Group D
Initiator Paper
Implants - Peri-implant (hard and soft tissue) interactions in health and disease: The impact of explosion of implant manufacturers

Saso Ivanovski

School of Dentistry and Oral Health, Griffith University, QLD, Australia

Introduction

Osseointegration is defined as "a direct, structural and functional connection between ordered, living bone and the surface of a load-carrying implant" (Listgarten *et al.*, 1991). Direct bone-to-implant contact was first described by Brånemark *et al.* (1969) and histologically demonstrated by Schroeder *et al.* (1978) as "functional ankylosis." Albrektsson *et al.* (1981) described successful clinical treatment outcomes of 2895 threaded titanium screw implants placed using a strict surgical protocol. Subsequent animal studies showed that implants with various designs and surface configurations become osseointegrated, and analysis of numerous retrieved implants documented that osseointegration is also a reality in humans (Schenk and Buser, 1998). The temporal wound healing events leading to osseointegration were shown to involve coagulum formation, granulation tissue formation, the development of a provisional matrix, woven bone formation, parallel-fibered bone formation, and eventually lamellar bone formation (Berglundh *et al.*, 2003).

The soft tissue attachment to implants is similar to teeth, with the presence of junctional epithelium and connective tissue fibers, although it is noteworthy that some important differences exist in that the fibers around implants are parallel rather than perpendicular to the surface, and the connective tissue surrounding the implant is less vascular than that surrounding teeth (Berglundh *et al.*, 1991). Berglundh *et al.* (2007b) showed that, while the formation of a junctional epithelium occurs within approximately 2 weeks of implant placement, the maturation of the soft tissue complex needs 6-8 weeks to establish after implant placement in an animal model. DeAngelo *et al.* (2007) concluded that soft tissue maturation, as evidenced by stable probing, was achieved in approximately 4 weeks from the time of implant placement in humans. Importantly, it is universally accepted that adhesion of the soft tissues to the implant is critical for the maintenance of osseointegration (Klinge *et al.*, 2006).

In terms of evaluating the performance of dental implant therapy, it must be recognized that it is no longer acceptable to simply consider the continuing presence of the implant at the site of insertion (implant survival) as a suitable measure of clinical outcome. Instead, it is important that the implant is free from biological, mechanical and aesthetic complications (implant success). In this regard, recent systematic reviews of longitudinal clinical studies of a mean 5-year follow-up have shown that implant survival rates were high, at 96.3% after 5 years and 89.4% after 10 years for single tooth restorations, and 96.4% after 5 years and 93.9% after 10 years for fixed prosthesis in partially edentulous patients (Jung *et al.*, 2012; Pjetursson *et al.*, 2012). However, the rate of technical, biological and aesthetic complications is also high, at up to a combined 33.6% (Pjetursson *et al.*, 2012).

It is widely recognized that implant-related characteristics can influence the outcome of treatment (Capelli, 2013). Combined with the continual increase in implant manufacturer numbers and the associated variations in implant design, this has the potential to affect the establishment and maintenance of osseointegration, as well as the incidence and management of complications. This review will evaluate implant-related characteristics that can influence soft and hard tissue healing around implants. Furthermore, the way that implant factors may affect the incidence and management of complications affecting the peri-implant tissues will be explored.

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Correspondence to: Saso Ivanovski, School of Dentistry and Oral Health, Gold Coast Campus, Griffith University QLD 4222, Australia
E-mail: s.ivanovski@griffith.edu.au

The 'explosion' of implant manufacturers

It is difficult to precisely estimate the number of companies providing implant components as this information is not available in the published scientific literature, but anecdotal evidence suggests that numbers have continued to increase exponentially over the years. One reason for this is that implant dentistry has been a high growth market over the past decade, growing at approximately 20% per year up to 2007, and more modestly since. Furthermore, as implants are treated as medical devices by regulatory bodies, the requirements for registering new products are less demanding than those required for pharmaceuticals, providing a low barrier to entry by new manufacturers. The method used by the industry to estimate the number of implant companies in the market is by evaluating the number of dental implant company exhibitors at dental conferences and trade shows. In this regard, an analyst report issued by the investment firm Morgan Stanley in March 2013 stated that "the number of dental implant competitors has increased by 29% in 2 years from 183 to 236" based on exhibitors at the International Dental Show. Similarly, internal research by a leading implant company found that the number of implantology exhibitors at various dental shows and conferences in 2013 was 480, compared to 413 in 2011 and 120 in 2003. Irrespective of the accuracy of these data, it is clear that the number of manufacturers is large and has increased significantly over the past decade.

Implant - peri-implant interactions in health

Albrektsson *et al.* (1981) concluded that there were six major factors influencing osseointegration. These were implant material, implant design, implant finish, status of the bone, surgical technique and implant loading conditions. These observations are still relevant today and it is important to note that the first three properties [material, (macro-) design and (micro-) finish] are related to the implant characteristics and can therefore be subject to variation during the manufacturing process.

Implant material

The primary consideration with regards to the implant material is its biocompatibility. The original Brånemark protocol used commercially pure titanium and this is still considered the gold standard material for implant use. Indeed, the vast majority of currently available implants are made of commercially pure (grade IV) titanium. Alternatives are titanium alloys (e.g., grade V titanium (Ti-6Al-4V) or titanium- zirconia alloy (TiZr)) and zirconia implants, made currently either of yttria-stabilized tetragonal zirconia polycrystals (Y-TZP) or yttria-partially stabilized zirconia (Y-PSZ) (Wenz *et al.*, 2008; Ehrenfest *et al.*, 2010). The alloys are generally used for increasing strength, especially in narrow diameter implants, while the zirconia implants have been advocated on the basis of improved aesthetics. Importantly, the vast majority of long-term studies report on commercially pure titanium implants with some short-term studies on titanium alloy implants (Barter *et al.*, 2012), while zirconia implants cannot be recommended due to a lack of long-term studies (Wenz *et al.*, 2008; Andreiotelli *et al.*, 2009).

Implant macro-features

The macro-design of implants can vary greatly, and there are several key considerations in the way that implant macro-design can affect treatment outcomes. Firstly, there is a requirement to achieve good primary stability of the implant, without excessive trauma at the osteotomy site which may result in necrosis. A second consideration is the ability to achieve a good seal at the implant-abutment margin in order to obtain good marginal integrity of the soft tissues, thus preventing future mechanical and biological complications. A third consideration is the ability to maintain the marginal bone levels during the initial physiological remodeling phase, which may be particularly important in aesthetic areas.

Implant shape and size

The shape of the implant body should allow implant insertion with adequate primary stability while minimizing trauma to the recipient tissue. The most common current design is the solid screw threaded implant (including parallel wall and tapered designs), which is supported by abundant long-term data. Alternatives are hollow screws and cylinders, which are usually inserted using the 'press-fit' method. A systematic review of randomized controlled trials that compared different implant types did not find differences in implant failures between different implant shapes (Esposito *et al.*, 2007). However, an earlier review found that press-fit implants were associated with more long-term marginal bone loss (Sennerby and Loos, 1998). A concern in regards to hollow cylinder designs is that the implants are impossible to treat if bone loss occurs (Baelum and Ellegaard, 2004). It should be noted that virtually all major implant manufacturers currently use the threaded solid screw design, with the press-fit designs having been abandoned some years back.

In terms of implant size, length and diameter do not appear to be related to implant failure (Lee *et al.*, 2005). A systematic review investigating short implants of 5-9 mm (majority 8 mm) found high (>99%) cumulative survival rates (Annibali *et al.*, 2012), suggesting that short implant length does not adversely affect treatment outcomes. Indeed, a recent meta-analysis of 12 studies with minimum 1-year follow-up has shown good treatment outcomes with 6 mm long implants (Srinivasan *et al.*, 2013). Similarly, narrow diameter implants (≤3.5 mm) have been shown to have good treatment outcomes (Sohrabi *et al.*, 2012), showing that implant diameter does not negatively affect treatment. However, mini-implants

(1.8-2.9 mm), commonly used for orthodontic and interim prosthodontic treatment, do not have sufficient evidence to support their use in definitive treatment (Bidra and Almas, 2013). It should be noted that implant manufacturers continue to push the boundaries in terms of implant length and diameter, and practitioners should exercise caution in using implants less than 6 mm long or 3 mm in diameter.

The implant-restoration interface

Generally implants have three components - the implant itself, an abutment that facilitates the attachment/retention of the restoration and the restoration itself. The design of the implant-abutment interface can have an influence on the nature of the post-loading remodeling process at the coronal margin of the bone crest. Traditional criteria for success of implant treatment have allowed for early crestal bone loss of up to 1 mm and ongoing annual bone loss of up to 0.2 mm to be considered a "normal" physiological response (Albrektsson *et al.*, 1986). However, this notion is now being challenged, with contemporary implant designs aimed at preventing marginal bone loss. This is achieved by improving the nature of the connection between the implant and the abutment/restoration, which then has the dual purpose of minimizing early crestal bone loss due to physiological re-modelling, as well as minimizing future mechanical and biological complications that may arise from poor fit between the implant componentry. Several implant design features may be important in this regard:

1. Internal vs external connection
2. Horizontal offset of the implant-abutment junction (platform switching)
3. Macrogeometry at the implant collar

1) Internal vs external connection

The connection that allows the prosthetic superstructure to attach to the implant can be either external (a projection outside the implant body) or internal (within the body of the implant). The original Brånemark implant design had an external hexagon that was developed to facilitate implant insertion (Brånemark *et al.*, 1985). Although this system was associated with good long-term implant survival outcomes, it does have the drawback of allowing micromovement under high off-axis occlusal forces, which may in turn result in abutment screw loosening or even fatigue fracture (Jemt *et al.,* 1991; Becker and Becker, 1995).

Internal connection implant systems have gained popularity because of a perceived higher resistance to bending and improved force distribution over external configurations (Asvanund and Morgano, 2011; Freitas *et al.,* 2011). This is achieved through their ability to dissipate lateral loads deeply within the implant and to resist joint opening due to a deep and rigid connection (Steinebrunner *et al.*, 2008; Bernardes *et al.*, 2009; Sailer *et al.*, 2009; Seetoh *et al.*, 2011), resulting in improved protection of the abutment screw from stress. A systematic review assessing internal and external connections (Gracis *et al.*, 2012) found that the type of connection influenced the incidence of screw loosening, with more loose screws reported for externally connected implant systems. However, it was acknowledged that appropriate pre-loading may decrease the incidence of screw loosening.

Internal connection systems adapted by various manufacturers differ in a variety of parameters, including the intimacy of approximation between the abutment's surface and the internal implant walls, depth of penetration of the abutment in the fixture, presence of anti-rotational interlocking, number and shape of anti-rotational or guiding grooves and abutment diameter at the platform level (Wiskott *et al.,* 2007; Steinebrunner *et al.*, 2008; Bernardes *et al.,* 2009; Coppedé *et al.*, 2009; Tsuge and Hagiwara, 2009). These factors can have a significant impact on clinical procedures and protocols, including length and number of appointments, component and laboratory costs, maintenance intervals, and incidence of complications.

Therefore, it is of great importance that clinicians understand the detailed characteristics of any systems that they intend to utilize. In this context, it is also noteworthy that there are a number of manufacturers who produce 'compatible' abutments to established systems that may not accurately fit the parent implant (Mattheos and Janda, 2012). Clinicians should ensure that appropriate componentry is utilized, including adequate communication and direction to the dental laboratory.

2) Horizontal offset of abutment at implant interface (platform switching)

It has been proposed that a horizontal mismatch between the diameter of the implant and the abutment can result in little to no change in crestal bone height following insertion (Lazzara and Porter, 2005). This has resulted in the development of several implant systems that feature an abutment-implant interface that is internally offset in relation to the external edge of the implant, a design feature that is referred to as 'platform switching.'

The rationale proposed for this approach is that the internal re-positioning of the implant-abutment interface would shift the inflammatory cell infiltrate formed at this interface away from the crestal bone, resulting in biologic width re-establishment in a predominantly horizontal rather than vertical dimension (Lazzara and Porter, 2005). This in turn minimizes vertical bone resorption associated with the physiological remodeling associated with biologic width formation. It has also been proposed that platform shifted implants have a biomechanical advantage by moving stress concentration away from the outer edges of the implant (Maeda *et al.*, 2007).

A recent systematic review and meta-analysis of nine clinical trials concluded that platform switching was indeed a desirable design feature that minimizes vertical crestal bone loss (Al-Nsour *et al.*, 2012). The authors identified several confounding factors that should be considered when interpreting the results, such as the apico-coronal position of implants in relation to crestal bone, the presence of various implant micro-textures, the degree of platform switching and the reliability of examination methods.

3) Macrogeometry of threads at the implant collar

Biomechanical modelling studies have found that peak horizontal and vertical loading forces occur at the top of the marginal bone (Stoiber, 1988). Based on these observations, a smooth implant collar was advocated to minimize the horizontal forces. However, this approach did not yield the desired outcome, and a modified implant macro-geometry with minute threads at the collar has been advocated as a more effective alternative (Hansson, 1999), particularly when combined with an internal conical implant abutment connection (Abrahamsson and Berglundh, 2009). The superiority of the micro-thread compared to the smooth collar design has been supported by animal and human studies (Abrahamsson and Berglundh, 2006; Lee *et al.,* 2007; Nickenig *et al.*, 2009). In contrast, the micro-topography of the implant surface does not appear to influence marginal bone loss (Abrahamsson and Berglundh, 2009). However, it has been proposed that laser micro-grooves at the implant collar result in perpendicular, rather than parallel, orientation of fibers to the implant surface, potentially resulting in a superior attachment, although the clinical implications of this are not yet known (Ketabi and Deporter, 2013). In summary, the implant-abutment/restoration interface in contemporary implant designs is focused on minimizing technical complications by reducing the incidence of screw loosening, as well as minimizing crestal bone loss during the initial remodeling phase.

While appropriately designed internal connections are largely responsible for improved outcomes in terms of screw loosening, reduction in crestal bone loss is likely to be the result of a combination of features, including internal connection, platform switching and micro-thread design of the implant collar. However, the precise combination of these interdependent parameters that results in the best outcomes is yet to be determined in long-term clinical trials.

Implant surfaces

Osseointegration is a biological process that involves a cascade of events which occur at the tissue-implant interface. These involve clot formation and the initial adsorption of serum components immediately following implant placement, an immune-inflammatory response to implant insertion, the migration and attachment of undifferentiated mesenchymal cells onto the implant surface, their proliferation and differentiation, the formation of extracellular matrix, and finally its mineralization and maturation. Several features of the implant surface can influence the rate and extent of bone-implant contact, and surface modification has been advocated as a method for enhancing osseointegration (Junker *et al.*, 2009; Wennerberg and Albrektsson, 2009; Ehrenfest *et al.*, 2010).

There are two broad methods used to modify the implant surface (Ehrenfest *et al*, 2010). In the first approach, the interface is improved chemically by incorporating inorganic phases, such as calcium phosphate, or organic molecules, such as proteins, enzymes or peptides, on or into the TiO_2 (titanium dioxide) layer. Implants with thick hydroxyapatite (HA) layers were initially advocated as a way to improve the speed and extent of osseointegration, but were found to result in implant failure due to delamination of the HA coating (Piattelli *et al.*, 1995). While thin calcium phosphate coating technology may solve the problems associated with thick calcium phosphate coatings, there is a lack of human clinical data to support their superiority over conventional micro-rough surface implants (Junker *et al.*, 2011). Furthermore, there is no convincing evidence to support the use of implants with organic molecule coatings (Junker *et al.*, 2011).

In the second approach, the interface is improved physically by modifying the architecture of the surface topography at the micrometer or nanometer level. In particular, it has been shown that the micro-level topography of the implant surface can influence the extent and speed of osseointegration around the implant (Wennerberg and Albrektsson, 2009). In the most widely recognized classification of micro-level topography proposed by Albrektsson and Wennerberg (2004), smooth surfaces were proposed to have an Sa value (arithmetic mean deviation of a surface) of <0.5 μm; minimally rough surfaces have an Sa of 0.5-1 μm, moderately rough surfaces have an Sa of 1-2μm, and rough surfaces have an Sa of >2 μm.

In animal studies, moderately rough titanium implants were shown to have a superior bone-to-implant contact compared to minimally rough implants (Buser *et al.,* 1991), as well as superior torque removal values (Buser *et al.,* 1998). These results have been replicated in histological analysis of human samples (Lazzara *et al.*, 1999; Ivanoff *et al.*, 2001; Ivanoff *et al,* 2003; Grassi *et al.*, 2007). Notably, histological analysis of the sequential healing events following implant placement demonstrated evidence of superior early healing associated with moderately rough compared to minimally rough

surfaces (Abrahamsson *et al.*, 2004). Furthermore, initial bone formation around the moderately rough surface implants occurred not only at the exposed bone wall of the surgically created recipient site (distance osteogenesis), but also along the osteophylic implant surface (contact osteogenesis), which was not observed on the minimally rough implants (Berglundh *et al.,* 2003; Abrahamsson *et al.*, 2004).

Additional changes to moderately rough surfaces via chemical modification has resulted in nanoscale features and changes in chemical composition and/or hydrophilicity, which have resulted in greater bone-implant contact in animal (Buser *et al.*, 2004; Berglundh *et al.*, 2007a) and human studies (Orsini *et al.*, 2007; Lang *et al.*, 2011). Notably, longitudinal time-course histomorphometric studies have shown that while moderately rough implants result in both earlier and ultimately greater bone-implant contact compared to minimally rough implants (Abrahamsson *et al.*, 2004), the chemically modified surfaces only accelerate osseointegration, with no differences in the final bone-implant contact values compared to moderately rough implants (Buser *et al.*, 2004; Berglundh *et al.*, 2007a; Lang *et al.*, 2011).

Many currently available implant systems employ a combination of chemical and physical modifications. However, it should be noted that implant surfaces are generally poorly characterized, with microscale topography being the most widely reported parameter, while other important parameters such as topographical uniformity, nanoscale features and purity have not been documented (Wennerberg and Albrektsson, 2009; Ehrenfest *et al.*, 2010).

Clinical relevance of implant surface modification

In the clinical context, while the original machined Brånemark implants had a minimally rough topography, the vast majority of implant systems that have been commercially available over the past decade have a micro-rough topography, which is within or very close to the Sa values of the moderately rough category (Sa 1-2 μm). More recently, a third generation of chemically modified surfaces with nanoscale features has become commercially available. It is noteworthy that there are a large number of studies that document the clinical performance of first generation machined and the various second generation 'micro-rough' implants, but there are relatively few clinical studies that report on the medium- to long-term performance of newly developed chemically/nanoscale modified implant surfaces.

It is important to note that excellent long-term results have been reported with the original first generation machined implants, with implant success of up to 99% reported at 15 years follow-up (Lindquist *et al.*, 1996). However, poorer results may be obtained in achieving osseointegration with machined implants in compromised sites, such as the posterior maxilla (Becktor *et al.*, 2004), and patients such as smokers (Balshe *et al.*, 2008). Animal data would suggest that moderately rough implant surfaces may result in improved clinical outcomes, such as decreased healing times and increased success in compromised sites and patients. However, there is a scarcity of human clinical studies to substantiate these hypotheses, as there are few randomized controlled clinical trials that directly compare the relative performance of different implant surfaces, especially in compromised situations. In a systematic review of the few available controlled randomized clinical trials, most of which involve a small numbers of patients, it has been shown that there is a clear trend towards a higher risk for implant failure in implants with machined surfaces compared with 'micro-rough' surface implants (Esposito *et al.*, 2007).

In the absence of large randomized controlled clinical trials, a review of cohort studies may be used to ascertain the relative performance of micro-rough and machined implants. Lambert *et al.* (2009) undertook a comprehensive assessment of 1- to 15-year survival rates of fixed implant rehabilitations in the edentulous maxilla incorporating 32 studies, including 1,320 patients and 8,376 implants. Implants with micro-rough surfaces showed a statistically higher survival rate than machined implants at all intervals (1, 3, 5, 10 and 15 year time-points). Furthermore, there is evidence from meta-analysis of cohort studies that micro-rough implants perform better than machined implants in augmented sites in the maxilla (Del Fabbro *et al.,* 2008; Lambert *et al.*, 2009), as well as in smokers (Balshe *et al.*, 2008).

In the clinical context, an important consideration is the influence of the emergence of micro-rough surfaces on the utilization of short implants. This is because implant survival is higher when short implants are used then when vertical bone augmentation is utilized to overcome bone deficiency, especially in the posterior mandible (Esposito *et al.*, 2009). In this context, it has been shown that short micro-rough implants have a greater survival rate than machined-surfaced implants (Feldman *et al.,* 2004; Renouard and Nisand, 2005; Annibali *et al.*, 2012).

In summary, moderately rough implants appear to improve the speed and extent of bone-implant contact in histomorphometric studies, which is also supported by meta-analysis of clinical cohort studies that suggest that these implants perform better than those with minimally rough machined surfaces. However, it should be noted that surface characterization of implants is generally poor, which has implications in the context of the ever increasing number of manufacturers. Further, it should be noted that new generation nanoscale modified implants have inadequate surface characterization, and are generally not supported by long-term clinical studies. So, although there is good clinical rationale for the use of micro-rough implants, practitioners should exercise caution when choosing implants for clinical use, and ensure that the relevant surfaces have good long-term clinical evaluation.

Implant — peri-implant interaction in disease

Peri-implant disease

The 6th European Workshop on Periodontology defined the term "peri-implant disease" as a "collective term for inflammatory reactions in the tissues surrounding an implant," with peri-implant mucositis described as "the presence of inflammation in the mucosa at an implant with no signs of loss of supporting bone" and peri-implantitis as an "inflammatory process around an implant, characterized by soft tissue inflammation and loss of supporting bone" (Lindhe and Meyle, 2008; Zitzmann and Berglundh, 2008). Peri-implant mucositis is a reversible disease whose pathogenesis and diagnosis does not fundamentally differ from gingivitis around teeth (Lang *et al.*, 2011). Peri-implantitis is a multi-factorial disease that is similar in clinical features and aetiology to periodontitis, although critical histopathological differences exist between the two lesions (Berglundh *et al.*, 2011). Notably, the apical extension of the lesion is more pronounced in peri-implantitis than in periodontitis, and in contrast to periodontitis lesions, peri-implantitis lesions lack a "self-limiting" process and extend to the bony crest, exhibiting signs of acute inflammation with large amounts of osteoclasts lining the surface of the crestal bone (Berglundh *et al.*, 2011; Lang and Berglundh, 2011).

The incidence of peri-implantitis has been reported in the range of 16 - 58%, and is highly dependent on the definition used to describe the disease (Fransson *et al.*, 2005, Zitzmann and Berglundh, 2008, Koldsland *et al.*, 2010). A systematic review by Heitz-Mayfield (2008) identified poor oral hygiene, history of periodontitis and cigarette smoking as strong risk indicators for peri-implant disease. The association between periodontitis and peri-implantitis (Ong *et al.*, 2008; Lee *et al.*, 2012) and the similarity in bacterial pathogens associated with the two lesions (Mombelli and Lang, 1998; Renvert *et al.*, 2007) point towards a common bacterial aetiology. Indeed, the aetiology of peri-implantitis appears to be multi-factorial, and changes in local ecological conditions that favor the growth of bacterial pathogens may be viewed as the true origin of peri-implant disease (Mombelli and Décaillet, 2011). The presence of the implant-abutment connection at the gingival/subgingival margin is important in this context, and given that this is the subject of great variation among different manufacturers, the choice of implant design may be important, especially in susceptible patients. Indeed, regardless of one's view on the relative importance of the bacterial biofilm in the initiation of the peri-implantitis lesion, it is widely accepted that multiple features of implant design, and the ability of the practitioner to appropriately manage these, have a significant impact on the development of peri-implant disease (Lang and Berglundh, 2011; Qian *et al.*, 2012).

Two aspects of implants that may play a role in the development and progression of peri-implant disease are the implant-abutment/restoration connection and the implant surface.

Implant-abutment connection and peri-implant disease

It has been shown that bacteria find their way through the microgap at the implant/abutment interface and reside within the internal components of implants, and this provides them with an environment sheltered from host defenses (Quirynen and van Steenberghe, 1993; Persson *et al.*, 1996; Jansen *et al.,* 1997). The design of the implant/abutment interface determines the size of the microgap and therefore will influence the degree of microleakage (Tesmer *et al.*, 2009), with the biological consequence being soft tissue inflammation that can lead to bone loss (Hermann *et al.*, 2001).

As previously discussed, the nature of the connection (external vs internal) can have an impact on technical complications, such as screw loosening (Gracis *et al.*, 2012). It is reasonable to expect that loosening of the restoration would have a negative impact on the health of the peri-implant tissues, as the interface between the implant and abutment is usually below the mucosal margin. Indeed, the incidence of biological complications has been linked to technical complications in a clinical study (Kim *et al.*, 2013). Clearly, the stability of the implant-abutment interface is important in minimizing biological complications, and in this regard an internal connection appears to offer an advantage (Gracis *et al.*, 2012).

It should also be considered that the nature of the implant-abutment connection (e.g., platform switching) may also influence the diagnosis of peri-implantitis, as it may influence the ability to probe around implants (Lang and Berglundh, 2011).

Another consideration in relation to the design of the implant-abutment/restoration connection relates to the potential for peri-implant tissue problems caused by clinician error. Incorrect seating of implant componentry, and in particular subgingival cement retention, are problems that can create a local environment that is conducive to the initiation of peri-implantitis, especially in susceptible patients. Wilson (2009) showed that excess luting cement was associated with peri-implant disease in 81% of 39 cases. Once the excess cement was removed, the clinical signs of disease resolved in 74% of cases. A recent study has shown a direct correlation of the depth of implant crown margin below the mucosal margin and the amount of undetected residual cement (Linkevicius *et al.*, 2013), underlying the importance of avoiding or limiting the sub-mucosal extent of the restorative margin.

It is generally recognized that iatrogenic factors (e.g., excess cement remnants, inadequate restoration-abutment seating, over-contouring of restorations, implant mal-positioning, technical complications) can initiate

peri-implant disease (Lang and Berglundh, 2011; Qian *et al.*, 2012). Clinicians should have appropriate clinical training and have a thorough understanding of the relevant implant system in order to avoid these problems, which may cause significant peri-implant tissue disease in susceptible patients.

Implant surface characteristics and peri-implant disease

With regard to the interaction of implant surfaces and peri-implant disease, the two key issues are whether certain implant surfaces are more prone to disease, and whether implant characteristics influence the treatment of peri-implantitis.

It has been suggested that the roughness of the implant surface as well as its chemical composition has a significant impact on the amount and quality of plaque formation (Teughels *et al.*, 2006). Indeed, hydroxyapatite (HA)-coated and rough-surfaced (Sa>2μm) implants have been associated with increased incidence of biological complications (Åstrand *et al.*, 2004; Piattelli *et al.*, 1995). However, these findings are of limited relevance to contemporary practice, as the implant systems used in these studies are no longer manufactured. Furthermore, the initiation of bone loss around HA-coated implants was associated with the delamination of the coating, and hence the biological mechanisms are different from conventional peri-implantitis pathogenesis. A recent systematic review based on human clinical trials found no evidence of increased susceptibility to peri-implantitis for currently available moderately rough surfaces, although it was acknowledged that there is a scarcity of available data on this topic (Renvert *et al.*, 2011). Of particular interest is a prospective, multicenter, randomized, controlled 5-year clinical trial comparing a hybrid implant design (coronal component of implant was machined) with fully micro-rough implants, which showed no difference in peri-implantitis incidence (Zetterqvist *et al.*, 2010). However, it should also be noted that there is experimental evidence from pre-clinical animal studies that some currently available moderately rough surfaces may be more susceptible to peri-implant disease progression (Albouy *et al.*, 2008; Albouy *et al.*, 2009), but these findings need to be validated by clinical trials.

In terms of treating peri-implantitis, the ultimate goal is to regenerate the lost bone and achieve re-osseointegration to the previously contaminated implant surface. In this regard, better outcomes have been reported with moderately rough compared to machined implant surfaces, although full defect resolution has not been demonstrated and there is variability in the way that different moderately rough implants perform (Renvert *et al.*, 2009). This finding is somewhat surprising because it has been shown that increased surface roughness has a significant impact on biofilm formation (Teughels *et al.*, 2006) and a smoother surface texture may be easier to decontaminate (Dennison *et al.*, 1994). A possible explanation is that the rougher surface may provide improved support for the developing blood clot after surgery and thus facilitate greater bone healing in contact with the implant surface (Persson *et al.*, 2001).

The impact of the 'explosion' of implant manufacturers

The obvious consequence of the increasing number of implant manufacturers is that the clinical and scientific community will have difficulties assessing and evaluating different systems. We can take some comfort in that over 90% of implants worldwide are produced by fewer than 10 of the top implant companies, most of which are supported by sound scientific evidence. However, many of the new manufacturers are marketing their products on the basis of cost effectiveness, rather than innovation aimed at achieving superior clinical outcomes. These manufacturers often have 'copycat' designs that are marketed as being 'compatible' with well-established manufacturers. This can result in poorly fitting componentry that predisposes to future technical and biological complications. Emerging evidence, in the form of case reports, suggests that 'compatible' or 'clone' abutments can have significantly different geometry compared to the original abutments (Mattheos and Janda, 2012), which may lead to future technical and biological problems. Inevitably, the quality of the components will vary, but the impact of this on clinical outcomes has not been evaluated in the scientific literature.

Another challenge of the increasing number of implant manufacturers is related to the nature of implant treatment, which often involves multiple visits over a prolonged period, followed by essential long-term maintenance. Combined with the increasing mobility of the population, this can result in cases where practitioners have to complete treatment initiated elsewhere or deal with complications involving treatment undertaken by another practitioner. This can pose significant challenges to even experienced clinicians and critical requirements for successful management would be the clinician's experience and special training, as well as access to the appropriate tools and devices.

It is widely recognized that peri-implant disease can be initiated by iatrogenic factors arising from poor management or understanding of implant componentry. Therefore, caution needs to be exercised by practitioners when choosing the source of implant componentry, including that utilized by the dental laboratory. Central to this is education to ensure that clinicians have a thorough understanding of the way that implant-related characteristics may influence clinical outcomes.

The 'explosion' of implant manufacturers - the developing world context

In many ways, the challenges of the increasing number of implant manufacturers are common to both the developed and developing world. Inevitably, as the living standards in the developing world improve, there will be increasing demands for dental implant treatment. There is also the issue of dental tourism, whereby patients from developed countries visit developing countries in order to obtain treatment at a lower cost (Barrowman *et al.*, 2010). Implant dentistry is attractive in this regard as it involves high value work and hence the savings can be considerable. However, because of the prolonged nature of implant treatment, the outcomes can be adversely affected by disjointed treatment and parts being undertaken in different countries. These problems may be exacerbated by differences in the availability of componentry from newer, less established manufacturers between countries.

With their focus on offering more cost-effective dental implant components, 'value' manufacturers will be major suppliers in the developing markets. Practitioners have a responsibility to carefully evaluate the implant systems that they utilize in order to ensure that quality clinical outcomes are achieved. The decisions should be made on the basis of a sound evidence base from publications in quality peer-reviewed journals. Furthermore, there is a need for manufacturer-independent undergraduate and postgraduate education in order to ensure that practitioners are familiar with the guiding principles of contemporary dental implantology, in order for them to be well placed to evaluate new products from implant manufacturers.

Summary

1. The best-documented implants have a threaded solid screw-type design and are manufactured from commercially pure (grade IV) titanium. There is good evidence to support implants ≥6 mm in length, and ≥3 mm in diameter.
2. Integrity of the seal between the abutment and the implant is important for several reasons, including minimization of mechanical and biological complications and maintaining marginal bone levels. Although the ideal design features of the implant-abutment connection have not been determined, an internal connection, micro-grooves at the implant collar, and horizontal offset of the implant-abutment junction (platform switch) appear to impart favorable properties.
3. Implants with moderately rough implant surfaces provide advantages over machined surfaces in terms of the speed and extent of osseointegration. While the favorable performances of both minimally and moderately rough surfaces are supported by long-term data, moderately rough surfaces provide superior outcomes in compromised sites, such as the posterior maxilla.
4. Although plaque is critical in the progression of peri-implantitis, the disease has a multi-factorial aetiology, and may be influenced by poor integrity of the abutment/implant connection. Iatrogenic factors, such as the introduction of a foreign body (e.g., cement) below the mucosal margin, can be important contributors.
5. Clinicians should exercise caution when using a particular implant system, ensuring that the implant design is appropriate and supported by scientific evidence. Central to this is access to and participation in quality education on the impact that implant characteristics can have on clinical outcomes. Caution should be exercised in utilizing non-genuine restorative componentry that may lead to a poor implant-abutment fit and subsequent technical and biological complications.

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