A patient’s growth factors

Prof. Liviu Steier and Gabriela Steier discuss how growth factors are a valuable addition to regenerative dentistry.

Blood clots are extremely valuable for initiating healing and regeneration for both soft and hard tissue. Platelet rich plasma (PRP) is becoming more accepted as a way of accelerating and enhancing natural wound healing, and has been successfully used for decades in orthopaedic surgery as well as in dermatology.

Growth factors

A variety of proteins and growth factors interact with each other to induce wound repair.

In a once-injured vessel, the platelets will start to stick to exposed collagen proteins and will release adenosine diphosphate, serotonin and thromboxane, contributing to the clotting cascade and hemostatic process, as well as to the platelet plug formation. The platelet plug is reinforced by an insoluble protein fibrin meshwork, as a product of the clotting cascade.

It’s important to note the fact that platelets actively extrude growth factors, such as:

Well-researched growth factors

1. Platelet-derived growth factor = PDGF
2. Transforming growth factor- = TGF-β
3. Insulin like growth factor = IGF-I

Under research

4. Transforming growth factor-alpha = TGF-β, etc
5. Epidermal growth factor = EGF
6. Vascular endothelial growth factor = VEGF
7. Hepatocyte growth factor = HGF

Here I will attempt to explain a bit about some of the benefits of these well-researched growth factors:

- **PDGF**
  - Proliferative activity on periodontal ligament fibroblast
  - Promotes collagen and protein synthesis
  - Enhances proliferation of bone cells.

- **TGF-β**
  - Activates intracellular proteins
  - Promotes extracellular matrix production for example in periodontal ligament fibroblasts
  - Stimulates the proliferative activity of periodontal ligament fibroblasts
  - Stimulates biosynthesis of type I collagen and fibronectin.

IGF-1

- In combination with PDGF will stimulate cementogenesis
- Bone formation; and many more.

It was Marx who in 1998 published a paper on the significance of increased bone formation and bone density after using thrombocyte growth factor. Rutherford et al. (1992) and Anitua (1999) published a paper on platelet concentrates for coating dental implants.

Commercial systems available for PRP

- Smart Prep autologous platelet concentrate system (Harvest Autologous Hemotherapeutics, Norwell, Massachusetts)
- Tisscel system (Baxter Health corp., Deerfield, Illinois)
- Curasan PRP kit (Curasan, Kleinostheim, Germany)
- Friadent-Schuetze PRP (Friadent-Schurtze, Vienna, Austria)
- PRGF by Anitua (G.A.C. Medicale San Antonio, Vitorto Espana).

How the systems differ:

1. Cycles of centrifugation
2. Speed of centrifuge
3. Amount of blood to be collected
4. Addition yes/no of bovine thrombin

I have used the Curasan approach for many years and switched to the PRGF technique almost three years ago. For the purpose of exemplification the latter technique will be briefly described.

As such, based on the technique used, the platelet count as well as the growth-factor content may differ. Differentiation of the above number may occur as well as a consequence of the donor.

The Anitua technique:

- Venous blood (between 10-30 mL) has to be collected in office and drawn into two to six sterile tubes containing an anticoagulant (here 3.8 per cent sodium citrate).
- Centrifugation: Eight minutes at 1800 rpm.
- Three different blood fractions will be identified and isolated by pipetting:
  - Fraction 1 = platelet poor plasma (the above 0.5ml)
  - Fraction 2 = platelet rich plasma (the above 0.5ml)
Fraction 2 = plasma containing a number of platelets (next 0.5ml)
Fraction 3 = platelet rich growth factor (remaining plasma above the buffy coat)
   this is the most important fraction.

The platelet then needs activation using 10 per cent calcium chloride (0.05ml per 1ml PRGF).

The coagulation will occur in five to eight minutes (best at 37 degrees Celsius – incubator).


The same study confirmed the absence of leucocytes in all three fractions.

One can use the gained material as follows:
a. Not activated for coating implants before seating
b. Activated:
   1. To be mixed with graft materials
   2. To make membranes.

Strengths of the technique
1. Needle-free approach which drops infection risk for practitioner
2. Duration for the preparation is about 20-25 min
3. Reduced centrifugation time
4. No need of additional bovine thrombin.

Weakness of the described technique
1. Lack of leucocyte might lead to a reduced anti-infective protection
2. High number of pipetting procedures (up to 30)
3. The use of a so-called “open system” implicates high sterilisation criterion.

Conclusion
PRP is a new tissue-engineering application suitable for the clinician. Among the different procedures available, I am describing the approach which in my hands currently works best. The use of the PRP here PRGF technique significantly changed the treatment outcomes in my practice: less complications, better healing and higher predictability of regeneration procedures.

Disclaimer
The author has no financial interests in any of the presented products or systems.
Clinical case study

A 54-year-old female patient presented to our practice requesting rehabilitation of the upper jaw with implant-supported fixed restorations.

The patient had not received dental assistance for the last 12 years and had no medical problems. The patient’s chief complaint was non-satisfactory chewing efficacy. She requested rehabilitation of the upper jaw with implant supported fixed restorations.

Her oral hygiene was adequate so she underwent a rigorous oral hygiene programme for three months. The soft tissue examination revealed no problems; TMJ and muscles showed no acute problems; occlusal assessment revealed a lack of occlusal support; implant assessment showed suspect teeth: 16, 15, 12, 22, 25, 26; available bone is moderate to poor; treatment plan includes planned extractions of teeth 16, 13, 12, 22, 25, 26 and a total of seven implants.

Esthetic risk analysis

We explained to the patient the high risks of smoking and it was agreed that the patient would attend a stop-smoking programme. Three months after this, the patient did stop smoking and treatment began.

The following treatment plan was agreed and discussed with the patient:

- Planned extractions: 16, 15, 12, 22, 25, 26.
- Number of implants: seven
- Position of implants: 15, 14, 15, 12, 22, 26, 27.
- Bone graft using: BioOss (Geistlich) and PRGF (a mixture of Grafton, BioHorizons) and BioOss, (Geistlich) soaked in PRGF) were performed concurrently in local anesthesia. Antibiotic coverage was assured for seven days.

The patient was asked not to wear temporary prosthesis for 10 days and an antibacterial regimen was prescribed.

The second-stage surgery was performed six months later. After a gingival healing/maturation time of 14 days, definitive impressions were taken, bite registered and a face bow made.

After two try-in sessions the definitive restorations were fitted.

The 12-month X-ray proved a stable outcome and it is expected that the patient will come back for rehabilitation of the lower jaw.

Conclusion

Wound-healing deficiencies do not often impose an obstacle in guided bone regeneration (GBR) procedures when associated with implant placement. The use of PRP techniques in medicine go a long way back and its application into dentistry represented a change of paradigm. The author can only anecdotally affirm, based on his own experience, that since using PRP (latest PRGF) techniques, wound-healing problems don’t occurred again and GBR procedures seem to have gained more predictability. 

References are available on request.

About the author

Dr. med. dent. Liviu Steier is a visiting professor at the School of Dental Medicine in Florence; visiting professor at Tufts School of Dental Medicine on its endodontic postgraduate programme; and an honorary clinical associate professor at Warwick Medical School. He is a registered specialist in endodontics (GDC) and Specialised Prosthodontics (www.dgzpw.de). He can be reached at lsteier@msdentistry.co.uk

About the author

Gabriela Steier is a BA from Tufts University Boston. She has conducted extensive research in the field of ozone in endodontics and has co-authored several articles, and textbooks chapters.
Introduction

The crestal area is the region to suffer initial breakdown when it comes to the implant tissue interface. Adell et al. (1981) first communicated 1.2mm of marginal bone loss from the first thread during healing time, with a continuation of 0.1 mm annually.

As a consequence, Smith and Zarb (1989) established the following as criteria for implant success: vertical bone loss of <0.2mm annually following the first year. This of course is a major issue in the anterior esthetic zone. Since then, clinicians and manufacturers have worked hard to try to improve this condition.

Factors affecting loss

The following factors are among the most discussed to cause crestal bone loss:
1. Surgical trauma
2. Biologic width/seal
3. Microgap
4. Occlusal overload
5. Crest module.

Causes of trauma

Overheating the bone during the drill procedure; extended full-flap raise; Screw-in forces higher than 35 N/cm² are optional causes for crestal breakdown. As such, these factors may only be responsible for bone loss prior to prosthetic load.

Biologic width/seal

This seal starts the day the abutment is mounted and continues for the next six weeks into treatment. Today’s surgical protocols control this fact by adequate three-dimensional implant positioning.

Microgap development

Two-stage implants seem to be prone to microgap development. Even with implant engineering work, it’s hard to control via different improved connections, glue, etc.

Occlusal overload

Crestal bone is mostly cortical bone. Forces occurring at the crestal level are described as shear forces. Cortical bone is highly susceptible to shear forces. Occlusal concepts have been developed specially for implant-supported restorations to address this issue.

Crest module

Implant professionals as well as implant manufacturers have introduced different remedies to address this issue: polished collar, Connective Contour (Astra), Laser-Lok Technology (Biohorizons), for example.

The peri-implant histology

Ericsson et al (1995) reported the following findings:
1. Plaque associated inflammatory cell infiltrate;
2. Implant associated inflammatory cell infiltrate.

As such implantologists addressed more attention to the area.
Serendipity

In the late 1980s, NobelPharma introduced a Branemark 5mm-diameter implant. The prosthetic components used a “standard” diameter. In 1991, Implant Innovations introduced wide diameter implants. Of course not all prosthetic abutments were available. As a result, prosthetic parts from a regular platform have been used.

Long-term observations of this demonstrated a reduced loss of bone height compared to the available standards.

The platform switching treatment concept

The platform is the crestal area of an implant. Let us say as an example that the diameter of the implant is 5.2mm and the abutment measures 4.1mm. The difference of the diameter between the implant and the abutment is the so called “platform switching”.

Manufacturers offering the concept

The concept of platform switching is only offered exclusively by a restricted number of implant manufacturers.

1. Wieland
2. BTI
3. 3I
4. Astra
5. Dentsply – Ankylos
6. Zimmer

Scientific evidence


Conclusion: The findings of the current trial indicate that the use of implants with an enlarged platform can result in better preservation of crestal bone when a reduced abutment is mounted.


Conclusion: This study suggests that in a limited time period of two years, immediately placed implants with subsequent platform switching can provide peri-implant tissue stability.


Conclusion: Results from this study showed the reduction of abutment diameter (for example, platform switching) resulted in a measurable, but minimal effect on Von-Mises stress in the crestal region of cortical bone.


Conclusion: The concept of platform switching appears to limit crestal resorption and seems to preserve peri-implant bone levels. A certain amount of bone remodelling, one year after final reconstruction occurs, but significant differences concerning the peri-implant bone height compared with the nonplatform-switched abutments are still evident 1 year after final restoration. The reduction of the abutment of 0.45mm on each side (5mm implant/4.1mm abutment) seems sufficient to avoid peri-implant bone loss.


Conclusion: This study strengthens the findings that the concept of platform switching is only offered exclusively by a restricted number of implant manufacturers.