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Science Radar is new in this issue of the magazine. We have located and summarised recent publications for you as well as providing information about current literature on materials, products or treatment concepts.

We hope you enjoy browsing through our first major magazine.

Best regards,

Walter Esinger
PERICARDIAL MEMBRANES

Characteristics of a resorbable collagen barrier membrane

Dr Nina Rätscho, Product Management Department, BEGO Implant Systems GmbH & Co. KG, Bremen, Germany

Abstract

The loss of volume of the alveolar ridge that regularly occurs after tooth extractions can compromise the hard and soft tissue situation for implants and thus the aesthetic outcome. The principle of membrane-supported guided bone regeneration (GBR) is currently the most commonly used technique for bone regeneration in the dental practice. The separation of the rapidly proliferating soft tissue from the more slowly regenerating hard tissue creates a protected compartment in which damaged or lost bone tissue can be regenerated.

Commercially available barrier membranes can be clearly differentiated from one another on the basis of several properties. Factors such as ‘source tissue’ and ‘preparation process’ have been just as exhaustively studied as the effect of the species from which the collagen was harvested or the networking properties. To what extent these factors are essential for the biodegradation time of a barrier membrane, for example, has been discussed in various studies. The BEGO Collagen Membrane is a resorbable barrier membrane derived from collagen that meets the requirements for use in guided bone and tissue regeneration and has proven itself in clinical use. The key features of the BEGO Collagen Membrane are considered to be the appropriate barrier function for the protection of areas of bone regeneration, the reliable exclusion of soft tissue from the regeneration zone and the permeability to nutrients.

Key words: Collagen, barrier membrane, porosity, GBR, GTR
1. Barrier membranes in membrane-supported guided bone regeneration

The principle of membrane-supported guided bone regeneration (GBR) is currently the most commonly used technique for bone regeneration in the dental practice (BOSSHARDT & SCHENK, 2010). The biological mechanism underlying membrane-supported guided bone regeneration is the insertion of a barrier membrane that serves to clearly separate hard and soft tissues (e.g., see BOSSHARDT & SCHENK, 2010; ROTHAMEL et al., 2005; HÄMMERLE & LANG, 2001; HÄMMERLE & KARRING, 1998; KARRING et al., 1993; DAHLIN et al., 1988; GOTTLOW et al., 1986).

The separation of the rapidly proliferating soft tissue from the more slowly regenerating hard tissue creates a protected compartment into which cells migrate from the bone defect region and where new bone tissue can regenerate (TAL et al., 2012).

As a rule, a bone defect is filled with bone substitute and a barrier membrane is applied to cover the bone substitute, which provides the necessary volume, while ensuring the membrane makes direct contact with the adjacent bone surface (BORNSTEIN et al., 2010) because immobilisation on the bone appears to directly influence the ossification (DIMITRIOU et al., 2012; AMANO et al., 2004).

In the protected cavity beneath the barrier membrane, a stable blood clot can form that acts as the initial matrix for regeneration.

In addition to cell occlusiveness, the requirements for the ideal membrane for GBR techniques include good tissue compatibility, easy application and tissue integration properties. It is an essential requirement that the ideal membrane remains intact until the desired bone regeneration phase is complete and is only then integrated into the surrounding soft tissue (e.g., see GHANAATI, 2012; BORNSTEIN et al., 2010; SCHWARZ et al., 2008; McALLISTER & HAGHIGHAT, 2007; HARDWICK et al., 1994; GOTTLOW, 1993).

Commercially available barrier membranes can be clearly differentiated from one another on the basis of several properties. The membranes can, for example, be divided into non-resorbable and resorbable membranes. Resorbability describes the property of the membrane to be biodegraded by physiological processes in the body of the recipient. Non-resorbable membranes are bio-inert. A surgical procedure is required to remove the membrane once the regeneration is complete. Along with the stress for the patient of a second surgical procedure, during the removal of non-resorbable membranes the underlying regenerated tissue can be damaged and there is a risk of subsequent crestal resorption of the alveolar bone (PIHLSTROM et al., 1983).

Non-resorbable membranes do offer the advantage of a temporally unlimited barrier function and the associated exclusion of the soft tissue from the area of the bone regeneration. In contrast, resorbable membranes can be broken down in the body of the recipient by physiological processes. A procedure to remove the membrane is therefore unnecessary. Unlike non-resorbable membranes, resorbable membranes can only provide a limited barrier function to exclude soft tissue from the area of bone regeneration.
The BEGO Collagen Membrane is indicated for use as a barrier membrane in guided bone and tissue regeneration techniques (Fig. 1).

The loss of volume of the alveolar ridge that regularly occurs after tooth extractions can compromise the hard and soft tissue situation for implants and thus the aesthetic outcome (ROTHEMEL et al., 2010). Rothamel et al. (2010) describe various techniques for preserving the alveolar ridge after extractions and discuss the treatment of an extraction socket with granular, allogeneic bone substitute and a pericardial membrane that underwent a clearly accelerated resorption process due to open healing. Open coverage of extraction sockets using a membrane is a special case because of the small dimensions of the defect (ROTHEMEL et al., 2011; ELIAN et al., 2007; FROUM et al., 2004). They also describe the use of the pericardial membrane on the buccal and crestal aspects after augmentation with a bovine bone substitute designed for volume stability to treat a large apical fenestration defect on tooth 26 (ROTHEMEL et al., 2010).

In a human histology case study by ROTHAMEL et al. (2011), the BEGO Collagen Membrane was used to cover a fascial maxillary sinus window with simultaneous crestal augmentation as part of an external sinus floor elevation. The key features of the BEGO Collagen Membrane are considered the appropriate barrier function to protect areas of bone regeneration, the reliable exclusion of soft tissue from the regeneration zone and the permeability to nutrients. The morphological structure of BEGO Collagen Membrane produces a multidirectional stability, which means the membrane is resistant to tearing but cannot be stretched.

Hydrating the BEGO Collagen Membrane achieves adhesion to the bone wall surrounding the defect. The membrane does not adhere to itself, which makes application as part of guided bone and tissue regeneration techniques easier. The BEGO Collagen Membrane can be applied wet or dry. The time required until the membrane is completely penetrated by fluid is determined by the viscosity of the medium. The viscous character of blood increases the time required for penetration of the porous, honeycomb-like internal structure of the BEGO Collagen Membrane. Moistening the membrane beforehand with sterile aqueous solution can shorten the time required until the blood penetrates the membrane. The BEGO Collagen Membrane is characterised by a very dense collagen fibre structure. Elastic fibres also run between the fibrils of the type I collagen and are directly responsible for the multidirectional stability.

2. Documented clinical use and key features of the BEGO Collagen Membrane

The BEGO Collagen Membrane is indicated for use as a barrier membrane in guided bone and tissue regeneration techniques (Fig. 1). The loss of volume of the alveolar ridge that regularly occurs after tooth extractions can compromise the hard and soft tissue situation for implants and thus the aesthetic outcome (ROTHEMEL et al., 2010). Rothamel et al. (2010) describe various techniques for preserving the alveolar ridge after extractions and discuss the treatment of an extraction socket with granular, allogeneic bone substitute and a pericardial membrane that underwent a clearly accelerated resorption process due to open healing. Open coverage of extraction sockets using a membrane is a special case because of the small dimensions of the defect (ROTHEMEL et al., 2011; ELIAN et al., 2007; FROUM et al., 2004). They also describe the use of the pericardial membrane on the buccal and crestal aspects after augmentation with a bovine bone substitute designed for volume stability to treat a large apical fenestration defect on tooth 26 (ROTHEMEL et al., 2010).

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Fig. 1: The BEGO Collagen Membrane is a resorbable barrier membrane derived from native, naturally cross-linked collagen (porcine fibrous pericardium).
Eight weeks after a tooth extraction, there is incomplete healing of the extraction sockets of 13 and 14 with a buccal defect formation. Palatal placement of an adapted BEGO Collagen Membrane and application of BEGO OSS S on the exposed implant thread. After rehydration, the BEGO Collagen Membrane showed outstanding adaptation to the contours to stabilise the augmentation material. Tension-free wound closure following a periosteal releasing incision is made easier thanks to the thinness of the membrane.

3. Intelligent surface design

As a result of different surface characteristics, barrier membranes are modified to stimulate certain biological responses (DIMITROIU et al., 2012). Along with the intramembranous porosity and interconnectivity (DIMITROIU et al., 2012), the surface design of barrier membranes is a feature that can be modified. The surface characteristics of the BEGO Collagen Membrane have been adapted to the two tissue types between which they are placed (Fig. 3). The dense and compact structure without obvious access to the membrane interior is characteristic of the smooth side of the BEGO Collagen Membrane (Fig. 3). The smooth surface serves to occlude connective tissue cells. The dense texture of the smooth side does not contain any pores or penetrating perforations that would allow connective tissue cells to migrate into the space beneath the membrane where the bone regeneration takes place. At the same time, thanks to its thinness, the BEGO Collagen Membrane meets the requirement for permeability to nutrients to provide nutrition to the zone beneath the membrane. The rough side of the BEGO Collagen Membrane has a
compact but clearly open porous character with many connections to the interior of the membrane (compare Fig. 2 and Fig. 3). The rough surface character satisfies the requirement for osteoconductivity and allows the migration of cells from the nearby bone bed (Fig. 3; C, D).
Histology 8 weeks after placement, perfect tissue integration of the BEGO Collagen Membrane with no inflammatory response.

1. Blood vessel
2. Structural 3D multilayered collagen network
3. Integration into the surrounding tissue, free of inflammation

5. Porosity and permeability versus barrier function?

DIMITRIOU et al. (2012) describe the importance of the pore size for the porosity of barrier membranes. On one hand, the pore dimensions must prevent the ingrowth of connective tissue into the covered zone of bone regeneration, but on the other hand they must allow angiogenic access of the membrane body. The three-dimensional topography of a barrier membrane and the presence of an interconnecting pore system can affect the cell occlusiveness and the biological response from different cell types (DIMITRIOU et al., 2012).

Studies of the temporal and spatial course of angiogenesis (ROTHAMEL et al., 2012; GHANAATI, 2012; SCHWARZ et al., 2008; SCHWARZ et al., 2006a; Van LEEUWEN et al., 2005; ROTHAMEL et al., 2005) of collagen barrier membranes or their degradation patterns in different animal models and physiological compartments (e.g. see ROTHAMEL et al., 2012; GHANAATI et al., 2012; Van LEEUWEN et al., 2012; MOSES et al., 2008; SCHWARZ et al., 2008; TAL et al., 2008; ZUBERY et al., 2007; SCHWARZ et al., 2006a; ROTHAMEL et al., 2005; von ARX et al., 2005; ZHAO et al., 2000; SIMION et al., 1996) describe varying observations (see Table 1 and 2 in the appendix). The results from a series of studies showed temporal differences in their biodegradation pattern, regardless of the type of cross-linking. Native cross-linked membranes degrade faster than chemically cross-linked membranes. It could also be demonstrated that the time required for the biodegradation increased with the degree of cross-linking. The degree of tissue degradation was inversely proportional to the longer breakdown period, decreasing over time (SCHWARZ et al., 2006a; ROTHAMEL et al., 2005).

Different temporal biodegradation patterns that are dependent on the source tissue and the preparation process were also detected for porcine collagen membranes (e.g. see ROTHAMEL et al., 2012; GHANAATI et al., 2012 and personal communication). In the opinion of the author, the factors ‘source tissue’ and ‘preparation process’ cannot be separated in the studies cited. If and whether factors such as species, source tissue, cross-linking characteristics and preparation process are critical for the biodegradation time or what influence the individual factors have must be investigated in further studies.
and good tissue integration after 2 weeks. For the same experimental design, ROTHAMEL et al. (2012) reported complete vascularisation of the membrane body after 4 weeks and almost complete degradation after 8 weeks. Twelve weeks after implant placement SCHWARZ et al. (2008) and ROTHAMEL et al. (2012) observed complete degradation of the membrane. ZUBERY et al. (2007) implanted the same membrane in the maxilla only of beagles and reported a temporal degradation pattern for the membrane that differed from the previous studies. Moderate degradation was observed after 16 weeks and complete degradation was only seen after 24 weeks. The membrane (BG) was also implanted in the mandible and maxilla of rats. After 2 weeks the researchers reported vascularisation of the membrane body and a mild inflammatory reaction and after 12 weeks they observed severe degradation of the membrane (van LEEUWEN et al., 2012). Vascularisation of the membrane body and an inflammatory reaction around the membrane were observed 2 weeks after placement of the same membrane subcutaneously in the backs of rats (ROTHAMEL et al., 2005; ZHAO et al., 2000). Resorptive processes were observed after 3 weeks (ROTHAMEL et al., 2005). A reduction in the thickness of the membrane and almost complete degradation after 4 weeks were described by ZHAO et al. (2000). SCHWARZ et al. (2006a) also observed significant degradation of the membrane 8 weeks after placement. Compared to the studies on rats that have been published, a different pattern of degradation of the BG was observed over time with subcutaneous placement in the backs of mice. The membrane thickness and volume stability were preserved, and 30 days after placement good tissue integrity and no signs of degradation were observed. The membrane body was also described as structurally intact 60 days after placement (GHANAATI, 2012). In the calvaria of rats, a reduction in the thickness of the membrane body of 60% was observed after 7 weeks (MOSES et al., 2009). In the calvaria of rabbits, a reduction in the thickness of the membrane body was reported 6 weeks after placement as well as full degradation after 12 weeks (ARX et al., 2005). The placement of another porcine membrane (pericardial membrane, PM) in the mandible and maxilla of beagles also showed good tissue integration after 4 weeks compared to the BG membrane in the same study but for the most part degradation only occurred after 12 weeks (ROTHAMEL et al., 2012). With the PM membrane placed subcutaneously in the backs of rats, an inflammatory response and mild vascularisation dependent on the particular surface property was observed by BARBECK et al. (2014). The volume and structural stability of the PM was comparable to that of the BG over 30 days (BARBECK et al., 2014; GHANAATI, 2012). The study results are summarised in tables 1 and 2 in the appendix. The transferability of the results from animal studies to humans and thus their clinical relevance is frequently and critically discussed (for a summary, see SHANKS et al., 2009; AUER et al. 2007; LIEBSCHNER, 2004).
**Supplement**

Tab. 1: Breakdown of the studies on the histological evaluation of different collagen membranes in various animal models and different physiological compartments. The different membranes investigated, their origin, the animal models used and the physiological compartments are indicated.

Tab. 2: Breakdown of the histological evaluation of different collagen membranes in various animal models and different physiological compartments. The breakdown shows that between the species and in the different physiological compartments there are different results observed for the vascularisation, tissue integration and degradation of the membranes.

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<tr>
<th>Barrier membrane</th>
<th>Manufacturer/Company</th>
<th>Material</th>
<th>Origin</th>
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### Table 2

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<tr>
<td><strong>Dog</strong></td>
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<td>PM</td>
<td>(1) reported good tissue integration and ingrowth of blood vessels after 4 weeks. After 8 weeks a high density of blood vessels was detected in the easily identified PM body with the PM body largely resorbed after 12 weeks. Isolated cloudy remnants of the PM were still observed.</td>
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<td>BG</td>
<td>(1, 7 maxilla and mandible; 8 mandible) Between 2 and 4 weeks a clear reduction was observed in the membrane thickness (7). The BG is already completely developed angiogenically after 2 weeks (7) and good tissue integration is reported. After 4 weeks full vascularisation of the BG body and good tissue integration are also reported by (1). Almost complete resorption was described after 8 weeks and full degradation after 12 weeks (1 &amp; 7). The pattern of degradation or resorption over time that is described by the authors (1) and (7) is consistent while the temporal pattern of the observations made by (8) deviate. Signs of degradation were described by (8) after 8 weeks, moderate degradation after 16 weeks and an inconsistent degradation pattern after 24 weeks. It must be noted that in (8) the membranes were implanted in the mandible, whereas in (1) and (7) they were implanted in the mandible and maxilla or in the maxilla only in the premolar and molar area. Differences in the temporal course of the resorption may be attributed to this fact.</td>
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<td><strong>Rat</strong></td>
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<td>PM</td>
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<td>BG</td>
<td>(Mandible) (2) reported vascularisation of the BG and a slight inflammatory response after 2 weeks. After 12 weeks severe degradation was observed that prevented detection of the BG in the tissue.</td>
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<td>BG</td>
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<td><strong>Rabbit</strong></td>
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[12] analysed the tissue response to the PM 3, 10, 15, 30 and 60 days after placement of the membrane subcutaneously on the backs of rats. Depending on the surface property of the PM, different tissue reactions were observed. The rough, sponge-like, porous side of the membrane primarily induced a response from mononuclear cells and acted as a stable barrier for the duration of up to 60 days. Transmembrane vascularisation in the sponge-like porous membrane area was not observed. On the compact surface of the PM a response from multinuclear cells together with slight vascularisation were observed over the course of the study. The compact side of the PM was degraded over the further course of the study and the multinucleated cells displaced as mononuclear cells appeared. After 60 days the PM was very well integrated into the implant bed and the material integrity was still maintained.

Consistent observations of the vascularisation of the BG after 2 weeks. [10] and [6] reported an inflammatory response around the BG after about 2 weeks. [6] reported of resorptive processes after 3 weeks, while [10] detected a reduction in the membrane thickness of about 40% and almost complete degradation or incorporation into the surrounding tissue after 4 weeks. [11] identified significant degradation after 8 weeks.

[9] reported a reduction in the membrane thickness of about 60% after 7 weeks in the calvarium.

Incipient vascularisation of the TD body was described by [11] after 2 weeks in different parts of the membrane which then progressed and was described as complete and homogeneous after 8 weeks.

[3] did not detect any changes in the membrane thickness (~650 μm) over the study period of 90 days. After 7 days incipient cellular infiltration of the BG body was reported and by day 15 progressive tissue ingrowth into the BG was observed with the original volume stability of the BG maintained. After 30 days good tissue integration but no signs of degradation were described. After 60 days newly formed connective tissue around the BG was described with the BG still detectable and appearing structurally intact.

After 2 weeks the BG was observed to be intact and surrounded by a fibrous capsule. After 6 weeks a reduction in the membrane thickness was described along with newly formed capillaries in the intrafibrillar network of the BG. The BG could not be distinguished from the host tissue after 12 weeks and after 28 weeks there was a consistent connective tissue layer over the previous defect [4].
SCIENCE RADAR
J Oral Implantol. 2014 Nov 11

Porcine dermis and pericardium-based, non cross-linked materials induce multinucleated giant cells after their in vivo implantation: A physiological reaction?


The present study analysed the tissue reaction to two novel porcine-derived collagen materials, i.e. pericardium versus dermis. Using the subcutaneous implantation model in mice, the tissue reactions were investigated at five different time points: 3, 10, 15, 30 and 60 days after implantation. Histological, histochemical, immunohistological and histomorphometrical analysis methodologies were applied. The dermis-derived material underwent early degradation while inducing mononuclear cells together with some multinucleated giant cells and mild vascularisation. The pericardium-derived membrane induced two different cellular tissue reactions. The compact surface induced mononuclear cells and multinucleated giant cells and underwent complete degradation by day 30. The spongy surface of the membrane induced mainly mononuclear cells and served as a stable barrier membrane for up to 60 days. No transmembranous vascularisation was observed within the spongy material surface layer. The present data demonstrates the diversity of the cellular tissue response to collagen-based materials from different tissues. Furthermore, it becomes obvious that the presence of multinucleated giant cells is associated with the material breakdown/degradation and vascularisation.

On the Screen

<table>
<thead>
<tr>
<th>Objective</th>
<th>Analysis of the tissue response to porcine collagens in the subcutaneous implantation model in mice.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model</td>
<td>Subcutaneous implantation in the back of mice.</td>
</tr>
<tr>
<td>Duration</td>
<td>5 times: 3, 10, 15, 30 and 60 days</td>
</tr>
<tr>
<td>Methodology</td>
<td>Histology, histochemistry, histomorphometry, immunohistochemistry.</td>
</tr>
<tr>
<td>Results</td>
<td>The porcine pericardial membrane investigated (BEGO Collagen Membrane) induced two different tissue responses that are dependent on the surface topography of the membrane. The porcine collagen derived from dermis (BEGO Collagen Fleece) underwent rapid degradation and induced both mononuclear cells and multinucleated giant cells together with mild vascularisation.</td>
</tr>
<tr>
<td>Conclusion</td>
<td>The analyses revealed the diversity of tissue responses to collagen-based biomaterials. The presence of multinucleated giant cells is associated with the material breakdown or degradation and the vascularisation of the BEGO Collagen Membrane and the BEGO Collagen Fleece.</td>
</tr>
</tbody>
</table>
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PERIIMPLANTITIS

Definition, aetiology, prevention and treatment of peri-implantitis – Current study results

Ole Jung, Dr med. Dr med. dent. Henning Hanken, Prof. Dr med. Dr med. dent. Max Heiland, Prof. Dr med. Dr med. dent. Ralf Smeets

Abstract

Peri-implant inflammations are serious complications following dental implants that affect both the surrounding hard tissue and the soft tissue. With prevalence rates of up to 56%, they can result in the loss of the dental implant if a multilateral treatment concept is not applied. Adequate patient-specific follow-up examinations (recall) and recording or eliminating risk factors are effective preventive measures. The type and structure of the implant surface also play a role in addition to aspects of the osseointegration. Various conservative and surgical treatment options are available for when peri-implantitis occurs. Conservative methods include the use of different manual ablations, laser-guided systems as well as photodynamic forms of therapy which can be supplemented by the administration of systemic and local antibiotics. Resective surgery is used primarily with peri-implantitis that has progressed further to eliminate pathogenic formations, while regenerative materials are used supportively. The CIST protocol can be applied as a guide for how to proceed with peri-implantitis. This article summarises the causes, epidemiology and therapy of peri-implantitis taking into account the current body of data.

Key words: Peri-implantitis, periodontitis, mucositis
1. Definition and pathogenesis

Analogous to gingivitis and periodontitis of the intact periodontium, inflammatory and destructive structural processes following implant restoration are referred to as mucositis and peri-implantitis (Fig. 1) (KHAMMISSA et al., 2012; ASTASOV-FRAUENHOFER et al., 2013; WILSON, 2013). The actual transitions are rather fluid and cannot be clearly differentiated clinically (SCHWARZ et al., 2008).

Mucositis refers to a bacterially induced, reversible inflammatory process of the peri-implant soft tissue with redness, swelling and bleeding on probing (KHAMMISSA et al., 2012; ASTASOV-FRAUENHOFER et al., 2013; WILSON, 2013; WALLOWY, 2012; SCHWARZ et al., 2008). Peri-implantitis in contrast refers to a progressive, reversible suite of inflammatory symptoms of the peri-implant hard and soft tissue that is associated with bone resorption, reduced osseointegration, increased pocket depths and suppuration (KHAMMISSA et al., 2012; ASTASOV-FRAUENHOFER et al., 2013; WILSON, 2013; WALLOWY, 2012; SCHWARZ et al., 2008).

Depending on the type of bone defect, an intrabony class I defect is differentiated from a supra-alveolar class II defect on the crestal implant transition according to SCHWARZ et al. (2008). According to SPIEKERMANN (1984), bone loss can be characterised as horizontal (class 1), crater-shaped (class 2), funnel- or trench-shaped (class 3 a, b) or horizontal circular (class 4). However, progression and prognosis are not taken into account in these classifications.

### General risk factors

- Inadequate patient compliance
- Ineffective oral hygiene
- Nicotine abuse
- Presence of IL-1 genotype as a polymorphism
- Systemic diseases
- Prior gingivitis and periodontal diseases
- Soft tissue damage / qualitatively poor soft tissue
- Iatrogenic causes
- History of implant failures

**Fig. 1:**
Schematic representation of factors favouring the development of peri-implantitis
At the microscopic and molecular level, there are fundamental differences observed in the peri-implant tissue compared to the intact dental periodontium (Tab. 1) Peri-implant tissue structures (including reduced vascularisation and parallel alignment of collagen fibres) generally encourage the development of inflammation, which is expressed immunohistochemically as an increase in the formation of inflammatory infiltrate, nitric oxide 1/3, VEGF, lymphocytes, leukocytes and Ki-67 (DEGIDI et al., 2012).

Table 1: Comparison of the peri-implant mucosa with the physiological periodontium

<table>
<thead>
<tr>
<th>Peri-implant mucosa</th>
<th>Physiological periodontium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epithelium or junctional epithelium (biologic width) is</td>
<td>Microscopic anchoring system of root cement, alveolar bone and</td>
</tr>
<tr>
<td>connected to the contact surface by (hemi)desmosomes</td>
<td>desmodontal fibre apparatus</td>
</tr>
<tr>
<td>Microscopically, direct bone-implant contact</td>
<td>More fibroblasts and vessels subepithelialy</td>
</tr>
<tr>
<td>More collagen fibres and fewer fibroblasts/vessels</td>
<td>Dentogingival, dentoperiosteal, circular and transseptal</td>
</tr>
<tr>
<td>subepithelially</td>
<td>collagen fibre alignment</td>
</tr>
<tr>
<td>Depending on the number of dental extractions:</td>
<td></td>
</tr>
<tr>
<td>Collagen fibres aligned parallel to implant surface</td>
<td></td>
</tr>
</tbody>
</table>

ZITZMANN & BERGLUNDH, 2008; SCHWARZ et al., 2008

Differentiating manifest peri-implantitis from other inflammatory processes of the periodontium using markers in human saliva such as osteocalcin, TRAP, DKK-1, OPG and CatK is not precise (HALL et al., 2011).

2. Aetiology and epidemiology

Mucositis and peri-implantitis occur with a prevalence of about 63.4% and 5% to 47.1% respectively, with the large fluctuations attributable to different study designs and population sizes in the publications with varying risk profiles and calculation profiles (SCHWARZ et al., 2008; ATIEH et al., 2012; CHARYEVA et al., 2012; SCHLOTTIG, 2011; ZITZMANN & BERGLUNDH, 2008, Smeets et al., 2014a).

ZITZMANN & BERGLUNDH (2008) quantified the incidence of the development of peri-implantitis in patients with prior periodontitis as being almost six times higher than for patients with no previous history of periodontal inflammatory formations. After 10 years, between 10% and 50% of all implants showed signs of peri-implantitis (ROOS-JANSÅKER et al., 2007; BEHRENS et al., 2004). According to the consensus report of the sixth European Workshop on Periodontology, LINDHE & MEYLE (2008) reported the frequency of mucositis as being 80% and that of peri-implantitis as 28% to 56% among patients with implant restorations. The prevalence of peri-implantitis was corrected by MOMBELLI et al. (2012) to 20% of all implant patients and 10% of all implants. The correction downwards was explained by the fact that to correctly determine the prevalence, only those studies can be considered in which the bone loss relevant for the peri-implantitis was determined from the time the suprastructure was inserted (baseline). This led to the recommendation for carrying out radiographic imaging after inserting the suprastructure and using this as the foundation for future evaluation of any peri-implant bone losses. Spectra consisting of P. intermedia/nigrescens, S. constellatus, A. actinomycetemcomitans, P. gingivalis, T. denticola and T. forsythia among others have been verified as marker bacteria.
**Excursus 1 Marker bacteria in the subgingival biofilm**

<table>
<thead>
<tr>
<th>Complex</th>
<th>Marker bacterium</th>
<th>Characteristics</th>
</tr>
</thead>
</table>
| A       | *Actinobacillus actinomycetemcomitans* | • Complex-independent  
• Significant at almost every level  
• Produces toxin  
• Invasive |
| A       | *Porphyromonas gingivalis*     | • Obligate anaerobe  
• Primary periodontal pathogen  
• Has a great number of proteases  
• Heavily involved in collagen and antibody degradation |
|         | *Tannerella forsythensis*      | • Obligate anaerobe  
• Very important for the clinical progression of periodontitis  
• High level of protease activity  
• Produces volatile fatty acids |
|         | *Treponema denticola*          | • Obligate anaerobe  
• Periodontal pathogen  
• Degrades proteins  
• Produces volatile fatty acids |
| B       | *Campylobacter gracilis*       | • Microaerophile  
• Importance in periodontal processes speculative |
|         | *Campylobacter rectus*         | • Microaerophile  
• Is often isolated with periodontitis  
• Produces a cytotoxin (similar to leukotoxin; *A. actinomycetemcomitans*)|
|         | *Eubacterium nodatum*          | • Obligate anaerobe  
• Gram-positive  
• Potential periodontal pathogen  
• Cell count is elevated in periodontal processes |
|         | *Fusobacterium nucleatum*      | • Obligate anaerobe  
• Early coloniser |
|         | *Peptostreptococcus micros*    | • Obligate anaerobe  
• Relatively well established Gram-positive periodontal pathogen  
• Also present physiologically  
• Protein breakdown  
• Early marker |
| B       | *Prevotella intermedia*        | • Obligate anaerobe  
• Early marker bacterium  
• Creates the anaerobic environment for the primary pathogens by consuming oxygen  
• Easy and widespread colonisation of mucous membranes |
|         | *Prevotella nigrescens*        | • Obligate anaerobe  
• Important role in infections of the tooth root  
• Similar properties to *P. intermedia*  
• Role is hotly disputed |
Depending on the type and antibiotic, variable levels of resistance of the individual pathogens have been described (Tab. 2) (ZITZMANN & BERGLUNDH, 2008; RAMS et al., 2014). According to RAMS et al. (2014), of 120 patients a total of 71.7% displayed resistance against at least one active substance.

### Excursus 1 Marker bacteria in the subgingival biofilm

<table>
<thead>
<tr>
<th>Complex</th>
<th>Marker bacterium</th>
<th>Characteristics</th>
</tr>
</thead>
</table>
| C       | *Streptococcus gordonii*  | • Facultative anaerobe  
          |                           | • Early coloniser  
          |                           | • Considered physiological if isolated |
|         | *Streptococcus mitis*     | • Facultative anaerobe  
          |                           | • Considered physiological if isolated |
| D       | *Campylobacter concisius* | • Microaerophile  
          |                           | • Speculative importance |
|         | *Capnocytophaga gingivalis* | • Of importance in periodontal diseases that develop early (prepuberty) |
|         | *Eikenella corrodens*     | • Aerobe or facultative anaerobe  
          |                           | • Cell count is elevated in periodontal processes |
| E       | *Actinomyces odontolyticus* | • Physiological marker  
          |                           | • Anaerobe to microaerophile |
|         | *Actinomyces viscosus*    | • Physiological marker  
          |                           | • Anaerobe to microaerophile |
|         | *Veillonella parvula*     | • Obligate anaerobe  
          |                           | • Gram-negative  
          |                           | • Minimal periodontal pathogenic importance  
          |                           | • Catabolises lactic acid  
          |                           | • Possibly anti-cariogenic  
          |                           | • Increases the mineralisation of dental plaque to form calculus |

Bacteria in complex A are associated strongly with deep pockets and bleeding on probing (BOP), while bacteria in complex B have a significantly increased association with the pocket depth. The bacterial communities in complexes C, D and E can be classified as physiological in isolation and when diagnosed as a collective are possibly of importance in processes in periodontitis and peri-implantitis. Modified from Socransky (1998).
A fundamental difference to periodontitis is that, in addition to the known marker periodontal bacteria, *Staphylococcus aureus* in particular appears to play an important role in peri-implantitis. This bacterium has a high affinity for titanium and has a high positive (80%) and a high negative (90%) predictive value according to studies carried out by SALVI et al. (2008). The occurrence of peri-implantitis can be influenced by the surface properties of the implant shoulder. However, current data cannot conclusively confirm whether a rough or a smooth surface favours the development of peri-implantitis (DEGIDI et al., 2012, SCHLOTTIG, 2011, SUBRAMANI et al., 2009).

### 3. Risk factors and prevention

Implant losses are divided into those occurring within a window of up to one year (early implant loss) and those occurring after one year (late implant loss) (ZITZMANN & BERGLUNDH, 2008). Peri-implantitis usually leads to a late loss situation, whereas mechanostatic factors usually result in an early loss situation.

General risk factors for the development of peri-implantitis include (WALLOWY, 2012; SCHWARZ et al., 2008; CHARYEVA et al., 2012; HUYNH-BA et al., 2008; HEITZ-MAYFIELD, 2008; GRIJICA et al., 2004; LAGERVALL & JANSSON, 2013; LORENZ & KLANG, 2013; LINKEVICIUS et al., 2013, Smeets et al., 2014a):

- Inadequate patient compliance and ineffective oral hygiene. This includes failing to attend recall examinations following the implant placement.
- Nicotine abuse with additional and significantly higher risk for any complications if an IL-1 genotype is present as a polymorphism
- Systemic diseases (e.g. poorly controlled diabetes, immunosuppression)
- Prior gingivitis and periodontitis paying particular attention to the remaining teeth
- Soft tissue damage or qualitatively poor soft tissue at the site of the implantation (including a lack of keratinised gingiva)
- Iatrogenic causes (e.g. cementitis, the presence of periodontitis)
- History of one or more implant failures

Existing periodontitis and smoking status increases peri-implantitis by 4.7 to 4.6 times respectively (WALLOWY, 2012). Over an observation period of 10 years, previously eliminated bacterial strains of *A. actinomycetemcomitans* and *P. gingivalis* could be detected again on the oral mucosa of periodontitis patients (ZITZMANN & BERGLUNDH, 2008). On the other hand, *P. intermedia* was detected throughout. This suggests that the bacteria survive in niches with the reappearance of the same microflora as before the extraction, whereas resective therapeutic procedures (gingivectomy and open curettage) with existing periodontitis led to consistently low level immune responses at the extraction site compared to non-resective procedures (open root planing). In particular, the remaining teeth must be considered a potential source of infection during therapy procedures. For diagnostic purposes, the matrix metallope-

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**Table 2: Antibiotic resistance**

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clindamycin</td>
<td>46.7%</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>39.2%</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>25.0%</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>21.7%</td>
</tr>
<tr>
<td>Amoxicillin &amp; metronidazole</td>
<td>6.7%</td>
</tr>
</tbody>
</table>

Antibiotic resistance in *Prevotella intermedia/nigrescens* and *Streptococcus constellatus* (n=120) (RAMS et al., 2014)
Elastase-8 (MMP-8) may be elevated by up to 971% in peri-implantitis compared to healthy teeth (Xu et al., 2008; Sorsa et al., 2011; Sorsa et al., 2010). Peri-implantitis induced by ‘cementitis’ occurs in almost one in 5 implants, with removal of the residual cement leading to reduction in the inflammatory reaction of almost 60% (Korsch et al., 2014). Regarding residual cement, Linkevicius et al. (2013) demonstrated obligatory development of peri-implantitis in a patient collective with a history of periodontitis (100%). In patients with no history of periodontitis, residual cement favours the development of peri-implantitis in 65% of cases. Differentiation using characteristic probing pocket depths must be considered an obligatory cofactor (Schwarz & Becker, 2013; Heitz-Mayfield, 2008). Any probing should use minimal force while noting that ‘platform switch’ abutments, in which the abutment diameter is less than that of the implant diameter, make probing more difficult and can thus conceal the true extent of peri-implantitis (Schlot Tig, 2011; Al-NSour et al., 2012).

Implant losses due to the following additional factors must be differentiated (Zitzmann & Berghlund, 2008; Wallowy, 2012; Schwarz et al., 2008; Flanagan et al., 2009; Mahnاما et al., 2013; SteigenGa et al., 2003; Georgiopoulos et al., 2007; Smeets et al., 2014a):

- Overloading of the implant
- Material defects, technical faults and incorrect choice of material taking into account essential factors that determine the success of the implant
- Inadequate availability or qualitatively poor bone at the implantation site
- Systemic diseases and pharmacotherapy that suppress bone modulation in accordance with Wolff’s law (bone density and strength increase with load and vice versa) and the mechanostatic theory

Thus implants > 10 mm with a square thread design have higher success rates than smaller implant lengths or shapes without a thread or sawtooth thread (SteigenGa et al., 2003; Georgiopoulos et al., 2007). Rough implant surfaces of > 2 µm also appear to have better osseointegration than smooth (< 0.5 µm) or moderate surfaces (1–2 µm) although more studies are required because of controversial findings (Schlottig, 2011).

With forces of more than 1300 Newton developing in the jaw joint, in the first few months healing implants can be shifted or moved by an average of 100 micrometres even with sagittally directed forces of just 50 N on average (Flanagan et al., 2009). These mean reference forces increase to 87 N with articulation angles of up to 60° in the horizontal.

As another preventive measure, implant systems with an internal junction and a microgap displaced inwards are preferable (Fig. 2) (Wallowy, 2012). However, the most important criterion remains best hygienic practice and consideration of all surgical preventive measures.
The effect of the microarchitecture of the different implant shoulder designs on the crestal bone level and the appearance of plaque accumulations are also discussed (HERMANN et al., 2011; SUBRAMI et al., 2009). Implant systems with microstructured shoulder zones are intended to create favourable factors for bone regeneration because of the rough surface and are therefore associated with reduced crestal bone loss (HERMANN et al., 2011) (Fig. 3; B, b). Machined implant shoulders, on the other hand, are intended to minimise plaque accumula-
tion and the associated risk of infection in comparison to rough surfaces (SUBRAMI et al., 2009; QUIRYNEN et al., 1996) (Fig. 3; A, a).

A recent Close Up review work by FIENITZ (2014, accepted) concluded that for endodontic implants a compromise between rough surfaces that encourage bone regeneration and smooth surfaces that are more resistant to biofilms must be found in accordance with the experience of the dentist and patients’ requests and compliance while taking into account other risk factors in peri-implantitis processes.

As well as providing advice and training patients in the best oral hygiene techniques, professional teeth cleaning and individually organised recall examinations at short intervals must be initiated as preventive measures (Tab. 3) (WALLOWY, 2012). In particular, reducing the risk factors listed above such as heavy smoking or diabetes mellitus must also be taken into consideration.

| Table 3: Number of recall examinations (RE) for particular patient collectives |
|---------------------------------|----------------|----------------|
|                                 | RE = 1 | RE = 2 | RE > 1 |
| Oral hygiene and ability to maintain hygiene of the implant | Good | Moderate | Poor |
| Smoking status | / | History | Given |
| Periodontitis, mucositis (with history) | / | / | Given |
| Other risks | / | / | Including systemic diseases, history of failed implant restoration |
So-called reference parameters (‘zero hour’) and clear follow-up processes with detailed documentation are essential for holistic therapy and recall examinations. Pre-, intra- and post-implant radiographic examinations must be used as reference parameters when recording the intra-implant site in which peri-implant inflammatory processes can be seen as radiolucent zones with respect to elevated bone resorption rates (WALLOWY, 2012). A recall examination should include determining the probing pocket depths and settling the next appointment along with advice, training and professional teeth cleaning. Bleeding, swelling and redness observed during the macroscopic manual probing suggest by definition possible peri-implantitis.

4. Therapy

As part of the therapeutic concept, the dentist must differentiate between a surgical and a nonsurgical approach with synergistic therapy plans an option depending on the case.

4.1. Conservative therapy

As well as pharmacotherapy and manual therapy forms (Teflon, carbon, plastic and titanium curettes, ultrasound and air-powder abrasive systems), innovative techniques such as laser-supported and photodynamic therapy can be used. In this regard, therapy using ultrasound or curettage deliver consistently worse results than treatments using air-power abrasive systems (SCHWARZ et al., 2008; TASTEPE et al., 2013; TASTEPE et al., 2012; PERSSON et al., 2010; RENVERT et al., 2009; SAHM et al., 2011; LOUROPOULOU et al., 2013; KARRING et al., 2005; Smeets et al., 2014a). PERSSON et al. (2010) and RENVERT et al. (2009) recorded significantly lower bacteria counts in some cases with a partial reduction in the plaque and bleeding scores after mechanical curettage, while SCHWARZ et al. (2008) reported 30% fewer residual biofilm areas with ultrasound treatments. Depending on the surface topography, different therapy approaches can be pursued. (Tab. 4).

<table>
<thead>
<tr>
<th>Smooth surface</th>
<th>Sandblasted and acid-etched surface (SLA)</th>
<th>Plasma-sprayed surface</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rubber cap</td>
<td>o</td>
<td>o</td>
</tr>
<tr>
<td>Curette made of metal; rotary titanium brushes</td>
<td>o</td>
<td>x</td>
</tr>
<tr>
<td>Curette made of plastic</td>
<td>o</td>
<td>o</td>
</tr>
<tr>
<td>Ultrasound systems with metal tips</td>
<td>o (polished)</td>
<td>o</td>
</tr>
<tr>
<td>Ultrasound system with plastic tips</td>
<td>o</td>
<td>x</td>
</tr>
<tr>
<td>Air-powder abrasive systems</td>
<td>x</td>
<td>x</td>
</tr>
</tbody>
</table>

Qualitatively determined effectiveness (x: yes/o: no) of various debridement methods depending on the titanium surface (LOUROPOULOU et al., 2013; Smeets 2014a).
The treatment outcome for air-powder abrasive systems, which are classified overall as effective, is dependent on the powder used with significantly better results achieved in the order hydroxyapatite/tricalcium phosphate, hydroxyapatite, glycine powder > titanium dioxide > water and air (control group) > phosphoric acid (TASTEPE et al., 2013). Abrasive powders can modify the surface of implants and form residues, while the cellular adhesion behaviour with lower cell response is preserved (TASTEPE et al., 2012, SAHM et al., 2011). The rate of re-osseointegration of titanium implants after air-powder abrasion is given as between 39% and 46% with an increase in the clinical implant attachment and a reduction in the pocket depth (TASTEPE et al., 2012). The occurrence of bleeding, one of the qualitative parameters for the presence of peri-implantitis, is not reduced (SAHM et al., 2011).

4.1.1 Pharmacotherapy

In vitro and in vivo studies of the pharmacotherapy of mucositis and peri-implantitis are numerous with contradictory results in some cases. Definitively stating the efficacy of a certain therapy or a certain antibiotic is not possible due to the poor comparability between the studies which is a result of the different study designs. The following three areas can be roughly differentiated:

1. Administration of systemic and local antibiotics taking into account the pocket depth
2. Administration of systemic and local antibiotics taking into account parameters other than those listed above
3. Disinfectant rinsing with reference to different parameters

In a review by JAVED et al. (2013) that referred to nine studies, systemic and local application of antibiotics (e.g. tetracycline, doxycycline, amoxicillin, metronidazole, minocycline hydrochloride, ciprofloxacin, sulfonamides + trimethoprim) led to significant reductions in the probing pocket depths over a period of between one and six years. The same phenomenon was observed by MOURA et al. (2012) for resorbable nanospheres that release doxycycline applied locally over a period of 15 months. LEONHARDT et al. (2003) reported an overall success rate of 58% for various systemic antibiotics and combinations of antibiotics after surgical exposure and debridement of the implant surfaces. ASTASOV-FRAUENHOFFER and colleagues (2013) detected complete growth inhibiting effects for the 10× MICs (minimum inhibitory concentrations) of amoxicillin and metronidazole on S. sanguinis and P. gingivalis with no combinations of active substances being able to achieve better results. BASSETTI et al. (2013) were not able to identify any differences in terms of the reduction in the probing pocket depths or reductions in the bacterial count in the dental pockets in a comparison of local...
administration of antibiotics and photodynamic therapy. Grapefruit juice, which is a known antioxidant, only acted bacteriostatically against S. aureus (SHRESTHA et al., 2012).

Rinses and applications of chlorhexidine led to a reduction in the probing pocket depths, greater implant adhesion and a general lessening of the inflammation for the inflammation parameters IL-1 beta, VEGF and PGE-2 in various studies (MACHTHEI et al., 2012; WAAL et al., 2013; DI CARLO et al., 2008). Compared to doxycycline, chlorhexidine led to significantly smaller reductions in the probing pocket depths (RENVERT et al., 2008; RENVERT et al., 2006).

With tissue engineering, LAN et al. (2013) demonstrated continuous release kinetics for metronidazole over 30 days using poly-ε-caprolactone/alginate rings. HOU et al. (2011) incorporated fluorouracil into cylindrical poly-ε-caprolactone implants of various diameters.

4.1.2 Laser therapy

With the advantage of having a bactericidal mode of action, CO₂, diode, Er:YAG (erbium-doped yttrium aluminium garnet) and Er,Cr:YAG (erbium, chromium-doped yttrium aluminium garnet) lasers are increasingly used to treat peri-implantitis but absorption and reflections must be minimised to protect materials and tissue. Er:YAG and Er,Cr:YAG wavelengths in a spectrum of 3 µm can reduce biofilms by up to 90% although possible biocompatibility and cell stimulating properties can be compromised, unlike most mechanical therapy approaches (SCHWARZ et al., 2008, YAMAMOTO & TANABE, 2013; SCHWARZ et al., 2006). Irradiation with a CO₂ 308 nm excimer laser produced satisfactorily effective results, mostly in the anaerobic bacterial spectrum (DEPPE et al., 2007).

Compared to mechanical treatment using plastic curettes, treatments with an Er:YAG laser produced significantly better results for the bleeding incidents with peri-implantitis, although probing pocket depths, clinical attachment level, plaque index and gingival recession did not differ significantly from one another for the two types of therapy but did improve compared to the baseline values (SCHWARZ et al., 2006) (Fig. 4).

PERSSON et al. (2011) investigated the effectiveness of Er:YAG lasers compared to a air-powder abrasive system: P. aeruginosa, S. aureus and S. anaerobius), after 6 months no long-term reductions were observed.

4.1.3 Photodynamic therapy

Reactive oxygen species are generated by multiplicity using high-energy single-frequency light, e.g. from diode lasers, combined with photosensitisers (e.g. toluidine blue). In a wavelength range of 580 to 1400 nm and toluidine concentrations between 10 and 50 µg/mL, photodynamic therapy developed bactericidal effects against aerobic and anaerobic bacteria (A. actinomycetemcomitans, P. gingivalis, P. intermedia, S. mutans, E. faecalis) (SCHWARZ et al., 2008; AL-AHMAD et al., 2013; MEISEL & KOCHER, 2005). In a study by DEPPE et al. (2013) on the effectiveness of phototherapy in the treatment of moderate to severe peri-implantitis, both the clinical attachment loss and the bleeding index were significantly reduced although more severe courses continued to exhibit bone resorption. For this reason, photodynamic therapy approaches should only be used for less advanced stages.

4.1.4 Treatment of mucositis

Taking into account the non-surgical therapy approaches discussed above, the treatment of mucositis as part of a general improvement in oral hygiene is divided into mechanical implant debridement (titanium and plastic curettes, ultrasound, air-powder abrasive systems, photodynamic therapy), oral (chlorhexidine gluconate, fluoride, hydrogen peroxide, sodium percarbonate) and local (e.g. povidone-iodone) antiseptic measures.

In two randomised clinical trials (HEITZ-MAYFIELD et al., 2011, HALLSTRÖM et al., 2012), anti-infective measures (chlorhexidine and Azithromax® (macrolide)) did not show any advantages compared to the relevant control group for the reduction of probing pocket depths, plaque index or suppuration. Reductions in the bleeding index were attributed to the general improvement in oral hygiene with reference to the potential importance of guidelines or treatment protocols (HEITZ-MAYFIELD et al., 2011; HALLSTRÖM et al., 2012; ZEZA & PILLONI et al., 2012).
4.2. Surgical therapy

Surgical therapy combines the non-surgical forms of therapy discussed above with resective and regenerative surgical approaches. The indication for therapy and the surgical approach itself have been demonstrated in patient trials (Tab. 5, 6) and among other items were assessed using the Cumulative Interceptive Supportive Therapy (CIST) concept (RUTAR et al., 2001; SCHMAGE, 2010; Smeets et al., 2014a).

According to the entire body of trial data, autologous, allogeneic and xenogeneic biomaterials are often used as augmentation materials for bone defects in terms of jaw surgery augmentation approaches, with allogeneic and xenogeneic transplants found to be almost equivalent to autologous material (FISCHER et al., 2011; KOLK et al., 2012; SMEETS & KOLK, 2011; Smeets et al., 2014b,c,d).

Table 5: Selection of clinical trials on surgical therapy of peri-implantitis

<table>
<thead>
<tr>
<th>Author</th>
<th>Methods</th>
<th>Results</th>
</tr>
</thead>
</table>
| Schwarz 2006    | Treatment of bone defects of 22 patients with xenogeneic bone and a collagen membrane (group 1) or hydroxyapatite and a collagen membrane (group 2) over 6 months | Group 1:  
  • Probing pocket depth: 7.0±0.6 to 4.9±0.6 mm  
  • Clinical attachment: 7.5±0.8 to 5.7±1.0 mm  
  Group 2:  
  • Probing pocket depth: 7.1±0.8 to 4.5±0.7 mm  
  • Clinical attachment: 7.5±1.0 to 5.2±0.8 mm |
| Roos-Jansäker 2007 | Comparison between:  
  • Group 1 (n=17): Algipore + membrane (Osseoquest)  
  • Group 2 (n=19): Algipore | Reduction in the probing pocket depth by 2.9 (group 1) and 3.4 mm (group 2) with defect filling of 1.5 and 1.4 mm respectively |
| Aghazadeh 2012 | Comparison between autologous (AG, n=23) and xenogeneic bone substitute (XG, n=22) in terms of:  
  • Bleeding index  
  • Probing pocket depth  
  • Bone growth | XG significantly better than AG and baseline |
| Schwarz 2012    | Treatment of bone defects of 24 patients with xenogeneic bone and a collagen membrane after defect cleaning with:  
  • Group 1 (n=12): Er:YAG laser  
  • Group 2 (n=12): Plastic curettes, cotton pellets, saline solution | Group 2 with significantly better bleeding index compared to group 1 and baseline |
| Wiltfang 2012   | 22 patients treated with a mixture of autologous and xenogeneic bone substitute | Mean probing pocket depth reductions of 3.5 mm |
| Mijiritsky 2013 | Treatment of 18 implants with titanium granulate with measurement of effect after 6 to 15 months | Bone ingrowth of 2.1 mm on average |
| Matarasso 2014  | Treatment of 11 implants with demineralised bovine bone matrix and collagen matrix subcristally and smoothing of supracrestal implant surface. Evaluation after 12 months | Significant changes:  
  • Probing pocket depth: 8.1±1.8 to 4.0±1.3 mm  
  • Clinical attachment: 9.7±2.5 to 6.7±2.5 mm |

Selection of clinical trials on surgical therapy of peri-implantitis
Table 6: CIST protocol

<table>
<thead>
<tr>
<th>Step</th>
<th>Findings</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Total failure: Implant failure, primary complication &lt; 6 months; bone loss along more than 2/3 of the implant length</td>
<td>Explantation</td>
</tr>
<tr>
<td>1</td>
<td>Infection due to foreign body (cementitis)</td>
<td>Mechanical debridement, polishing</td>
</tr>
<tr>
<td>2</td>
<td>Mucositis                    PPD &gt; 3 mm with no radiological bone loss</td>
<td>Mechanical debridement, polishing, disinfection with CHX</td>
</tr>
<tr>
<td>3</td>
<td>Mild peri-implantitis        PPD &gt; 4 mm</td>
<td>Mechanical debridement, polishing, disinfection with CHX, systemic antibiotic therapy (metronidazole 3x400/d + 3x/500/d amoxicillin) for 7 d</td>
</tr>
<tr>
<td>4</td>
<td>Advanced peri-implantitis    PPD &gt; 5 mm</td>
<td>Surgical intervention: Expose site, remove calculus and biofilm, smooth the implant surface, insert bone substitute to stabilise the defect, membrane and close tightly, particularly around the implant, antibiotic therapy with metronidazole + amoxicillin</td>
</tr>
</tbody>
</table>

PPD: Probing pocket depths

In a retrospective study by LAGERVALL et al. (2013) with 150 patients (382 implants), the type of operation most used was periodontal flap surgery with osteoplasty (47%) followed by the use of bone substitutes (20%). For both procedures a cumulative success rate of 69% was recorded which was significantly lower for patients with risk factors such as smoking, periodontitis and poor oral hygiene.

5. Conclusion

In summary, the number of studies and the in part contradictory results make a conclusive evaluation of the ‘ideal peri-implantitis therapy’ difficult.

As the simplest instrument, prevention with recall examinations at short intervals should be given the highest priority. Various risk factors regarding the patient and the treating dentist must be taken into account here. As well as smoking status, poor oral hygiene and comorbidities (e.g. periodontitis, systemic infectious diseases, bone diseases), the dentist must pay attention to possible factors such as remaining teeth, cementitis, choice of implant, bone status, familiarity with the handling of dental implants and recall examinations at short intervals.

For non-surgical therapy, combinations of mechanical debridement with metal curettes and air-powder abrasive systems (e.g. hydroxyapatite + tricalcium phosphate) in particular must be considered promising. These measures can be supplemented by systemic antibiotic combination therapies. Laser or photodynamic therapy has produced less promising results and should primarily be used in a supportive role or in less advanced cases.

Based on the non-surgical therapy, surgical approaches add to the therapy regime with resective and regenerative procedures. The bone substitute materials used here (e.g. BEGO OSS or BEGO
Collagen Membrane) can be considered good materials that are almost equivalent to autologous bone substitute.

In the absence of guidelines, the CIST protocol must be considered a definitive guide whereby scrupulous incorporation of all existing risk factors must be considered.

The ideal peri-implantitis therapy must therefore be considered a multifactorial therapy regime that occasionally must draw on individually tailored treatment models in order to accommodate the diversity of the multifactorial genesis, therapy options and study results.

### Literature

- You can find the full list of references here.
Self-tapping, conical, modern, bionic

BEGO SEMADOS®
RS/RSX Implants

- FLEXIBLE: One surgical tray for both systems – facilitates an intraoperative system change
- CUSTOMISED: Machined (RS-Line) or microstructured (RSX-Line) shoulder with platform switch, according to the preference of the dentist
- MODERN: Bionically optimised microgrooves (patent pending) – for reduction of stress peaks in the bone and enlargement of the implant surface
- QUICK AND EASY: Self-tapping thread design with optimal cutting angle – self-centring function makes it easy to use and quick to insert with just a few turns

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Partners in Progress
Bionic requirements for the implant design of modern systems
von See C.

As well as functional aspects, implant patients expect immediate relief as well as an aesthetic provisional restoration in light of the unquestionable success of promising implant therapy. These high demands also mean that there a new suite of requirements for the implant design itself. Superior surface quality, primary stability and good osseointegration in particular are among the desired system features. Professor Constantin von See explains the various parameters that characterise a modern implant design in detail in the following article.

Further literature
SHOULDER DESIGN

Machined versus microstructured implant shoulder – Which is better?

Dr Tim Fienitz, Clinic for Oral, Maxillary and Facial Plastic Surgery, University Hospital Cologne

Abstract

The majority of the implants currently available on the dental market have good and comparable implant survival rates. In light of this, the aesthetic outcomes when using different implant systems is becoming increasingly important. The aesthetic outcomes are essentially determined by the surrounding soft tissue which is in turn directly dependent on the crestal bone level. The crestal bone level can be affected by the macroarchitecture of the implant body as well as the microarchitecture of the implant surface. This review article examines the importance of the implant shoulder with special consideration of the surface properties in this area using a recent literature review.

A microstructured implant shoulder appears to have a positive effect on the crestal bone resorption, whereas a machined implant shoulder is associated with a reduced risk of infection if the implant is exposed to the oral cavity because there is less plaque accumulation. On the basis of the current body of trial data, no clear statement can be made about the superiority of one particular type of implant shoulder and the choice of one of the two options should be made taking the patient’s individual situation into consideration.

Key words: Implant shoulder, machined, microstructured, platform switching
1. Dental implants in the dental practice

Implant dentistry is an important area in the dental practice. With the help of dental implants, fixed restorations can be prepared that maximise patients’ comfort. Individual teeth can be restored using implants and implant-borne bridge constructions can also be anchored. With prosthetic restoration using implants, preparing clinically normal adjacent teeth can also be avoided. Edentulous patients can also be treated with fixed restorations using implants.

‘All implant-borne prosthetic solutions require a stable implant integrated into the jaw bones that bears the resultant chewing forces. The bony integration of dental implants can be influenced by various factors. As well as factors related to the patient such as smoking behaviour and oral hygiene, implant-specific properties can also affect the bony integration. These factors include both the microarchitecture of the implant in terms of the surface properties as well as the macroarchitecture or the implant design. In this context, great importance is attached to the implant shoulder and its effect on crestal bone loss.

2. Macroarchitecture of dental implants / implant design

Dental implants come in a variety of designs that enable the individual patient situation as well as the preferences of the dentist to be considered. There is a choice between
- different implant lengths and widths
- a cylindrical or conical shape
- one-part or multi-part implant systems
- or a different number and arrangement of the thread grooves.

The choice of implant length is usually determined by the patient’s individual bone situation and the location of the inferior alveolar nerve in the mandible. In compromised bone situations, shorter or reduced diameter implants can be also be used to avoid bone augmentation or nerve lateralisation with the associated risk of complications. Shorter implants (< 10 mm) have been described as being more susceptible to failure (MISCH, 2005). Diameter-reduced mini implants (< 3 mm) initially have comparable survival rates to standard implants but the long-term survival rates of these implants have not yet been adequately demonstrated (BIDRA et al., 2013).

Both the implant diameter and the length and angle of the implant neck appear to have a critical influence on the loads that develop at the contact point between the cortical bone and the implant surface (bone-implant interface) (FAEGH et al., 2010). An increase in the implant diameter, a longer implant neck and a positive implant neck angle, that is, an increase in the diameter towards the implant tip, can reduce the loads developing between the two surfaces, for example (FAEGH & MUFTU, 2010).

The choice between one- or two-part implant systems depends primarily on the patient’s individual indication. Two-part implant systems are made up of an implant screw that is inserted into the bone and is located beneath the gingiva and an abutment that acts as a connective element between the implant and the crown construction. With one-part systems, the implant itself includes a connection to the prosthetic restoration that protrudes above the gingiva after implant placement. One-part implants are therefore particularly suitable for cases in which immediate loading is desired, whereas in most cases two-part implant systems are exposed only after an initial healing phase and at this later point an abutment can be attached. Studies that compare the advantages and drawbacks of the two systems in terms of the influence of both systems on the surrounding hard and soft tissues show very different results in some cases (for a review: PRITHWIRAJ et al., 2013). While some studies have described less bone loss and a smaller reduction in the biologic width for one-part systems (HERMANN et al., 2001), other studies have found a lower success rate and an increase in bone resorption for one-part implant systems (OSTMAN et al., 2007; ZEMBIC et al., 2012). One reason for this discrepancy may lie in the fact that the implants used in the individual studies differ not only as to whether they are one- or two-part implant systems but also in terms of other properties which therefore makes a direct comparison between the studies difficult.
2.1 Biologic width

The biologic width mentioned previously is an increasingly important dimension in the area of implant dentistry. While only the bony healing of the entire implant was usually noted in the past, improvements in implant survival rates have also increased the demands placed on the aesthetics, which are fundamentally determined by the surrounding soft tissue. The biologic width of natural teeth differs only slightly from the biologic width of implants. With natural teeth the area between the highest contact point of the gingiva to the tooth crown and the highest point on the alveolar bone is referred to as the dentogingival complex. This complex is made up of the sulcus (0.2–0.5 mm) and the biologic width, which can in turn be divided into the epithelial attachment (about 1 mm) and the connective tissue attachment (about 1 mm). This complex has a primarily protective function and is intended to effectively delineate the underlying tissue from the oral cavity by means of the connective tissue fibres and the epithelium (SICHER, 1959). The fibres of the connective tissue attachment on the natural teeth have a three-dimensional arrangement (FENEIS, 1952) along and across the tooth axis, whereas the connective tissue fibres of the biologic width of implants only run parallel to the longitudinal axis of the implant (BUSER et al., 1992; BERGLUND-DH et al., 1991) (Fig. 1). It has been demonstrated that the height of the dentogingival complex of about 3 mm (GARGIULO et al., 1961) is relatively constant and with a stable dentogingival complex a change in the alveolar bone height leads to a corresponding change in the gingival height. For implant dentistry this means that a reduction in the crestal bone at the implant results in regression of the gingival height and thus an aesthetically unappealing exposure of the implant neck. With two-part implant systems, a dependency between crestal bone resorption and the location of the microgap has been observed in this context (HERMANN et al., 1997; HERMANN et al., 2000). This microgap develops between the implant shoulder and the attached abutment. The design of the implant shoulder and the seated abutment can alter the location of the microgap and thus directly influence the crestal bone resorption.

Fig. 1: The biologic width on natural teeth and implants

The dentogingival complex has a protective function

The connective tissue fibres and the epithelium form the junction to the oral cavity. The fibres in the connective tissue on natural teeth are arranged three dimensionally along and across the tooth axis. In the connective tissue of the biologic width around an implant, the fibres run parallel to the longitudinal axis of the implant. This parallel fibre arrangement affects the protective function of the dentogingival complex.
2.2 Platform switching

Platform switching is one method that takes into consideration the dependence of the crestal bone resorption on the location of the microgap to improve the marginal bone situation. A two-part dental implant is used with an abutment that has a smaller diameter. This displaces the microgap between the implant and the abutment horizontally from the outer wall of the implant to the centre of the implant. Several studies observed reduced marginal bone resorption in this context in both animal studies (BECKER et al., 2009) and in patients (ATIEH et al., 2010) which was lower the greater the size difference between the implant and abutment.

Various reasons have been proposed to explain the curbing of the marginal bone loss through platform switching.

- The space available for the tissue in the biologic width may be optimised by the platform switching (DEGIDI et al., 2008)
- The inflammatory connective tissue around the implant abutment connection is displaced horizontally to the centre of the implant (LUONGO et al., 2008)
- The area of maximum biomechanical load is displaced towards the implant axis (CHANG et al., 2010)

A systematic review by Annibali and colleagues (ANNIBALI et al., 2012) confirmed the reduced marginal bone resorption on dental implants. However, no noteworthy difference was demonstrated between implants with and without platform switching regarding the implant survival rates.
Along with the design and the location of the implant shoulder, considerable importance must also be attributed to the surface properties in terms of the crestal bone loss. In principle, the implants currently available can be divided into implants with machined implant shoulders (Fig. 5 & 3) and implants with microstructured implant shoulders (Fig. 4 & 5) in which the largely rough implant surface covers the entire implant. In contrast to the different surface properties of the implant shoulder, these days the remaining surface is roughened in almost all titanium implants using various procedures. This is done to modify the surface properties to favour cell adhesion because slower rates of colonisation by cells have been observed for untreated smooth titanium surfaces compared to roughened surfaces (NISHIMOTO et al., 2008). Furthermore, it has also been observed that osteoblasts are highly sensitive to increased surface roughness and the production of various growth factors is elevated. This means that shorter healing times are needed before the final implant loading and that smaller implants than usual can be used (NASATZKY et al., 2003).

The procedures that can be used to modify implant surfaces include:
- anodic oxidation
- mechanical blasting with various particles (e.g. titanium oxide, aluminium oxide, hydroxyapatite) and chemical etching with various acids (e.g. hydrochloric acid, hydrofluoric acid)
- combinations of mechanical and chemical procedures

Along with modifying the implant morphology, these procedures can also create a more hydrophilic implant surface. An increase in the hydrophilicity was demonstrated to be another factor favouring initial adhesion of bone cells (WATANABE et al., 2012).

For implants with microstructured implant shoulders, the focus is on the concept of encouraged formation of new bone on rough surfaces around the implant shoulder as well and an associated reduction in the marginal bone loss. This result was observed in various studies. Sandblasted and acid-etched titanium implants without machined implant shoulders have less peri-implant crestal bone loss compared to implants with machined shoulders (HERMANN et al., 2011). A similar study even observed marginal bone ingrowth with the microstructured SLA® implants and bone loss with the machined implants after one year (VALDERRAMA et al., 2010). In this context, that the
marginal bone loss is lower the smaller the machined shoulder also applies to machined implants. One study in which the same implant system was investigated with different machined implant shoulders (0.4 mm and 1.6 mm respectively) showed that the implants with the smaller machined implant shoulders had significantly less marginal bone loss and greater bone-to-implant contact (BIC) (SCHWARZ et al., 2008). These advantageous effects on the formation of bone are, however, accompanied by an increased risk of plaque colonisation. This risk is particularly high if there are complications during wound healing and the implant shoulder is exposed to the bacterial flora in the oral cavity. In this context, a review article by Subramani and colleagues (2009) concluded that an increase in the surface roughness of implants and abutments is associated with an increase in biofilm formation. In terms of the subgingival plaque, an accumulation 25-times higher on rough surfaces compared to smooth surfaces was measured (QUIRYNEN et al., 1996). The resultant biofilm is often responsible for inflammations in the oral cavity such as gingivitis, peri-implantitis or periodontitis and its formation should therefore be prevented as far as possible (DHIR, 2013). To reduce the risk of peri-implantitis, which can ultimately lead to the loss of the implant, a rough implant shoulder and abutment surface should be avoided in addition to the classic risk factors such as smoking and poor oral hygiene (QUIRYNEN et al., 2002). Unlike with abutments, which are regularly exposed to the oral cavity and the bacterial flora living in it, for endodontic implants a compromise between a rough surface that encourages the formation of bone and a smooth surface that is more resistant to biofilm formation must be found.

4. Conclusion

Based on the current body of trial data, the question of whether machined or microstructured implant shoulders are preferable for implant dentistry cannot be answered adequately. Microstructured implant shoulders appear to have an advantage in terms of the marginal bone resorption because the rough surface that encourages the formation of bone continues to the implant shoulder. Machined implant shoulders have lower plaque accumulation and are thus associated with a lower risk of infection if the healing proceeds with complications, including exposure of the implant.

The choice between implants with machined or microstructured implant shoulder should therefore be made based on the experience of the dentist and also depends on the patient’s wishes and compliance as well as the oral hygiene status of the patient.

Literature

- You can find the full list of references here.
# CLINICAL CASE STUDY

## Navigated implant placement with simultaneous sinus lift

Dr med. dent. Sebastian Stavar, MSc. Oral Implantology Houten, Netherlands

### Indication profile

<table>
<thead>
<tr>
<th>Background and focus of the case</th>
<th>Guided implantation with simultaneous sinus lift tooth 26 and region 44–47 with simultaneous horizontal alveolar ridge augmentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
<td>Male □ Female ☒</td>
</tr>
<tr>
<td>Age</td>
<td>56 years</td>
</tr>
<tr>
<td>Indication profile</td>
<td></td>
</tr>
<tr>
<td>Area</td>
<td>Maxilla ☒ Mandible ☒</td>
</tr>
<tr>
<td>Aesthetic zone</td>
<td>Non-aesthetic zone ☒</td>
</tr>
<tr>
<td>Single tooth restoration</td>
<td>Restoration of several teeth ☒</td>
</tr>
<tr>
<td>Bone situation</td>
<td>No bone defect ☒ Bone defect ☒</td>
</tr>
<tr>
<td>Augmentation and implant placement</td>
<td>Augmentation before implant placement □</td>
</tr>
<tr>
<td>Soft tissue</td>
<td>Note: adequate keratinised gingival situation in the maxilla and the mandible</td>
</tr>
<tr>
<td>Prosthetic concept</td>
<td>Single tooth crown screwed onto 26, bridge screwed onto 44–47</td>
</tr>
</tbody>
</table>

### Figures

**Figure 1: Initial situation in the maxilla**
- Occlusal view.
- Planned implant position in region 26.

**Figure 2: Initial situation in the mandible**
- Occlusal view.
- Planned implant position in regions 44, 46 and 47.

**Figure 3: Trial of the drilling guide in the maxilla**
- Perfect fit of the drilling guide in situ.

**Figure 4: Sinus floor elevation**
- Elevated Schneiderian membrane.
Figure 5: Filling the maxillary sinus
Positioning the drilling guide after inserting the volume-stable bovine bone substitute BEGO OSS in the sinus.

Figure 6: Implant bed preparation
Guided preparation of the implant bed using the BEGO Guide RS/RSX-Line tray.

Figure 7: Final augmentation of the vestibular maxillary sinus
Over-augmentation of the maxillary sinus after insertion of the implant via the lateral window.

Figure 8: Tension-free wound closure
Occlusal view after wound closure.

Figure 9: Postoperative radiograph of region 26
Postoperative follow-up radiograph. Optimal implant position and location of the augmentation material.

Figure 10: Incision in the mandible
Crestal incision through the sulcus of the adjacent teeth to avoid a mesial relief incision. Preparation of a mucoperiosteal flap.
Figure 11: Trial of the drilling guide in the mandible
Drilling guide in situ.

Figure 12: Preparation of the implant bed using reduction sleeves
Preparation of the implant bed through the drilling guide with the help of the BEGO Guide RS/RSX-Line tray.

Figure 13: Implant placement
Implant placement at position 44 through the drilling guide with the help of the BEGO Guide Connectors with depth stop.

Figure 14: Implant position
Implants region 44 and 46 in situ.

Figure 15: Augmentation
Minimal buccal bone level in regions 44 and 46. Defect lies outside the alveolar ridge. Opening of the medullary cavity using multiple drill holes for bleeding in the defect space.

Figure 16: Augmentation
Augmentation of the buccal defect with the volume-stable bovine bone substitute BEGO OSS and coverage with a BEGO Collagen Membrane.
Case report

**Conclusion**

In this clinical case the virtual implant planning was transferred to a fully navigated drilling guide. There were no problems associated with the clinical and intraoperative handling. The dental support and the exact fit of the BEGO Guide drilling guide enabled safe insertion of the implants in the maxilla and mandible in accordance with the plan. Using the BEGO Guide Connector, the implant can be precisely inserted through the drilling guide and thus completes the precise implementation of the preoperative implant planning.

**References and further reading**

- Rothamel D, Fienitz T, Gerstenberg M, Hofmaier, F, Zöller JE. Initial formation of new bone after critical-size calvarial augmentation with sintered and non-sintered bovine bone substitute (Initiale Knochenneubildung nach critical-size Kalotten-Augmentation mit gesinterten und nicht gesinterten bovinen Knochenersatzmaterialien.) German Association of Implantology (Deutsche Gesellschaft für Implantologie, DGI), poster presentation 2014

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**Figure 17: Positioning of the collagen membrane**

Positioning of the collagen membrane over the augmentation material and fixation with titanium pins.

**Figure 18: Tension-free wound closure**

Tension-free wound closure for primary healing and problem-free integration of the augmentation material.

**Figure 19: Postoperative follow-up radiograph**

Implant position in region 44, 47 at crestal level – slightly subcrestal positioning at 46. The vestibular defect filled with bone substitute at 46 cannot be seen because of the limitations of a two-dimensional panoramic radiograph.

**Figure 20: Suture removal**

Suture removal after 14 days. Healing without any complications.