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Dear readers,

Just a few months prior to his death, Dr. Peter Geistlich was honoured with the Distinguished Humanitarian Award from Loma Linda University. He was honored for his pioneering achievements in materials research along with his visions in the field of regenerative medicine and his decade-long commitment to research benefiting patients. Dr. Peter Geistlich’s visions continue to be our visions.

“Regenerating rather than just repairing” - this is the motto of our work. Our products are unique in their ability to be integrated into endogenous structures, for their comfort to the user and, not least, for their high degree of safety. We also pay close attention to the innovative capacity of our research and the quality of our employees. We invest considerable sums in both. To further bolster interdisciplinary collaboration in our research and development division, new structures were set up in January 2015. They ensure that our research and product development will continue to be among the best that regenerative dentistry and orthopaedics have to offer.

In the future everything from Research to Development, Approval, Manufacture and Sales will remain under one roof and under our responsibility. Only by controlling each individual step ourselves, are we able to vouch for the quality of our products. This justifies the key award which our products receive around the world: trust.

Dr. Terance Hart
CSO, Geistlich Pharma AG
MAJOR BONE AUGMENTATIONS.

What techniques are most suitable?
Will there soon be brand new techniques?
Major Bone Augmentations: Contemporary techniques and materials

Nowadays, using modern biomaterials and autologous bone transplants, it is possible to place implants in patients experiencing considerable bone deficits – if appropriate surgical techniques are used and the patient’s circumstances permit.

Bone augmentations are no longer just performed to allow thorough osseointegration of dental implants. They are also used to enhance the:

1. Aesthetics,
2. Prosthetic function, and
3. Prognosis for the restoration.

For example, augmentation can help avoid unnaturally long crowns in the mesial maxilla (1) and impression difficulties or eccentric screw channels with non-axially aligned implants (2). If adequately sized implants are covered by bone on all sides, they have a good prognosis – both mechanically and biologically (3).

For instance, in an edentulous maxilla it can be important to use bone augmentation to facilitate good prosthetic function in tetrapodal or hexapodal prosthetic support with large antero-posterior abutment spread and a large support polygon. In an edentulous, atrophied jaw a bone augmentation can normalise the occlusal position and the integrity of the mimic facial muscles and so improve facial aesthetics.

Augmentation surgery can be complex. When planning surgery, indication restrictions use and contraindications need to be taken into account (Tab. 1).

Avoiding compromises

Although it is sometimes possible to compromise by using implant prostheses with implants that are dimensionally-reduced, angled or anchored to the cheekbone, it can be assumed that implant planning will then often be bi-directional. In other words, the implants will not be aligned along the axis of the prosthesis and mediatory, so that awkward prosthetic structures are required. A proper augmentation, however, builds the bone where it is needed to fit the prosthetic tooth axis. This allows implants to be planned unidirectionally with a correspondingly dedicated crown-bridge prosthesis.

Augmentation techniques

Depending upon the defect type, inlay, interpositional, appositional and onlay osteoplasties can be used (Fig. 1). The degree of surgical complexity grows correspondingly because it becomes increasingly complex to reliably cover the bone transplants with soft tissue and avoid a subsequent dehiscence.

The more difficult the defect class, the more active the bone transplant itself has to be. But beware that using autol-
ogous chips from a bone filter increases the chance for infection, necessitating a good antibacterial regimen and an antiseptic procedure.

**Challenge: angiogenesis**

Today it is not yet clinically predictable to provide vertical augmentation with blocks made of bone replacement material. This is in part due to angiogenesis. Since vascularization occurs only a few vertical millimeters from the bone substrate. Biomaterial which is further than 3 to 4 mm away from the bone substrate tends to heal with scarring.

**Sandwich technique and bone splitting**

An internal bone defect presents the possibility for the good healing tendencies of inlay and interpositional osteoplasties (sandwich) with angiogenesis from all sides of the graft. Internal bone defects occur when, for example, a vertical defect is transformed into a sandwich osteoplasty by a horizontal osteotomy or when a horizontal defect is carried over into bone splitting.

A major advantage of sandwich-interpositional osteoplasties compared to appositional and onlay osteoplasties is that the soft tissue remains attached to the alveolar ridge and does not need to be shifted in a lingual direction. This facilitates soft tissue coverage, improves peri-implant tissue and reduces the likelihood of resorption (Fig. 2). A modification of the sandwich osteoplasty is a Schwing interposition, which allows a ridge to be raised and broadened, if moderately atrophied knife-edge ridges are involved (Fig. 3).

**Problem: transplant resorption**

Free bone transplants – whether cancellous or cortical – can permanently heal only through internal bone resorption and subsequent reconstruction (“creeping substitution”). Whereas internal resorption of bone is necessary for the transformation, surface resorption on a larger scale is undesirable because it causes the augmentation material to lose volume and produces clinically unpredictable results. Thus, resorption occurs in about 40% of cases with large pelvic bone transplants, particularly early in the healing process. To counteract this uncontrolled resorption, autologous bone blocks can be covered with Geistlich Bio-Oss® and Geistlich Bio-Gide®. Geistlich Bio-Oss® inhibits osteoclast precursor cells, while Geistlich Bio-Gide® forms a barrier against soft tissue in-growth without inhibiting vascularisation, which is crucial for new bone formation. Free bone transplants – whether cancellous or cortical – can permanently heal only through internal bone resorption and subsequent reconstruction (“creeping substitution”). Whereas internal resorption of bone is necessary for the transformation, surface resorption on a larger scale is undesirable because it causes the augmentation material to lose volume and produces clinically unpredictable results. Thus, resorption occurs in about 40% of cases with large pelvic bone transplants, particularly early in the healing process. To counteract this uncontrolled resorption, autologous bone blocks can be covered with Geistlich Bio-Oss® and Geistlich Bio-Gide®. Geistlich Bio-Oss® inhibits osteoclast precursor cells, while Geistlich Bio-Gide® forms a barrier against soft tissue in-growth without inhibiting vascularisation, which is crucial for new bone formation. Augmentation materials containing Geistlich Bio-Oss® exhibit volume preservation for many years.

**Long term prognosis**

Implants in augmented bones have an excellent five-year survival rate, which is generally as good as native bone or over 95%. Cone beam computed tomography (CBCT) studies have provided excellent prospective proof of the constancy of volume with alveolar ridge augmentations both for bone blocks and for the membrane (GBR) technique over five years. Even major augmentations like Le Fort 1 interpositional osteoplasties exhibit an implant survival rate of 94.5%.
The augmented volume remains stable over the long-term when implants are subjected to stress from chewing, as ten-year studies have shown. On the other hand, the augmentation is 100% resorbed if it does not undergo normal stress from masticatory function. Nowadays, using augmentation surgery, experienced surgeons are able to obtain very reliable results. In the future, new techniques, such as tissue engineering, could reduce surgical complexity and morbidity.

**References**

Geistlich News 01 | 2015

Horizontal augmentations using granulate material

Granulate graft material has to be well stabilised, and Geistlich Mucograft® can be combined with a gingival strip graft. Prof. Istvan Urban explains his techniques.

“\textit{A membrane should allow vascularisation from the periosteum.}”

Professor Urban, you use granulate graft material for horizontal ridge augmentations. Why?

\textbf{Prof. Urban:} I never liked using the autogenous bone block, because I found them very invasive to harvest and sometimes very complicated to adapt perfectly to host bone. Another disadvantage is the resorption that we usually see in blocks. Today we prefer particulate graft materials for two main reasons: Firstly, our histological examinations show that they are easily vascularised, which is very important for graft incorporation and new bone formation. Secondly, the particles adapt to any surface irregularities. However, we have to completely immobilise the graft and cover the granules. In the beginning, we used non-resorbable, titanium-reinforced membranes for both horizontal and vertical augmentations. The membranes worked well, but they were sometimes very demanding and not well accepted by many clinicians. Then we asked ourselves why not use the remaining bony wall in a smarter way. We started to apply resorbable, rigid membranes for horizontal augmentations with good results. Today we are using a native collagen membrane, the Geistlich Bio-Gide®.

Why have you called your approach the “sausage technique”?

\textbf{Prof. Urban:} We fix the collagen membrane with titanium pins into the bone walls and fill the space under the membrane to form a very stable graft. The whole graft looks like a densely filled sausage. Geistlich Bio-Gide® acts like an immobilised “sausage” skin during the early weeks of healing.

What are your results?

\textbf{Prof. Urban:} We get very predictable results with this technique using a 1:1 mixture of Geistlich Bio-Oss® and autogenous bone particles. We can usually harvest enough bone using bone scrapers. The Geistlich Bio-Oss® particles incorporate well and help to reduce graft resorption. This has been nicely demonstrated both clinically and histologically in our recent prospective case series 1.

What properties should a membrane have for this procedure?

\textbf{Prof. Urban:} First, I think a membrane should allow vascularisation from the periosteum. This enables nutrient transfer, capillary in-growth and other potential stimulating effects. The elasticity of a membrane is also important, so that I can stretch it when I fix it with the pins and form the stable “sausage bone graft”. The membrane should disappear in a good prompt manner so that it does not interfere with bone maturation. I do not think a long resorption time is needed, and it may even slow down bone formation. Geistlich Bio-Gide® has all these properties. The lack of titanium reinforcement can be overcome reliably by fixing the membrane both lingually or palatally and vestibularly. Today we use titanium-reinforced membranes exclusively for vertical defects.
I also think that we understand the principle of Guided Bone Regeneration much better now than 20 years ago, when we believed long resorption times were necessary. The interaction with the periosteum might be a very important part of good bone maturation, and this is better when native collagen membranes are used.

What complications have you faced so far with the sausage technique?

**Prof. Urban:** In the past ten years I have had only one posterior mandibular case in which the patient developed a postoperative infection. I can only blame myself for this complication as I think the infection emerged from a third molar, which I should have extracted. Anyway, in general, the procedure is very successful and predictable. We can even reconstruct completely resorbed maxillary edentulous ridges using this technique. But of course, adequate patient preparation and post-op management as well as precise surgical techniques are key factors in reducing the rate of any complication.

Soft tissue management is often a problem in horizontal augmentations. How do you handle this?

**Prof. Urban:** Advanced ridge augmentation procedures usually result in a severe displacement of the mucogingival line and vestibular loss. In the past we performed mucogingival surgery using epithelialised gingival grafts or free connective tissue grafts. We left these grafts to heal in an open healing environment because this is a prerequisite for the reformation of the vestibule and keratinised tissue.

Graft harvesting from the palatal mucosa, however, may be associated with significant patient morbidity. This was usually the treatment phase that patients did not like at all. When we heard of Geistlich Mucograft®, we were very interested in it because we saw potential for soft tissue regeneration – and because I was fed up with the big connective tissue grafts.

**“Graft harvesting from the palatal mucosa may be associated with significant patient morbidity.”**

What are your experiences with the strip technique?

**Prof. Urban:** In a study of a prospective case series, which is now accepted for publication, we found that we could in fact regenerate the amount of keratinised tissue needed. We achieved an average of 6.3 mm of keratinised tissue after one year. In the anterior maxilla, which was one of the major indications, it was even 7.8 mm.

We also found very favourable results for pain intensity: on a visual analogue scale of up to 10 – with 10 being the strongest pain – the average pain in the first week was 2.3, and it was 0 for the following weeks of healing. Ten out of the 20 patients did not take any pain medication, and one patient only needed medication for the palatal wound.

What are the clinical prerequisites for using these techniques?

**Prof. Urban:** I like things to be both simple and reproducible. Both the sausage technique and the strip technique using Geistlich Mucograft® are easy for clinicians with adequate surgical skills. Surgeons, however, should train for the techniques in hands-on courses. Live surgery and video tutorials will also help them to become more familiar with these options for tissue regeneration.

Professor Urban, thank you very much for this interview!

References

SAUSAGE TECHNIQUE

1. Intraoperative view demonstrates insufficient ridge width.
2. Geistlich Bio-Gide® is applied over a mixture (1:1) of bone chips from the retromolar area, and Geistlich Bio-Oss® is rigidly fixed with pins.
3. Sufficient amount of augmented bone for implant placement after 8 months.

Also see the Geistlich brochure on oral and maxillofacial surgery for more information on the sausage technique and the strip technique.

STRIP TECHNIQUE

1. Insufficient vestibular depth and keratinised tissue after an augmentation procedure.
2. Application of a palatal keratinised strip toward the vestibulum, suturing of Geistlich Mucograft® over the previously augmented area where it is left exposed for healing.
3. Increased vestibular depth and keratinised tissue 3 months later.

Brochure “Innovative Treatment Concepts in Oral and Maxillofacial Surgery”
Large vertical augmentations require a staged approach that may consist of several treatment steps to ensure optimal hard and soft tissue results, as presented in this complex case.

The patient was a 55-year-old female, non-smoker in good systemic and periodontal health. Teeth 11, 21, 23, 24 had to be extracted due to extreme periodontal attachment loss. The extraction sockets were filled with Geistlich Bio-Oss® Collagen, and a free gingival graft was used to close the cavity and enhance clot formation. After 4 months, vertical bone augmentations were performed: two non-resorbable titanium-reinforced membranes protected grafts consisting of a 1:1 mixture of autogenous bone and Geistlich Bio-Oss®. The membranes were fixed by 4 bone fixation pins and sustained by a tenting screw, which was exposed over the portion corresponding to the vertical defect. Periosteal releasing incisions allowed the flap to be advanced coronally. The flap was sutured using horizontal mattress U-stitches to ensure proper flap apposition.

Six months later, machined implants were inserted, and a horizontal bone augmentation was performed using Geistlich Bio-Oss® and Geistlich Bio-Gide® to enhance the aesthetic outcome. After another 4 months, the soft tissue thickness was augmented using a Geistlich Mucograft®. Two months later minimally invasive re-entry allowed the connection of the implant abutment and the beginning of prosthetic procedures.

Are there any special considerations?

Vertical bone augmentation by means of Guided Bone Regeneration (GBR) is a well-documented procedure that insures good long-term results. It allows a proper prosthetic rehabilitation with a crown length ideally proportioned to the adjacent teeth. However, the efficacy of this technique strictly depends on a standardised surgical protocol.

Ridge Preservation techniques may be performed to minimise soft tissue and bone contraction that generally follow tooth extraction. Eventually, a horizontal GBR in relation to implant positioning and a soft tissue augmentation may be performed to increase tissue thickness, resulting in a better blood supply and ultimately optimum long-term stability of the peri-implant tissues.

References

**CASE**

1. Teeth 11, 21, 23, 24 are irredeemable due to vertical bone loss.
2. Sockets are filled with Geistlich Bio-Oss® Collagen and covered with free gingival grafts.
3. Residual vertical and horizontal bone defects are still present at 4 months.
4. The tenting screws are positioned to support the membranes.
5. A 1:1 mixture of Geistlich Bio-Oss® and autogenous bone is placed.
6. Non-resorbable titanium-reinforced membranes are positioned and fixed with pins (2 palatal and 2 buccal for each membrane).
7. After 6 months the membranes are removed to insert the implants. Note the regenerated bone.
10. Before implant abutment connection, soft tissue thickness is increased using a collagen matrix (Geistlich Mucograft®).
11. Final result: correct prosthetic rehabilitation avoiding excessive crown length.

**CAPTIONS:**

1. Teeth 11, 21, 23, 24 are irredeemable due to vertical bone loss.
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11. Final result: correct prosthetic rehabilitation avoiding excessive crown length.
Horizontal augmentations with blocks

Surgeons can avoid complications with autogenous bone blocks if they use adequate incision techniques, rigidly fix the block and cover it with a suitable granulate bone substitute and membrane.

After tooth extraction the alveolar ridge undergoes a physiological resorption leading to narrowing. In the aesthetic area and for specific indications, such as lateral upper incisor agenesis or absence of lower incisors, the use of narrow diameter implants is considered a first choice option. But on a routine basis, a residual ridge width of at least 5 mm has to be present to allow the placement of a standard diameter implant (Ø 3.8 mm). In posterior areas clinicians should choose wider implants for prosthetic reasons, therefore, the lack of an ideal width is more frequent. One proven technique for optimising the horizontal ridge is autogenous block grafts. The main advantages of autogenous blocks are their osteoconductive, osteoinductive and osteoproliferative properties. However, since the amount of bone is limited, this technique is not suitable for large defects and complete maxillary reconstructions.

Intraoral donor sites

Surgeons can harvest autogenous bone blocks from intraoral sites such as the chin or mandibular body under local anaesthesia in an outpatient procedure. Grafts from a mandibular symphysis consist of both cortical and cancellous bone. They allow the surgeon to increase the ridge width by up to 7 mm, while grafts from the mandible can be used to obtain only 3 to 4 mm in width due to the presence of the inferior alveolar nerve. In addition, they are composed of cortical bone only.

FOCUS

RISK: SUPERINFECTIONS

ANTIBIOTICS

A full dosage antibiotic therapy is used to avoid superinfections at the surgical site.

How to avoid problems in horizontal augmentations with block grafts

DRILLING OF RECIPIENT CORTICAL PLATE

The cortical plate should be drilled until it bleeds.

RIGID FIXATION

The block should be fixed with at least 2 screws.
**Adequate Incision Techniques**

Usually periosteal horizontal incisions are performed in a deep position from the inner portion of the flap and running from one releasing incision to the other. In doing so, the length of the flap can be increased up to 4 to 5 mm.

**Larger reconstructions:** Combinations with sliding partial thickness palatal flaps, detachment of the muscular fibres from the mylohyoid line and periosteal or vascularised connective tissue flaps are effective ways to totally passivate the flaps.

**If Exposed: Removal of Necrotic Parts**

Necrotic portions of bone may have to be removed with a tungsten carbide bur.

**Early exposure**: the exposed bone has to be decorticated. Rinsing with antibiotic is recommended before closing the defect.

**Late exposure**: remove the necrotic portion until bleeding from the graft is noticed.

**If Exposed: Graft Coverage**

In absence of soft tissue inflammation, surgical corrections using sliding flaps, sometimes associated with connective tissue grafts, may allow the graft to be covered.

**RISK: Graft Exposure**

**Risk: Graft Resorption**

**Filling of Gaps**

Gaps between the block and the recipient plate should be filled with autogenous bone chips.

**Risk: Insufficient Graft Integration / Blood Supply**

**Anti-EDEMA Drugs**

**Block Coverage with Granules and a Collagen Membrane**

The block is covered with a thin layer of Geistlich Bio-Oss® and Geistlich Bio-Gide®. The granules allow new bone formation that balances the bone loss due to remodelling. Clinically, the original graft volume is maintained so that implants can be placed approximately 4 months later.
Risk: graft resorption

While autogenous blocks perform excellently in terms of quality of the reconstructed ridge, a main problem is the 5 to 20% graft resorption due to remodelling. One possibility for overcoming this resorption is to oversize the graft, but then closing the soft tissues without tension is a bigger challenge. An alternative procedure, that can be easily performed at the end of the augmentation surgery is to cover the block with deproteinised bovine bone granules and a collagen membrane.

Risk: graft exposures

In order to limit the risk of graft exposure, the flap margins have to overlap at least 3mm to allow for a tension-free wound closure. In addition, surgeons should avoid ischaemia during suturing by using an adequate incision technique.

Even if the mentioned procedures are performed in the correct way, the risk of graft exposure cannot be 100% eliminated. If exposure occurs during healing, surgeons should remove necrotic tissue and obtain soft tissue coverage to avoid major graft resorption or infections.

Risk: insufficient graft integration

If there are no exposures during healing, graft necrosis is an uncommon event. More frequently, problems may arise due to the in-growth of connective tissue into the gaps between recipient site and blocks. This may result in a lack of graft integration as well as an insufficient blood supply. The risks are minimised by drilling the recipient cortical plate until it bleeds, by rigidly fixing the block and by filling the gaps with autogenous bone chips. Adequate medication with antibiotics and anti-edema drugs is also recommended to reduce the complication risks.

References

Vertical augmentations are challenging. The sandwich technique facilitates soft tissue management and allows experienced surgeons to achieve good results in patients with greater vertical bone deficiencies.

When the ridge has to be augmented vertically to allow implant placement, sandwich osteoplasty offers important advantages over onlay techniques. Due to the repositioning of the keratinised soft tissue, no further soft tissue surgery is usually necessary. In addition, only native bone is located in the sensitive area crestally around the implant. Moreover, the grafted bone blocks are supported apically and coronally, thus facilitating bone in-growth and allowing considerable vertical gain.

As a general prerequisite for this technique, a residual bone height of 4 mm above the inferior alveolar nerve should be available. The horizontal ridge width should be large enough to allow the insertion of a dental implant. Otherwise, the surgeon should exercise alternative augmentation methods. Also, due to the rigid palatal mucosa, the technique is limited primarily to the lateral part of the mandible.

**Planning**

In the situation of reduced vertical dimensions, a CBCT (Cone Bean Computer Tomography) is often required to weigh the option of short implants versus a vertical bone augmentation. While short implants may also yield good long-term outcomes, a vertical augmentation will allow placement of implants with regular dimensions in an optimal three-dimensional position. This may facilitate the prosthetic treatment steps and improve the aesthetic result.
Nevertheless, the patient should be informed about possible complications such as graft failure or nerve lesions before surgery.

The key for success: flap preparation

In the sandwich technique, the soft tissue is left on the crestal part of the ridge. This allows optimal nutrition of the transposed bone. A successful interpositional grafting procedure requires an adequate incision technique for the soft tissues that does not compromise blood supply. Under local nerve block anaesthesia (buccal and inferior alveolar nerves), a subperiosteal poncho flap (repositioned perforated attached gingival flap) starting from the vestibulum is prepared and elevated. The critical step in this phase is the identification of the mental foramen. Afterwards the flap is raised close to the attached mucosa of the crest, while the crestal and lingual mucosa is left attached to the bone.

Osteotomy and interpositional grafting

The osteotomy above the nerve is performed using piezo surgery, since this technique allows higher precision and control than saws or burs in cutting just the bone. Palpating the tip of the piezo with a finger at the lingual sides can further help avoid damage to the soft tissue. Care is taken to keep the soft tissue attached to the cranial segment. After performing the osteotomy with a chisel, the mylohyoid muscle can easily be stretched. The cranial segment can be elevated and stabilised by inserting a block of Geistlich Bio-Oss® – pre-shaped by piezo instruments – into the emerging gap. With interpositional grafting in a sandwich osteoplasty, vertical augmentations of up to 8 or 10 mm can usually be achieved without problems. Following the graft placement, a mini plate with short, self-tapping screws is attached to fix the bone and to avoid nerve damage. This fixation method is also used in more extensive maxillofacial surgery for internal and stable fixation of transposed bone elements. The thick poncho flap can be closed with a double layer suture without further releasing incisions. The time until implant placement depends on the height of the vertical augmentation, but a healing phase of 6 months is sufficient in most cases. For implant placement, a crestal incision is performed, which allows the mini plate to be removed at the same time.

Pitfalls

The sandwich technique provides good success rates if there is careful patient selection and planning, and adequate surgical techniques are used. However, complications may arise from some typical pitfalls:

› If the cranial segment is too thin, it might fracture during transposition.
› A residual infection or osteomyelitis after extraction can lead to graft infection and failure.
› Soft tissue and osteotomy problems may occur at the distal tooth due to the close spatial relationship.

References

The exciting future of regenerative dentistry

Prof. Alan Herford | USA
Oral and Maxillofacial Surgery,
Loma Linda University

Tissue engineering and regenerative medicine (TERM) is a highly multidisciplinary field in which bioengineering and medicine merge. Integrative approaches using scaffolds, cells, growth factors or gene therapy are developed to overcome today’s limitations in augmentation procedures.

Patients with defects due to congenital disorders, trauma or tumor removal often suffer from serious functional and aesthetic deficiencies that strongly compromise their social lives. Current therapy options are highly invasive, associated with severe morbidity or are simply unavailable. However, the progress in technology has enabled advances. Promising techniques are now being studied that may shift the frontiers in regenerative dentistry and medicine. TERM techniques include:

› Injecting cells into the damaged tissue, either with or without a degradable scaffold.

› Growing a complete three-dimensional tissue to maturity in the laboratory and then implanting it into a patient.

› Implanting a scaffold directly into the injured tissue and stimulating the body’s own cells to regenerate the tissue.

› Introducing a gene encoding a therapeutic protein into cells, which can then express the target protein.

Cells + scaffold + growth factors

Three components are needed for successful tissue engineering: cells (such as stem cells), scaffold or matrix (which provides a degradable physical base for cell growth), and growth factors. Simply put, the cells grow along a physical scaffold, and specific growth factors stimulate cell activity and differentiation into the desired tissue.
One of the first tissues to be engineered and used clinically is bone. Engineered bones may one day eliminate the need for more invasive therapy.

Stem cells

Reconstruction of craniofacial and dental defects using mesenchymal stem cells avoids many of the limitations of both auto- and allografting. Clinical studies are underway using stem cells for alveolar ridge regeneration as well as long-bone defects. Dental stem cells from the pulp, periodontal ligament, and associated healthy tooth structure have shown promise in treating a number of diseases.

3D scaffolds

A scaffold is necessary to enable cell growth. It should contain growth factors such as Bone Morphogenic Protein (BMP), fibroblast growth factors, and endothelial growth factors to aid in stem cell proliferation and differentiation. Furthermore, it should provide nutrients promoting cell survival and growth. The scaffolds studied have included natural or synthetic, biodegradable or permanent materials.

3D printing of tissue

Technological advances in biomaterials, printer technology and computer-aided design allow replacement tissues and organs to be “printed”. The idea is to use patient data, such as from a CT scan, to first create a computer model of the organ. This model is used to guide the printer as it prints layer-by-layer a three-dimensional structure made up of cells and the biomaterials to hold the cells together. This printer is unique in that it can use biomaterial gels as well as rigid polymers – so that any three-dimensional shape can be created. In addition, it can print proteins, growth factors and other liquids into the structure to help promote regeneration once the device is implanted. This device is still experimental and is being explored for organs such as the kidney and structured tissue such as the ear.

Challenge: vascularisation

Many challenges remain, however. For example, if an engineered tissue is placed into the body, it has to be vascularised quickly or the tissue will die. This presents a greater challenge in larger engineered tissues. The timing and appropriate doses of growth factors are still under investigation.

Next evolution

Researchers are also developing engineered skin, which will help treat massive burns, chronic wounds and missing soft tissue in the oral cavity. Skin and cartilage substitutes are available through regenerative medical techniques, and laboratory-grown tracheas, blood vessels and other tissues have been implanted into patients. Other tissues that are at the early stages of engineering include heart valves as well as bladders. In fact, a whole bladder has been engineered and transplanted in a dog. The bladder appeared to be normal and demonstrated normal function. Nearly every body tissue is being engineered for future applications in medicine.

As we continue on this exciting journey of exploration, thus expanding the frontiers of tissue regeneration, we should keep the words of Christopher Columbus in mind:

“You can never cross the ocean unless you have the courage to lose sight of the shore”.

Christopher Columbus

References
“Thin and narrow keratinised mucosa may lead to a greater mucosal recession”

Zigdon & Machtei 2008
How much keratinised tissue is needed to maintain healthy tissues around implants? Which augmentation techniques are successful? Prof. Mariano Sanz has selected milestone studies on the relevance and management of keratinised tissue.

Whether or not presence or a certain zone of keratinised mucosa (KM) is required around dental implants to maintain peri-implant health is still a controversial issue. Yet evidence is accumulating that KM tissues around functioning implants are important in the long-term maintenance of both soft and hard tissues.

Animal models: more plaque-induced tissue loss

After 9 months of spontaneous plaque accumulation, ➔ Warrer et al. 1995 found no significant differences between implants surrounded by lining or KM with respect to changes in “attachment level”, recession or peri-implant bone level (5 monkeys, 30 implants). In contrast, ligature-enhanced plaque accumulation in implants without KM resulted in significantly more recession and slightly more attachment loss. This suggested that the absence of KM around dental implants increases the susceptibility to plaque-induced tissue destruction.

Reviews: heterogenic data

In three recently published systematic reviews the authors evaluated whether a reduced band of KM (< 2 mm) around dental implants is associated with disease and/or has a significant predictive value for bone loss2–4. However, the limited number and heterogeneity of the studies made it difficult for the authors to draw clear conclusions. In the first systematic review ➔ Wennstrom and Derks 2012 found that “inadequate” width of KM was associated with a significantly higher plaque score (12 studies)2. Although some studies reported significantly higher bleeding scores and recessions at implants with < 2 mm of KM, others found no differences. Evidence about the effect of KM on bone level changes or implant loss was non-existent, and no conclusions could be drawn. No predictive value

In the pooled analyses, ➔ Gobbatto et al. 2013 found that the Gingival Index (GI) and Plaque Index (PI) were significantly higher in the group with KM width of < 2 mm, while the Bleeding Index (BI) was also higher but only marginally significant (review with 8 studies, meta-analysis with 7 studies)1. The authors concluded that a reduced KM width around implants was associated with clinical parameters revealing inflammation and poor oral hygiene. However, there was not enough evidence to define a predictive value of keratinised mucosa width.

Wide keratinised mucosa favorable

➔ Lin et al. 2013 found statistically significant differences in PI and modified PI, modified GI, mucosal recession (MR), and attachment loss (AL), and all these parameters favoured implants with wide KM (7 cross-sectional, 4 longitudinal studies)4. However, comparisons of other parameters (BI, modified BI, GI, probing depth, and radiographic bone loss) did not reach statistically significant differences.
Clinical data: more recessions

Zigdon & Machtet 2008 found that a wider band of KM (>1 mm) was associated with less mucosal recession compared with a narrow (≤1 mm) band (63 implants). Similarly, a thick mucosa (>1 mm) was associated with less recession compared with a thin mucosa. In a similar study design, Chung et al. 2006 found statistically significantly higher gingival and plaque indexes as well as mucosal recession in areas of deficient KM (<2 mm) compared with areas with sufficient soft tissue (69 patients, 339 implants, 3 years follow-up).

Schrott et al. 2009 performed a prospective case series (58 patients, 307 mandibular implants, 5 years follow-up). When the width of KM was <2 mm, they found statistically significantly higher plaque accumulation, bleeding tendencies and larger soft-tissue recession buccally, compared to sites with ≥2 mm of KM. Crespi et al. 2010 followed partial reconstructions after immediate implant positioning without flap elevation and immediate provisional restoration in the anterior jaw region (29 patients, 132 implants, 4 years follow-up). Implant sites with <2 mm of KM showed a significantly greater amount of recession compared with implant sites with ≥2 mm of KM.

1. Can absent keratinised mucosa result in problems?
2. How can sufficient keratinised tissue best be formed?
How to augment keratinised tissue

In a systematic review, Thoma et al. 2014 evaluated the efficacy of different soft tissue augmentation procedures aimed at increasing the width of KM around dental implants (9 clinical studies)\(^9\). They found a significant increase in KM for the combination of apically positioned flap/vestibuloplasty (APF/V) plus graft material compared to APF/V alone. When the authors compared different graft materials, they found similar outcomes for free gingival graft, free connective tissue graft as well for a xenogeneic collagen matrix (CM). In a randomized controlled clinical trial Basegmez et al. 2012 compared classic vestibuloplasty versus free gingival graft on implants with a minimal KM (<1.5 mm) and signs of peri-implant mucositis (64 patients, 64 implants, 12 months follow-up)\(^10\). With free gingival graft, the width of the attached mucosa and the final gains in KM width were significantly greater.

Less morbidity and surgical time

With a collagen matrix, the gain in KM is as effective and predictable as with autogenous free connective tissue grafts. This was demonstrated in two randomised controlled clinical trials by Lorenzo et al. 2012 and Sanz et al. 2009 (24 patients, 6 months follow-up and 20 patients, 6 months follow-up)\(^11,12\).

“The keratinised tissue gain is effective and predictable using a collagen matrix.”
Lorenzo et al. 2013, Sanz et al. 2009

Although the authors found more graft contraction at 30 days with the collagen matrix (67.2% vs. 59.7%)\(^12\), they reported statistically significantly more favourable outcomes for the collagen matrix with respect to surgery time and patient morbidity\(^11,12\).

References
Regeneration was long thought to be impossible for sufferers of spinal cord injuries. This might change in years to come.
Why after cutting yourself with a bread knife is it possible to regenerate nerves in your finger but not in your spinal cord? What was still true 20 years ago takes on a new perspective thanks to the pioneering discoveries of Prof. Martin Schwab from Zurich.

Is this growth inhibition the case for all vertebrates?

**Prof. Schwab:** This is true for all higher vertebrates, i.e., frogs, reptiles, birds and mammals, not, however, fish and salamanders. Salamanders can regenerate and regain function in fibres cut off in the spinal cord or brain over long distances. They even renew whole legs. So these animals are of great interest to us. With this in mind we have scrutinised the processes after injuries in the mammalian spinal cord very closely, and we have indeed been able to observe very limited growth, but after about half a millimetre of nerve budding it was over. Why is this the case? At some point we realised: in central nerve tissue, mainly in myelin, there must be substances which inhibit growth.

So you set out in search of these substances...

**Prof. Schwab:** In cell culture we observed that extracted spinal cord strongly inhibited fibre growth. In contrast, extract from peripheral nerves was not inhibited at all. So there had to be an inhibitor in the CNS. And after a long search, we found it. This potent protein ensures that further growth is prevented in the spinal cord and “nothing else works”. We called it “Nogo A”. Then we developed an antibody to block a receptor of the protein using a lock & key mechanism. And guess what? When we applied the antibodies to a rat after a spinal cord injury, the nerve fibres did not cease to grow after half a millimetre, but were...
suddenly able to sprout for centimetres. That – a good 20 years ago - was the first proof that regeneration is possible in the spinal cord.

**Do these new nerves tend to grow more on the periphery or more in the center of the cord?**

**Prof. Schwab:** We very rarely find injuries to the spinal cord where the nerve pathways are completely severed. Ballistic wounds sometimes result in such a thing, but with "conventional" spinal cord injuries due to traffic or sports accidents we still tend to find thin bridges of tissue. It is these very bridges which use the regenerating fibres. But the time window for regeneration is limited owing to nerves retracting and scarring – in rats one week to ten days, in man probably about a month after an accident.

**How far along are we from application in man?**

**Prof. Schwab:** For the past few years we have been conducting clinical studies in cooperation with Novartis and a European network looking at people who have just been paraplegically injured. Phase I with 52 patients is complete, and a Phase II study is in the pipeline.

**When will we see a drug?**

**Prof. Schwab:** So far we have been in a highly experimental phase, and there is no therapy available yet. If we succeed clinically, it will still take a few more years for such a drug to be commercially available. We mustn't forget: such an injury to the spinal cord is a catastrophic event. It is like hitting a computer with an enormous sledge hammer. You cannot simply patch it up. Many small steps are needed, but – just as for the patients themselves - even small steps are a success.
BACKGROUND.
The right concept for each case

Susanne Schick

Linking art to surgery

Leading experts present clinical cases with major bone augmentations in “Innovative therapy concepts for oral and maxillofacial surgery” (picture top left). Innovative techniques for horizontal and vertical alveolar ridge augmentations are shown, in addition to orthognathic treatment with Geistlich Biomaterials. The brochure not only links art to surgery, but also provides printed and digital content on the topic.

Solutions for peri-implantitis

The number of studies on peri-implantitis has risen in the last few years. The brochure “Therapy Concepts for Treating Peri-implantitis” is a collection of clinical cases and studies showing non-surgical and surgical approaches with Geistlich Biomaterials.

Ridge Preservation

The new brochure “Therapy Solutions Following Tooth Extraction” explains the restoration of extraction sockets with subsequent bridge restoration or implant placement on the basis of the clinical examples of Dr. Manuel Neves (Portugal) and Dr. Fernán López (Colombia) (picture top right). The newly revised brochure “Therapy Concepts for Extraction Sockets” provides the right concept for each case on the basis of the latest scientific and clinical data. Practical QR codes in the brochures link you to the original literature or follow-up film material.

Digital training

Three films offer new visual aids for Ridge Preservation: (1) An animated 3D film (QR code above) features Ridge Preservation with Geistlich Biomaterials after an atraumatic dental extraction. Ridge Preservation with an intact or defective buccal bone wall is shown in the surgery film by (2) Dr. Raffaele Cavalcanti (Italy) or the film by (3) Dr. Holger Janssen (Germany). Dr. Rui Figueiredo (Spain) demonstrates the simple use of Geistlich Bio-Oss Pen® for sinus floor elevation.

Interested? You can request these tools through your local partner at: www.geistlich-pharma.com/mycontact.
Power – 70 percent self-sufficiency

Verena Vermeulen

Using its own hydroelectric power system Geistlich Pharma is able to fill 70 percent of its energy needs. The future could raise this figure even higher.
Every form of energy has pros and cons. But with a mind to political crises, which repeatedly jeopardize gas or oil supplies, and the threat of safety and end storage problems with nuclear power, there is some sense in the ecological production of one's own power. Geistlich has been pursuing its own power production since the beginning of the 20th century. In 1906 Eduard Geistlich started building a small hydroelectric power system to supply electricity to his adhesive and fertilizer factory. The energy was sourced from an underwater channel he built, which was 4,600 ft long and had a 50 ft drop.

**Electricity as a top export**

Going by today’s average energy consumption, the power levels back then appear tiny. In the supply crisis during the First World War and until 1927 Geistlich Pharma supplied electricity to third parties too. The company supplied 62 electricity subscribers with a total of 588 lamps, one heater, one cooker, 19 irons and 11 electric motors. Nowadays, through its own production Geistlich Pharma meets 70 percent of its energy needs for manufacturing all the Geistlich products it sells around the world. For this, just over 1,000 gallons of water a second cascade through each of two turbines. Along with researchers at the University of Zurich the company is working to further optimise its independent energy supply.

The annual power consumption of the Geistlich site = 3000 MWh per annum. This equates to 750 2-person households a year (= a small village in Switzerland)
Prof. Dr. Jan Lindhe, Periodontist and Professor Emeritus at the University of Gothenburg (Sweden), is one of the pioneers of scientific research in the field of oral tissue regeneration. We spoke to him about the Foundation’s work and its role in research.

**The Osteology Foundation**

The interview was conducted by Dr. Kay Horsch and Dr. Heike Fania

**Prof. Lindhe, you were one of the founding members of the Osteology Foundation, and you have contributed significantly to its development. Could you explain to us what the particular strengths of the Foundation are?**

The greatest strength of the Osteology Foundation is its autonomy. When Dr. Peter Geistlich created the foundation, he provided the start-up funding and also ensured further support. The Foundation Council, nonetheless, never had the feeling that it was acting under instructions. This is the strength of the Osteology Foundation: it is an independent organization presided over by a Foundation Council that thinks independently and expresses its opinion independently.

**The Osteology Foundation focuses on tissue regeneration. We normally think of bone regeneration, but some years ago you said: “The bone sets the tone, but the tissue is the issue” – Should we therefore concentrate more on soft tissue?**

If you talk about periodontitis and peri-implantitis, the difficulty is always the soft tissue. That’s where the inflammation is, and the bone tissue vanishes as a result. I am afraid that we are too unaware of this fact. For instance, we see articles entitled “Using biomaterials to treat peri-implantitis”. This is wrong because the problem is not hard tissue. The problem is that the soft tissue around the implant has to close to eliminate the source of infection. Only when the infection has been eliminated and the soft tissue problem solved, can a bone augmentation be practical.

**It appears that there is a trend away from evidence-based dentistry toward “experts’ opinions”. Can you see this trend – too?**

“Evidence-based” is an extremely demanding requirement. We generally say that randomised controlled clinical studies are the best way to assess the validity of a procedure or a material. If the evidence is based on corresponding research results, it is of course important and high-calibre. Experts... well they have often made up their minds in advance. If these opinions are also based on randomised clinical studies, it is of course all right. But if they only rely on “personal experience” then it is doubtful.

**The Osteology Foundation sets out to impart scientific findings to dentists in order to benefit patients. What topics are important?**

Everything the Foundation is doing and will continue to do is to a patient’s benefit. And for it to reach a patient, we have to go via the dentist. Creating knowledge and presenting it at conferences, in publications and so forth is the best thing we can do. I think the Osteology Foundation is already very well placed here.
Osteology fosters research

Osteology Research & Education Grants

In 2015 researchers in the field of oral regeneration can once again apply for funding for their projects. The Osteology Foundation offers two established programmes: the Osteology Advanced Researcher Grants and the Osteology Young Researcher Grants, which systematically target young researchers to help them implement their own, early career projects. The next application cut-off date for these programmes is 15 June 2015. In 2015 researchers can apply for Osteology Large Clinical Grants for the first time. This new program is aimed at experienced and established groups of researchers. Another new program in 2015 is the Osteology Research Scholarships for young clinicians or researchers, who want to train further in the area of clinical or basic research. Novice researchers, who want to participate in the Osteology Research Academy courses in Lucerne or Kiel, can also apply for Osteology Education Grants.

All the details on Osteology Grants are on the internet at www.osteology.org

The second volume of the Osteology Research Guidelines is out

Following the successful first volume on preclinical research, the anticipated second book on clinical research is now available. The “Clinical Research Guidelines” published by William V. Giannobile, Niklaus P. Lang and Maurizio S. Tonetti deals with every aspect of clinical research.

For further information and ordering go to the Osteology Foundation’s website: www.osteology.org

Dates

Core Module
Lucerne, Switzerland
14–18 September 2015

Expert Module
Kiel, Germany
2–4 November 2015

NATIONAL OSTEOLOGY SYMPOSIUMS

Osteology Symposium
Baden-Baden, Germany
18–19 September 2015

Osteology Symposium
Florence, Italy
1–3 October 2015

International Osteology Symposium

MONACO 2016

It’s time! The next international Osteology Symposium in Monaco will be held from 21–23 April 2016. You can look forward to an exciting scientific program, internationally prominent speakers, fascinating workshops and many other highlights.

Further information and registration is available at the Symposium’s website: www.osteology-monaco.org
Here’s to a “picture” with Rainer Schmelzeisen

Reto Falk conducted the interview

You work as a surgeon and an artist and are presently showing your work here in Freiburg. What is hard to get right, a good picture or a good treatment result?

Prof. Schmelzeisen: Basically neither should be easy, but a good treatment result is more difficult to achieve in some respects because the stakes are higher and a patient’s expectations are critical.

How about the art scene’s expectations for a good picture?

Prof. Schmelzeisen: A good picture must transcend expectations and surprise the beholder again and again.

What do you perceive to be difficult in your profession?

Prof. Schmelzeisen: When complications occur which might jeopardise treatment. Major, nasty failures are fortunately a rarity. But that makes them all the more tragic and they often hit me hard, even now.

Is there a recipe for how best to deal with problems?

Prof. Schmelzeisen: Over the years I have tended to become more sensitive and try to see things from the patient’s perspective.

Does this make you a better surgeon?

Prof. Schmelzeisen: We always confront the challenges.

Your greatest professional success?

Prof. Schmelzeisen: Patients our team has hopefully helped live longer.
FOCUS
Ridge Preservation
With the appropriate technique for maximum benefit

JOURNAL CLUB
Periodontology
Can periodontal ligament be regenerated?

OUTSIDE THE BOX
Skin cells with blood and lymphatic vessels
Success for the first time in manufacturing a skin substitute similar to full-thickness skin.

IMPRINT
Periodical for customers and friends of Geistlich Biomaterials
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