GEISTLICH BIOMATERIALS

NEWS

VOLUME 14, ISSUE 1, 2019

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LEADING REGENERATION.

Editorial

Of planning, chance and the curiosity needed

Photo: Roger Schuler

Only those who recognize an opportunity will really discover something new.

Read about fortunate discoveries in our article about “serendipity.” We describe scientific breakthroughs that are not the result of meticulous planning. Instead, capable scientists have stopped to examine the unexpected. We owe penicillin, X-ray technology and much more to their cuiosity.

Serendipity is also at work for Geistlich. By chance Peter Geistlich browsed trough an oral surgery journal at the beginning of the 1980s and wondered whether he could contribute his bone and collagen processing expertise to the new science of bone regeneration, laying the foundation for Geistlich Bio-Oss®.

On one hand, fortunate discover, and on the other hand, foresight and tenacity – that’s what counts.

Geistlich has existed since 1851, and we owe this long history to both planned and unplanned events. But what has remained, is our passion for regenerating tissue, along with our corporate values. One of these values is “pioneering,” because only those who can explore and change remain true to themselves.

With this in mind, I look forward to striking out on a new path with you...

Dr. Mirjam Kessler
Director Corporate Communications

Issue 1 | 2019

NEWS

10 Research and Practice

Research questions are endless, and the answers can be hard to find. A series of tips and tricks and lessons learnt from the experts can help learned.

FOCUS

34 Inside the Matrix

How do cells react on a biomaterial implanted into bone or soft tissue? Prof. Shahram Ghanaati and his team are investigating the process.

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Regeneration pays off in the long-term

Treating intra-bony defect with a regenerative procedure instead of flap surgery is an initial investment that pays off.

Periodontally affected sites treated with a regenerative approach are clinically more stable, show less recurrences and less tooth loss than sites treated with access flap surgery alone. The initially higher costs of periodontal regeneration are partly offset over time. Better tooth retention and lower periodontitis progression over time means: lower investment to manage periodontitis progression and tooth loss. This is the result of 20-year data published by **Cortellini et al.** and awarded the R. Earl Robinson Periodontal Regeneration Award 2018 by the American Academy of Periodontology.

20-year data

Cortellini et al. have compared the outcomes obtained with regenerative approaches and flap surgery over a follow-up period of 20 years. They performed a recurrence analysis to check costs of re-intervention. So far, no prospective controlled studies with observation periods above ten years have compared the long term outcomes of the two treatment alternatives. (Ed.)

Cortellini P, et al.: J Clin Periodontol 2017; 44(1): 58-66.

Fewer scars after Ridge Preservation

Geistlich Mucograft® Seal adopts better to the surrounding mucosal tissue than an autologous punch graft. So, the matrix causes fewer scars.

"As soft tissue grafting with a porcine collagen matrix seems to be associated with improved aesthetics, lower costs, shorter treatment times, and decreased patient morbidity, it may be a valuable alternative to soft tissue grafting with free gingival punch grafts." This is the authors' conclusion in a recently published case control study.

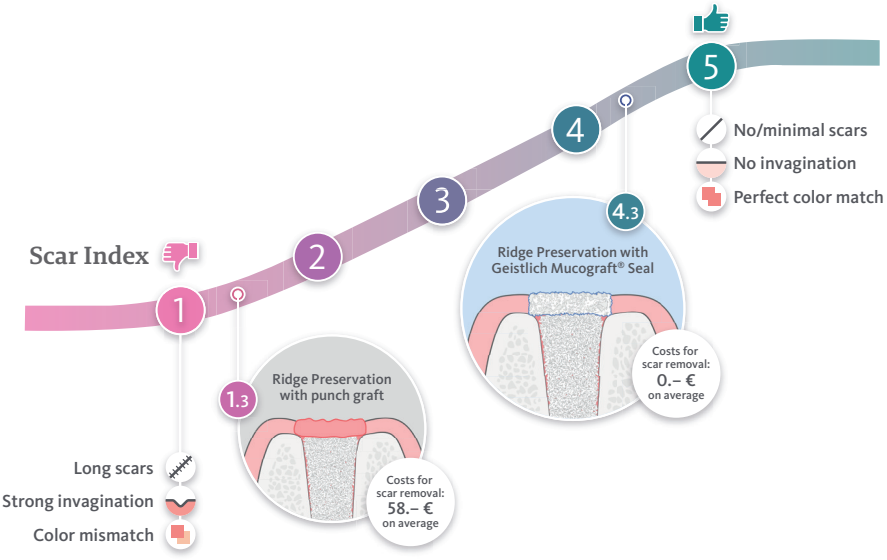
Fickl et al. investigated whether a free gingival punch graft or Geistlich Mucograft® Seal causes fewer scars when used to close an extraction socket filled with Geistlich Bio-Oss® Collagen.

The authors modified a scar score from dermatology for their evaluation. This is based on the scar size, invagination and color.

Fewer scar means better aesthetics

In all categories patients treated with the collagen matrix were in the lead. Fewer scars means for the patient: fewer measures for scar removal and a better aesthetic result. Volume preservation and implant success were similar in both treatment groups. (Ed.)

Fickl S, et al.: Int Journal Periodontics Restorative Dent 2018; 38(1): e1-e7.



With or without Geistlich Bio-Gide®? With.

Geistlich Bio-Gide® in combination with Geistlich Bio-Oss® and enamel matrix derivative can positively influence the reconstruction of the lost periodontal tissue.

Various treatment methods have been developed to reconstruct lost periodontal tissue due to periodontitis with intra-bony defects.

Some case reports have shown good results for the combination Geistlich Bio-Oss®, enamel matrix derivative, and Geistlich Bio-Gide®. However, it is unclear whether these results are attributable to the addition of the membrane. **Nemoto et al.** have now compared the effect of regenerative therapy using enamel matrix derivative and Geistlich Bio-Oss® with or without Geistlich Bio-Gide®.

Patients with thick biotype benefit

Patients treated with Geistlich Bio-Gide® demonstrated significantly improved probing pocket depth and Miller tooth mobility compared to patients only treated with Geistlich Bio-Oss® and enamel matrix derivative. The gain in clinical attachment level was better with Geistlich Bio-Gide®, although the difference did not reach statistical significance.

Interestingly, the results of the stratified comparison showed that Geistlich Bio-Gide® had a bigger positive impact on probing pocket depth and clinical attachment gain in patients with thick biotype. The authors conclude: "Combinational regenerative therapy including Geistlich Bio-Gide® appears to be a predictable method, particularly in patient with thick gingiva." (Ed.)

Nemoto Y, et al.: Int J Periodontics Restorative Dent 2018; 38(3): 373-81.

Soft tissue management favors peri-implant health

Soft tissue augmentation has been recommended primarily to improve aesthetics. A recent systematic review and meta-analysis now investigated its impact on peri-implant health.

Soft tissue augmentation with autologous grafts reduces marginal bone loss over time. Also surgical procedures to gain keratinized tissue have a positive impact. They improve bleeding indices and lead to higher marginal bone levels. This is the result of a systematic review published by **Thoma et al.** in the context of the **Osteology Consensus Conference 2017** on "Evidence based knowledge in the aesthetics and maintenance of peri-implant tissues".

An answer to the lack of scientific evidence

The authors answered the question: What is the effect of soft tissue grafting procedures to increase the width of keratinized tissue or the mucosal thickness at dental implant sites in terms of peri-implant health?

Soft tissue grafting procedures are performed for a number of indications in conjunction with dental implant therapy. However, there has been a lack of scientific recommendations whether or not to perform surgical procedures to establish peri-implant health and to limit the incidence of peri-implant disease. (Ed.)

Thoma DS, et al.: Clin Oral Implants Res 2018; 29 Suppl 15: 32-49.

Indication sheet 2.0 with additional features

Geistlich Biomaterials has been publishing clinical treatment concepts for more than 10 years – explained and commented on by the surgeons themselves. Geistlich Indication Sheets are standard literature in dental practices worldwide.

New are these indication sheets not only in paper form, but with additional features also digitally available and have the name "BioBrief". The new added values are a short webinar including additional information by the same author on the same case and access to an online library with other case studies and literature.

Do you like the indication sheets? Then you will love the BioBrief. Please visit: www.bio-brief.com and check the first BioBrief. (Ed.)

Major investment at Wolhusen site

Geistlich extends its Research & Development and its Production facilities in Wolhusen/Switzerland.

The foundation stone for the “888plus” extension building at the Geistlich Pharma AG Headquarters in Wolhusen was laid on 1 February 2018. With this investment in the tens of millions, Geistlich demonstrates its commitment to its Switzerland location.

In addition, the company strengthens its areas of Strategy, Research & Development, and Production "under one roof". The main reasons for the decision to invest here include the access to qualified professionals, the close proximity to leading Swiss universities for dentistry, and the cooperation with Lucerne University of Applied Sciences and Arts.

The new building, designed over three floors and covering a surface area of 2194 m², boasts a flexible building concept with separate production areas.

Learning from the best

In 2019, Geistlich Biomaterials is offering seven new webinars – accessible worldwide, free of charge and with a live Q&A session.

All webinars are held by experienced and recognized experts and focus on evidence-based techniques, scientific backgrounds and practical tips.

These are the topics and speakers:

Assistant Prof. Richard Bauer | USA
Hard and soft tissue augmentation
April

Dr. Daniele Cardaropoli | Italy
Soft tissue management
May

Prof. Bilal Al-Nawas | Germany
Complex bone augmentation
June

Ass. Prof. Dieter Bosshardt | Switzerland
Bone biology
September

Prof. Istvan Urban | Hungary
Horizontal bone augmentation
October

Prof. Li Dehua | China
Alveolar bone augmentation
November

Prof. Massimo Simion | Italy
GBR Surgery
December

For further details and to sign up visit our website: www.geistlich-pharma.com

Geistlich's blog – A wealth of expert knowledge

Interested in interviews with experts in the field of dental regeneration? Techniques, tips, comments? Or stories about regeneration in nature and medicine?

Geistlich's blog **www.regeneration-expert.com** is a treasure trove of knowledge and a reference book for anyone interested in oralregeneration. (Ed.)

Visit now: www.regeneration-expert.com

Research and Practice.

Some insights on research in the dental practice, research organizations and funding opportunities plus tips and tricks for dental photography.

Photo: Roger Schuler

The iMc Institute: An example for practice-based research

Dr. Michael K. McGuire | USA
The McGuire Institute™ & Perio Health Professionals™,
Houston

The truth is that as clinicians we are all practice-based researchers. When we diagnose our patients, choose treatments and follow results, we are really performing research, whether we know it or not.

"The validity of our conclusions needs to be tested, continually, because as medical techniques and technologies evolve, there are more alternatives we should also be studying."

Our research questions are endless. We have many diagnostic tools, like patient medical and dental histories, probing measures, periapical radiographs and CBCT scans; but we should continually be asking ourselves which diagnostics are appropriate and how they should best be used to form treatment options.

Should we use antibiotics, and if so, what type and dosage? Which incision and flap techniques are best? What biomaterials are most successful, and what post-operative care is most beneficial?

In reality our diagnoses, prognoses and treatment plans are our "study hypotheses and methods," and our patient outcomes are our "study results." No matter what we learned in dental school or through continuing education, the longer we practice the more we get to observe our clinical results, perhaps comparing with other clinicians or the literature, so that we arrive at what we believe are our best practice "study conclusions." But the validity of our conclusions needs to be tested, continually, because as medical techniques and technologies evolve, there are more alternatives we should also be "studying." Therein lies our role in continuing, practice-based research. The only question is whether we want to formally plan, record and publish our "research results."

The first steps

My own path toward practice-based research started in the 1970s. Early in my career I desperately wanted to contribute to the literature, and as a young practitioner I did not know how to get grants and was certainly not going to find a company willing to support my research. So I looked for a project that I could do in my own practice. There was some classic literature (Hirschfield, Wasserman, McFall and others) retrospectively evaluating patient populations, and I remember reading a paper about patient maintenance and thinking, "Gee, I could have done that!"

So one day after giving a lecture to the residents in San Antonio, I began thinking about prognosis and what we really knew about it. I retrospectively analyzed 100 of my patients, examining whether the prognoses (and associated treatments) I had assigned were predictive of outcomes 5- and 10-years later. I was the sole author, and it was the first time I had ever attempted to publish anything, so I did not really understand the publication process (manuscript organization, submission and review). I submitted my work to the *Journal of Periodontology*, and it was rejected, without reviewer comments.

While I was very disappointed, I thought I had no recourse, until Dr. Raul Caffesse, who knew that I had been writing the paper, asked me about it. After I told Dr. Caffesse my experience, he contacted the journal editor and asked him to "give the kid a chance." I eventually received the reviewers' comments and was able to make corrections that satisfied the journal. Ultimately the paper was published, and it is interesting that this paper is one of the publications I am now known for around the world.[1] It's now considered classic literature.

The achievement

Now I find myself leading a network of 16 practice-based investigators - Periodontists and Oral Maxillofacial Surgeons, and more recently general dentist sub-investigators helping us with restorative research. We have practices across the United States, and we are like-minded. We all want to use research to understand how best to treat our patients, and we appreciate the value of practice-based research, where real patients are treated in real practices. (We also appreciate and collaborate with universities, where particular types of research – for example, inflammatory biomarker diagnostics, gene therapy development and government grant projects – are best developed and studied.)

Our investigators have published more than 350 peer-reviewed papers, and every year they provide an average of 70 regional, 45 national and 15 international lectures. They are active at all levels of organized dentistry and are editors or on the editorial boards of respected, peer-reviewed journals. We all believe in the power of practice-based research and think it provides more rapid translation of new therapies into clinical practice.[2]

What it will take

Decide whether you really want to be a practice-based researcher. Consider that you might make less money and actually work harder and longer than you would if you simply treated patients in your practice. You will be creating study protocols, looking for grants or industry sponsors, filling out clinical reporting forms (CRFs), analyzing results, writing study manuscripts and shepherding them through journal review processes. If you have a practice partner, it helps if they support your work, and it's even better if they collaborate with you. I am very grateful my partner Dr. E. Todd Scheyer not only supports practice-based research but also has been a collaborating investigator and author, while supporting the founding of The McGuire Institute (iMc).

I think the biggest challenge is incorporating high quality clinical research into a busy private practice. In order to do that, it takes the development of systems and staff so that you can function smoothly and not disrupt your practice. You will need dedicated office staff to recruit patients, coordinate study progress and help record and report results. I would be nowhere without the excellent hygienists, surgical assistants and our Study Coordinator who, as a team, make sure our research works!

I created iMc primarily as a legacy project. After I give lectures, especially at big periodontology meetings, someone often comes up to me and says, "Hey, that's cool. I would like to do that. Tell me how you do it." Through iMc we are able to help clinicians learn how to run high-level studies in an efficient way that benefits them, the profession and their patients.

"We all believe in the power of practice-based research and think it provides more rapid translation of new therapies into clinical practice."

Help, tools and references

Find r**esearch mentors**. You have read (above) how Dr. Caffesse and others helped me. But the opportunity that really got me started was a study organized by Drs. Ken Kornman and Mike Newman for a local delivery, tetracycline-impregnated cord for periodontitis. To my knowledge this was one of the first, large, practice-based clinical research studies done in dentistry.[3] Ken, Mike and their team helped train one of our hygienists and me in the basics of practice-based research, and it was "love at first study."

Find **expert study collaborators and partners**. Dr. Newman taught me about evidence-based dentistry (and was the founding editor of the *Journal of Evidence-Based Dental Practice*). Biostatistician Dr. Jack Gunsolley calibrates our examiners (so we can measure our study results consistently and accurately across the country), creates the statistical designs that power our studies

The McGuire Institute – Facts & Figures

Practice-Based Clinical Research Network

THE INSTITUTE

16 clinicians
13 practices
256 combined years of experience
350 articles to-date
70 regional lectures/year
45 national lectures/year
15 international lectures/year

Fields of research:

Tissue Engineering, Surgical Orthodontic treatment, CBCT / CT Imaging, Dental Implants, Periodontal and Bone Regeneration, Dental Practice and Insurance Models, Soft Tissue Plastic Surgery, Tooth Regeneration and Transplantation, Live Cell/ Biologics treatments, Pathology, Prosthodontics and Pathogenesis

Clinical Research Pathway

A clinical research project involves many steps.

TREATMENTS

20,000 patients in maintenance treatment
200 hygiene appointments/day
14,000 patients in active treatment

Every month, on average:

460 implants in **430** patients with **300** bone regeneration procedures, **85** soft tissue augmentation procedures, and **60** peri-implant procedures

365 periodontal surgeries, with **215** bone grafts and **160** periodontal regeneration procedures

310 non-surgical treatments

270 soft tissue augmentations

220 root coverage procedures, **120** tissue thickening and **100** keratinized tissue augmentation procedures

Illustration: Quaint

"If you enjoy dentistry and you enjoy research, and what both can do for your patients, you too might want to consider a practice-based research."

and statistically analyzes our results. Researcher Dr. Thiago Morelli, University of North Carolina, recently introduced us to a new, super-accurate, 3-D digital intraoral scanning technique for measuring oral soft tissue changes within 0.05 mm accuracy. Dr. Alan Herford (Loma Linda University) has helped us with histological analyses. Dr. Will Giannobile, the University of Michigan, the University of Pittsburg and the Harvard/Wyss Institute have partnered with iMc under an NIDCR tissue engineering and regenerative medicine research grant. In this very competitive process, new technologies are selected to receive funding, and iMc has been chosen to help select and shepherd these new therapies through pre-clinical studies and into human clinical trials. In addition, our patient reported outcomes "PROs pro," sociologist Chad Gwaltney, PhD (Brown University), helps interview patients who undergo, for example, laser procedures, and then creates the PROs questions and questionnaires that tell us about pain, anxiety and what therapies patients really prefer.

iMc has also partnered with the clinical research organization Medelis, Inc., which helps us organize, initiate and monitor our multi-center studies. Regularly we gather with Medelis for good clinical practice (GCP) training. GCP guidance for the US can be found within the Food and Drug Administration's Code of Federal Regulations (21 CFR), and there is a similar guidance for European studies. This year many of our study coordinators and examiners traveled to Houston and Phoenix for calibration and GCP training in preparation for our ongoing laser and Geistlich Fibro-Gide® studies.

Besides 21 CFR, there are other helpful guides and references, like the *Osteology Guidelines for Oral and Maxillofacial Regeneration – Clinical Research*.[4] This useful book includes advice and tools for designing and conducting clinical studies. There are also "how-to" guides for writing manuscripts, like Dodson's *A guide for preparing a patient-oriented research manuscript*,[5] or conducting PROs.[6,7] All the help you need is out there. It just takes a bit of effort (and some late night reading) to get it.

Rewards

The rewards? I'm very grateful for where my career and my research have taken me. Practice-based research has certainly made my practice more interesting, and it has allowed me access to technologies and devices that I would not have experienced otherwise. Dr. Scheyer and I have been able to offer some of the newest treatment options for our patients. Research has also set our practice apart from others and often times provided our patients with free therapy or therapy at a reduced cost. Clearly we have enjoyed the notoriety research brings, and I have enjoyed the travel and the camaraderie my speaking engagements have provided. In the end, it's all about job satisfaction. If you enjoy dentistry and you enjoy research, and what both can do for your patients, you too might want to consider practice-based research.

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98 shades of grey

Dr. Pasquale Loiacono | Italy
Private Practice, Tropea
Interview conducted by Dr. Giulia Cerino

Photo: ©iStock.com/martin-dm

Photography has become a valuable resource in daily dental practice, revolutionizing the way clinicians diagnose, treat and communicate with patients and colleagues. We gave the floor to the expert, Dr. Pasquale Loiacono, who shared tips and tricks for achieving a quality dental image.

You teach dental photography. What is the question most frequently asked by your audience?

Dr. Loiacono: Surely the biggest question is how to set up the camera correctly. Listening to my audience, I realized setup is really a weak point that generates anxiety; it is as people fear the instrument itself.

What is the most basic equipment a dentist needs to create good clinical photos for publications and presentations?

Dr. Loiacono: For basic dental photography, you need a camera with a dedicated macro lens and flash (see details in **Box 1**: Camera, flash, and lens).

In their free time, most people use their mobile devices for taking photos. Is this also an option for dental photography? Or are mobile phones a total "no go?"

Dr. Loiacono: Let's say they're not 100% "no go" but definitely a less desirable option. The main limitation of mobile phones is their lack of photo uniformity plus the in-



Basic equipment: Camera, flash, and lens.

Camera. Mid-range digital single lens reflex **(DSLR)** camera (800 – 1200 Euros) with a **24 x 18 mm sensor**.
Larger sensors, such as 24 x 36 mm, are a disadvantage for the dentist because they offer less depth of field and magnification.

Flash. Ring flashes for intraoral photographs. They are mounted on the front of the lens with dedicated mount rings, allowing the source of light to be positioned close to the subject and the lens.

Dual flash on a bracket for anterior areas or prosthetic procedures. By controlling the distance and flash head position, you can easily capture more details, but above all improve the perception of dimensions for the dental elements.

Lens. Macro lenses are definitely the best option, as long as you keep in mind two main features at the time of purchase: focal length and magnification ratio.

> **Focal length**. 100 mm, but please be aware that not all 100 mm lenses are macro lenses.

> **Magnification ratio 1:1.** This means that at the shortest focal distance (i.e., the closest distance from the lens to the object that still produces a sharp image) it is possible to produce an image of an object the same size as the object itself, which translates into considerable magnification.

Initial settings

- **Mode:** Manual. In this way we increase or decrease the aperture of the diaphragm to increase or decrease the depth of field to always have the right sharpness.
- **Focus:** Never use autofocus setting, since the depth of field extension is decided by the plane of focus. I suggest using autofocus only for extraoral pictures of the face.
- **Color space:** Adobe RGB
- **Image quality:** RAW + jpg
- **White balance:** I always suggest pre-measuring a value to set the white balance, using the appropriate procedure and the white card balance, not to be confused with gray balance at 18%, which is quite different. This procedure is used to recognize the light temperature of the the flash, allowing the camera to properly manage the colors. Using the manufacturer's default settings may lead to an approximate result.
- **ISO:** 100 or 200 (depending on the camera) are considered the standard.

ability to provide RAW format storage (the only format with legitimate value) and the macro option, thus causing a distortion of the images. The only advantage they could offer is greater focal depth.

Which camera brands are used most often?

Dr. Loiacono: I have a preference for Nikon, which for me, as a company, is more concerned with scientific photography. But I have also shown that, with the same settings, Canon offers the same results. Regardless of the brand, you have to ask yourself: "Is this picture acceptable?" The camera becomes an instrument for measuring reality, and all brands produce "measuring instruments." The device is neutral; the difference is made through the eye and mind of the person behind the lens.

A doctor has bought a new camera for taking good clinical pictures, which initial settings would you recommend?

Dr. Loiacono: The three pillars for a correct scientific photo are correct magnification, depth of field, and perspective. These three pillars must be found in the settings (see details in **Box 2**: Initial settings).

Any recommendations for accessories such as retractors, mirrors or contrasters?

Dr. Loiacono: Dental photography accessories help produce better pictures. Because they come in contact with the patient's oral cavity, they should be autoclavable (see details in **Box 3**: Retractors, mirrors, and contrasters).

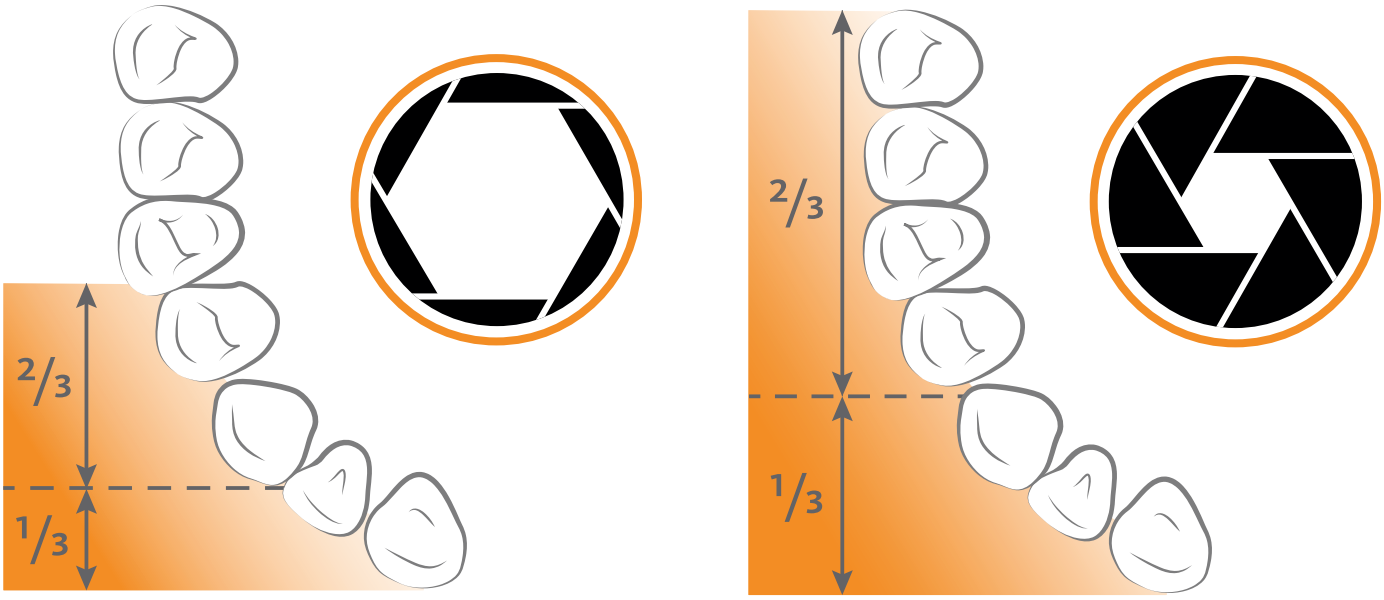


FIG. 1: Example of how the depth of field (highlighted in the orange area) changes depending on the aperture of the diaphragm.

Suppose a dentist wants to document a GBR treatment for a publication. What shots should they take?

Dr. Loiacono: First of all, it is necessary to obtain a basic documentation of the pre-operative state that includes at least the extraoral photos of the face and lips at rest, both frontally and laterally, and the smile in its three positions (light, medium and forced). The area of surgical interest must then be photographed in a perspective that is at least frontal, but if possible, also occlusal, using a mirror, to show the breadth of the bone and gum volumes. If the area to be treated is lateral, lateral mirrors must obviously be used. It is recommended to take intra-surgical photos with the same perspectives and magnifications in order to facilitate comparisons between different therapeutic steps. Regarding the settings, it should be remembered that the more you enlarge, the more you close the diaphragm and extend the depth of field. **(Fig. 1)** The big problem with surgical photography is bleeding, so it is necessary to carefully prepare the equipment and decide the framing, and only when all the photographic parameters have been established, invite the assistant to aspirate and remove as much blood as possible, while taking the photo as quickly as possible.

Storing pictures can be a challenge. Do you recommend a particular strategy?

Dr. Loiacono: The strategy is definitely never to trust your own PC (laughs)! I suggest having at least one backup disk activated for daily backup. To this should be added a second backup disk, but kept in a place away from the first one (in case of unfortunate events). Alternatively, other possibilities are obviously network-attached storage (NAS), a file-level computer data storage server connected to a computer network providing data access to a heterogeneous group of clients, or Cloud storage. The physical connections of the hard disks are an additional concern. They often change with new digital development processes, so you always have to update your hard disks.

Do you recommend modifying pictures?

Dr. Loiacono: We should, of course, modify as little as possible. The photo must already be beautiful and usable to start. Moreover, the idea of acquir-

Dental photography accessories: Retractors, mirrors, and contrasters.

> **Retractors** are often used to lift the lips away and provide better access to the oral cavity. They can be made of plastic or metal and come in different shapes and sizes. Self-retracting retractors are used primarily for frontal views and also occlusal shots. Single-sided retractors are primarily used for lateral views.

> **Mirrors** are used to capture the reflected image of the teeth, avoiding interference from the cheeks and lips. They can be made from different materials and using different techniques, and they come in different shapes and sizes according to the different situations. However, in daily practice I would recommend having at least an occlusal and a lateral mirror.

> **Contrasters** are rubber or metal pallets or even disposable, opaque cards, which create a black background behind the teeth to enhance the translucency and perception of the teeth themselves, increasing the contrast with white dental elements. This allows you to delete information that is not necessary for understanding the image. As for retractors and mirrors, they are available in different shapes and sizes for anterior, occlusal and lateral views.

Photo: ©iStock.com/Talaj

ing a wrong or ugly photo and thinking there are many corrections possible using software is a misconception. Allowed are magnification and exposure corrections, and it is always better to slightly overexpose. On the other hand, you should not correct perspective and/or depth of field.

Any preference for any particular software?

Dr. Loiacono: One of the best software packages available on the market for these purposes is Adobe® Photoshop Lightroom. The Develop Mode has all the necessary tools for making the improvements we just discussed. One of the most important features of Lightroom software is the way it treats files. It is not destructive, the original files remain untouched, so you can always return to the original file in the file history. In addition, the software allows working with different file types, including RAW, jpg, TIFF, psd, and png. However, I always recommend working with the RAW file.

What would be a summary of how images should look for lectures or publications and print?

	Lectures	Print
Format	jpg	TIFF (but it depends on the publisher/ print house)
Quality	Max	Max
Resolution	72 pixels per inch	240 pixels per inch
Color space	sRGB	Adobe RGB
Compression	Corresponding to the highest quality	None
Possible modifications	Magnification / Exposition	Magnification / Exposition

“Doing research is not just about performing experiments”

Prof. William Giannobile | USA
School of Dentistry, University of Michigan, Ann Arbor
Interview conducted by Verena Vermeulen and Todd Scantlebury

He is one of the most experienced researchers in the field of regenerative dentistry and editor-in-chief of the Journal of Dental Research. Prof. William Giannobile talked with us about impactful research, the tenacity needed and the Osteology Foundation’s role in educating and funding researchers.

Prof. Giannobile, can you recall the publication which made the biggest impression on you?

Prof. Giannobile: When I was a graduate student at the Harvard School of Dental Medicine and the Dana-Farber Cancer Institute, I read a paper about gene therapy.[1] It showed that by using gene therapy to regenerate lost tissue one could harness the body’s own ability to produce growth factors instead of applying exogenous proteins. At that time the paper really inspired my own research.

For several reasons many research projects do not end up in a scholarly publication...

Prof. Giannobile: True. If we look at the abstracts presented at scientific meetings and try to track that work, we see that on the average only ten to twenty percent of the findings are eventually published in a peer-reviewed journal. There is a large amount of work that is initiated but not completed and promoted thru scholarly publication.

That’s a sobering statistic! What are the reasons?

Prof. Giannobile: One example: overly optimistic expectations. Researchers want to investigate a hypothesis, and if the data don’t fit the hypothesis, they doubt the data, which leads to retesting, follow up with a larger sample size, demonstration that the data are reproducible, etc. During this process people can lose their enthusiasm or realize the work is too preliminary. But we encourage our students to be

tenacious. There are other reasons for not completing research, like insufficient funding or negative publication bias. There is actually a *Journal of Negative Results in Biomedicine*, but it's not a common journal in which people think of publishing.

You have been the editor-in-chief of the Journal of Dental Research for many years. Has your perception of a good research paper changed over time?

Prof. Giannobile: I have seen the complexity and the need for collaboration growing in dental research. Thirty years ago the average number of authors on a paper was two or three. Now it's seven or eight. Research questions are being approached more collaboratively, combining, for example, biological sciences with engineering or clinical sciences with computational biology. These collaborative projects are challenging, but the results are also very exciting.

How about the social factors of collaborative research?

Prof. Giannobile: I think in any type of collaboration mutual respect for the individuals with whom you are working is key. Mark Kelly, former NASA astronaut, said during his opening presentation at the 2018 AAP Annual Meeting that he likes to work with people who are competent and not "yes people." Those two components are important in any type of collaborative research: competence to perform sophisticated types of experiments and being critical but also open and transparent when interpreting results. As a faculty member, I encourage students by letting them know it's okay to have negative results. We want to know what is really going on.

FIG. 1: The Osteology Foundation promotes research, mainly, through the Osteology Research Academy and by providing research guidelines and funding.

You are also collaborating with the medical device industry. What is their role in research?

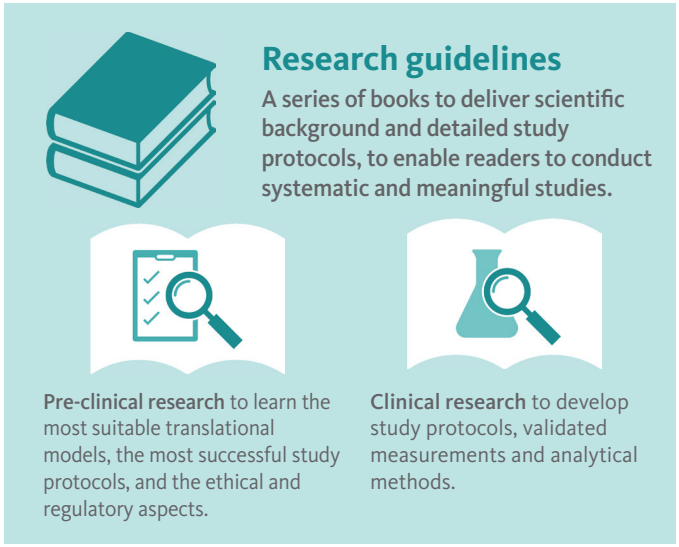
Prof. Giannobile: Industry can help academia because industry focuses on a goal: the desire to bring something to clinical application. It is a great privilege in academia to be able to explore a plethora of ideas, but eventually, if you want to find a real device application or a drug or diagnostic tool for a specific human condition, you are going to have to prioritize and set clear goals. Partnerships between academia and industry can therefore be synergistic.

You are the president elect of the Osteology Foundation. Their motto is "Linking Science with Practice in Regeneration." Also your motto?

Prof. Giannobile: Yes. I feel very privileged to be part of the Osteology Foundation. The theme of bringing solutions into the clinic and balancing clinical practice and science is key. We have the national and international symposia for clinicians and the Osteology Research Academy to train young researchers, and we also have grant programs supporting basic, preclinical and clinical research **(see Fig. 1)**. These pillars are what we think is needed to support evidence-based dentistry.

Do you plan to further extend the Osteology Foundation's research support in the future?

Prof. Giannobile: Yes. There will be more Osteology Research Academies in the next years, teaching also young researchers in the expanding global community. This is not only a valuable source of knowledge. It is also a great opportunity to build up a scientific network with like-minded people.
As the incoming Osteology Foundation president I will strive to walk in the footsteps of our past outstanding leaders in Profs. Christoph Hämmerle and Mariano Sanz. They have emphasized the balance of research and education in oral tissue regeneration. Last year, the Osteology Foundation engaged in a strategic plan-



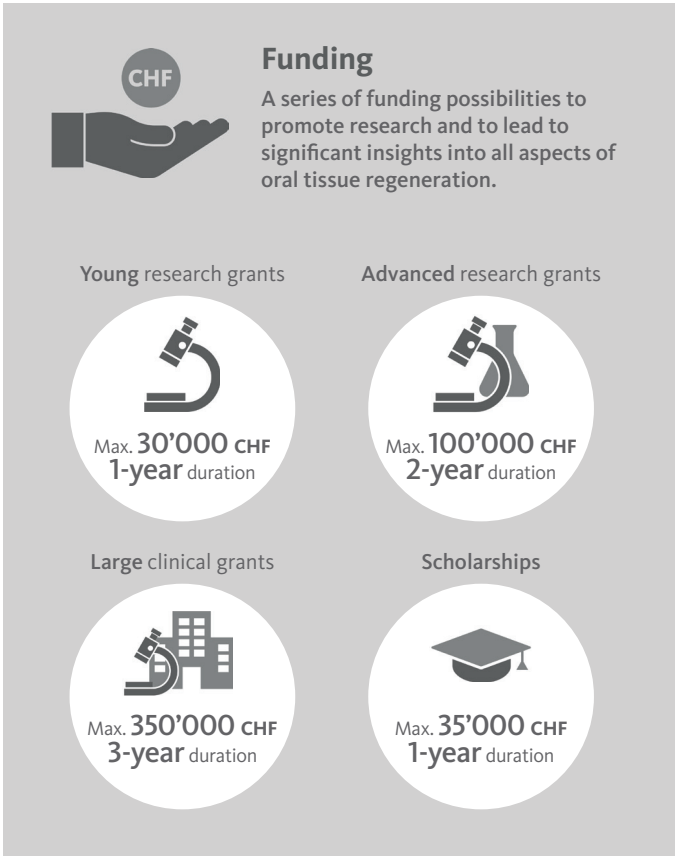


Illustration: Quaint

ning process that sought to further promote oral tissue regeneration in a global fashion through our many programs to reach out to the next generation of researchers and clinicians in dentistry. This should be an exciting period for the foundation that recently celebrated its 15th birthday.

What is your advice for somebody who wants to start research outside the university?

Prof. Giannobile: It's important to realize that doing research is not just about performing experiments and testing study hypotheses. It is also about study coordination, institutional review board approval, staff support to gather quality data, etc.

If not well organized, the quality of the data that comes out is not going to be translatable to clinical practice. So I would encourage people who want to embark in this area to get some additional training.

For example, the Osteology Foundation organizes one-week research academy programs for clinicians who are interested in embarking on clinical research. We are teaching basic principles ranging from grant writing and overt ethical conduct to study management and manuscript preparation, and so on.

What is the research result of which you are proudest?

Prof. Giannobile: A study that comes to mind concerns personalized medicine. In a population of about 5'000 patients we looked at three key risk factors associated with periodontal disease: smoking, diabetes and the expression of a genetic polymorphism. Using these three factors and the patient's recall interval we were able to predict which patients would lose more teeth and have more adverse dental events.[2]

It was exciting to see that for the first time we could use a personalized medicine approach to predict patient outcomes in dentistry. It was also a real learning experience for me because initially there was some push back from the dental community. But I was very proud to be a part of it since translation to the clinical is a process bringing together research, clinicians and policy-makers.

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Research that should influence clinical practice

Dr. Ulpee R. Darbar | United Kingdom
Consultant in Restorative Dentistry
Eastman Dental Hospital & Institute, London

Systematic reviews, despite heterogeneity and standardization issues, can give the clinician a framework from which to assess and plan their patients, temporarily making up for the current lack of randomized controlled trials particularly in the field of dental implantology. This article provides a short overview of key published systematic reviews and their relevance to the clinician.

SOFT TISSUE AUGMENTATION[1]

Gain of keratinized tissue: Free gingival grafts to increase the keratinised tissue results in a significant decrease of the bleeding on probing and gingival index, probing depths, higher marginal bone levels and reduced plaque scores when compared to maintenance sites with no grafting.

Gain of mucosal tissue thickness: Connective tissue grafts have a positive effect on reduction of the marginal bone levels, but result in no significant improvement in the bleeding or plaque indices or probing depths.

Clinical relevance: Clinicians should include soft tissue quality and morphology assessment during the planning of implant treatment. Enhancing the keratinized tissue and/or thickness during implant treatment can be of great benefit to improve outcomes.

SMOKING[2]

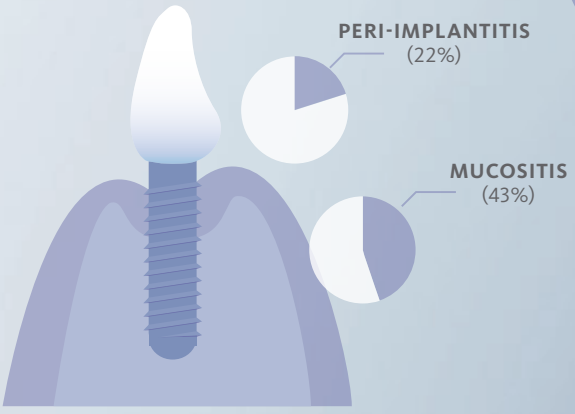
Marginal bone loss is worse in smokers than in non-smokers, with the loss being worse in the maxilla than the mandible. Smokers have also been shown to have a higher risk of complications and smoking is reported to have a negative effect on implants placed in regenerated sites – most likely due to the effect of the nicotine on blood supply and bone healing.

Clinical relevance: Clinicians should take into account the role of smoking in treatment outcomes and be aware of the increased risk of implant failure and marginal bone loss particularly if grafting is planned. They should also understand the importance of a baseline reference of the bone levels after implant rehabilitation against which to monitor the marginal bone loss over time.

PRISTINE VS AUGMENTED SITES[3]

Patients receiving implants in augmented sites display higher variability in outcome and predictability than those receiving implants in pristine sites. In the literature this is partly due to eligibility criteria, patient sample, different techniques used for augmentation, and variable case definitions used for the biologic complications.

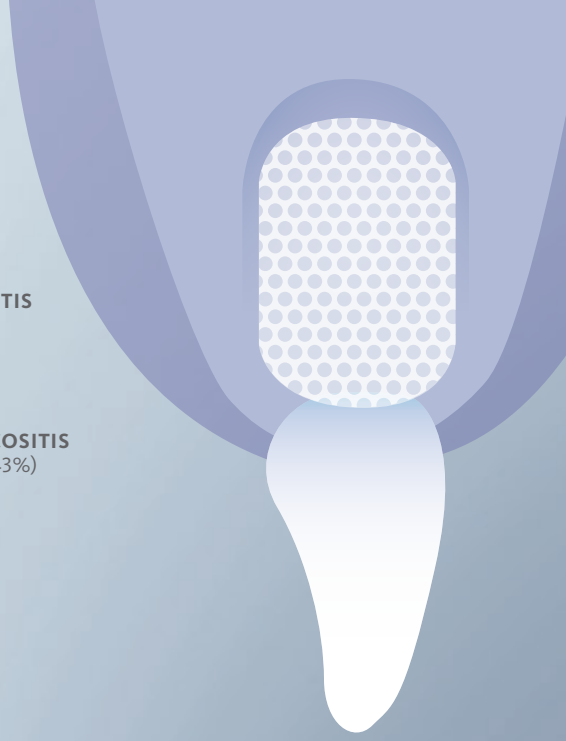
Clinical relevance: Clinicians need to be aware of the limitations in comparative data looking at augmented vs pristine sites. They should consider the importance of assessing patient related factors when planning implant treatment with augmentation.



PERI-IMPLANT DISEASES[4,5]

The prevalence, extent and severity of peri-implant disease as reported by Derks et al. in their first paper was peri-implant mucositis 19-65% (weighted mean 43%) and peri-implantitis 1-47% (weighted mean 22%). This review highlights the limitations of the reported prevalence, extent and severity of peri-implant disease due to the lack of a standard case definition of peri-implant disease, the variable follow up time periods and the issues with using convenience samples as opposed to randomly selected samples. The EFP/AAP World Workshop 2017 has addressed these issues as reported in the second paper by Derks et al. where new standardized definititions for peri-implant health and disease have been included and the need for using these highlighted.

Clinical relevance: Increasing reports suggest the rise in the prevalence of peri-implant disease. However, clinicians should consider the limitations of the published evidence and whether the reported data is inflated. The role of planning and careful preoperative assessment of risk factors and predictability should not be overlooked, as a number of these factors will affect the post treatment predictability. Clinicians should be aware of the new definitions for peri-implant health and apply them when considering a diagnosis of peri-implant disease.



ALVEOLAR RIDGE PRESERVATION[6]

Alveolar ridge preservation techniques may prevent bone loss in the horizontal and vertical dimensions. Better outcomes are achieved when a flap is raised and a membrane applied with a xenograft or allograft, especially in the mid-buccal and mid-lingual height.

Clinical relevance: Clinicians need to understand the need for preserving bone after tooth loss. Alveolar ridge preservation should therefore be considered for all extraction sites to minimize the extent of bone loss and also reduce the need for extensive grafting and augmentation at a later stage.

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Science Talk

“May the force be with the bone”

Interview with Prof. Jung-Chul Park and Niklaus Stiefel conducted by Dr. Giulia Cerino and Verena Vermeulen

Photo: Alfons Gut

Does bone regeneration work better in a defect site loosely filled with a bone substitute material, or is compression of the biomaterial beneficial? Prof. Jung-Chul Park, Korea, is among the first researchers to investigate this question in a clinical study. Here he talks with Niklaus Stiefel from Geistlich's research department about existing evidence and speculation in the field of compressive forces.

Prof. Park, you conducted the first clinical study on how different compressive forces affect Ridge Preservation outcome. Why?

Prof. Park: When performing Ridge Preservation, we sometimes find that the bone particles are pushed out of the socket over time. That's why we decided to compact the bone graft inside the socket. There were no previous studies on what compressive forces work best in Ridge Preservation or Guided Bone Regeneration. Thus, we decided to investigate the effects of extreme pressure versus low pressure.[3]

How was the investigation done?

Prof. Park: We included 20 patients who required the extraction of a single maxillary or mandibular molar tooth. After tooth extraction, the sockets were filled with 250 mg of Geistlich Bio-Oss® Collagen, applied with either very low pressure, 5 Newton, or with extreme pressure, 30 Newton. Then we covered the sockets with Geistlich Bio-Gide® membranes in a double layer technique and made a hidden cross suture on top.

What did you observe?

Prof. Park: Focus was on hard and soft tissue volume changes, implant survival and new bone formation. To investigate the latter, we analyzed histologies from core biopsies. While volume gain and implant survival were similar in both groups, we saw an increased amount of new bone formation in the sockets filled with higher compressive forces.

Photo: Alfons Gut

FIG. 1: How much pressure can Geistlich Bio-Oss® withstand before the particles crush? Prof. Jung-Chul Park (middle) and Niklaus Stiefel (right) discuss the product properties.

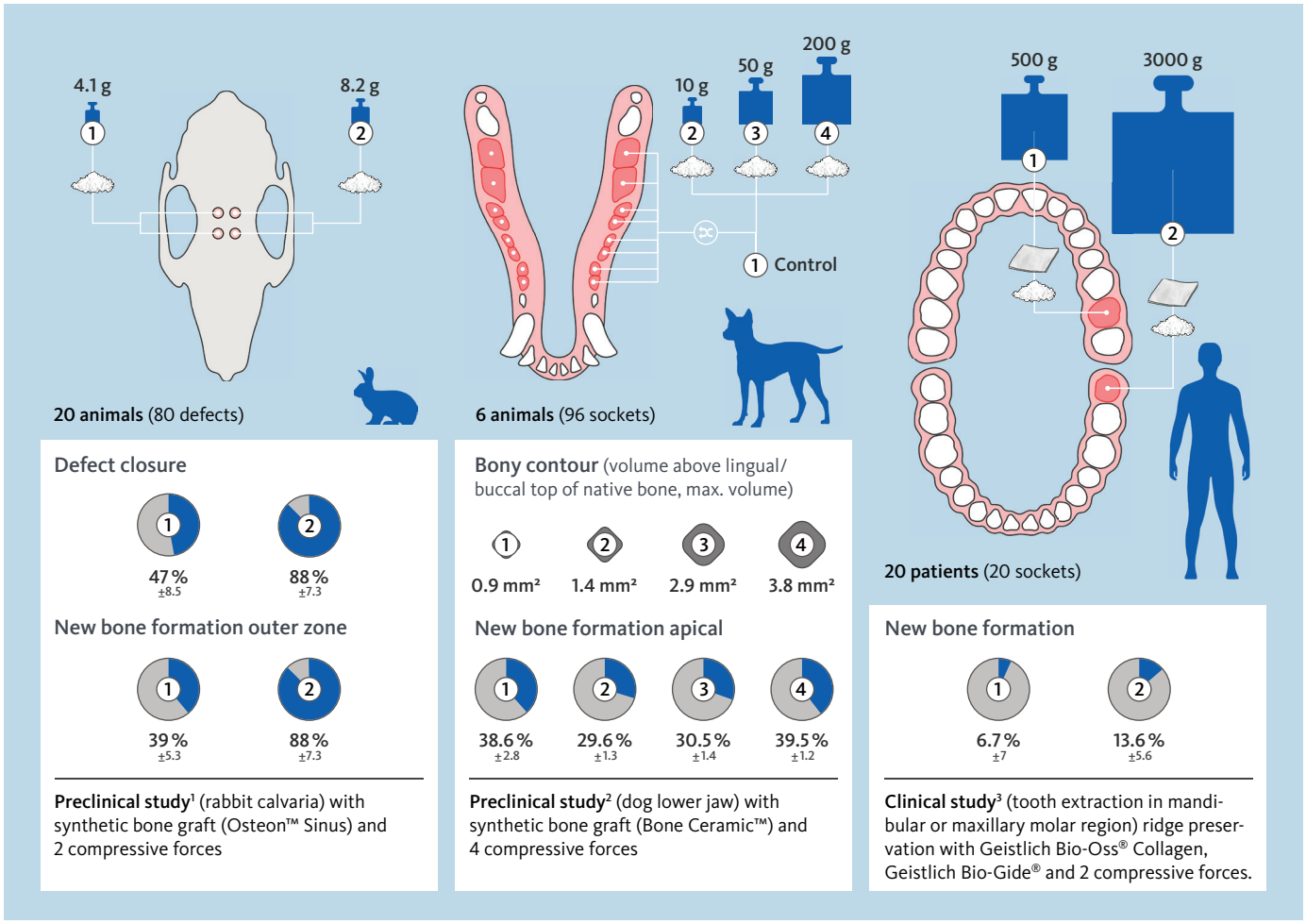

FIG. 2: Does compression of biomaterials lead to superior bone formation in the grafted area? This is the existing evidence.

You did, however, not find differences in volume gain or implant survival.

Prof. Park: True. We already have a great success rate with common treatment planning, implants and bone graft biomaterials.

So, if everything works out so well, why should we care about compressive force? Though it may not make a big difference for all patients, compression may have a tremendous impact on patients with impaired medical conditions, such as osteoporosis or diabetes, or patients with major bone deficiencies.

Nik Stiefel, you follow the development in this field. Is the finding that compression can lead to more new bone formation surprising for you?

Nik Stiefel: Yes and no. Yes, because in dentistry it is recommended to apply particulate bone graft materials as gently as possible to not lose trabecular architecture and porosity of the graft. And no, because compression increases the mechanical stability of a particulate graft and there is no reason why the principles of mechanobiology "more stability means more bone" should not apply in cranial bone formation.

Could you explain the positive effect of compression?

Nik Stiefel: According to mechanobiological laws, nearly no movement leads to bone formation while large amounts of movement lead to soft tissue formation.

Because compression increases the mechanical stiffness of the particulate material, less movements and by that less soft tissue formation and more bone formation are expected.

Is this a proven principle?

Nik Stiefel: Yes. We know that blood clot stability and overall stability of the wound play a crucial role in bone regeneration. For example in tibial mid-diaphysis fractures of rats certain types of strain lead to formation of cartilage instead of bone.[4] And while contained bone defects do fully ossify during bone regeneration using particulate bone material[5], mechanical stabilization is needed for vertical defects to enable bone formation.[6] In addition, there is evidence that at tissue level mechanical strains and fluid movement affect relevant celltypes such as osteoblasts[7], endothelial cells[8] or human mesenchymal stem cells[9] that are relevant for tissue regeneration.

Prof. Park: Several other factors might be involved. Mechanical transduction with integrin-beta signaling in osteocytes is a well-investigated principle. The facilitated formation of bony bridges in a densely packed cavity is another - we call it contact osteogenesis. Or the simple fact that via compaction we force the biomaterial into the most apical part of the socket. All we know currently is that when we put more force on the biomaterial we get more new bone, but we don't know whether it's this force that enhances bone formation or something else, for example the stability of the biomaterial.

Would you expect the same effect with another biomaterial?

Prof. Park: Our study was conducted with Geistlich Bio-Oss® Collagen where the collagen fibers might act as space maintainers between the bone particles and prevent crushing of the biomaterial. With Geistlich Bio-Oss® particles, things might be different. Further variables need to be considered, like: the type of procedure (horizontal or vertical ridge augmentation vs ridge preservation), source of biomaterial (xenograft, allograft, synthetic graft), particle size (small vs large), quality of surrounding bone (e.g., 3-wall vs 1-wall defect). How should one decide? When thinking that compression is an important factor, a ton of questions appear.

But is there research going on in this field?

Prof. Park: There is a lot of research on how to enhance bone regeneration with growth factors, anabolic or anti-resorptive agents, etc. All these adjunctive therapies have side-effects. But by adapting a routine clinical procedure only slightly, we can make a difference. And I, as a clinician, would do almost anything to have better and faster bony healing.

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Further voices on the question: "To compress or not to compress?"

Prof. Maurício Araújo
State University of Maringa | Brazil

"When doing a Ridge Preservation, I usually compress the biomaterial until I feel resistance. In order to have the best possible wound stability, I don't want to have biomaterial granules loose inside the defect. Indeed, I favor Geistlich Bio-Oss® Collagen because the collagen provides extra stability to the granules."

Dr. Mario Roccuzzo
University of Torino | Italy

"When doing a Ridge Preservation, usually I only use Geistlich Bio-Oss® Collagen and cover it with Geistlich Mucograft® Seal. I compress it to make sure there are no voids in the socket."

Adj. Prof. Thiago Morelli
University of North Carolina | USA

"During Ridge Preservation procedures most clinicians (including myself) have a tendency to compress biomaterials into bone defects in order to stabilize the graft particles and fill the space with the maximum amount of biomaterials possible. Although clinically it fits the purpose, I do have concerns regarding excessively crushing biomaterials. The crushing action can potentially damage the particles and thereby destroy the scaffold for new bone formation. The use of collagen-based biomaterials such as Geistlich Bio-Oss® Collagen can reduce the need for over-compression by providing the graft stabilization itself."

5 clinicians and 5 questions

5 clinicians.
5 questions.
5 precise answers.

We selected five renowned clinicians and asked them to answer five research-related questions, sharing their points of view with fellow clinicians. Result: 25 professional and personal insights.

Prof. Kristina Badalyan | Russia
CNIIS, Oral implantology department, Moscow

Which famous researcher would you like to meet?
Jan Lindhe. His books and articles are the "Bible" for periodontists and oral surgeons.

What was your first research about?
Influence of microsurgery on soft and hard tissues during implantation.

A moment in your research career that made a big impression on you?
I attended a congress in 2004 in Lucerne, which allowed me to see the direction of future developments and gave me the opportunity to use new knowledge in my clinical practice.

If you were a researcher in another area, what idea would you develop?
Periodontal ligament cells preservation and cultivation, and how to use them for regeneration.

A researcher should always...
"Make things as simple as possible, but not simpler." Albert Einstein.

Prof. Nikos Donos | UK
Queen Mary University of London

Which famous researcher would you like to meet?
Alexander Fleming and currently, Shinya Yamanaka, who has revolutionized stem cells research.

What was your first research about?
Evaluation of the use of autologous bone grafts with the combined use of non-resorbable membranes.

A moment in your research career that made a big impression on you?
The development of GTR principle and the relevant clinical application.

If you were a researcher in another area, what idea would you develop?
Early diagnosis of oral cancer through biomarkers in saliva.

A researcher should always...
Be both critical and open to new ideas and technologies, but also humble enough to understand that every new finding leads to new, exciting questions.

Prof. Andreas Stavropoulos | Sweden
Department of Periodontology, Faculty of Odontology, University of Malmö

Which famous researcher would you like to meet?
I'd like to have met Sture Nyman; he is considered among the fathers of oral tissue regeneration and, apparently, he was also a character!

What was your first research about?
Evaluation of the impact of a bone substitute on bone formation by means of guided bone regeneration.

A moment in your research career that made a big impression on you?
The fact that doing research *per se* can indeed make you happy!

If you were a researcher in another area, what idea would you develop?
I find the idea of guided cell rejuvenation and reprogramming fascinating.

A researcher should always...
Look honestly at the data and use some common sense during the interpretation of the results. Also to study and never give up!

Prof. Giuseppe Romito | Brazil
Periodontic Division, Dental School, USP – Universidade de São Paulo

Which famous researcher would you like to meet?
Niklaus Lang and Jan Lindhe to discuss their opinions about future perspectives in periodontology and implantology.

What was your first research about?
Relationship of subgingival and salivary microbiota with gingival overgrowth in heart transplant patients following cyclosporin A.

A moment in your research career that made a big impression on you?
When I understood that the most important thing besides results is the entire investigative process.

If you were a researcher in another area, what idea would you develop?
Tissue engineering with stem cells to improve the patient's ability to, for example, go back to walking!

A researcher should always...
Be a restless and open-minded person, be persevering, and be enthusiastic about academic area.

Dr. Rachel Schallhorn | USA
Private Practice, Aurora, Colorado

Which famous researcher would you like to meet?
I've met him already! My grandfather Dr. Robert Schallhorn.

What was your first research about?
Investigation of the mechanism of apoptosis with a drug used to treat prostate cancer during my undergraduate education.

A moment in your research career that made a big impression on you?
The day I finalized my master's thesis. I realized that I had learned much more than I expected.

If you were a researcher in another area, what idea would you develop?
Epigenetics and the influence of external, environmental factors on gene expression.

A researcher should always...
Remain objective. We keep our mind open to new discoveries we may not have predicted or expected.

Keratins that make a difference

Prof. Istvan Urban | USA and Hungary
School of Dentistry, Loma Linda University
Advanced Education of Implant Dentistry

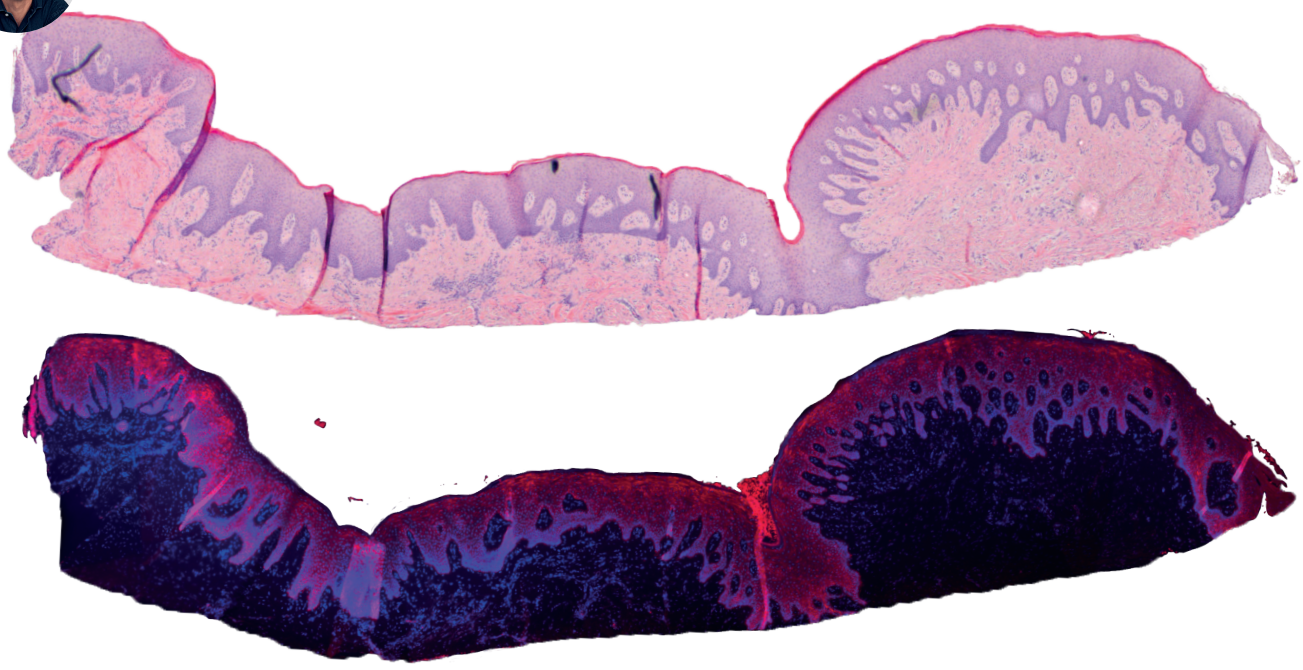

FIG. 1: Hematoxylin and eosin (H&E) staining of a treatment biopsy (top). Staining of a treatment biopsy for keratin 14 (red) and DAPI (cell nuclei, blue) to confirm physiological distribution of basal keratinocytes (bottom).

The surgical intervention tested in this prospective study[1] was called the "combination graft technique," since it consisted of combining an apically positioned autologous strip gingival graft with a coronally positioned Geistlich Mucograft®. This technique is indicated for correcting large mucogingival defects resulting from advanced regenerative procedures, while limiting autograft harvest and patient morbidity. It is a minimally invasive approach used to regenerate large amounts of missing keratinized tissue.

Since we use only a single strip graft apically and most of the exposed wound bed is covered with a collagen matrix, we were interested in finding out what type of tissue we achieved after healing. In addition to traditional histology, we assessed the expression pattern of different keratins, as they reveal the state of the gingiva and can detect abnormal differentiation. Histological staining as well as immunofluorescence examination revealed that the regenerated tissue was keratinized with no differences compared with "normal" keratinized tissue.

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"When I saw the beautiful immunofluorescence images and the right keratins were shining like small, beautiful Christmas lights, I felt a shiver. This is a small but vivid, successful and useful example of tissue engineering!"

The science of serendipity

In the age of computer-aided drug design, many believe accidental discoveries in the natural sciences and medicine are a thing of the past. However, and fortunately, that is not the case.

Photo: Getty Images/Chad Baker/Jason Reed/Ryan McVay

Even now random observations and unforeseen failures open up completely new paths to groundbreaking innovations. For such unintentional discoveries, the scientific world has a special term: "serendipity".

The word is derived from an oriental fairy tale. On their adventurous travels three Princes of Serendip – an old name for Sri Lanka – constantly made discoveries they had not been looking for. However, serendipity goes beyond pure coincidence, since only those who recognize an opportunity can turn surprises into discoveries.

The following scientists worked in their fields for years and were, therefore, able to consider the value of happenstance. Their particulary talent was the ability to recognize serendipity and capitalize on it.

Photo: ©iStock.com/jarun011

FIG. 1: Nearby an antimicrobial drug bacterial growth is inhibited. The principle and the first antimicrobial drug penicillin were discovered by Alexander Flemming in 1928.

X-rays – a strange glow

A single event can be decisive, and a number of momentous discoveries can be pinned to a certain date or even time of day. Such was the case with physicist Wilhelm Conrad Röntgen, who on the evening of 8 November 1895, was conducting an experiment with a Crookes tube (a vacuum tube in which cathode rays propagate in a straight line without a magnetic field) at the University of Würzburg, Germany. When he applied voltage, a fluorescent paper that happened to be lying around in the darkened room suddenly began to glow.

Röntgen tried to prevent the disturbing glow with black cardboard – in vain. Soon he realized that certain materials, such as bone and metal, were less permeable to this "X radiation," and lead blocked it completely. Using a photo plate mounted behind his wife's hand, he was able to depict her internal tissues – one of the first x-ray images ever taken. The accidental discovery and, later, thorough study of X-rays earned Röntgen the Nobel Prize for Physics in 1901.

Penicillin – lid forgotten

The research of the Scottish bacteriologist Alexander Flemming was marked by his experiences during World War I. More soldiers had died in the trenches from wound infections than from combat injuries. The breakthrough search for a cure was due to a coincidence. When Fleming left for the summer holidays in August 1928, he forgot to close the lid on his *staphylococci* Petri dishes. When he returned to his laboratory at St Mary's Hospital in London on 28 September, he noticed that mold had grown in one of the dishes. But wherever the fungus had come into contact with the *staphylococci*, the bacteria had disappeared.

Flemming cultivated the fungus and found that it was secreting an antibacterial poison. However, more than a decade elapsed before this poison, later known as penicillin, could be produced in large enough quantities to be used as an antibiotic. Flemming, who together with two other bacteriologists received the Nobel Prize in 1946, remained modest throughout his life. Asked about his great discovery, he said: "Nature created it. I just stumbled upon it."

Genetic fingerprint – runs in the family

On 10 September 1984 in his laboratory at Leicester University in Great Britain, biochemist Alec John Jeffreys was continuing his research on what is known as mini-satellite DNA. Mini-satellites are sections in the human genome that consist of variable repetitions of a short DNA sequence.

Jeffreys examined blood samples from several members of the same family, side by side. He noted that the mini-satellite DNA images could be individually assigned to each person like a barcode. Family relations could also be seen – the more agreement, the closer the relationship.
Jeffreys immediately recognized the importance of his discovery. He had found what we now call the genetic fingerprint. Today it is impossible to imagine criminal investigations, as well as paternity tests, without the genetic fingerprint of DNA profiles.

PDE-5 inhibitors – unexpected side effects

In 1989 two British researchers Peter Ellis and Nick Terret were looking for a drug to prevent heart attacks and other cardiovascular disorders. They were focusing on the active substance and vasodilator sildenafil. After two years of study sildenafil's efficacy for coronary disease could still not be proved, but the drug had an unexpected side effect: Male participants had more erections, and the erections persisted. Sildenafil had inhibited the enzyme phosphodiesterase-5 (PDE-5), and the concentration of the secondary messenger substance cGMP in the erectile tissue of the penis remained high, which in turn led to dilation of the vessels and produced unexpected and durable erections.
One of the most common causes of erectile dysfunction to date, namely constricted blood vessels and insufficient blood supply to the penis, could now be treated pharmaceutically.

Today the accidentally discovered side effect has made PDE-5 inhibitors one of the world's most widely used drugs.

Photo: ©iStock.com/puflic_senior

Hemangioma – suddenly shrinking

The bright red, rubbery birthmark on the nose of the newborn had grown rapidly and was already beginning to press on the baby's trachea.
Hemangioma is a nodule of extra blood vessels in the skin, and although in 2007 pediatrician Christine Léauté-Labrèze from the University Hospital in Bordeaux had started treatment with systemic corticosteroids, the treatment had not been successful. Instead, at the age of three months the baby also developed a serious heart muscle disorder, so therapy with the beta-blocker propranolol was initiated.
Just a few days later something completely unexpected happened: The conspicuous growth changed color from red to purple and became softer. Within a few weeks it began to shrink. When the beta-blocker was discontinued at 14 months, the hemangioma had almost completely disappeared.

"Only those who recognize an opportunity can turn surprises into discoveries."

Nine more children with problematic facial hemangiomata were soon cured in the same manner. For doctors, for parents and above all for thousands of children, this random observation from southern France has been one thing above all: a great stroke of good fortune.

Giant viruses – stuck in the bacterial sieve

In 2003 at a British clinic Didier Raoult from the Université de la Méditerranée in Marseille was not searching for viruses but for a special type of bacteria: *legionellae*.
When Raoult examined the contents of a bacteria filter more closely, he discovered previously unknown giant viruses, and they were to turn some existing ideas about viruses upside down. With a length of 0.4 µm and containing about 900 genes, they were not only considerably larger than all known viruses, and larger than many bacteria as well, but also a kind of hybrid organism that included the ability to produce proteins.
Such giant micro-organisms had already been seen by researchers in the 1990s, but they had been thought to be new bacterial species.
Didier Raoult not only found the organisms but also identified them as megaviruses. Since then an entire spectrum of even larger virus giants has been described. Their study indicates that the line between viruses and bacteria, between lifeless and alive, is now fluid. A completely new chapter of virology was started, by chance.

Literature

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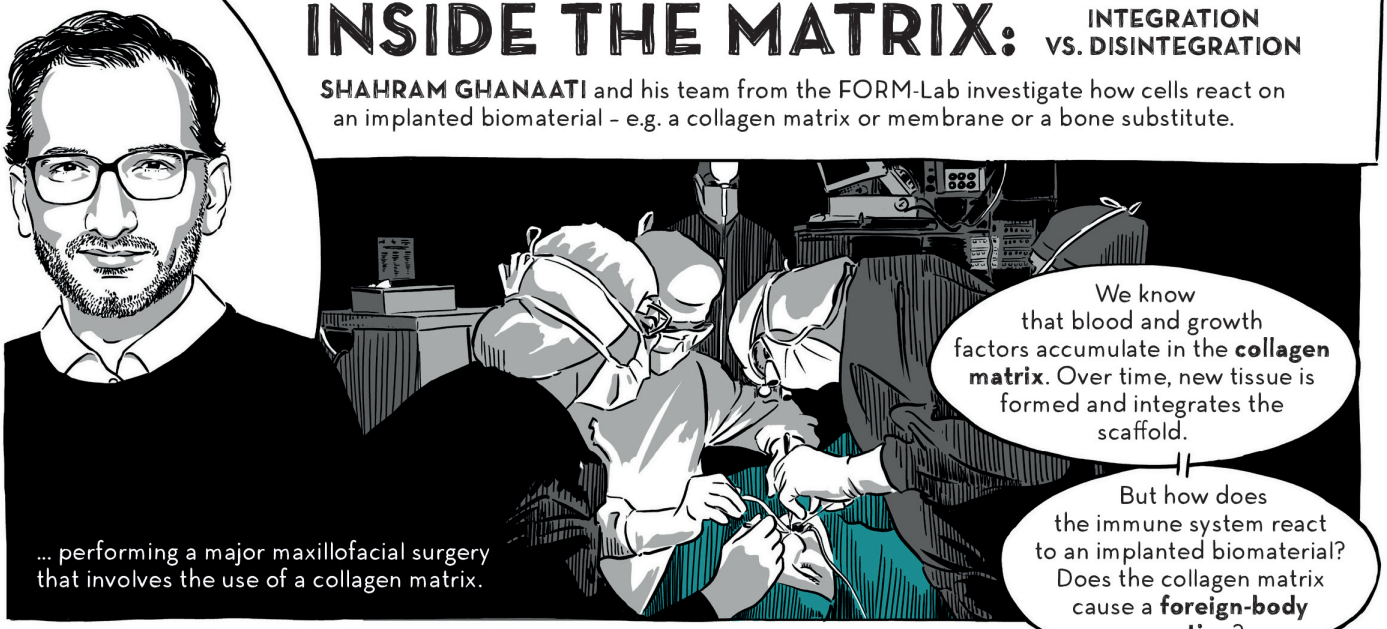
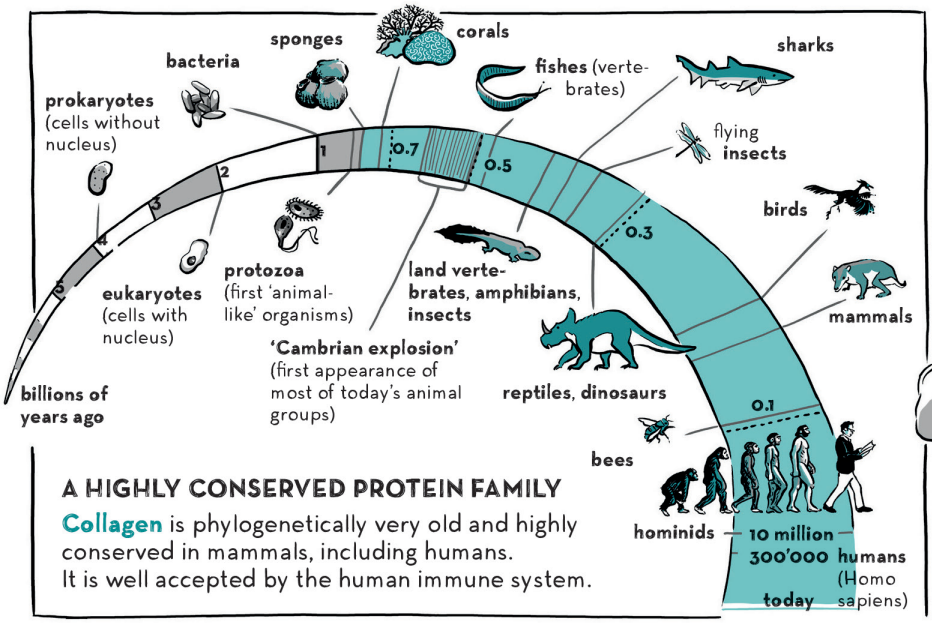
INSIDE THE MATRIX: INTEGRATION VS. DISINTEGRATION

SHAHRAM GHANAATI and his team from the FORM-Lab investigate how cells react on an implanted biomaterial – e.g. a collagen matrix or membrane or a bone substitute.



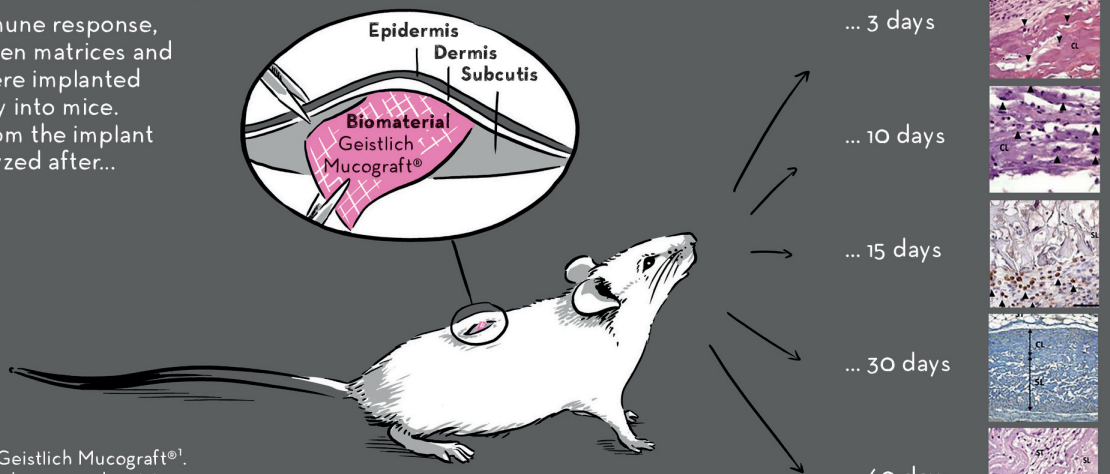


A HIGHLY CONSERVED PROTEIN FAMILY

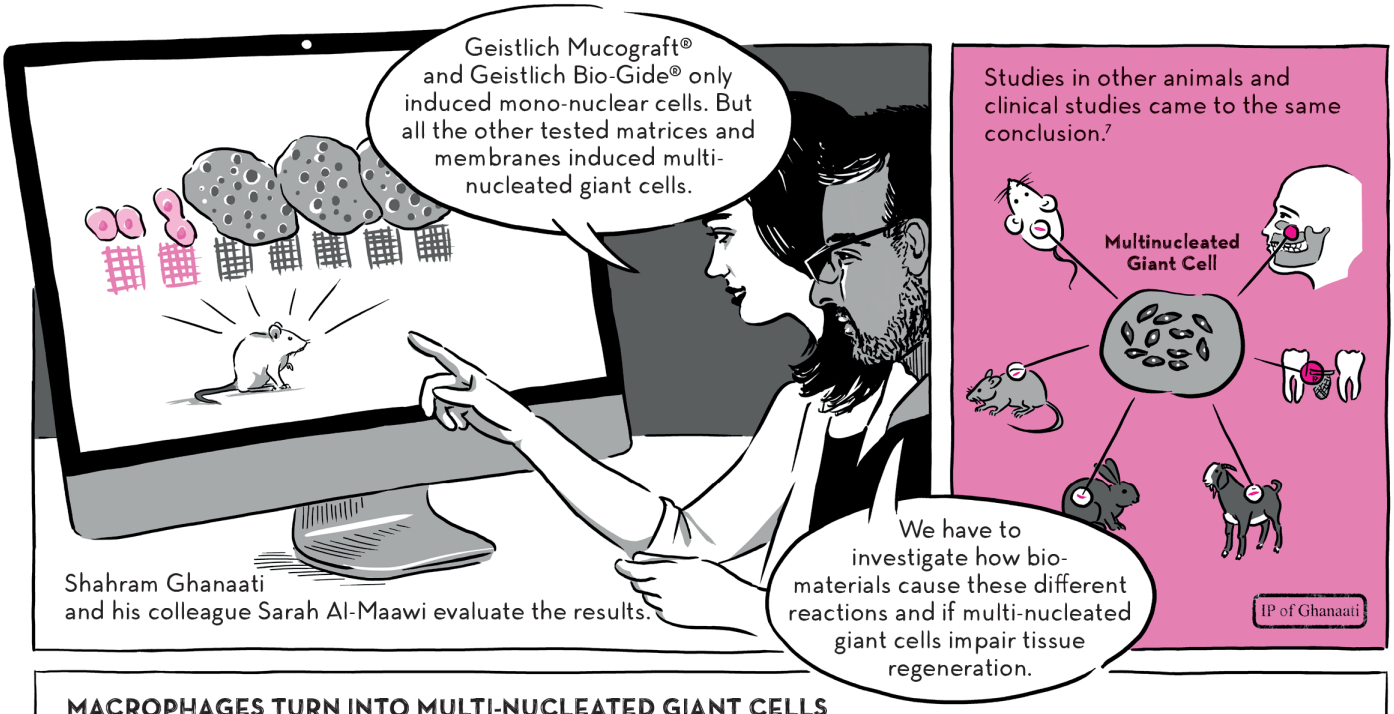
Collagen is phylogenetically very old and highly conserved in mammals, including humans. It is well accepted by the human immune system.

HOW DOES THE BODY REACT?

To test the immune response, different collagen matrices and membranes were implanted subcutaneously into mice. Histologies* from the implant bed were analyzed after...



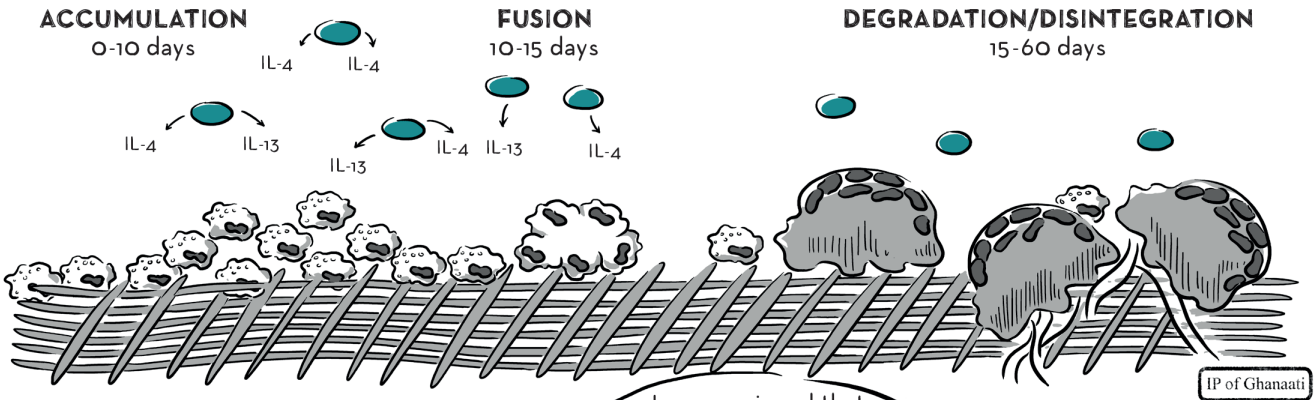
*Histologies show Geistlich Mucograft®[1].
Further tested membranes and matrices were:
Geistlich Bio-Gide®[2], BEGO collagen membrane[3], Ossix® Plus[4], Mucoderm®[5], Symbios collagen membrane SR and Collprotect®[6].



MACROPHAGES TURN INTO MULTI-NUCLEATED GIANT CELLS

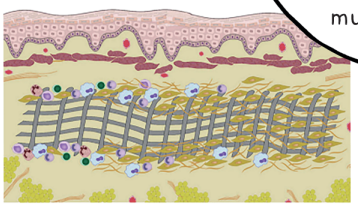
Macrophages are **mono-nuclear cells**. Their phagocytic activity and their capacity to release growth factors and cytokines are important in wound healing, repair and maintaining tissue integrity.[7-10]

But failing to eliminate foreign particles (e.g. an implanted biomaterial) by phagocytosis, they can fuse to form multi-nucleated giant cells. And then, they overdo it.

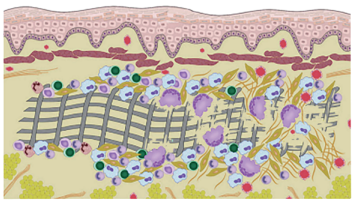


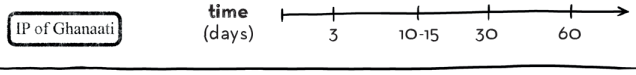
Depending on the **immune reaction**, two patterns can be distinguished:

A) Physiological integration
The biomaterials are well-integrated into the host tissue without any sign of foreign body reaction or premature breakdown.



B) Pathological disintegration
The biomaterials evoke a foreign-body reaction characterized by multi-nucleated giant cells. This is associated with premature loss of function and integrity.[7]





References: see page 39

Osteology Foundation: Where we are now, and where we are going

Interview with Prof. Mariano Sanz, Spain, conducted by Basil Gürber

The motto 'THE NEXT REGENERATION' combines the Osteology Foundation's key focus in Barcelona 2019. This includes the next generation of regenerative therapies as well as the next generation of dentists – not only as attendees of the program but also featuring upcoming experts in the field of oral tissue regeneration.

Looking back, how has the Osteology Foundation developed since the last International Osteology Symposium in held in Monaco in 2016?

Prof. Sanz: The Osteology Foundation's main mission is to link science with practice in the field of oral tissue regeneration, and, therefore, as new scientific advances and technologies have developed in this field during these last three years, the Osteology Foundation has significantly broadened its activities. This has included the increase and diversification of the funding research program, the widening of our research training programs through the expansion of Oral Research Academy courses into South America and Asia, and the increase in our education and training programs by establishing key collaborations with the most important global scientific associations.

What are the future goals of the Osteology Foundation?

Prof. Sanz: We have just elaborated a strategic plan projecting the course that the Osteology Foundation will take over the next 10–15 years. We envision the Osteology Foundation becoming a key global entity promoting research and education in the field of oral tissue regeneration.

A new generation of dentists is entering the field – how can the Osteology Foundation support their professional careers?

Prof. Sanz: This global ambition of reaching every oral health professional can only be accomplished if we have the appropriate communication tools. Direct electronic contact with the individual professional must be combined with well-planned educational and scientific transfer activities, which collaborate with the most prestigious associations and educational and scientific entities from around the world.

What tools has the Osteology Foundation developed to support these changing needs?

Prof. Sanz: To fulfil this mission, the Osteology Foundation needs both human and technical resources. We have an elected Board and an Expert Council that includes the most prestigious researchers and clinicians in the field, as well as exceptional, dedicated staff, all prepared to face these changing needs. As for technical resources, we have a powerful electronic platform (THE BOX), which beautifully serves the needs for direct education and communication between the individual dentist and our organization.

Compared to Monaco in 2016, what is new in Barcelona 2019?

Prof. Sanz: In Barcelona we would like to engage more young professionals, more interested dentists, and for that we have prepared an exciting scientific program combining lectures by the top international speakers with the upcoming new generations. We will maintain the high-quality scientific content that has always characterized the Osteology Foundation's International Symposium, with newly designed modalities of interaction within the congress, which will allow the most appropriate networking using current technologies. By transferring the international symposium from Monaco to Barcelona, we want to make this congress more accessible, mainly to young professionals, and for that we have introduced special registration fees for them and have designed new activities specifically suited for their needs.

What are you most looking forward to at Osteology Barcelona 2019?

Prof. Sanz: Barcelona is one of the most beautiful cities in the world. It perfectly combines modernity, culture, freshness and the light of the Mediterranean Sea. It has, therefore, a magnetic attraction for both young and older generations worldwide. Combined with the quality of the scientific program and professional networking that we have come to expect at the Osteology Foundation's International Symposium, this is the perfect cocktail for success. On a personal note, what will make this congress a very special one for me is that it's taking place in my home country during my last year as President of the Osteology Foundation. I would love to personally welcome all delegates attending this International Symposium, and I am sure that they will thoroughly enjoy both the congress, this beautiful city and the well-established Spanish culture, culinary delights and hospitality.

Osteology Research Academy Courses 2019

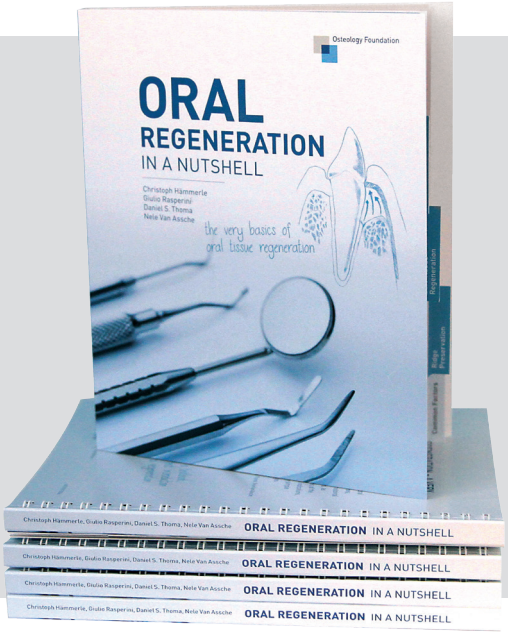
Research drives advances in science. This is why the Osteology Foundation is committed to running intensive courses on research design and methodology. Moreover, one course with different focuses on hard tissue research is offered in 2019.

> **Research Design and Methodology**
3-6 June 2019, University of Hong Kong, SAR, PR China
9-13 September 2019, University Lucerne, Switzerland
22-25 October 2019, Rio de Janeiro, Brazil

> **Hard Tissue Research**
4-6 November 2019, University of Bern, Switzerland

Oral Regeneration in a nutshell: About the book

The aim of the authors of this booklet was NOT to produce another comprehensive text book. It was rather to introduce novices to the complex but fascinating field of oral regeneration and to provide a basic overview on indications, procedures and materials used. The essentials of periodontal regeneration, regeneration of bone and soft tissues, as well as ridge preservation, are introduced. The aims of the different therapies, underlying principles, clinical indications, and surgical procedures, are presented in a very simple way by means of illustrations and clinical images. Find out more on www.oral-regeneration.org



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Interview

Together with Gong Ping in Xi'An

Interview conducted by Yun Yang

This issue of Geistlich News focuses on Research and Practice. What is your experience?

Prof. Gong: Research and practice complement one another. Before any technique or product is used in a patient, the first step must always be research-based. As an experienced dentist, when I am introduced to a new product, I am always very cautious. I really want to check if the product is as good as I am told. I check the scientific literature myself, and I do several studies and tests. Following this approach, I have a better understanding of the materials and of the clinical applicability. As an old Chinese saying goes: "Know what and why at the same time."

How do you like being a teacher?

Prof. Gong: I've had, and still have, brilliant students. They study and work very hard. All of my students who decided to stay at my university after graduation have received at least one grant from the National Natural Science Foundation, one of the first institutes in China. That is a great honor for me! I try to keep in contact with all of them. We have group chats. We talk and share information from around the world. It's a pleasure to be a teacher!

But you are also dealing with patients... What is your attitude toward them?

Prof. Gong: I always try to put myself in their shoes. What kind of treatment would I accept? Besides that, I always try to become familiar with the patient's background. I believe that a treatment based on empathy is the best solution for long-term benefits. I also teach this approach to my students. It is important that the patient feels comfortable, especially in a university hospital. I offer my students the opportunity to interact with the patients. I am by their side, listening and supporting them. When I see or hear something wrong, I take the time to talk to the student separately.

An approach that may seem tough...

Prof. Gong: I'm not a tough teacher, but I have my rules. You have to be committed to the patient. The mobile phone is not allowed during work, and no one should interrupt me when I visit with a patient. After the treatment, I encourage my students to call the patients for follow-up. Whether you have many patients to treat and are very busy every day or not, you have to finish what you started.

What did you dream of becoming as a child?

Prof. Gong: I was born in a family of doctors. My mother is a pediatrician; my father is an orthopedist. We never had a family dinner, not even in the Chinese New Year. While I couldn't stand the fact that my parents were always busy, I also understood that they had very respectable occupations. Therefore, I decided to become a doctor as well.

And why dental implantology?

Prof. Gong: When I was a child, I had a lot of problems with my teeth, and not many dental hospitals were near my house. So when I went to the university, I didn't consider any faculties other than dental medicine. Once I was told: "Teeth are the indicators of your entire life. Dental care will be there forever!" So I wouldn't say it was my dream, but rather an obsession!

Photo: Jia Degang

Prof. Gong Ping is professor, doctor advisor and director of the Implant Center of West China College of Stomatology. Besides being the associate director of the Dental Implantology Specialty Committee of Chinese Stomatological Association, she is an active member of the American Academy of Implant Dentistry (AAID) and the International Association for Dental Research (IADR). She is author and co-author of several articles in peer-reviewed journals and textbooks, and she gives lectures at national and international meetings.

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will be published in August 2019.

FOCUS

Around implants

› Peri-implantitis: How to regenerate the defect

› Treatment sequences: How to combine bone and soft tissue augmentation

› How to treat thinning soft tissue

SCIENCE TALK

Yxoss CBR® vs titanium-reinforced membrane

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