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Biological Dentistry

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Health, disease, death – where do we stand?

Dr. med. dent. Sebastjan Perko

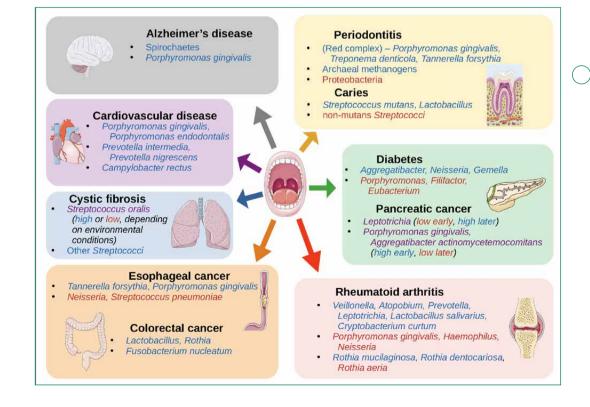
Biological Dentistry – The microbiome and osteoimmunology as key factors for systemic health

Perhaps a somewhat surprising title for dentistry and yet nowadays any dentist who reads and follows research should automatically associate the mouth with the body. Yet, the common conscience separates the two as if we remove the mouth from the body when we go to sleep. The strictly biological dentistry that we have developed over the last 10 years with biological doctors, such as Prof. Dr. Thomas Rau, gives us a serious insight into the relationship between the two. Being aware of Pischinger's space or internal milieu, it is no surprise that this could be a major pathway through which inflammatory mediators, bacterial byproducts and microorganisms themselves can travel to other parts of the body.

As it turns out, this pathway is more important than the cardiovascular or lymphatic systems, especially in chronic disease. So obvious and close in anatomy and yet so far in understanding is a recent publication titled: "Can oral microbiota affect the microbiome of the gut?" [Olsen et a., 2019]. The authors show that another pathway is the ingestion of pathogens and their products with saliva, e.g. Porphyromonas gingivalis, which causes dysbiosis in the gut microbiome. To connect the past with the present and the future, it is appropriate to quote Ibn Sina (980 - 1037), who said that if a doctor knows that the chosen therapy works in treating a particular disease, it is up to science to prove why it works, as the doctor should lay his focus on treating patients.

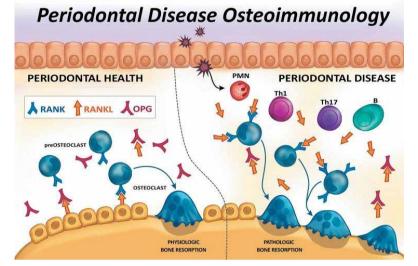
In biological dentistry, there are many areas that need special attention, and we have divided them into four main groups, namely microbiome, osteoimmunology, materials, and musculoskeletal system. This is only an artificial division, and all four areas are on stage at the same time and need to be addressed together. Traditionally, dentistry is never considered part of medicine, but with this division, there is a clear physical connection in each of the four areas. Let us start with the microbiome: the mouth is inhabited by 700 different species of bacteria, which harbor many viruses and fungi. For many people, the number could be greater than in the colon. When we produce between 0.7 I and 1 I of saliva a day, various "guests" enter our intestines along with the saliva we swallow.

It has been proven that Porphyromonas gingivalis survives stomach acid and disrupts the gut microbiome. It has also been proven that gingipain, secreted by the same bacteria, plays a role in the development of Alzheimer's disease. Another very aggressive bacterium,



Aggregatibacter actinomycetemcomitans, increases the metastatic potential of pancreatic cancer and much more. Locally pathogenic bacteria destroy soft and hard tissues in the mouth, causing either periodontal disease or periapical periodontitis, or both simultaneously. The inflammation is hidden below the gum line, where a true periodontal wound forms. The same thing happens with endodontically treated teeth. It is almost impossible to completely disinfect the root canal completely, regardless of the technologies used. The 10-year survival rate of endodontically treated teeth is about 80 %, which is not enough even for pharmaceutical medicine, especially if the patient suffers from one or another systemic disease. The link between inflammation and bone metabolism has led to the emergence of the field of osteoimmunology in the last 20 years. Bones were long believed to be relatively inert, but modern science shows that they play an important physiological role in maintaining electrolyte balance and are also a site for the development of haematopoietic progenitor cells. Bone is indeed a very dynamic tissue that is constantly remodeled by the balanced action of haematopoietic osteoclasts and mesenchymal osteoblasts. Bone remodeling can be physiological or pathological. The first is coordinated by vitamin D, parathyroid hormone and fibroblast growth factor 23; the second is called osteoporosis and osteopetrosis and is coordinated by the activation of osteoclasts by chronic or acute inflammation. Two important molecules involved in this process are RANKL (receptor activator of nuclear factor kappa B ligand) and OPG (osteoprotegerin), which up- or down-regulate osteoclasts. For a long time, it was believed that bacteria such as Porfyromonas gingivalis and Aggregatibacter Actinomycetemcomitans directly destroyed the periodontium. Today, however, it is known that the destruction occurs through an over-activation of the innate and acquired immune system against the bacterial biofilm. For example, the lipopolysaccharide of Porphyromonas gingivalis has been shown to increase RANKL expression in osteoblasts, which increases bone loss in periodontal disease via Toll-like receptor 2. Kawai et al. (2006) demonstrated that in patients with healthy gingiva, less than 20 % of T and B cells express RANKL, whereas in periodontitis-affected tissue, over 50 % of T cells and over 90 % of B cells are positive for RANKL. For those interested in details, I recommend reading an article by Kevin A. Thomas, The osteoimmunology of alveolar bone loss. More clinically relevant and measurable is the balance between Th1 and Th2 immune systems, the former secreting IFN-gamma and the latter IL-4, both of which inhibit osteoclast formation. In fact, Th17 cells produce IL-17 and the cytokine stimulates osteoclast development. In addition to IL-17, these cells secrete IL-1, IL-6 and TNF-alfa, which

induce RANKL expression. To make a long story short: Lipopolysaccharides (LPS) from bacteria found in periodontal disease and periapical granulomas activate our immune system – not to sound too dramatic – to use it to break down tooth-bearing tissues and feed on itself. What is important for biological medicine is that this can happen silently over many years, triggering inflammation throughout the human body through the mechanisms mentioned.



With some basic knowledge of the very well established relationship between inflammation and bone metabolism, we come to FDOJ, namely fatty degenerative osteonecrosis of the jaw bones, which has been observed and studied for some time and still receives general recognition. Lechner et all have done most of the work and the following thoughts are summarised from their articles.

It is a clear fact that no other organ in the human body is so frequently subjected to invasive surgical procedures as the tooth-jaw complex. These include tooth extractions in the mixed dentition and permanent dentition, the surgical removal of wisdom teeth, the insertion of dental implants, the drilling and filling of cavities and endodontic procedures (root canal treatment) on inflamed teeth. Some of the procedures only affect the hard tissue of the teeth, while the others break through the epithelial barrier and directly affect the inner milleu. Any procedure that creates a wound can lead to wound healing disorders. The resulting impaired healing and insufficient new bone formation of the alveolar bone, which take the form of silent inflammation, are thus inevitable. Such maxillary cavities are medullary cavities characterised by dying or dead bone marrow and can remain asymptomatic for years as FDOJ. As early as 1989, Bouquot introduced the term "neuralgia-inducing cavitary osteonecrosis (NICO)" to describe a chronic, osteolytic, medullary change in the jawbone with accompanying neurological symptoms.

In the first weeks after surgery, the wound is filled with mesenchymal stem cells, which can primarily differentiate into either osteoblasts or adipocytes. If differentiation into osteoblasts is disturbed, this can lead to a reduction in bone mass and an increase in adipose tissue as the number of adipocytes increases and the number of osteoblasts decreases. The result is osteolytic and osteoporotic areas filled with "fatty tissue" as seen in FDOJ. The typical cytokine profile of such degenerative osteonecrosis/osteolysis of the "fatty tissue" includes six molecules, the most important of which are IL-6. TNF- α and Rantes with the modern name CCL5. The study by Lechner et all confirmed that FDOJ reliably overexpresses the inflammatory messenger Rantes/CCL5. Rantes is a very well-studied molecule and has many important functions in our body, including the development of many modern diseases, when it is chronically secreted from FDOJ lesions and travels mainly through Pischinger's space to other parts of the patient's body.



The phenomena described represent almost half of what may be a problem with your patient that simply does not get better with your treatment. In many cases it is not enough to have a biological dentist, you need to work with a biological oral surgeon who has knowledge of biological medicine to support transformation of mesenchymal stem cells into osteoblasts and achieve perfect bony healing and osseointegration of dental implants with a bone content of more than 90 %.

This first part focused on the topic of microbiome and osteoimmunology as key factors for systemic health. The second part will cover harmful materials and how dental problems can affect the musculoskeletal system. The third part will explain preventive measures and therapeutic approaches to promote bone and soft tissue healing.

Biological Dentistry – Harmful materials & how dental problems can affect the musculoskeletal system

It is common knowledge that the contamination with toxins (in addition to sedentary lifestyles, unhealthy

diets and increased calorie intake) are changing our world and seriously contributing to the development of many chronic diseases, including neurological diseases, cardiovascular diseases, cancer, and many more. Of the many trillions of dollars spent on medical care in western countries, most is spent on treating chronic diseases. In the US, 90 % of the \$4.1 trillion spent on medical care in 2021 was used to treat people who were already sick. Obviously, this system of "sick care" is just too expensive to provide a decent margin of health. At first I thought that only in Slovenia we were separating the mouth from the body, but by treating many patients from all over the EU and the US it is obvious that this is a worldwide problem. At our clinic, our top priority is to reconnect dentistry with medicine. Our team currently consists of 35 people, each of whom is closely involved in the treatment of patients. Sadly, 99 % of our patients' initial therapies must be performed in the oral environment for the body's treatments to be successful. In part one of this article series we talked about the microbiome and in this second part we will focus on the mouth as a source of contamination from metals, plastics and other chemicals. In reality, there are materials that are only in the mouth for a short time and those that stay there as long as possible. In the latter group there are usually different metals that form alloys. There is a good book by B. W. Darvell called "Materials Science for Dentistry" (662 pages).

As mentioned in the first article, we produce 0.7 to 1 litre of saliva every day, which is swallowed with microorganisms and pollutants that not only come from the environment, such as pesticides from food, metals from water, chemicals from toothpastes, etc., but are often in the patient's mouth in the form of mercury amalgam fillings, prosthetic alloys, metallic implants that contain 4 % to 6 % aluminium, etc. Endodontic cements contain bisphenols and many of the "white" filling materials contain suspect monomers. The oral environment is very challenging because of temperature and pH variations in beverages and foods, different physical properties such as abrasiveness and hardness and, on the other hand, properties and quantity of saliva and the composition of the microbiome. In cases of GERD or bulimia nervosa, acidic challenges comes from the stomach.

Inflammation is very acidic by nature. I will never forget a patient from Prof. Dr. Thomas Rau's practice who suffered from severe ALS. When I examined his DMPS urine metal profile, it was clear to me that his bridgework is based on a Cr-Co-Mb alloy with some Ni in it. Even the panoramic X-ray clearly showed that he had severe periodontal inflammation under the bridge and that the root of one tooth had broken through due to decay. A perfect environment for "corrosion" of the bridge alloy and from there via GIT and also directly via the oral mucosa into the central nervous system. Another case that comes to mind, is my professor from the Josef Stefan Institute with six titanium implants, three of which had severe peri-implantitis clinically and radiographically. She had some systemic problems and I suggested a DMPS urine metal test. It was no surprise that she was full of aluminium and during the metal detox her situation improved significantly. She is very happy now because she was afraid of Alzheimer's. The latter was a real danger in her case considering the microbiome and pollution from titanium implants. I just spoke with Mr. Igor Akrapovič, whom you may know from the motorbike industry, about the issue and he too is guite surprised why titanium alloys with aluminium are used in medicine, as there are much more suitable materials. He was invited to make medical subperiosteal implants because he is an expert in titanium alloys and has studied the effects of metals in the biological environment

Fortunately, we live in a time when non-metallic materials are readily available and we have been using them since the foundation of our clinic. For fixed prosthetics, zirconium oxide ceramics are very well established, for removable prosthetics we use the material PEEK from a well-known German manufacturer, with which we have had experience for about 10 years and which works perfectly. For dental fillings we always recommend ceramics, if a patient chooses a composite, we recommend special materials developed by the Fraunhofer Institute that do completely without classical monomers and are classified as ormocer. In the field of biological jaw surgery, we have to be extremely careful with bone grafting materials, as the integration of artificial or animal materials in a thickness of more than 2 mm is guestionable and one could get foci. For this reason, we only perform autologous bone grafting and use synthetic materials only in sinus floor elevation procedures. There are promising new materials coming into play, but that is beyond the scope of this article. The most popular of all is in the field of implant dentistry and here too there are several manufacturers on the market. Finally, there are bone-like zirconium implants that we have had good experiences with so far. What is crucial in everything is that the body can regenerate and that the diagnostics and decisions are in order. Preserving the biological tissue, especially the bone, is of utmost importance. Especially in patients who are already ill. The musculoskeletal system is the last of the four topics of biological dentistry and the least studied. Fascia and muscle are extremely complex and occlusal disharmony and overload due to teeth grinding or bruxism are very common. Unexplained pain in the teeth, parts of the jaw, TMJ, headaches, neck and even further down the line can originate in our mouth.

Vice versa, pain in a specific tooth can be a diagnostic indication for a medical issue elsewhere. In order to find such connections, especially at an early stage, lon-Induction-Therapy (IIT) can be used to detect hidden pain regions. While applying IIT as part of my protocol specifically designed for post-op osseointegration of implants (Dr. Perko's papimi protocol for osseointegration), I discovered the benefits of additionally treating pain regions, which can be felt only during the therapy.



Occlusion (the bite) is the foundation of dentistry. For a dental procedure to be satisfactory, a good bite must be ensured. Traditional dentistry has focused on the teeth - like a 'one dimensional' dentistry. Today we know that the masticatory system consists of teeth, of course, but also of muscles, nerves and the temporomandibular joint, which connects the lower jaw to the skull. Without muscles, the masticatory system is dysfunctional.

Neuromuscular dentistry (NMD) is a term that links teeth/occlusion, muscles and the temporomandibular joint (TMJ) and was introduced to dentistry by Dr Bernard Jankelson in 1967. It is a controversial topic in dentistry and remains contentious. The issue of good occlusion and good health has been debated many times. Very often the signs of inadequate occlusion are overlooked and the whole situation is misdiagnosed and wrongly treated. Evidence of this is patients who have persistent pain in or around the temporomandibular joint, headaches, migraines, non-specific orofacial pain or neck pain and are treated unsuccessfully with analgesics, antiepileptics, antidepressants, beta blockers, etc.

The interconnection of the elements of the masticatory system is based on anatomical, physiological and skeletal-muscular principles and allows dental contacts (occlusal proprioceptive sensory information) to influence both the masticatory system and many other musculoskeletal systems of the body. Conversely, musculoskeletal dysfunction at other levels of the body can influence occlusion. The therapeutic goal is to reestablish an occlusion that minimises the need for adaptive compensatory muscle activity to move the teeth into a comfortable intercuspal position. Minimising the need to adapt to a suboptimal intercuspal position facilitates muscle relaxation. When compensation reaches its maximum, pain and dysfunction of the affected structures occur. This applies to every level of the postural chain, not just the craniomandibular mechanism.

A pilot study "The Role of Dental Occlusion and Neuromuscular Behaviour in Professional Ballet Dancers' Performance" (Henri Didier et al; 2021; Milan, Italy) showed that the use of a customised occlusal device improved the dancers' neuro-muscular coordination and overall performance over a 6-month period.

Stress and tension can cause silent, asymptomatic temporomandibular disorders (TMD) or exacerbate an existing temporomandibular condition. Common signs of TMD include pathological occlusal wear and tooth fractures/restorations, tooth hypermobility and cervical dentin hypersensitivity (CDH). Abfractions are



highly controversial, carious lesions are not usually caused by pathological lateral forces, but like most diseases, these lesions are multifactorial. All these signs can be multifactorial, so it is necessary to investigate the cause of them in each patient individually. Anamnesis helps us a lot in this regard. Fremitus may also be present. This is a vibration felt in the teeth when patients bite with their natural bite or in maximum intercuspal occlusion. Patients usually suffer from the following symptoms: stiff neck, headache, facial pain, earache, cracking when opening and closing the mouth or even if the symptom lasts too long, it can lead to arthritis in the joints. People who have any of these signs or symptoms should be thoroughly examined to determine the cause. Diagnosing and treating occlusal disease is as important as treating caries and periodontal disease or any other disease of the oral cavity. In the long term, occlusal disease can have a detrimental effect on the patient's general well-being. Diagnosis includes intraoral and extraoral

examination, intraoral and extraoral palpation of the masseter muscles as well as the neck muscles, palpation and auscultation of the temporomandibular joints, examination of mandibular function, which may be supplemented by Computerised Mandibular Scan (CMS), Electromyograph (EMG), Electrosonograph (ESG) and radiographic examination.

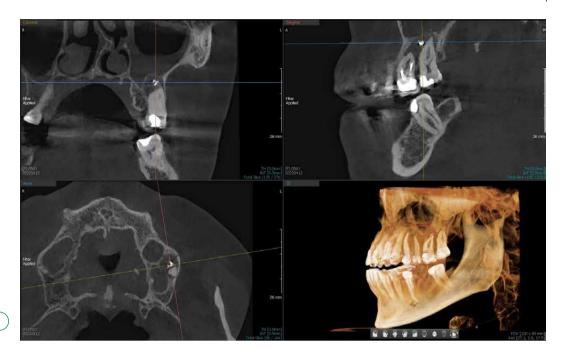
Therapy consists of removing all afferent and efferent noxious proprioceptive stimuli from the occlusion. The aim is to achieve comfort and normal function and eliminate pain and discomfort. This is achieved with minimal or major changes in occlusion and/or splint therapy.

In the third part of this article series we will focus on diagnostic procedures such as CaviTAU, regenerative protocols such as infusions with curcumin, vitamins and minerals, ozone, pulsed electromagnetic field (PEMF) therapies such as papimi lon-Induction-Therapy (IIT) and local restorative injections and more. We use virtually no antibiotics as we use protocols to normalise the oral microbiome, remove foci with modern surgical techniques, also intelligently combining PRF approach with modern biologic oral treatment. The selection of appropriate, strictly non-metallic materials in each situation is crucial to support systemic therapies.

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Preventive measures and therapeutic approaches to reduce systemic influence

Dr. med. dent. Sebastjan Perko, Phd.

The true benefits of biological medicine and biological dentistry lie in the treatments carried out according to the perspectives described in the first two parts of this article (issue 182, page F62). In this article we will describe only the supportive pre- and post-operative therapies, those that are not used in "normal" dental practises, with the aim of significantly reducing the use of antibiotics and painkillers. Of course, it all depends on the disease being treated and the well-being of the patient's body at that particular moment. We could divide them into local, i.e., intraoral, and systemic treatment modalities, in any case there are always multimodal approaches with restorative properties. A functioning immune system and bone metabolism are of paramount importance, especially because of osteoimmunology, which links the two. Osteoimmunology is a relatively recent direction in bone research, having first been mentioned in Nature by Takayanagi, Sato and Takaoka in 2002. Recovery and osseointegration begin with inflammation, which is an immune response that is in turn triggered by inflammatory cytokines released by white blood cells. According to Choukroun (Dohan et al., 2006), acute inflammation after an injury is only beneficial if it lasts for a maximum of 5 days or less. If it lasts longer, it becomes harmful because free radicals are formed and RANKL is produced, which activates transformation of macrophages into osteoclasts. Clearly, antioxidative capacity is of the utmost importance as free radicals trigger oxidative stress and consequently delay wound healing and cause a higher rate of failure and complications. Choukroun et al. reported in 2014 that LDL cholesterol and vitamin D are two important blood markers by which we can assess the patient's readiness for oral surgery.

Low vitamin D levels appear to be pandemic. In 2008, Holick published that 70-90% of the population is deficient. Figure 1 shows our analysis of vitamin D, folate and B12 in the serum of 460 patients performed on the same day as the surgical procedure. The results are catastrophic for all three for both genders and we can confidently say that low levels of vitamin D-hormones result in postoperative complications like inflammation with throbbing pain. It has been shown by Zhou et al in 2022 that vitamin D deficiency has a causative role in the systemic inflammation since low levels relate to higher serum CRP levels. Normal serum levels to achieve immune stimulation are from 50 ng/ml and above, from 10ng/ml to 30 ng/ml we can call insufficiency and below 10 ng/ml a deficiency. It is important to consider the systemic status of our patient, e.g., smoking, diabetes, allergies, etc. and through that decide on dosing. If one is healthy with appropriate lifestyle, we prescribe 2000 ie. to 5000 ie,

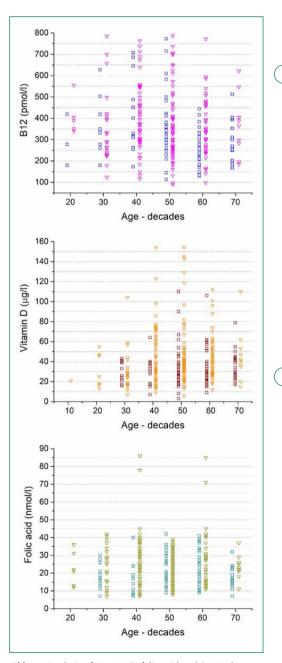


Abb. 1 Analysis of vitamin D, folic acid and B12 in the serum of 460 patients.

if one has some disease that is based on systemic inflammation and increased oxidation, we prescribe from 5000 ie. to 10000 ie. After approximately one month on the day of surgery it is tested and then we decide the dosing for the next 6 months when we retest again.

Because of these low levels in the general population, we have established a preoperative protocol in which patients are prescribed 2000 IU to 10000 IU of vitamin D daily, stronger type of B complex, Mg, Zn, etc. for one month prior to periodontal or surgical intervention. If vitamin D levels are below 10 ng/ml, we administer vitamin D intramuscularly. Vitamin C, selenium and curcumin are also prescribed and, if possible, intermittent fasting for at least five days before and after the surgery to induce self-detoxification and improve patients' immunity and accelerate wound healing. There also are articles that claim that osseointegration of an implant will be delayed if LDL is higher than 1.4 g/l and it is impossible if LDL is higher than 1.8 g/l so keeping an eye on cholesterol profile is also recommended.

In our clinic we have two multipotent formulations that cover most antioxidative needs. Antioxidant infusions, intravenous ozone and curcumin infusions are also highly recommended. In all surgical procedures we use various forms of second generation PRF technique. The first generation was called PRP. There are significant differences which are beyond the scope of this article. With PRF – platelet rich fibrin we centrifugate white blood cells, platelets and mesenchymal stem cells. These form a clot which is densely packed into the wound or covering bone graft, etc. PRF membrane can act as substrate with high concentrations of growth factors which improve angiogenesis and improve wound healing.

PRF -based matrices contain various inflammatory cells, such as platelets and leukocytes, in combination with various plasma proteins embedded in a fibrin network. It is known that the components of PRF -based matrices play an important role in wound healing. Platelets are the first cells to appear in the region of an injury. In addition to their role in haemostasis, platelets also have inflammatory potential, including the recruitment of other inflammatory cells such as neutrophils and macrophages, and promote angiogenesis and tissue repair. In this context, platelets can express a number of biologically active signaling molecules and growth factors, such as platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF) and transforming growth factor beta (TGF- β). These growth factors are essential for tissue vascularisation and the formation of new tissue. In addition, platelets contain granules of cytokines, chemokines and other inflammatory mediators that are released after platelet aggregation to improve haemostasis and

to activate and deliver cells to the site of inflammation. Leukocytes also contribute to angiogenesis and lymphangiogenesis by participating in cell-cell crosstalk and expressing various signaling molecules. The extracellular matrix in the wound bed supports blood vessel formation and fibrin provides a scaffold for the inflamed cells.

As blood is drawn for PRF as mentioned above, we check the levels of vitamin D, folic acid and B12. After periodontal or surgical procedures, procaine, selenium, vitamin D and B12 are infiltrated locally submucosally. Homeopathics such as Arthrokehlan A are highly recommended.

We must remember that we are dealing both with soft and hard tissue healing in the mouth and each has its own dynamics. Normally, the soft tissue heals quickly and effectively while the bone has its own dynamics. Generally, the soft tissue is not a problem, we just have to be careful that the incisions do not scar, and metallic tattoos are not as rare as one might think. Usually, a bluish stain is observed in the mucosa, which usually extends throughout the thickness and can even infiltrate the bone. Metallic tattoos are remnants of metal drilling, where extremely small metal particles are pressed into the gingiva or mucosa. We also have to pay strict attention to the width of the attached gingiva before implantation and sometimes we opt for a free soft tissue graft from the palate.

The healing of the bone is much more demanding and generally requires a good antioxidant capacity. Extraction sockets, implant integration, etc. require



Abb. 2 Placement of an implant



Abb. 3 papimi Ion-Induction-Therapy (IIT)

stem cells that can differentiate into osteoblasts or adipocytes. It is of utmost importance that we get as many osteoblasts as possible and for this we use papimi lon-Induction-Therapy and IV-ozone. It has been shown that the partial pressure of O2 in the peripheral tissue affects the differentiation of stem cells into osteoblasts, and it is also known that IV-ozone shifts the dissociation curve of hemoglobin to the right, which means that oxygen dissociates more easily in the peripheral tissue, including in the wound.

Several studies have shown that PEMF (Pulsed electromagnetic fields), can accelerate bone healing in both animal and human models, with benefits seen in both fracture healing and spinal fusion surgery. PEMF are thought to enhance bone healing by increasing cellular activity and promoting the production of growth factors and cytokines that are involved in bone formation. They may also stimulate the differentiation of osteoblasts and the activity of osteoclasts, leading to improved bone remodeling. The treatment is generally well-tolerated and has few reported side effects. We use the papimi lon-Induction device, a particularly powerful type of PEMF device that has a magnetic induction field which will reach as far as 25cm into the body.

Biological dentistry therapies offer a unique and innovative approach to oral health care. By focusing on supporting the body's natural healing processes, reducing the use of antibiotics and painkillers, and using multimodal approaches with up-building properties, these therapies can help patients achieve optimal oral health and overall well-being. With a deep understanding of osteoimmunology, stem cell biology, and the importance of antioxidants, biological dentists can provide their patients with personalized treatment plans that address their individual needs. By embracing this approach, we can truly revolutionize the way we approach dental care and empower patients to take control of their health and lead happier, healthier lives.

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