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“The Geistlich Way”

Geistlich Pharma’s collagen researchers have two clients: you, our distinguished readers, and the body’s own cells. For you, our researchers work to optimize product handling. Is the biomaterial intended to create volume? Should it simply be easy to hydrate? And for the cells, our researchers make sure our collagens remain as similar as possible to “original tissue” – because only then will the somatic cells that contact collagen react naturally.

Over the past 160 years Geistlich Pharma has dedicated itself to building its collagen expertise. The guiding principle behind all of our efforts remains the same: “Geistlich’s collagen membranes and matrices should lead to predictable success by providing the solution to a patient’s problems.”

We can let the numbers speak for themselves. As most of you know: 1+1=3, when you can exploit successful synergies. But Geistlich has even more to offer: 20+30=1000. Are you still following us? We have much to celebrate in 2016: 20 years of experience with collagen membranes and 30 years with bone replacement biomaterials – all supported by 1,000 scientific publications. This is the “Geistlich Way”, which has clearly proven that this pioneering company’s products and concepts always work superbly well.

I hope that you enjoy reading “Geistlich News” and find the content engaging and helpful.

Mario Mucha,  
Chief Operating Officer
RIDGE PRESERVATION.

Each extracted tooth presents a new challenge. What can Ridge Preservation measures achieve?
Extraction sockets: the key facts

Following tooth extraction, how much surrounding bone is lost? Can this process be slowed? Our current understanding.

In a jaw that has been edentulous for years, the alveolar ridge can resorb completely\(^1\). Also, single tooth gaps are subject to dramatic contractions. In order to describe such dimensional alterations following tooth extraction, the edentulous ridge has been measured in numerous studies, clinically, radiographically and using casts. According to the Osteology Consensus Conference, the mean ridge reduction is 3.8 mm horizontally and 1.24 mm vertically\(^2,3\).

Adaptation to a new, edentulous state

What are the reasons for bone resorption following tooth extraction? First we have to be clear that the jaw is made of basal bone and alveolar process. It is the bone of the alveolar process that is mainly resorbed. In addition, it is not the entire alveolar process but a significant part of it, about 30% (for individual tooth gaps in the first year following extraction). The remaining jaw, the basal bone, is resorbed to a lesser extent, i.e., about 10%\(^4\). The amount of bone resorption depends on anatomical factors, site of extraction and function.

Often the bone of the alveolar process is made up of very thin socket walls, especially at the buccal aspect, and parts of the alveolar process are often outside the envelope of the jaw. In addition, since the purpose of the alveolar process is to support a tooth, once the tooth has been removed, bone is resorbed because the body adapts to the new, edentulous state.

Bone loss in posterior and anterior sites

The extent of bone loss varies according to the site and the patient. Our studies show that net loss of bone is greater in the posterior than the anterior regions. Fortunately, the posterior sites contain so much bone that resorption is often not a major clinical problem.

On the other hand, due to the limited amount of anterior bone, the loss of less bone in the anterior region can be problematic. As alluded to above, facial bone walls are very thin and often lost completely after a tooth has been extracted. Accordingly, the net bone loss is lowest in the incisor region, but the percentage of bone reduction is the highest (37%).

Lack of bone vs. lack of volume

There is another phenomenon to be considered. Despite alveolar process and basal bone reduction, there is more bone after tooth extraction than before – because new bone is formed in the space previously occupied by the root.

Thus, frequently we will have bone enough to hold an implant, especially a narrow diameter implant. But to restore a tooth with implants, not only is bone necessary but also ridge volume to provide the mucosa profile for aesthetics.

Now, if we have enough bone for placing the implant but not enough volume, in reality we don’t necessarily need more bone but any graft that could provide volume, whether it is a gingival graft, a soft-tissue matrix, a bone substitute or anything that is compatible and stable. However, the best-documented way to preserve volume after tooth extraction is Ridge Preservation with biomaterials.
Less bone loss through Ridge Preservation

Ridge Preservation prevents volume loss after tooth extraction, but not always 100%. Results depend, again, on the tooth region and the patient. We have recently shown that, for the vast majority of patients, preserving ridge dimension provides enough bone tissue to place an implant in a proper 3-dimensional orientation and with an ideal amount of bone surrounding the implant. Animal studies have shown that in extraction sockets Geistlich Bio-Oss® Collagen supports new bone formation, particularly in the cortical region, and contributes to ridge profile preservation. Given these studies, we can assume that Ridge Preservation modifies bone modelling and alleviates buccal bone loss.

How long does Ridge Preservation last?

Many studies on Ridge Preservation are limited to a six-month observation period. There is, however, reason to believe that extraction sockets filled with Geistlich Bio-Oss® continue to be stable much longer. Long-term studies measuring lateral augmentations and sinus floor elevations have revealed that, if there is no loss caused by inflammation, Geistlich Bio-Oss® preserves ridge volume long term. Further extraction socket studies would, however, be helpful in confirming this assumption.

These factors influence bone loss

Facial bony walls are frequently thinner than 1 mm, and these thin walls are almost exclusively bundle bone. Because it is a completely tooth-dependent structure, the bundle bone is resorbed after tooth extraction.

The extent of surgical trauma influences bone loss after tooth extraction, so there are good reasons not to extract teeth with dental pliers but with a periosteum or vertical tooth extractor.

Loss of functional stimulation of the bony walls is a confirmed factor contributing to bone loss after tooth extraction.

References

4 Unpublished data
The new thinking post tooth extraction

Immediate implantation, spontaneous healing or Ridge Preservation – these are the available options after a tooth has been extracted. Which option is the best, and when?

There is new thinking in implant dentistry, much like the new thinking that occurred with cariology some 50 years ago. Treatment in cariology used to involve the “Extension for prevention” approach: the more hard tooth substance that could be replaced with an amalgam filling, the less that could go wrong. But since the 1960s, dentists have made retention of hard tooth substance their aim. And between 1964 and today, a prevention program has helped reduce the prevalence of caries in Switzerland by over 90%.

And a similar new thinking is happening today at the “alveolar process” level. Again, retention instead of replacement is the key. At conferences we should no longer be measuring ourselves against those who can regenerate the largest bone defects, but rather we should seek to impress others with our predictable and low-risk procedures. Because alveolar ridge preservation has its part to play in this new approach, it is not just another technique in the treatment repertoire, it is much more significant.

Three options after tooth extraction

The first decision that the dentist must make: Should I let the extraction socket heal spontaneously, fill it with a bone replacement material or insert an immediate implant? The best procedure depends on different factors in day-to-day clinical practice: tooth location, the condition of the bone and soft tissue, as well as the patient’s general state of health, his or her personal circumstances and financial situation, to name but just a few factors.

It is important that the treatment decision is discussed before the tooth is extracted. Depending on the option, the bone lost during the first four to six months is:

› 50 % for spontaneous healing,
› 56 % for immediate implantation,
› 15–20 % for immediate implantation with “gap filling”, and
› 15 % for Ridge Preservation.

The advantages and disadvantages of the treatment options are depicted in Fig. 1.

When should the ridge be preserved?

In our clinic, Ridge Preservation is always carried out if no implant is placed within the first 8 weeks after tooth extraction (Fig. 2, Page 10). There is another approach, however, which involves Ridge Preservation after every tooth extraction, if an implant or bridge restoration is planned. Above all, private practitioners claim that this pre-emptive measure gives them a greater degree of security. The alveolar ridge is always sufficiently

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**Fewer interventions**

The shorter treatment time and the reduced number of surgical interventions are major advantages of an immediate implantation. Also, blood-thinning medication taken by older patients has to be discontinued only once (lower risk).

**Comply with the indication**

Immediate implantation can cause bone and soft tissue recessions. Anterior teeth should only be replaced with immediate implants when the buccal socket wall is sufficiently thick. Increased bone absorption can occur in the molar region.

**Optimization**

Fill the gap between the buccal socket wall and the implant with a bone replacement material and cover the defect with a membrane. Some surgeons close the socket over the implant with a connective tissue transplant in order to gain additional volume.

**The right procedure**

The tooth should be extracted atraumatically after the soft tissue has been released using a desmotome or scalpel. Orthograde apparatuses can help with the extraction, but they can be complex to use. In general you can say: the gentler, the better. The extraction socket should then be curetted. This step must be performed carefully, as it can help prevent later complications. Using a periodontal probe – and a CBCT scan, if one is available – it is possible to establish whether the buccal socket wall is intact. The procedure depends on this diagnosis. If at least 50% of the buccal bone lamella has been resorbed, volume should be gained by contouring. After a flap has been prepared, the bone replacement material is poured into the socket and applied in a buccal direction. A collagen membrane is laid over the graft and ridge to stabilize the graft and prevent soft tissue invasion. Primary wound closure improves prognosis. The membrane itself does not need to be sutured. If the buccal lamella is largely intact, the bone replacement material is poured into the socket without it being opened up, and the socket is then sealed – with a disc of collagen matrix Geistlich Mucograft® Seal or with an autologous soft tissue punch graft or a connective tissue palatal harvest graft. This “sealing” procedure has an advantage over the contouring approach, as the mucogingival border is not displaced. If a collagen matrix is used, which means that no harvest graft needs be taken from the palate, then the procedure is even less invasive. If, however, the soft tissue has to be thickened, an autologous transplant is absolutely necessary.
There is very little convincing evidence for an approach using only bone replacement material, i.e., without a soft tissue transplant, wound closure, membrane or matrix. A randomized comparative study from our group has shown that, in the event of a Ridge Preservation without a collagen membrane or matrix, even more bone volume is lost than with spontaneous healing (bone material used: beta-tricalcium phosphate with a special coating)\(^4\).

When and how to optimize the soft tissue?

Above all, in the anterior maxillary region a sufficient quantity of keratinized soft tissue can be critical for aesthetics. At extraction, sometimes it is possible to predict when a larger bone augmentation will be necessary later. In such cases, soft tissue management at the time of tooth extraction can be of enormous help. An autologous connective tissue or soft tissue punch graft from the palate, or a disc of collagen matrix can be used. After such a procedure, the soft tissue should be allowed to mature for at least two months before an implant is inserted.

References

FOCUS

Is implant insertion within 2 months possible / indicated?

<table>
<thead>
<tr>
<th>NO</th>
<th>YES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are there bone defects in the socket?</td>
<td>Can the soft tissue situation be improved?</td>
</tr>
<tr>
<td>SMALL &lt; 50%</td>
<td>LARGE &gt; 50%</td>
</tr>
<tr>
<td>Socket Seal Technique</td>
<td>Bone augmentation = GBR</td>
</tr>
<tr>
<td>Geistlich Bio-Oss® Collagen</td>
<td>Geistlich Bio-Oss® Collagen</td>
</tr>
<tr>
<td>Geistlich Mucograft® Seal</td>
<td>Geistlich Bio-Gide®</td>
</tr>
</tbody>
</table>

Type 4 implantation | Fixed dental prosthesis | Adhesive bridge | Partial tooth replacement | Type 1 or Type 2 implantation | Type 3 implantation

2 Decisions after tooth extraction

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Socket Sealing with collagen matrix

Should the extraction socket be sealed with a soft tissue punch graft or with a collagen matrix? The matrix has some advantages over the autologous punch.

Studies over the past few years have clearly shown that Ridge Preservation significantly reduces ridge volume loss after tooth extraction. Animal and clinical trials have demonstrated that the combination of a xenogeneic bone replacement biomaterial (Geistlich Bio-Oss® Collagen) with an autologous soft tissue punch graft can achieve the most effective volume preservation. But this technique is not without its clinical disadvantages, which include high patient morbidity and the danger of scar formation in the buccal region due to incomplete healing.

Preconditions for Socket Sealing

A xenogeneic soft tissue replacement material for the sealing of the extraction socket (Geistlich Mucograft® Seal) appears to provide Ridge Preservation results similar to an autologous soft tissue graft. At the same time, postoperative levels of patient morbidity are clearly lower. It also appears that the collagen structure of Geistlich Mucograft® Seal reduces the risk of scar formation, ensuring a more pleasing tissue match with surrounding native tissues. The preconditions for a successful application of the Socket Seal technique are an inflammation-free marginal soft tissue situation, precise suturing and an intact extraction socket with retained buccal bone lamella. In these cases – and as found by the Geistlich Mucograft® Seal Advisory Board Meeting in February 2013 in Geneva – no additional barrier membrane is needed. An early implantation time (8–10 weeks after extraction) is possible. If portions of the buccal bone lamella are dehisced, a membrane should also be used to protect the bone replacement biomaterial, and the healing time should be extended.

References

Ridge Preservation instead of sinus lift?

Sinus floor elevation is still a major surgical intervention and is associated with the risk of complications. How can one avoid it?

Prof. Rasperini, the benefits of Ridge Preservation appear to be confirmed by the latest systematic reviews. In your opinion, what are the benefits of Ridge Preservation in the posterior region?

Prof. Rasperini: Ridge Preservation is performed in posterior regions in order to reduce the need for a sinus lift. The upper jaw has limited basal bone due to significant pneumatisation of the sinus and, of course, incurs additional bone loss after tooth extraction. So, a sinus lift is needed to create sufficient bone for implant placement. However, peremptory Ridge Preservation reduces the need for bone regeneration at the time of implant placement.

Did you find an advantage for Ridge Preservation over spontaneous healing?

Prof. Rasperini: After 6-months the major benefit was a significantly reduced need for sinus floor elevations. The bone is almost completely mature at that time, and a flapless implant placement can be performed easily, because of the ridge volume obtained with the grafting biomaterials. The simple procedure makes a big difference compared with sinus floor elevation, which is a major surgical procedure.

What is the patient benefit?

Prof. Rasperini: Most of the patients who undergo molar extractions are more than 70 years old. They are often on medications like Coumadin, Aspirin or other anticoagulants, and they can be diabetic. These are factors that influence wound healing and the outcome of any surgery. The patients appreciate avoiding a major surgery, and treatment time is shortened, so they have less pain and, of course, they avoid possible post-operative complications.

You have also evaluated the healing process histologically. What did you find?

Prof. Rasperini: Our histological evaluation revealed normal healing with a lack of inflammatory cells. Geistlich Bio-Oss® Collagen as well as Geistlich Bio-Gide® appeared to be surrounded by newly formed bone. This is advantageous for the dentist: on the one hand, the bone is stable – due to the mineral component of the graft that resorbs slowly; and on the other hand, the biological activity of the new and vital bone promotes osseointegration of the implant.

Your publication includes a finding of “delayed bone formation process and incomplete resorption of bovine bone particles” at the grafted sites. How do you interpret this finding?

Prof. Rasperini: It is well known that the body’s own cells incorporate the grafting granules in the bone remodelling processes. In the case of the Geistlich bovine bone mineral particles, this process takes place over a long period of time.
Ideally, when the bone is mature, the newly formed bone of the regenerated area will be mineralised. With Geistlich Bio-Oss® we place mineralised particles in the socket from the beginning. After six to nine months, histopathology shows that biologically active tissues surround these particles, i.e., newly formed woven and lamellar bone. With grafting we achieve ideal physical and mechanical results.

According to a study performed by Prof. Cattaneo’s group, less than 20% of Geistlich Bio-Oss® is still present after ten years. So at that time we have over 80% mature, mineralised bone.

You used Geistlich Bio-Gide® as a collagen membrane to protect the augmented site. What makes you sure that this membrane has the right barrier function for this indication?

Prof. Rasperini: Wound healing consists of three phases: first comes the inflammatory phase, which takes about three days, then the proliferative phase, which takes about 15 days, and finally the maturation phase, which continues over three months. In the beginning a scaffold is needed that prevents any shrinkage of the tissue and graft loss. But after one month, every cell in the wound “knows” exactly what to do, and the barrier function is no longer needed. That’s why Geistlich Bio-Gide® with its short barrier function is appropriate. The advantage of Geistlich Bio-Gide® compared to other non-resorbable membranes is that it does not interfere with vascularization and nutrition processes between the soft tissue flap and the underlying graft. Cells and blood vessels from the flap integrate with the membrane quickly and start to deliver nutrients and oxygen to the surgical site, contributing to the maturation of the graft and the healing process. A recently published paper from our group provides this evidence. If, on the other hand, a non-resorbable membrane is used, the graft receives nutrition from the bone site only and lacks nutrition from the flap. But there is another fact to be considered: how quickly the graft resorbs. Geistlich Bio-Oss® resorbs slowly and, thereby, preserves volume in the augmented site. Autologous bone, in contrast, resorbs quite quickly so that volume is lost. To compensate for this loss, a different type of membrane that resorbs slower than the scaffold is needed – not for the barrier function, but for volume stability. With Geistlich Bio-Oss® and Bio-Gide® we achieve the ideal combination of volume stability and barrier function.

References
Ridge Preservation creates better bone conditions for later implantation and provides more forgiving implant placement conditions for dentists with less experience, says Dr. Dietmar Weng.

To put the question as simply as possible: Isn’t it always “Tooth out – bone replacement in”?

**Dr. Weng:** No, you really can’t make such a generalization. It depends on several variables, for example: the treatment you are planning, the bone condition and the level of inflammation.

The German Society for Implants in its 2011 Consensus Conference noted that GBR-measures are five-times less likely to be needed at the time of the implantation if a Ridge Preservation was already performed. That is going to save a considerable amount of operating time and pain for the patient, don’t you think?

**Dr. Weng:** Ridge Preservation, above all, is less traumatic for the patient than later GBR-measures. A periosteal incision must often be performed after a lateral bone augmentation so that the soft tissue can close without being under tension, which can cause both haematomas and swelling.

The time aspect, on the other hand, is of secondary importance. If one performs a Ridge Preservation, the tooth extraction takes longer, because one wants to remove the tooth more gently and damage the bone structure as little as possible. Ridge Preservation done correctly also takes time.

How can you tell beforehand whether a Ridge Preservation is necessary in order to avoid a later GBR?

**Dr. Weng:** According to Jan Lindhe’s research, the thickness of the buccal bone lamella plays a role here. The loss of buccal-lingual alveolar ridge width with a thick buccal bone lamella, shall we say wider than 0.8 mm, is less than in sockets with a thin buccal wall. Unfortunately, the latter defects exist almost exclusively in the anterior maxillary area of bundle bone, which is resorbed after tooth extraction, at least up to a height of 2–3 mm from the ridge.

In practice, it is hard to measure the socket walls accurately either before or after an extraction, and without a flap it is also difficult to judge the bone situation.

In your view, when should Ridge Preservation be recommended?

**Dr. Weng:** I would always carry it out – both in the anterior and lateral tooth areas – if an implant is planned, but not when an immediate implantation is under consideration. And then I always fill the gaps between the implant and the socket walls!

Which situations do you find unsuitable for immediate implant placement?

**Dr. Weng:** Molar sockets, severely inflamed sockets, or sockets with demonstrable wall dehiscences are not cases for an immediate implantation, in my view. I would carry out a Ridge Preservation first in such cases.

Does the patient’s biotype play a role?

**Dr. Weng:** Over the years I have developed my treatments so that I can operate independently of biotype. As for Ridge Preservation, I would say it is just as effective for patients with thick or thin bony walls.

Would you also carry out a Ridge Preservation in order to preserve the volume under pontics?

**Dr. Weng:** Probably not, because of the financial considerations involved. When someone decides on a bridge reconstruction instead of an implant, he or she tends to do so on the
grounds of cost. For such patients, Ridge Preservation is also a financial matter.

Often the person who removed a tooth does not insert an implant later himself, but refers the patient on to an oral surgeon...

**Dr. Weng:** Many dentists don’t feel confident about implants, because they are associated with complex augmentations. But Ridge Preservation makes treatment much simpler. The measure itself is uncomplicated and minimally invasive. And it creates a sufficiently wide alveolar ridge, which means that a later implantation can be performed by less experienced dentists.

So we should have “more confidence when it comes to implants”?

**Dr. Weng:** Yes. When you use a suitable procedure, the whole treatment from extraction to prosthetic restoration can be done in a minimally invasive way.

**References**

A case series investigation of whether it is possible to insert an implant just four months after a Ridge Preservation.

A 75-year-old female patient was referred for the extraction of teeth 21 and 22. An implant restoration in region 21 (screw-retained) with an extension bridge was planned. Both teeth had gingival recessions, although the patient had a thick biotype. The patient had a deep smile line.

After the careful removal of tooth 21, the extraction socket was filled loosely up to the crestal edge of the socket walls with Geistlich Bio-Oss® Collagen. A disc of collagen matrix, Geistlich Mucograft® Seal, was adapted to the deepithelialised wound margins over the bone replacement material and stabilized with a mattress suture. Tooth 22 was initially left in situ and served as an anchoring point for the temporary Flieger crown x22.

The healing progressed smoothly. After three weeks, the epithelisation over the collagen matrix was complete. After four months, the implant (Straumann Bone Level NC Implant Roxolid SLActive) was inserted in the correct prosthetic position. The newly formed bone had matured by this time, and there was sufficient primary stability. After a further two-month healing phase, the reopening took place, and a conical healing cap was inserted. The patient was referred back to the dentist treating her for the prosthetic restoration and the extraction of tooth 22. Two years later, the probe values around the implant were 3 mm. The extension of the crown (tooth 22) had no contact in the articulation. The patient was very happy with her treatment.

**What should be taken into consideration?**

The case is part of a case series, in which the effectiveness of Ridge Preservation in combination with a late implantation was tested. One of the objectives of the case series was to evaluate the earliest possible time for implantation after Ridge Preservation. For this reason, the implant was inserted after just four months, although this is a relatively early implantation time after bone regeneration with bovine bone replacement material.

A biopsy was taken in order to assess the condition of the bone after four months. The degree of maturity of the new bone was sufficient for a primary stable implant insertion.

**Aftercare planning**

Cooperation with the referring dentist is of great importance for a successful treatment. The patient’s oral hygiene barely fulfilled the requirements for implant placement. We recommended that the dentist arranges more frequent recall appointments for professional tooth cleaning.
1 Radiograph of teeth 21 and 22, which were not worth retaining
2 Clinical situation of the area to be treated
3 De-epithelialisation of the sulcus after tooth extraction
4 Geistlich Bio-Oss® Collagen placed in the extraction socket
5 The extraction socket sealed with Geistlich Mucograft® Seal
6 Stabilisation suturing
7 Healing after one week
8 Installed implant with a sealing screw
9 New healing cap for the emergence profile after 2 months
10 Radiograph 2 months after implant insertion
11 Clinical situation 2 years after extraction
12 Radiograph 2 years after extraction
KEY STUDIES SELECTED.

Dr. Hector Rios | USA
Department of Periodontics and Oral Medicine
University of Michigan
Ann Arbor
Can novel therapeutic approaches regenerate the periodontal ligament? And which findings contribute to personalized periodontal therapy?

Over 30 years have passed since the first successful application of regenerative therapy for treatment of periodontal diseases. A plethora of biomaterials and protocols have been developed since then and are now available for clinical application. Nonetheless, periodontal regeneration is still a challenging task. Once the integrity of the tissue attachment is compromised and the alveolar bone starts deteriorating, restoring the function and structure of the periodontal organ to its original state becomes an unpredictable clinical outcome.

How do we overcome this situation? Key developments in periodontal research have included:

- The establishment of advanced diagnostic methods that help anticipate and prevent severe periodontal disease progression,
- 3D imaging to better diagnose defects,
- Optimized biomaterial scaffolds, e.g., in combination with biologically active molecules or genes for the “holy grail” of periodontal ligament (PDL) regeneration, and
- New surgical protocols and instruments that minimize trauma and enhance wound healing.

The following collection of recent papers sheds light on the current state of knowledge and gives hope for the future.

**Early Diagnosis**

Today, our understanding of wound healing and periodontal regeneration should incorporate gene, protein and metabolite information into a dynamic, biological network that includes disease initiation, susceptibility, and resolution. But today periodontal disease is diagnosed based on clinical findings such as probing pocket depth, bone loss, loss of attachment and other clinical measures. How can we anticipate severe disease progression early and prevent periodontal destruction? What is needed is a proper understanding of the biological processes of the PDL. And this understanding should help us discover new “early stage” markers for periodontal disease. In this paper the most important features of a biomarker are discussed – that it must be highly specific, highly sensitive, biologically stable for feasible detection, predictive (i.e., proportionate to the degree of disease) and noninvasively measurable.

**A Potentially Novel Biomarker?**

Molecules such as peristin are potential biomarker targets that could help us with our understanding of periodontal cell-matrix dynamics and homeostasis. Peristin is found within the periodontal ligament and is a key extracellular matrix protein involved in periodontal tissue homeostasis. In peristin-knock-out mice, the loss of peristin leads to rapid deterioration of the structural and functional integ-
rity of the periodontium, advanced alveolar bone loss, severe clinical attachment loss and a significant widening of the PDL space. Periostin expression in the PDL is strongly induced during cell differentiation and mineralization. The identification of PDL biomarkers such as periostin could help us predict regenerative outcomes and complement traditional clinical measures.


3D-imaging for diagnosis

Cone beam computed tomography (CBCT) gives an undistorted 3-D assessment of a tooth and surrounding structures and provides axial, coronal and sagittal multi-planar reconstructed images without magnification. What are the advantages of this imaging technique compared to conventional radiography, when it comes to the diagnosis and treatment of periodontal defects?

Acar & Kamburoğlu’s paper highlights advantages of 3D imaging for the assessment of intrabony defects, the diagnosis of interradicular bone loss and the measurement of regenerative therapy outcomes. For example, CBCT imaging of maxillary molars gives more detailed information about furcation involvement than conventional radiology. In this sense, the volumetric assessment of the periodontal structures assists us with case selection and helps us anticipate challenging anatomies. It helps us choose surgical options, such as apically repositioned flaps with or without tunnel preparations, root amputation, hemi-/trisection or root separation.


Tissue engineering, cells and genes

Tissue engineering has the potential to improve the regeneration of lost periodontium in a more predictable manner than conventional therapies. Novel approaches include combinations of scaffolds with living cells and/or biologically active molecules.

Scaffold matrices: In the last two decades, scaffold matrices have been investigated extensively for periodontal regeneration. Current research is focused on the optimization of physicochemical and mechanical properties of novel scaffolds to overcome contemporary structural and biological limitations that have hindered the predictability of periodontal regeneration. One possibility is region-specific variations in microstructure porosity and scaffold surface topography. Another potential is the combination of scaffolds with cell- or gene-based therapies.

Cells: Mesenchymal stem cells (MSCs) from oral or extraoral sources are able to differentiate into a variety of cell types, such as osteoblasts, fibroblasts and cementoblasts, and thus promote regeneration. Though theoretically possible, the use of MSCs for regeneration has so far lacked the sophistication to be predictable in mainstream clinical practice.

A more recent technology utilizes confluent cell sheets. Cells from the PDL are grown on a temperature-sensitive sheet in culture plates, and the entire sheet, which includes not only cells but also an intact extracellular matrix with cell-cell junctions, can be harvested by simply lowering the temperature. The sheet can then be implanted directly into the intended site of therapy. The advantage of this technique lies in its improved preservation of cells within an extracellular environment.

Genes: The idea behind gene therapy is the transfer of genetic material to direct a patient’s cells to produce a therapeutic effect. Using gene therapy for PDL regeneration has several advantages over cell therapy. For example, it avoids the challenges associated with *ex vivo* protein expression and purification, and the genes can be expressed *in vivo* for weeks to years. Possible target genes for gene therapy are PDGF, BMP and glycoproteins from the WNT pathway.

Nonetheless, due to the safety and efficacy issues involved in regulatory approvals, the clinical application of gene therapy for periodontal defects remains more of a theory than a mainstream clinical practice.

Limitations and lessons learned: Our outcome limitations when working with growth factors frequently relate to our limited understanding of the biology of the healing periodontium, i.e., specific target cells and their differentiation requirements, release kinetics of growth factors delivered
to the site and stability of the regenerated tissues. In addition, many scaffold-based strategies have failed because the investigators confused tissue ingrowth with tissue maturation. A defect filled with immature tissue should not be considered “regenerated,” and premature scaffold degradation can adversely affect treatment outcomes.


3D printed scaffolds

Imaging-based and computer-aided scaffolds provide a personalized tissue engineering solution. The three-dimensional anatomical geometry of a defect is acquired by high-resolution computed tomography data, which can function as a template for a scaffold. The scaffold is fabricated with desired biomaterials by 3D printing that, in turn, will precisely match the spatial dimensions of the defect volume. Due to the complexity of the periodontal apparatus, application of this technique requires a heterogeneous internal scaffold design, including region-specific variations in porous microstructure and scaffold surface topography. These structural variations, in turn, help regulate the fate of ingrowing cells in a spatial specific manner. The scaffold tested in this study featured a fiber guiding structure and was able to compartmentalize different cell phenotypes within the volume of the scaffold.


Results from the AAP workshop

The report from the 2014 AAP Regeneration Workshop sheds light on emerging therapies like systemic anabolic agents, local delivery of growth factors and cell therapy. As emerging therapies, most of these treatments lack high levels of evidence, i.e., randomized and controlled trials. Nonetheless, the report provides some clinical scenarios and gives background information on mode of action and indications. For example, the well-known bone anabolic agent teriparatide acts on preosteoblasts to increase proliferation and on osteoblasts to decrease apoptosis. Its main indication could be for patients with known metabolic disorders.


Regeneration of periodontal defects in daily practice

The last paper is a literature review and provides an excellent overview of the contemporary management of periodontal osseous defects by the periodontist-hygienist team. According to the authors, key principles for successful periodontal regeneration are: (1) case selection, identification and resolution of etiologic and contributing factors, (2) the proper surgical technique, including defect debridement, root preparation and materials selection and (3) follow-up. Currently used biomaterials are bone grafts, bone graft substitutes, barrier membranes and bioactive agents such as growth factors.

SUBSTITUTE SKIN WITH A SUPPLY SYSTEM.

Recently developed natural artificial skin could revolutionize skin regeneration.

Cell biologist Ernst Reichmann has developed a substitute skin.
At the University Children’s Hospital in Zurich a substitute skin has been successfully cultured for the first time, which, along with other cell types, also contains blood and lymph vessels. With this development, “cultured skin” is becoming more like natural human skin.

Although generations of scientists have already tried to reconstruct a natural skin substitute, the results have not been satisfactory. This largest of human organs seemed to be too complex, with its various functional layers and multitude of cell and tissue types, all of which have to be brought together in artificial skin to form a functional unit.

Juvenile skin: a special problem

As long ago as the 1970s, doctors in Boston, USA, attempted to develop a new skin from bovine skin, collagen and shark cartilage. But the powerful defence mechanism of the human immune system meant that all these attempts came to nothing. By the end of the 1980s, scientists were able to culture certain skin cells, although they were still very far from achieving a true skin substitute.

Until now burn victims have received mostly endogenous skin transplants. This is disadvantageous in particular for small children for whom only limited donor surfaces are available. Moreover, the transplants can cause new wounds and disfiguring scars. For children there is another serious problem, as the scar tissue will not keep pace with the body’s future growth. On the contrary, scars tend to contract over time, which can lead to restrictions in movement or physical distortions that mean many stressful subsequent operations could be necessary.

Vessels to supply the skin

Whether it is for burn victims, for people with chronic open wounds or for a substitute to animal testing – the demand for artificial skin is enormous. To date, skin substitutes have contained no blood or lymph vessels, no pigmentation, no sweat glands or hair follicles, and no nerves. Due to the lack of a vessel system, which in natural skin is responsible for supplying oxygen and nutrients as well as removing excess water, there is an immediate oxygen and nutrient deficiency in the critical, initial healing phase, which clearly reduces the artificial skin’s chances of survival.

But now for the first time, scientists working with Ernst Reichmann, Martin Meuli and Clemens Schiestl at the University Children’s Hospital in Zurich have succeeded in creating a double-layer artificial human skin consisting of hypodermal cells (fibroblasts), epidermal cells (keratinocytes), melanocytes and the endothelial cells of blood and lymph vessels. In these trials, skin biopsies one to two centimeters in size are divided into layers and then broken down by enzymes into individual cell types. The cells are then placed in special nutrient media to allow them to multiply. The remarkable thing about the artificial skin is that

OUTSIDE THE BOX
the epithelial cells from the blood and lymph capillaries reform themselves spontaneously into the two vessel types on a jelly-like carrier matrix. These tiny capillaries have all the characteristics of their natural counterparts and are fully functional. The new sections of skin are 7x7 cm square and take about three weeks to grow before they can be transplanted.

It has been a long road

Over the last decade and a half, it has taken a huge technical effort and enormous financial outlay for the 15-person team to reach this stage. It took five years alone to develop a suitable carrier substance for culturing skin cells. And it was this special matrix that paved the way for the creation of real skin transplants. The recently developed laboratory-grown skin with its own supply capillaries is being tested in a clinical trial at the University Children’s Hospital in Zurich; and, according to the lead researcher, Ernst Reichmann, it is the best in clinical use anywhere in the world.

Such skin substitutes are urgently needed. Approximately 1,000 people are burnt so severely that they require hospitalisation every year in Switzerland alone – to which can be added hundreds, perhaps even thousands, of people who, because of extensive birthmarks, accidents, infections or cancerous ulcers, have to have large sections of skin removed. If these trials are successful and the substitute skin can grow with natural skin in the long term, this will mean fewer operations for paediatric patients and, above all, fewer scars.

References
1 Kemp AM, et al.: Arch Dis Child (online) 3. Februar 2014

Baby skin in danger

According to one study, about 25,000 children and juveniles under the age of 15 scald or burn themselves in England and Wales every year; and some 3,800 have to be hospitalized. 1-year-old babies suffer ten times as many burns and scald injuries as school-age children.

Our skin is always changing

The epidermis renews itself completely approximately every 28 days. New skin cells form during this time in the lower epidermal layers and migrate toward the surface. As a result, the older cells lying above them are pushed upwards and are shed. This is how we lose about one to two grams of skin every day.

Taking a closer look at skin

One square centimeter of skin contains 600,000 to 2 million skin cells, 5,000 sensory cells, 100 sweat glands, one meter of the smallest blood vessels, 15 sebaceous glands (although not on the palms of the hands or the soles of the feet), five hairs and 150,000 pigment cells.
BACKGROUND.

Geistlich Pharma & Osteology Foundation
A conversation with the collagen experts

Interview by Verena Vermeulen

Collagen plays an important role in the regeneration of tissue. This is why Geistlich Pharma has devoted itself to collagen expertise.

Eleven scientists working at Geistlich Pharma have dedicated themselves exclusively to collagen research. Dr. Lothar Schlösser, Niklaus Stiefel and Daniel Suppiger have advanced the company’s 160 years of collagen expertise with their work, as they have developed innovative biomaterials for tissue regeneration.

Dr. Schlösser, collagen performs so many different functions in the body. Is it also the same for the collagen in Geistlich biomaterials?
Dr. Schlösser: It certainly is. The Geistlich Bio-Gide® collagen membrane is a good example. The dense collagen of the upper layer acts as a dividing wall between a bone graft and the soft tissue. The lower layer has a more open structure in comparison. It adheres well to the tissue, allows cells to colonize and contains fibers that serve as “guiding templates” for somatic cells. Although these are very different properties, Geistlich Collagen has them all.

How can one modify a protein so that it has either this or that property?

N. Stiefel: Many people think that it has something to do with which one of the 30 different types of collagen one uses, but in fact it is a question of the original tissue and how it is processed. It’s like when you are looking for a house. You can either buy a complete, ready-built detached house, or you can buy the individual bricks and assemble something completely new.

And which approach does Geistlich use?

Dr. Schlösser: Both strategies have a role to play for us. Some of our products, for example, if they should be strong to retain sutures, contain native organized collagen tissue obtained using a gentle preparation process. In other cases we have designed our collagen tissue completely from scratch using natural collagen components in order to obtain a specific effect, for example, to achieve good volume stability when healing.

Is the competition doing the same thing?

Dr. Schlösser: Other membranes are frequently assembled from collagen components, but in order to make them strong for suture retention, they must be chemically cross-linked, which can compromise the biology and healing response, which is exactly what we don’t want!

How do the cells react when you alter the collagen?

D. Suppiger: That is the crucial question for our cell laboratory. We continually optimize our collagen products until the right cells do what we want them to: mucosal cells, bone cells, cartilage cells, etc. And to go back to the analogy of houses for a moment, after doing the cell tests, we can really say: here’s the nursery, there’s the living room and that’s the cellular, i.e., testing particular “rooms” to make sure they “attract” the right cells.

1 Niklaus Stiefel says: “We optimize our products on the one hand for the sake of the body’s cells, and on the other hand to make them easier for dentists to use.”

2 Daniel Suppiger (left) and Dr. Lothar Schlösser are quite certain: “Collagen products must be made in such a way that cells can behave naturally in them.”
How would you complete the sentence: “When a clinician uses Geistlich collagen membranes or matrices he can be sure that...”

N. Stiefel: ...the outcome is predictable, that no surprises will occur, and that he will be able to send his patient home happy. That’s why we do our research: to push for successful outcomes, no matter how experienced a clinician might be.

How can this be guaranteed?

D. Suppiger: A large part of our work consists of optimizing the handling of a product without compromising its proper effect on cells. Our focus is on the clinician from the very beginning. What’s important to the dentist or orthopedic surgeon? Does the product have to create volume? Must it be easily hydrated? For the requirement analysis, we work together with many clinicians around the world, from top surgeons to less experienced dentists.

Dr. Schlösser: And we test the prototypes in the same way, of course. Finally, we always have animal cadaver models in the lab so that in-house and external specialists can test how the new products perform in use.

One last question: What is a collagen researcher’s dream?

N. Stiefel: In principle, all tissue can be regenerated using the right collagen. It really would be a dream come true to be able to facilitate this: to be able to help cells so that they themselves can regenerate tissue that has been lost or destroyed, like skin, heart or liver tissue. In this regard, we hope to “turn back the clock” – to encourage tissues to regenerate to their former, healthy states.
QUANTITY
If all the collagen molecules in a human body were unfolded and laid out end to end, they would reach from the Earth to the Moon.

APPLICATION
In the pharmaceutical industry collagen is used, above all, for coating tablets.

POTENTIAL
Collagens can absorb tensile forces up to ten thousand times their own weight.
Global reach

Thomas Pfyffer

Geistlich Pharma has further consolidated its network of biomaterial providers with the opening of its ninth affiliate. Along with its nine agencies, about 60 licensed distribution partners work to ensure that Geistlich's products are available in almost 100 countries around the world.

What is the benefit of this impressive network to you, the customer? Geistlich's expertise is based on 160 years of experience. This accumulated knowledge and an active network of exceptional researchers working around the world all influence our products and procedures.

What's the difference? The products originate from a single source – all the research, development and production takes place in Switzerland. This is why we enjoy such a high level of confidence. Our family-run company has an extraordinarily high proportion of staff involved in research and development. We are continuously making considerable investments – both our research and our corporate philosophy are designed for the long-term.

Success is predictable

“We want to give patients some of their quality of life back. As a specialist in regenerative medicine, we are always exploring new avenues,” is how CEO Paul Note outlines Geistlich's philosophy. Our company developed the market for oral regenerative biomaterials, and today we are a world leader in this field. Moreover, our company is the leading supplier of natural medical devices for cartilage and bone regeneration in orthopaedics, and we also supply other medicinal products for selected indications.

Our strictly scientific approach is one of the most important pillars of our lasting success – yesterday, today and tomorrow. You can benefit from this comprehensive knowledge by taking part in the advanced training courses we offer. They will let you see for yourself just how much our safe and quality-assured products can achieve.
Studies pass the 1,000 mark
Evelyn Meiforth

Over one thousand publications attest to the high scientific and clinical standards of Geistlich Biomaterials.

If we assume that a typical study in dental regeneration takes about a year and a half with at least six researchers intensively involved, then 1,000 publications represent 6,000 scientists, who have spent the equivalent of 9,000 years investigating Geistlich’s Biomaterials. This is why, when it comes to bone replacement and membranes for oral regeneration, Geistlich Bio-Oss® and Geistlich Bio-Gide® are considered the No. 1 referenced biomaterials around the world.

A pioneering achievement
The close cooperation between Geistlich and researchers at various universities began in the 1980s. The potential for regenerative biomaterials was only a possibility when Dr. Peter Geistlich had an unusual idea for a new biomaterial solution. Together with Professors Myron Spector (Harvard University) and Philip J. Boyne (Loma Linda University), he developed a new kind of bone replacement material: Geistlich Bio-Oss®. Geistlich Bio-Oss® was followed in the 1990s by Geistlich Bio-Gide®, which was distinguished by its special bilayer structure and by the way it simplified the GTR and GBR techniques used at the time.

Inspired to research
The exceptional biofunctionality of Geistlich biomaterials has fascinated scientists and clinicians around the world. Numerous studies have demonstrated that Geistlich Bio-Oss® is highly osteoconductive, because of its extremely porous structure and hydrophilicity. Geistlich Bio-Gide®’s natural collagen fibers promote vascularized wound healing. The slow resorption of Geistlich Bio-Oss® and the ideally matched protective function of Geistlich Bio-Gide® favor long-term volume stability of the augmented bone. As the most recent development, Geistlich Mucograft® has inspired numerous research groups to conduct studies in which the new 3D collagen matrix has been used in the regeneration of soft tissue. Geistlich Mucograft® has provided successful treatments for over five years.

Committed to dental regeneration
Geistlich will be celebrating two important anniversaries next year: 30 years of Geistlich Bio-Oss® and 20 years of Geistlich Bio-Gide®. But today the company has already set a new benchmark for regeneration with over 1,000 scientific publications – works that have made a decisive contribution to the field of oral regeneration and provided successful treatments for patients around the world.

References
Osteology Foundation has a new President

Dr. Heike Fania

For over twelve years and since its establishment, Prof. Christoph Hämmerle has been the President of the Osteology Foundation. His successor, Prof. Mariano Sanz, took office on 1 June 2015. The official transfer of the presidency took place at the Osteology Board Meeting on 22 June 2015 in Zurich.

Looking back, Christoph Hämmerle stated that the key to the Osteology Foundation's success has been, on the one hand, the outstanding teamwork within the Foundation itself and, on the other hand, the financial support and academic freedom that Dr. Peter Geistlich granted to the Foundation.

Advanced training and research

The successful development of the Osteology Foundation has been a continual step-by-step process. Christoph Hämmerle pointed to the National and International Symposia held by the Foundation, which have grown steadily in size and reputation over the years. Alongside these symposia, an important mainstay of the Foundation has been its grant program, providing support for research projects. The grants have produced important knowledge about oral regeneration along with corresponding publications. And as a truly special and innovative development of the Foundation, Christoph Hämmerle points to the Osteology Research Academy, in which prospective researchers receive advanced training in scientific method.

Driving expansion forward

Christoph Hämmerle stated that, with Mariano Sanz as his successor, he knows the Foundation is in good hands. He has known Mariano Sanz for a long time and has worked with him on various projects over the years, and he knows Dr. Sanz has a great deal of experience in both science and practice, and as a leader. Mariano Sanz said on the occasion of this change in leadership that under Christoph Hämmerle’s guidance the Foundation had succeeded in achieving the highest levels of quality in both science and practice: “I have no intention of changing anything, but rather I will follow the same path and keep on working to increase the Foundation’s importance as well as continue to drive its geographical expansion.” What is important is to make even greater use of new technologies and media in order to continue to ensure long-term growth and continuous development.

A new Osteology Foundation Board

Simultaneous with this change at the top, there have been other changes in personnel: Professors Myron Nevins, Friedrich Neukam and Massimo Simion have stepped down from the Foundation Board, as their time in office had come to an end. They were succeeded in June 2015 by Dr. Pamela McClain and Professors Frank Schwarz and Istvan Urban.
Osteology Monaco 2016 – Registration opens in October

Dr. Heike Fania

Great events cast their shadows before them, and in April 2016 it will be that time again: The International Osteology Symposium will return to Monaco!
The congress’s Chairmen, Prof. Friedrich W. Neukam and Prof. Myron Nevins, have put together a truly outstanding scientific program under the slogan “Learning the WHY and the HOW in regenerative therapy”.

With 85 internationally renowned speakers, interactive sessions, innovative technologies and concepts, approximately 20 workshops and three new Master Clinician Courses (which are included in the registration fee), Osteology Monaco 2016 will once again be the highlight of next year’s congress calendar!
The latest research discoveries will be presented and discussed in the Research Forum and Poster Presentation. The deadline for submitting abstracts is 1 December 2015.

You can find all the details of the program, a schedule and organization on the congress’s homepage. You can register online starting in October 2015.

You can find more information about the Osteology Foundation’s grants, along with its other activities, at the website: www.osteology.org

The Osteology Foundation has been awarding Young Researcher Grants since 2015. These one-year scholarships are intended for young scientists aspiring to a scientific career in the field of oral regeneration. In the first round, numerous applications have already been received for the Osteology Scholarship Centres in Zurich (Christoph Hämerle), Vienna (Reinhard Gruber), Gothenburg (Christer Dahlin) and Ann-Arbor (William Giannobile). In the next round of applications, requests will be accepted for the Osteology Scholarship Centres in Bern (Daniel Buser), Madrid (Mariano Sanz), Dusseldorf (Frank Schwarz) and Harvard/Boston (David Kim).

The application period ends on 1 December 2015.
**INTERVIEW**

On a lab tour with Todd Scheyer

The interview was conducted by Verena Vermeulen

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We are on tour in Geistlich’s research and production departments. What is your first impression?

**Dr. Scheyer:** Very interesting, especially because my own research began using Geistlich biomaterials in 1998. So, now, to finally see how it all happens is really fascinating.

You have helped establish a practice-based clinical research network (PBCRN) called The McGuire Institute in the United States. What’s the main idea behind the network?

**Dr. Scheyer:** It’s a non-profit organization that helps translate research ideas into clinical applications – the first one in the US built around private practice Periodontists. Meanwhile, even the National Institute of Dental and Craniofacial Research is looking for PBCRN’s to collaborate with academic centers for critical research efforts over the next ten plus years.

What is the major advantage of a PBCRN compared with academic research?

**Dr. Scheyer:** The results are very translatable to patient care. And with such an efficient organisation, it doesn’t take years to transition from an initial idea to a clinical application.

Are there major differences between dental research in Europe and the US?

**Dr. Scheyer:** I think the differences are based on history. For example, in the US bone grafts have usually meant “allografts” – that’s what we know best, and because of the relative regulatory ease of using tissue bank biomaterials, research has been driven in that direction. But my view has broadened so much just through my research. There’s a lot of opportunity to find the similarities between Europe and the US and use them for future research.

If you were not a dentist, what would you like to be?

**Dr. Scheyer:** Maybe a traveling adventurer... I love to travel, and I love sports like mountain biking and fly fishing. But this would probably only be nice for a while... before missing patient interaction and scientific advances!
FOCUS
30 years of oral regeneration
Biological basis, applications, outlooks

JOURNAL CLUB
Membranes in GBR
Just a barrier – or more?

BACKGROUND
Celebrate anniversaries with us
30 years of Geistlich Bio-Oss®, 20 years of Geistlich Bio-Gide®

Free attendance to Osteology Monaco!

Scan the QR code or type in the URL to take part in the Geistlich News-Reader Survey. Duration: 2 minutes

All participants will be entered into a drawing for 3 free passes to Osteology Monaco (including the “Osteology Night” in the Salle des Étoiles)