

Healing of Soft Tissue and Bone Around Implants: A Review of Literature

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ABSTRACT

Background: The introduction of implant-supported prostheses has contributed to a significant improvement in restoring the masticatory function of patients. This literature overview aims to discuss the biological processes of predictable bone and soft tissue healing around an implant leading to its success. It also discusses the factors that affect healing some of which are the quantity and quality of bone, the patient's age and health, location of implant placement, dimensions of implant, axial loading, and oral hygiene maintenance. The evidence collected from literature with respect to soft tissue and bone healing around implants was collected, categorized and summarized. To be successful, implant must integrate with the surrounding hard tissues, which is termed as osseointegration. The soft tissue following the implant surgery requires 6–8 weeks for complete healing and follows the same phases as skin wound healing.

Keywords: Dental implants, healing, osseointegration, soft issue integration.

INTRODUCTION

A dental implant (also known as an endosseous implant or fixture) is a surgical component that interfaces with the bone of the jaw or skull to support a dental prosthesis such as a crown, bridge, denture, facial prosthesis or to act as an orthodontic anchor. In the past 20 years, the number of dental implant procedures has increased steadily worldwide, reaching about one million dental implantations per year. (1) The introduction of endosseous implant-supported prostheses has contributed to a significant improvement in restoring the masticatory function of partially or completely edentulous patients. (2,12,13).

The clinical success of oral implants is related to their ability to integrate with the surrounding tissues prior to prosthetic rehabilitation. The implant must integrate with both the surrounding soft tissues as well as the hard tissues i.e. bone which is termed as osseointegration. **Osseointegration** is the direct

association of osseous tissue with an inert alloplastic biomaterial surface. (12)

The dental implants should be stable mechanically and biologically, thus, biocompatible metallic devices have been the material of choice. Pure titanium (c.p.Ti) and titanium alloy (Ti-6Al-4V) are among the most biocompatible metallic materials. Animal experiments indicating that direct bone anchorage to titanium alloplastic surfaces was possible was first published in the late 1960s by Branemark et al. The phenomenon later accepted as osseointegration was clearly demonstrated in independent studies. (12) With the advancement of medical research, biomaterial science and technology, an improvement in the knowledge of oral health and an increase in the average life expectancy, there is a growing demand for the design and development of implants with improved longevity, minimum failure rates and expanded use. Until a defined technology for regenerating

Received: July. 21, 2019; Accepted: Sept. 11, 2019

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tooth structure becomes available, significant opportunities and challenges exist in developing a new generation of dental implants with variations in surface microtopographies. (12) The geometry and surface topography are crucial for the short- and long-term success of dental implants. These parameters are associated with delicate surgical techniques, a prerequisite for a successful early clinical outcome. After implantation, titanium implants interact with biological fluids and tissues.

There are two types of response after implantation:

- a. The first type involves the formation of a fibrous soft tissue capsule around the implant.
- b. The second type of bone response is related to direct bone-implant contact without an intervening connective tissue layer. This is what is known as osseointegration.

Soft and hard tissue integration is a prerequisite for implant success. The primary function of a soft tissue barrier at implants is to effectively protect the underlying bone and prevent access for microorganisms and their products. A soft tissue seal, with structures similar to that at teeth with a true connective tissue attachment to the implant may improve this protective function.

Soft tissue healing around implants has become a focus of attention because it plays a central role in esthetic outcomes. Fibrin clot serves as a provisional matrix allowing epithelial and fibroblast migration towards the implant surface. Epithelial and connective tissue contact to the implant or abutment surface is established within 1–2 weeks and further maturation follows up to at least 12 weeks. Orientation of collagen fiber bundles also differs from natural tooth. Instead of attaching to the neck of the implant, collagen fibers run parallel and circumferentially around the implant. (11)

This literature review aims to discuss the biological processes of predictable bone and soft tissue healing around an implant leading to its success. It also discusses the factors that affect

healing some of which are the quantity and quality of bone, the patient's age and health, location of implant placement, dimensions of implant, axial loading, and oral hygiene.

The inflammatory phase allows the body to control bleeding and bacterial invasion and, additionally, to recruit the cells that are needed to restore the injured area. During the proliferative phase, new tissue components are produced to fill the void caused by the tissue damage. This phase is completed when the barrier has been restored. The remodeling of the tissues continuous up to 2 years after injury but the greatest changes occur between 6 and 12 months. (3)

The soft connective tissue determines the characteristics of the overlaying oral epithelium. Within 7–14 days, epithelial healing of surgical wounds at teeth is completed. Soft tissue healing following surgery at implants requires 6–8 weeks for maturation. The resulting tissue resembles scar tissue. Well-designed pre-clinical studies providing histological data have been reported. Few controlled clinical studies with low numbers of patients are available for some of the treatments reviewed at teeth. Whereas, histological new attachment has been demonstrated in pre-clinical studies resulting from some of the treatments reviewed, human histological data commonly report a lack of new attachment but rather long junctional epithelial attachment and connective tissue adhesion. (3,15)

BIOLOGICAL PROCESSES OF HEALING AROUND IMPLANTS.

SOFT TISSUE HEALING

Oral soft tissue healing around implants follows the same phases as skin wound healing.(15)

Soft tissue interface around implants

To be functionally useful, oral implants have to pierce the gingiva or oral mucosa and enter the oral cavity, thus establishing a transmucosal connection between the external environment and the inner parts of the body. In order to avoid bacterial penetration that could jeopardize either initial healing or long-term behaviour of

implants, the formation of an early and long-standing effective barrier capable of biologically protecting the peri-implant structures is mandatory.

From a comparative study in dogs, it is known that the soft tissue interface is slightly longer at (two-piece) implants than at teeth: if the junctional epithelium has comparable dimensions at teeth and implants (2.05 vs. 2.14mm), the connective tissue is 1.12mm long around teeth vs. 1.66mm around implants. These results were obtained with transmucosal implant components made of machined titanium and cannot be extrapolated to other materials. (5)

Biologic process of soft tissue healing around implants

Dental implants are anchored in jaw bone through a direct bonding between bone and the implant. Success and survival of an implant do, however, not depend solely on osseointegration. A soft tissue, which surrounds the transmucosal part of a dental implant, separates the periimplant bone from the oral cavity. This soft tissue collar is called "periimplant mucosa". The attachment of the soft tissue to the implant serves as a biological seal that prevents the development of inflammatory periimplant diseases (i.e. peri-implant mucositis and peri-implantitis). Thus, the soft tissue seal around implants ensures healthy conditions and stable osseointegration and therefore also the long-term survival of an implant. Around teeth, a sophisticated soft tissue collar seals the tissues of tooth support (i.e. alveolar bone, periodontal ligament and cementum) against the oral cavity. While the soft tissue seal around teeth develops during tooth eruption, the peri-implant mucosa forms after the creation of a wound in oral soft and hard tissues. The wound healing phase may occur following the closure of a mucoperiosteal flap around the neck portion of an implant placed in a so-called one-stage procedure or after a second surgical intervention for abutment connections to an already installed dental implant (two-stage procedure). (14)

Dental implants lack root cementum and collagen fiber bundles in the peri-implant

mucosa were mostly found to be aligned in a parallel direction with the implant surface. Some studies have suggested the presence of perpendicularly attached collagen fibers to dental implants.(3)

A series of experimental studies demonstrated that the formation of a barrier epithelium was initiated after 1-2 weeks of healing and completed at 6-8 weeks after surgery. The collagen fibers in the connective tissue became organized after 4-6 weeks of healing. The findings indicated that the overall dimension of the soft tissue interface to titanium, i.e. "biological width" was established after 6 weeks following surgery (study 1). Similar soft tissue dimensions and composition of the connective tissue were found at collagen coated and uncoated titanium implants after 4 and 8 weeks of healing (study 2). Abutments made of titanium and zirconia promoted proper conditions for soft tissue integration, while abutments made of gold-alloy failed to establish appropriate soft tissue integration (study 3) Bone formation coronal of the junction between the implant and the abutment was possible when 2-part implants with sufficient surface characteristics were placed in a subcrestal position. The connective tissue interface to abutments with a TiOblast surface was comprised of a higher density of collagen and a lower fraction of fibroblasts than at abutments with a turned surface (Study 4). Different marginal bone levels at the lingual and buccal aspects were obtained when 2-part implants with suitable surface characteristics were placed in sites with buccal bone defects (Study 5). (3)

Influence of material characteristics on soft tissue integration is due to:

1. **Chemical composition** - c.p. titanium is the only material that has proven his biocompatibility towards the soft tissues in long-term clinical studies
2. **Surface free energy** (wettability)
3. **Surface contamination** - the surface of the core material can be contaminated, altering the composition of the interface. Saliva has

shown deleterious and hardly reversible effects in vivo. (5)

Influence of surfaces' topography on soft tissue integration is due to:

1. Surface texture
2. Contact guidance
3. Surface form

No clinical studies are currently available on the effect of altered surface topographies

on implant prognosis. (5)

Influence of implant components and connections on soft tissue integration is due to:

1. Surgical procedure
2. Use of one or two piece implants
3. Abutment disconnection (5)

Summary of key points:

1 Oral mucosal and skin wound healing follows a similar pattern of the four phases haemostasis, inflammation, proliferation and maturation/matrix remodelling.

2 Infection control is important for undisturbed oral wound healing and is a prerequisite for the transition of the inflammatory to the proliferative phase.

3 Granulation tissue derived from the periodontal ligament induces epithelial cells to form a keratinized masticatory gingiva.

4 The soft connective tissue determines the characteristics of the overlaying oral epithelium.

5 Epithelial healing around teeth following non-surgical and surgical periodontal therapy is completed after 7–14 days.

6 Functional stability between the denuded root and soft tissue is achieved approximately 14 days after surgery.

7 The formation of the biological width and maturation of the barrier function around transmucosal implants requires 6–8 weeks of

healing. The established peri-implant soft connective tissue resembles a scar tissue in composition, fibre orientation and vasculature. The peri-implant junctional epithelium may reach a greater final length under certain conditions such as implants placed into fresh extraction sockets versus conventional implant procedures in healed sites. (15)

BONE HEALING

An in vivo study was done to compare bone healing and crestal bone changes following immediate (Im) versus delayed (De) placement of titanium dental implants with acid-etched surfaces (Osseotite) in extraction sockets. The survival rates were 91% in the Im group and 96% in the De group. In the Im group, the mean reductions in parallel width, perpendicular width, and depth of the largest defect of each implant amounted to 48% (from 4.4 to 2.3 mm), 59% (from 2.2 to 0.9 mm), and 48% (from 6.9 to 3.6 mm), respectively. The corresponding mean reductions in the De group amounted to 39% (from 3.1 to 1.9 mm), 77% (from 1.3 to 0.3 mm), and 34% (from 4.4 to 2.9 mm). The reduction over time was statistically significant in both groups. For both groups, a higher degree of bone healing was achieved in the infrabony defects (60% for depth) than in dehiscence-type defects (approximately 25%). Furthermore, 70% of the 3-wall infrabony defects with a parallel width of up to 5 mm, a depth of maximum 4 mm, and a perpendicular width of maximum 2 mm had a capacity of spontaneous healing within a period of 3 months. It was concluded that new bone formation occurs in infrabony defects associated with immediately placed implants in extraction sockets. (2)

Increasing surface roughness and coating with tricalcium phosphate of titanium and titanium alloy implants has been proposed to provide better rates of osseointegration. An in vivo study was done which found that histology indicated no differences in the amount or pattern of bone formation within the healing tissue surrounding the different implant surfaces. Bone healing occurred predominantly on exposed bone surfaces (distance osteogenesis) and not on the implant surface (contact osteogenesis). No differences were observed in the number or

timing of PCNA, osteopontin and osteocalcin positive cells within the bone healing tissue around each of the implant analysed. Thus, it was concluded that for immediately placed implants, the surface modifications investigated appeared to have little influence on the activity of bone forming cells surrounding the implant, probably due to the high level of distance osteogenesis seen within this scenario. (17)

The major challenge in implantology today is therefore to combine current knowledge in materials science, tissue engineering, and biology to design metal implant surfaces capable of optimal bone bonding and at the same time providing epigenetic signals to cells in the peri-implant tissues to elicit proper biological responses that favor bone healing and osseointegration over adverse effects and sub-optimal treatment outcomes. Thus, to achieve an optimal biological reaction in the bone following the placing of an implant, and to develop new biomimetic strategies for improved implant performance in bone, three major factors must be optimized and carefully controlled:

- the surface structure and surface chemistry of the implanted device.
- the nature and quality of the tissue-implant interface and the peri-implant environment.
- the physiology and biology of the healing process in the compromised bone. (8)

Biologic process of bone healing around implant

Osseointegration has been used to describe the successful healing of an implant within a host bone. It is the ability of the bone to bond to the surface of a synthetic material, such as a titanium implant.³

The biological process behind osseointegration occurs within the normal human bone as a part of physiological bone remodeling. In bone remodeling, osteoclasts remove the old bone and in so doing provide a surface on the old bone with the appropriate topography, with which the newly formed bone may bond. This bonding occurs as the cement line interdigitates with the surface of the old bone. The cement line

is the first matrix developed during *de novo* bone formation. Evidence suggests that this process may occur at an implant surface, and thus result in osseointegration, if the implant's surface topography is three dimensionally complex, with pores and undercuts. (16)

The bone healing is initiated with a coagulum that is substituted by a provisional matrix at 1 week. Bone formation started concomitant to a marked bone resorption. At 2 weeks, woven bone formation was evident and gradually remodeled into lamellar bone at 4 and 8 weeks. (9)

Evaluation of bone density changes in the jaw bones in the periimplant regions is of interest when studying the healing response after bone grafting procedures. The use of subtraction radiography is not a new concept and has been utilized in dentistry for several decades. It was found that digital subtraction radiography was effective in detecting minimal changes of bone density around dental implants. Studies have shown massive increase of the mean bone density scores at 12 months when compared to immediate postoperative records. Other studies have concluded that implant loading protocol induced mineral bone gain around single tooth implants after the first year under function. The bone healing in immediate and immediate delayed placement occurred predominantly on exposed bone surfaces (distance osteogenesis) and not on the implant surface (contact osteogenesis). (9)

Fig 19. Scanning electron micrographs showing the apatite coatings formed on chemically modified titanium in the absence (control) and the presence of recombinant rM179 amelogenin in 40 ml of calcifying solution. Note the formation of apatite bundles on the surface in the sample containing 100 lg/ml amelogenin.[Source 12]

FACTORS AFFECTING HEALING AROUND DENTAL IMPLANTS

Important factors for clinical consideration which affect healing around implants (13):

A. Patient dependent factors

1. Bone quality and quantity
2. General health – irradiation, infection, systemic diseases
3. Oral hygiene/ untreated dental disease
4. Oral lesions
5. Patients oral habits
6. Age and gender

B. Clinician dependent factors

1. Case selection
2. Site selection
3. Implant design
4. Implant number/spacing
5. Surgical technique
6. One or two stage policy
7. Premature loading/ axial loading
8. Design of prosthesis
9. Commitment to recall protocol

Quantity and quality of bone

Various research studies have been done to assess the bone quantitatively and qualitatively around the implants. (4)

Immediate implant placement in extraction sockets in combination with barrier membranes also seems to be a predictable treatment modality. Lazzara introduced the use of expanded polytetrafluoroethylene membranes after immediate implantation with a positive outcome. Later, bioresorbable barriers were developed, which offered the advantage that membrane removal was not needed; however, these possessed other drawbacks such as lack of stiffness (thus requiring a membrane-supporting material). In animal and human studies, it has been shown that resorbable barriers can be successfully used for bone augmentation purposes. Furthermore, the combination of resorbable barriers and immediately placed implants seems to be comparable with the combination of nonresorbable barriers and immediately placed implants in terms of integration of the implants.

Animal studies have indicated that osseointegration of immediately placed implants in extraction sockets can be achieved without bone augmentation procedures, and with a success rate comparable to that of delayed implant placement. This was supported

by a case series including 109 implants¹⁵ and a prospective clinical study in which high success rates of immediately placed implants were obtained without the use of membranes or grafts. In reviews of the literature, it was concluded that there is no consensus whether the use of bone grafting, bone substitutes, osteogenesis-stimulating substances, and/or membranes in combination with implants immediately placed in extraction sockets yields better results than the use of immediately placed implants alone.

Since simplified surgical procedures and low treatment costs are preferable to the patient, it is desirable that the necessity for the various bone-reconstructive treatment strategies for achieving osseointegration of immediate implants be evaluated. Therefore, it is important to identify the type and size of peri-implant bone defects that heal spontaneously with bone. More controlled, prospective clinical studies are needed to define the potential for spontaneous healing, for instance, in 1-wall and 2-wall infrabony peri-implant defects, as well as the long-term prognosis of immediate implant placement into fresh extraction sockets. (2)

A clinical trial showed that the placement of implants immediately in fresh extraction sockets affected by periodontal disease followed by immediate restoration may be a valid operative technique that leads to predictable results if adequate preoperative and postoperative care is taken. Several studies have shown that immediately loaded implants' micromovements can improve osseointegration and can dramatically increase the bone density. Also it was shown that immediate loads can increase the mineralization rate in bone-implant interface as there is potential for increased bone healing and remodelling in fresh extraction sockets. (9, 10)

Patient's age and health

Today, the placement of implants immediately after tooth extraction has proven to be a predictable treatment strategy with a very high success rate. Several authors carried out immediate loading of implants placed in fresh extraction sockets in the anterior (premolar to

premolar) region to maintain an excellent soft tissue esthetic profile around the implant-prosthetic restoration with a survival rate of 100%. However, contradictory results were reported with cumulative survival rate of 82.4% for implants placed in fresh extraction sockets and 100% for implants placed in healed ridges. The definition of periodontally compromised/periodontally susceptible patients has been used when evaluating survival and success rates of implants, because periodontal disease has been considered a risk factor for implant therapy. Greater long-term periimplant marginal bone loss versus periodontally healthy subjects, sometimes statistically significant, has been observed in this category of patients. Immediately loaded implants present an alternative treatment modality for periodontally compromised patients that might provide a better opportunity to meet patient needs [9].

Surface topography of implant : There are a number of surfaces commercially available for dental implants. Most of these surfaces have proven clinical efficacy (>95% over 5 years).

Surface roughness of dental implants:

1. Roughening of implants by titanium plasma-spraying
2. Roughening of implants by grit-blasting
3. Roughening of implants by acid-etching
4. Roughening of implants by anodization

Future trends in dental implant surfaces:

1. Surface roughness at the nanoscale level
2. Biomimetic calcium phosphate coatings on titanium dental implants
3. Incorporation of biologically active drugs into titanium dental implants.

However, the development of these surfaces has been empirical, requiring numerous in vitro and in vivo tests. Most of these tests were not standardized, using different surfaces, cell populations or animal models. The exact role of surface chemistry and topography on the early events of the osseointegration of dental implants remain poorly understood. Furthermore, comparative clinical studies with different implant surfaces are rarely performed.

The future of dental implantology should aim at developing surfaces with controlled and standardized topography or chemistry. This approach is the only way to understand protein, cell and tissue interactions with implant surfaces. The local release of bone-stimulating or resorptive drugs in the periimplant region may also respond to difficult clinical situations with poor bone quality and quantity. These therapeutic strategies should ultimately enhance the osseointegration process of dental implants for their immediate loading and long-term success. (1)

Surface topography influences bone response at the micrometre level. Some indications exist that surface topography influences bone response at the nanometre level. (6)

As demonstrated in the available literature dealing with recently developed and marketed oral implants, surface-roughening procedures also affect the surface chemical composition of oral implants. There is sufficient proof that surface roughening induces a safe and predictable implant-to-bone response, but it is not clear whether this effect is due to the surface roughness or to the related change in the surface composition. The review of the experimental surface alterations revealed that thin calcium phosphate (CaP) coating technology can solve the problems associated with thick CaP coatings, while they still improve implant bone integration compared with non-coated titanium implants. Nevertheless, there is a lack of human studies in which the success rate of thin CaP-coated oral implants is compared with just roughened oral implants. No unequivocal evidence is available that suggests a positive effect on the implant bone integration of peptide sequences or growth factors coated on titanium oral implants. In contrast, the available literature suggests that bone morphogenetic protein-2 coatings might even impede the magnitude of implant-to-bone response.

MATERIALS & METHODS

This dissertation is an analysis of over 500 articles published on this topic. Many databases such as PubMed and MedLINE were searched

for relevant publications centering on the research on healing around dental implants. The search was done using the keywords. All types of studies were included in the search including in vitro experiments, in vivo studies on animal models and clinical trials in humans. The abstracts of all the articles were read and analysed. Of these, most of the articles had to be disregarded because they did not accurately present relevant information on healing around dental implants. The remaining 50 articles were again scrutinised in detail and 18 articles were shortlisted and formed the basis for this review. The evidence collected from this literature with respect to soft tissue and bone healing around implants was finally categorized and summarized.

RESULTS

Healing time

- In general implants are allowed to heal for 2–4 months before they are used to support crowns, bridges, or dentures. Some studies have shown that early loading of implant may not increase early or long term complications. However, if an implant is loaded too soon, it is possible that the implant may move which results in failure. Therefore it is important for patient to follow post operative instructions closely to maximize implant success.

Table 1. Factors influencing primary stability of implants.

The available data indicate the following about soft tissue wound healing around dental implants: (14)

- (a) Oral wounds follow a similar pattern.
- (b) The tissue specificities of the gingival, alveolar and palatal mucosa appear to be innately and not necessarily functionally determined.
- (c) The granulation tissue originating from the periodontal ligament or from connective tissue originally covered by keratinized epithelium has the potential to induce keratinization.
- (d) Epithelial healing following non-surgical and surgical periodontal therapy appears to be completed after a period of 7–14 days.

(e) The formation of the biological width and maturation of the barrier function around transmucosal implants requires 6–8 weeks of healing.

(f) The established peri-implant soft connective tissue resembles a scar tissue in composition, fibre orientation, and vasculature.

(g) The peri-implant junctional epithelium may reach a greater final length under certain conditions such as implants placed into fresh extraction sockets versus conventional implant procedures in healed sites.

Table 2. Comparison of tooth with implant.

Features	Tooth	Implant
Clinical characteristics		
Biologic width	Supracrestal	Subcrestal
Probing depth	Normal = 2–3 mm	Increased ≥ 4 mm
Bleeding on probing	Reliable inflammatory sign	Less reliable as bleeding is unrelated to the amount of inflammation in the peri-implant tissue ⁽¹²⁾
Tissue quality		
CT composition	Low collagen and high fibroblast	High collagen and low fibroblast
Vascular supply	Increased (supraperiosteal, vascular plexus of PDL)	Less (supraperiosteal only)
Hard tissue interface	Resilient connection	Rigid connection
	Bone-periodontal ligament-cementum connection	Osseointegration, periodontal ligament and cementum absent
Others	Periodontal ligament can allow tooth movements with its adaptive capacity	No adaptive capacity and no movements possible
Soft tissue interface		
Connective tissue fibers	Perpendicular insertion into cementum	Collagen fibers parallel to the tooth surface
Junctional epithelium	Originates from the reduced enamel epithelium	Originates from the adjacent oral epithelium

PDL= Periodontal ligament

There are many factors which influence bone healing around a dental implant. A huge number of the experimental investigations have demonstrated that the bone response was influenced mainly by the implant surface topography; smooth (Sa0.5 mm) and minimally rough (Sa 0.5–1 mm) surfaces showed less strong bone responses than rougher surfaces. Moderately rough (Sa41–2 mm) surfaces showed stronger bone responses than rough (Sa42 mm) in some studies. (6)

CONCLUSION

Manipulations of soft tissues as therapeutic steps associated with teeth and implants are

common clinical procedures. An understanding of the biological process of wound healing helps to better understand the possibilities and limitations of such clinical preventive or corrective interventions. A range of different products are available aimed at improving the conditions of the soft tissues at teeth, implants and the edentulous ridge. These products encompass scaffolds, cells and biologicals. Histological evidence from human studies provides valuable guidelines for clinical application of these products. (15)

Recommendations for future research

Strategies for future research investigation to advance the field of oral wound healing around teeth and implants included the following target areas recommended by the expert review panel:

- Need more information on the inductive influences of the connective tissue environment on tissue neogenesis. Study at the cellular and matrix levels could be important in determining environmental cues. Cell: cell interactions (e.g. epithelial-mesenchymal influences) may instruct cell fate and determination. Identification of the cytokine, chemokine and intercellular signalling networks that are involved in the wound healing process may better inform on regenerative and reparative approaches. The study of existing and newly discovered growth and differentiation factors may lead to new information on the repair and regeneration of oral tissues.

Evidence gained from genetic models (i.e. transgenic and gene deletion) relevant to skin morphogenesis and regeneration may be instructive and translate to the oral wound healing situation. More study is warranted to examine the oral wound healing response in the face of the microbial challenge and local salivary molecules that may influence epigenetic changes of oral epithelia.

- To identify host and immunological cellular and soluble factors that regulate the healing process during periodontal and periimplant wound repair. Determine what genetic biological phenotypes may regulate an exacerbated healing responses depending on

immunological profiles. It would also be valuable to study ageing on oral soft tissue wound healing responses on cellular senescence and telomere length on stem cell progenitors contributing to the reparative process.

- To investigate the mechanisms of connective tissue graft (CTG) integration, re-vascularization and re-epithelialization as it relates to tissue remodelling (increases or decreases in tissue volume and quality) in different soft tissue biotype situations.

- To identify the basic mechanisms and relevance of scar-like periimplant connective tissue and epithelial interface. To determine the mechanisms of connective tissue adhesion to the implant material surface. The field would be advanced to better understand the biological consequences of implant/abutment biomaterial surface characteristics on the influence of biological width formation. The role of implant biomaterial surface characteristics on dental biofilm formation and proliferation should be considered. (15)

For immediate placement of implants into fresh extraction sockets, titanium implants with roughened surfaces and coating with tricalcium phosphate have negligible influence in accelerating the early bone healing events of osseointegration. (17)

To be functionally useful, oral implants have to pierce the oral mucosa and enter the oral cavity, thus establishing a transmucosal connection between the external environment and the inner parts of the body.

In order to avoid bacterial penetration through this transmucosal piercing, the early formation of a long-standing effective barrier capable of biologically protecting the peri-implant structures is of paramount importance. It is a critical part of tissue integration, and may in part depend on: Material chemistry; Surface topography and Implant components and connections. (5)

In the light of the current literature, it has to be noticed that there is an increasing trend to install oral implants on more challenging cases, especially in elderly patients with poor wound

healing due to, e.g., diabetes, other metabolic malconditions, osteoporosis, radiation therapy, etc. As a consequence, there is a need to establish surfaces that will lead to a predictive improvement of implant-to-bone response. Evidently, the currently available methods to modify implant surface composition show potential to control the biological activity of the implant surface. Still additional animal as well as human studies are needed to provide more insight into the bone response as evoked and to generate a predicted bone response. (7)

CONFLICTS OF INTEREST

The authors declare they have no potential conflict of interests regarding this article.

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