions during maintenance for these patients.

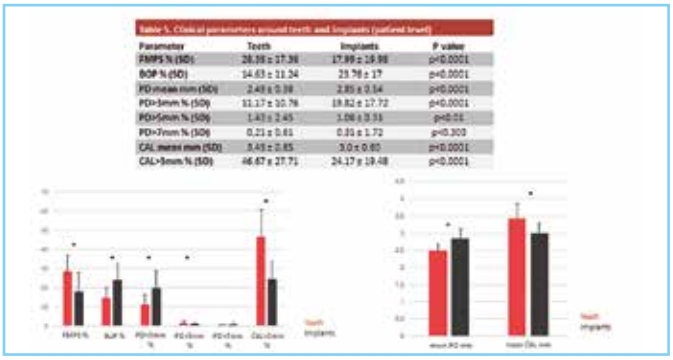

Figure 5. Clinical parameters around teeth and impants (patient level)

6. VEGF release from a polymeric nanofibre scaffold for improved angiogenesis

(**Alaa Khutaba**, *Rambam Medical Center, Haifa, Israel*).

Angiogenesis is critical in all aspects of tissue regeneration and this study sought to develop an electrospun fibre scaffold that permits the controlled release of recombinant human vascular endothelial growth factor (rhVEGF) to enhance angiogenesis.

Scaffolds composed of core-shell fibres were fabricated by electrospinning. The shell solution was composed of polycaprolactone 8% and polyethylene glycol (PEG) in various concentrations (0.25-3%) to produce pores of different sizes on the shell. The core solution was composed of polyethylene oxide (PEO) 4% mixed with rhVEGF.

Scanning electron microscopy (SEM) was used to characterise the scaffold and measure pore size. The releasing kinetics of rhVEGF were monitored by enzyme-linked immunosorbent assay (ELISA). *In vitro* biological activity of rhVEGF was determined by trans-well migration assay. *In vivo* angiogenesis was evaluated by subcutaneous implantation of the scaffold in a mouse model. Recruitment of cells into the scaffold and angiogenesis was evaluated via confocal microscopy and histomorphometry after three and 14 days.

Core-shell fibres of 6-8µm diameters were obtained.

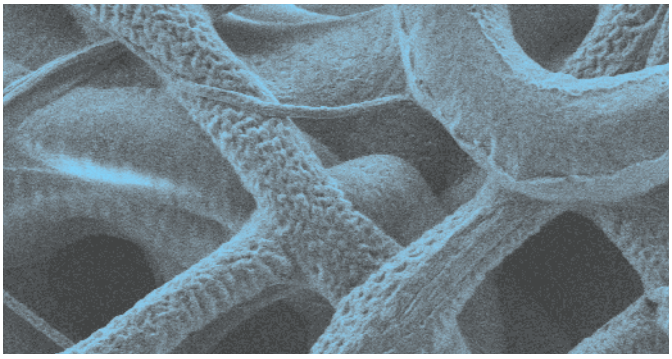

Figure 6. A representative image of the nanofibre scaffold with 1% PEG concentration. The image was acquired by scanning electron microscope. Scale bar= 2um

Mean pore size of the shell was 503.497±64nm in 3% PEG and 205±60nm in 1% PEG ($p<0.05$). A positive correlation between PEG concentration and pore size in the shell was found. Similarly, changes in PEG concentrations influenced rhVEGF release: burst release of rhVEGF was observed in the 3% PEG (large pores) scaffold, with a maximum release of 23% within four hours; while in the 1% PEG (smaller pores) scaffold, a more gradual release of rhVEGF was observed: 38% of rhVEGF was released within 18 hours.

Trans-well migration assay demonstrated that the 1% PEG scaffold loaded with rhVEGF enhanced the migration of endothelial cells (EC) 80-fold compared with negative control (1% PEG scaffold without rhVEGF; $p<0.05$). Analysis of subcutaneous transplants (*in vivo* model) showed increased recruitment of cells in the test group after three days and angiogenesis was significantly higher in the test group after three and 14 days ($p<0.01$).

Conclusion: The results of this study suggest that PEG concentration in the electrospinning system deployed influenced the pore size of the scaffold shell, thereby modifying hVEGF165 release kinetics. Released hVEGF165 promoted EC migration *in vitro* and significantly enhanced blood vessel formation *in vivo*.

[*This research was published in Journal of Biomedical Materials Research Part A*: 105A: 2712-2721, 2017, https://doi.org/10.1002/jbm.a.36127.]

The other research presentations at the symposium were: Anti-inflammatory potential of a sage-based mouthwash in elderly subjects enrolled in supportive periodontal therapy: a six-week randomised controlled clinical trial (Kevin Guldener, University of Bern, Switzerland); and The association between periodontitis and the risk of obstructive sleep apnoea syndrome (ASAS): a pilot study (Alexander Verhelst, ACTA, Amsterdam, Netherlands).

There were also eight clinical cases presented at the symposium by students at universities in France, Italy, Israel, Spain, Sweden, Turkey, and the UK. These will be covered in the next edition of Perio Insight.

The 8th EFP Postgraduate Symposium took place from September 5 to 7 at the Aspenäs Herrgård Hotel in Lerum, near Gothenburg. The event was sponsored by Procter & Gamble and Dentsply Sirona.

Focus on Perio Master Clinic 2020: novel concepts in regeneration - 'the future is already here'

Perio Master Clinic 2020, the EFP event for clinicians which takes place in Dublin on March 6 and 7 next year, will focus on current and future challenges of hard- and soft-tissue aesthetic reconstructions around teeth and dental implants. The two-day event, preceded by a day of hands-on workshops, brings together leading clinicians to explain the latest clinical techniques in one of the most challenging areas of periodontal practice. The session "novel concepts: outlook for the future" explores what the future might hold for new techniques and materials. Two of the speakers in this session outline the issues: *Darko Božić* on combined periodontal and bone regeneration and *Lior Shapira* on bone regeneration in the digital era.

Combined periodontal and bone regeneration

*By **Darko Božić***

When Prof Sculean, the scientific chair of Perio Master Clinic 2020, asked me to give a lecture about combined periodontal and bone regeneration it was a great honour – but also a difficult task and a great responsibility as this is a topic that is not often covered at meetings.

When we talk about simultaneous bone and periodontal regeneration, we are always confronting an extremely difficult task because of the biological limitations of periodontal regeneration. It is much easier to rebuild the bone than the periodontium.

Our current knowledge about the biological capabilities and response of cells and about the biomaterials we use tells us that these cases are probably the most challenging ones. In order to treat these cases, we should use the entire armamentarium that is currently available – growth factors in particular – in order to have a chance of a successful outcome. Many of these cases involve the maxillary anterior region, where the aesthetic component further complicates the treatment.

So, you can see the complexity of the treatment approach. As this lecture will be in the section "Novel concepts: outlook for the future", I will focus on growth factors – both those that are well-established and a new one that I use in treating these demanding cases. I think the future is already here and that our knowledge about cell response to growth factors has significantly grown, which helps us in our decision-making.

These advances in the last few years – and especially in basic biology – have been pivotal, in my opinion. We have learnt how cells respond in contact with bone-grafting materials and how they respond when treated with growth factors.

A good example of how something that was highly promising did not really translate into the initial expectations of clinical practice because of the lack of such information is represented by bone morphogenic proteins (BMP).

We knew that BMPs were highly osteogenic and able to differentiate mesenchymal stem cells into osteoblasts, but we did not know that they also stimulate osteoclasts and, in fact, in coupling bone

BMPs first induce bone resorption.

Then there was the issue of the correct dosage of the protein, carrier, etc. It took years to understand this and even today many issues are still unresolved.

That said, we must keep in mind that research from *in vitro* studies does not necessarily represent real *in vivo* responses, although when they are coupled with *in vivo* animal studies we gain an insight into how osteoblasts, cementoblasts, and periodontal ligament cells (PDL) behave in contact with growth factors and different biomaterials. This understanding of cell behaviour and events during healing is of paramount importance when you try to simultaneously reconstruct the periodontium and bone for future implant placement.

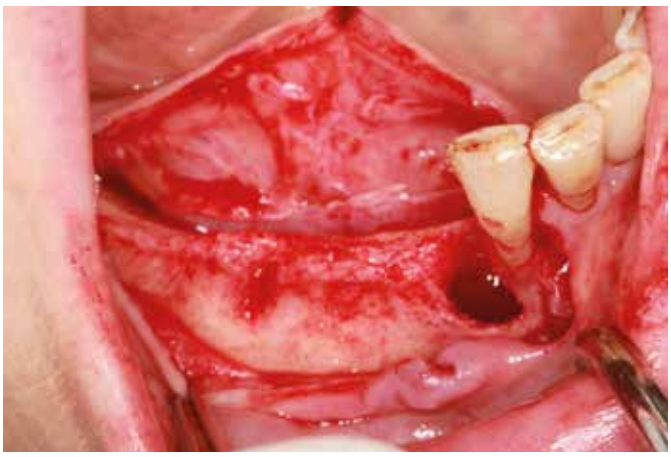

Figure 1. A knife-edge edentulous ridge with a severe periodontal defect distal to the second incisor extending close to the apex of the tooth. The bone and periodontal defect was managed with a combination of Emdogain (EMD) and allogeneic bone covered and fixed with a collagen membrane.

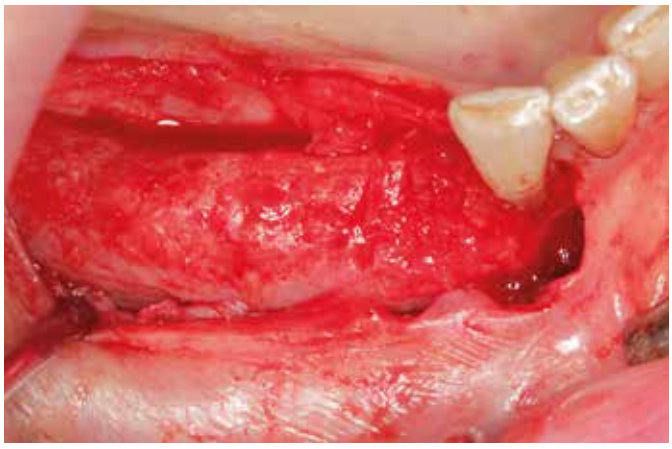

Figure 2. Six months post-operation, with a clear resolution of both the periodontal and knife-edge defect with significant bone regeneration.

So when you ask me "what's new in regeneration? ", I think that we have learned to use the existing materials in a better way, we have deciphered many unknown actions of growth factors, and I deeply believe that in the coming years – no more than a decade – researchers will resolve the current issues with stem cells and that they will be routinely utilised.

We must acknowledge that much more research lies ahead if we are to achieve the ultimate goal, which is complete and predictable regeneration of the periodontium to a much larger number of patients than is currently possible. These are exciting times since we are in a period of rapidly evolving technology and there is something new coming out every week, every day. You never know what is in the pipeline.

Darko Božić *is an associate professor of periodontology at the University of Zagreb in Croatia and a member of the EFP communications committee. He is also president of the Croatian Society of Periodontology.*

Guided bone regeneration in the digital era

*By **Lior Shapira***

A few decades ago, Per-Ingvar Brånemark invented the concept of osseointegration and started a major change in dentistry. Since then, implant dentistry has moved from being an invasive, time-consuming, costly, and semi-predictable procedure to one that is minimally invasive, efficient, friendly, and predictable in the dental practice.

Within the last decade, technology in the areas of telecommunication, radiology, and imaging has been evolving and integrating with great speed and simultaneity, changing the face of traditional dentistry. Distances and time have been shortened through the internet, affecting the process of diagnosis and treatment possibilities.

The digital revolution has embraced the evolution of implants in terms of implant placement and implant restoration, and today it is also doing so for guided bone reconstruction.

My presentation at Perio Master Clinic 2020 in Dublin will focus on digital means that help the surgeon plan and perform bone regeneration for implant placement, for more accurate and efficient procedures.

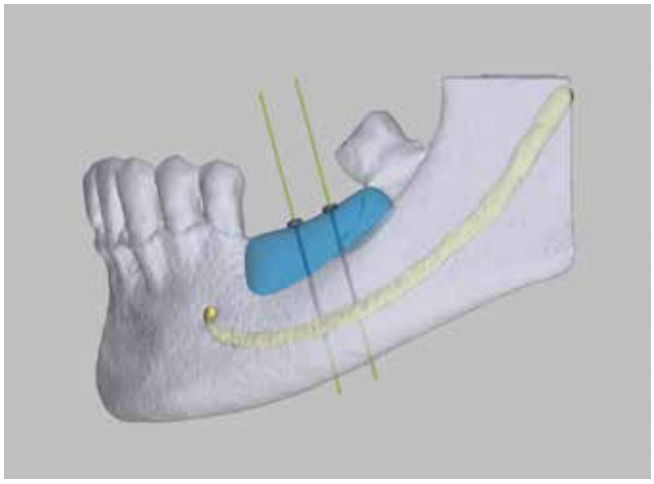

Figure 1. Computer planning of a bone graft

Figure 2. 3D model of a patient mandible with the planned area for bone regeneration

Today, 3D printing of the patients' jaws and CAD-CAM technologies have become available, allowing the surgeon to utilise the "personlised medicine" approach. The digital approch is more accurate, shortens the surgical procedure, and has fewer adverse effects.

This is not the future of bone regeration – it is already the present, and the new bio-technologies that are being developed will make it more simple and more predictable. As Albert Einstein once said, "I never think of the future. It comes soon enough."

Lior Shapira *is professor of periodontology and chair of the department of periodontology at the Hebrew University-Hadassah Faculty of Dental Medicine in Jerusalem in Israel. He is an elected member of the EFP executive committee and will be the federation's president in 2021-2022. He was the co-ordinator of Gum Health Day 2019.*

Latest research from the EFP's Journal of Clinical Periodontology

The *Journal of Clinical Periodontology (JCP)* is the official scientific publication of the European Federation of Periodontology. Editor: Maurizio Tonetti. Impact factor of 4.164. Special Issue: *Bone Regeneration. Proceedings of the XV European Workshop of Periodontology jointly held by the Osteology Foundation and European Federation of Periodontology*. Published June 2019.

Biological factors involved in alveolar bone regeneration: Consensus report of working group 1

Working group 1, chaired by Tord Berglundh (EFP) and William V. Giannobile (Osteology Foundation), focused its discussions on four reviews: (1) *Mesenchymal cells and differentiation factors leading to bone formation* (Mark Bartold et al); (2) *The critical interplay between bone-resorbing and bone-forming cells* (Ulf H. Lerner et al); (3) *Osteoimmunology: Inflammatory osteolysis and regeneration of the alveolar bone* (Reinhard Gruber); (4) *Self-regenerative capacity of intra-oral bone defects* (Anton Sculean et al). The working group formulated and addressed critical questions, covering (1) the critical biological phases that characterise bone regeneration, (2) the biologic/growth factors involved in bone regeneration; (3) the role of mesenchymal stem cells, their niche and extracellular matrix in bone regeneration; (4) coupling factors that regulate bone remodelling; (5) coupling factors involved in bone remodelling that have regenerative potential for clinical use; (6) the role of inflammation and its resolution in the process of bone regeneration; (7) the role of different macrophage phenotypes – especially osteomacs – in bone regeneration; (8) the role of lymphocytes in bone regeneration; (9) the role played by osteoclasts in bone regeneration; (10) whether bone regeneration in alveolar extraction sites in animals reflects the clinical situation in humans; (11) whether the morphology and location of the defect affect the regenerative capacity; (12) the regenerative capacity of cystic defects or intra-oral bone graft donor sites. The group identified areas of future research, highlighting the need to target both stem cells and biologics through well-controlled clinical trials, based on results of *in vitro* and pre-clinical studies. The report notes that combining cell-based therapies with controlled temporal delivery of regulatory molecules, using tissue-engineering approaches, offers many exciting prospects for bone regeneration. But it cautions that "it is not until we understand the process of bone formation that regeneration will become an achievable and predictable clinical endpoint for managing disease and trauma."

Authors: William V. Giannobile, Tord Berglundh, Bilal Al-Nawas, Mauricio Araujo, P. Mark Bartold, Philippe Bouchard, Iain Chapple, Reinhard Gruber, Pernilla Lundberg, Anton Sculean, Niklaus P. Lang, Petter Lyngstadaas, Moritz Kebschull, Pablo Galindo-Moreno, Zvi Schwartz, Lior Shapira, Andreas Stavropoulos, Janne Reseland

Full article:
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Biomaterials and regenerative technologies used in bone regeneration in the craniomaxillofacial region: Consensus report of working group 2

Working group 2, chaired by Mariano Sanz (EFP) and Christer Dahlin (Osteology Foundation), explored the regenerative technologies used in bone regeneration, basing discussions on four reviews: (1) *Bone grafts: which is the ideal biomaterial?* (Havard J. Haugen et al); (2) *Barrier membranes: more than the barrier effect?* (Omar Omar et al); (3) *The use of bioactive factors to enhance bone regeneration: a narrative review* (Nikos Donos et al); (4) *Cell therapies for orofacial bone regeneration: a systematic review and meta-analysis* (Siddharth Shanbhag et al). The group's consensus was that biomaterials used as bone grafts must meet specific requirements for biocompatibility, porosity, osteoconductivity, osteoinductivity, surface properties, biodegradability, mechanical properties, angiogenicity, handling, and manufacturing processes. Currently used biomaterials have demonstrated advantages and limitations based on the fulfilment of these requirements. Similarly, membranes for guided bone regeneration (GBR) must fulfil specific properties and potential biological mechanisms to improve their clinical applicability. Three main approaches using cell therapies to enhance bone regeneration have been evaluated: (a) "minimally manipulated" whole-tissue fractions; (b) *ex vivo* expanded "uncommitted" stem/progenitor cells; and (c) *ex vivo* expanded "committed" bone-/periosteum-derived cells. Based on the evidence from clinical trials, transplantation of cells – most commonly whole bone-marrow aspirates (BMA) or bone-marrow-aspirate concentrations (BMAC) – in combination with biomaterial scaffolds has demonstrated an additional effect in sinus augmentation and horizontal ridge augmentation, and comparable bone regeneration to autogenous bone in alveolar cleft repair. Highlighting the clinical relevance of these findings, the report notes that bone-regenerative interventions in the jaw bones are widely used, mainly in conjunction with dental implant therapy. The outcome of these interventions depends largely on the appropriate selection of the regenerative technology, which should be based on a careful diagnostic assessment of the defect site.

Authors: Mariano Sanz, Christer Dahlin, Danae Apatzidou, Zvi Artzi, Darko Bozic, Elena Calciolari, Hugo De Bruyn, Henrik Dommisch, Nikos Donos, Peter Eickholz, Jan E. Ellingsen, Håvard J. Haugen, David Herrera, France Lambert, Pierre Layrolle, Eduardo Montero, Kamal Mustafa, Omar Omar, Henning Schliephake

Full article:
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Management of the extraction socket and timing of implant placement: Consensus report and clinical recommendations of working group 3

Working group 3, chaired by Maurizio S. Tonetti (EFP) and Ronald E. Jung (Osteology Foundation) discussed the management of the extraction socket and the timing of implant placement. Discussion focused on four systematic reviews: (1) *Effect of alveolar ridge preservation interventions following tooth extraction: a systematic review and meta-analysis* (Gustavo Avila-Ortiz et al); (2) *The effectiveness of immediate implant placement for single tooth replacement compared to delayed implant placement: a systematic review and meta-analysis* (Jan Cosyn et al); (3) *Effectiveness and clinical performance of immediate implant placement for the replacement of single teeth in the anterior area: a systematic review* (Filippo Graziani et al); (4) *Efficacy of lateral bone augmentation performed simultaneously with dental implant placement: a systematic review and meta-analysis* (Daniel S. Thoma et al). The working group, which produced 23 consensus statements and 12 clinical recommendations, emphasised that the evidence base relates mostly to single-tooth extraction and replacement, so its applicability to multiple extractions requires careful consideration. The group identified six considerations to assist clinical decision-making:

(1) presence of infection; (2) inability to achieve primary stability in the restoratively driven position; (3) presence of a damaged alveolus; (4) periodontal phenotype; (5) aesthetic demands; and (6) systemic conditions. The group also concluded that more high-quality research is needed to develop evidence-based clinical guidelines.

Authors: Maurizio S. Tonetti, Ronald E. Jung, Gustavo Avila-Ortiz, Juan Blanco, Jan Cosyn, Stefan Fickl, Elena Figuero, Moshe Goldstein, Filippo Graziani, Phoebus Madianos, Ana Molina, José Nart, Giovanni E. Salvi, Ignacio Sanz-Martin, Daniel Thoma, Nele Van Assche, Fabio Vignoletti

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Regeneration of alveolar-ridge defects: Consensus report of working group 4

Working group 4, chaired by Søren Jepsen (EFP) and Frank Schwarz (Osteology Foundation) discussed four systematic reviews: (1) *Efficacy of lateral bone augmentation prior to implant placement: a systematic review and meta-analysis* (Nadja Naenni et al); (2) *Long-term effectiveness of maxillary sinus floor augmentation: A systematic review and meta-analysis* (Gerry M. Raghoebar et al); (3) *Effectiveness of vertical ridge augmentation interventions: a systematic review and meta-analysis* (Istvan A. Urban et al); (4) *Efficacy of reconstructive surgical therapy at peri-implantitis-related bone defects: a systematic review and meta-analysis* (Cristiano Tomasi et al). Substantial evidence supports lateral bone augmentation before implant placement as a predictable procedure to gain enough ridge width for implant placement. Many studies showed that vertical ridge augmentation was effective in treating deficient alveolar ridges to allow implant placement. However, both procedures had a high rate of associated complications. The adjunctive benefit of reconstructive measures for treating peri-implantitis-related bone defects has been assessed in few RCTs, while meta-analyses demonstrated a benefit in terms of radiographic bone gain but not for clinical outcomes. Lateral-window sinus-floor augmentation was shown to be a reliable procedure in the long term for the partially and fully edentulous maxilla. The evaluated bone-augmentation procedures were proven to be effective, but some procedures are demanding and bear a higher risk of post-operative complications.

Authors: Søren Jepsen, Frank Schwarz, Luca Cordaro, Jan Derks, Christoph H. F. Hämmerle, Lisa J. Heitz-Mayfield, Federico Hernández-Alfaro, Henny J. A. Meijer, Nadja Naenni, Alberto Ortiz-Vigón, Bjarni Pjetursson, Gerry M. Raghoebar, Stefan Renvert, Isabella Rocchietta, Mario Roccuzzo, Ignacio Sanz-Sánchez, Massimo Simion, Cristiano Tomasi, Leonardo Trombelli, Istvan Urban

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