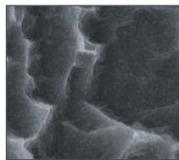


Immediate loading: The role of the implant surface on biological stabilization

John E. Davies, BDS, PhD, DSc



Clinicians who are immediately restoring and loading dental implants must consider a hierarchy of clinical parameters, including the choice of the implant surface. The latter plays a crucial role in orchestrating many of the cellular mechanisms in peri-implant tissue healing. The phenomenon of bone bonding is also critically dependent upon the design of the implant surface. This article reviews the cascade of post-placement healing responses and examines the role of implant micro- and nanotopography within that sequence of events.

Key Words: implant surface, biologic stabilization, bone bonding, nanotopography, osteogenesis

Introduction

Treatment planning is of cardinal importance in clinical procedures. When placing dental implants, consideration of parameters such as the dental base relationship, occlusion, and planned implant positioning with respect to the residual alveolar bone are all critically important, while surgical technique can also dramatically affect the therapeutic outcome. Similarly, the three-dimensional design of the implant (the gross dimensions and shape, including screw thread design) significantly influences the biomechanical environment created upon implant placement. Finally, increasing the complexity of the implant surface microtopography has been recognized for more than a decade to profoundly affect healing, particularly in cancellous bone.

Figure 1 illustrates this hierarchy of clinical parameters. The more advanced the implant procedure, the more

important it is for clinicians to pay careful attention to each aspect of this hierarchy. This is particularly true when immediately restoring and loading endosseous dental implants, an increasingly popular approach to the rehabilitation of edentulous patients.

Early studies of occlusal loading of immediately placed implants reported bone loss due to excessive implant micromotion¹ and the formation of a fibrous peri-implant connective tissue layer.² However, more recent studies have documented a high level of bone-to-implant contact in humans around immediately loaded implants.³ Over the past 10 years, immediate loading therapies have shown success rates ranging from 97% to 100% with comparable or better histological and histomorphometric outcomes than delayed loading protocols.⁴

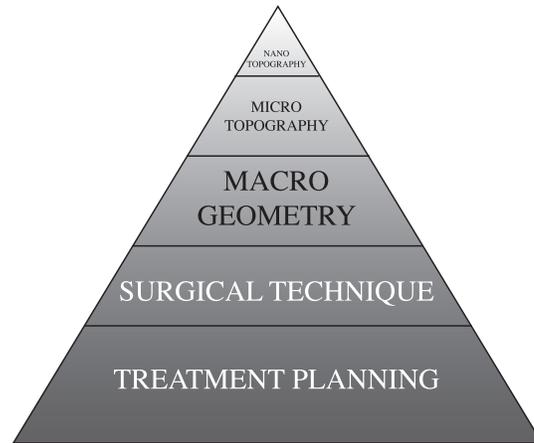


Fig. 1

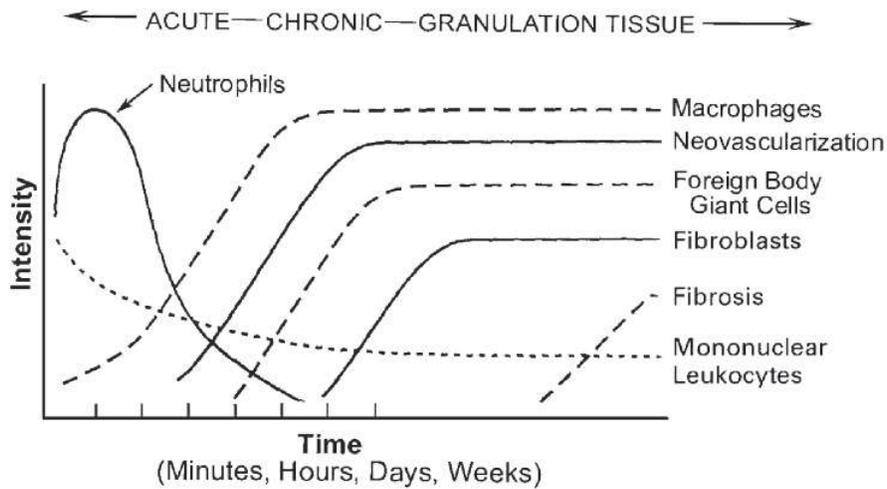


Fig. 2

The Basis of Immediate Loading: Implant Stabilization

Successful immediate loading depends upon three main strategies: (1) achieving primary stability and avoiding implant micromotion in the early stages of healing, (2) achieving secondary (biological) stability as a result of osteogenesis in the peri-implant area, and (3) controlling bone resorption caused by deleterious loading forces that lead to implant instability during healing.⁵

Primary stability is one of the most critical factors.⁶ It must be obtained at the time of the implant's insertion, before any load is applied. Primary stability involves securing the implant within the host bone with sufficient rigidity to preclude any significant micromotion.⁷ The lack of primary stability contributes to fibrous encapsulation of the implant, which represents one of the main factors of implant failure.^{6,8}

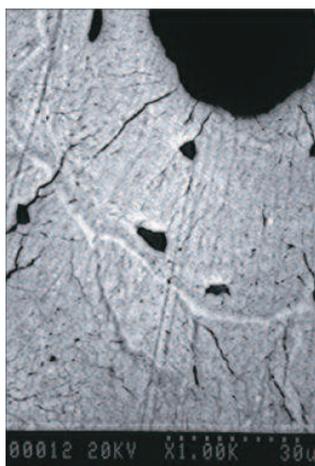


Fig. 3a

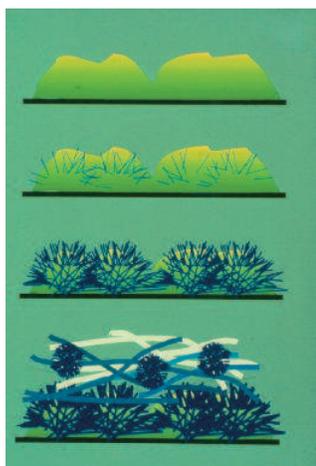


Fig. 3b

Fig. 1.

The hierarchy of parameters for successful implant therapy. Successful clinical outcomes rely on proper treatment planning and surgical technique, which provide an essential foundation for success. The overall implant design, shape, size, and screw thread geometry will have major effects on both early and long-term biomechanics. Surface microtopography has been shown to dramatically influence the early stages of peri-implant bone healing and to be particularly important for contact osteogenesis. Refinement of the surface nanotopography can further accelerate contact osteogenesis and also result in bone/implant bonding.

Fig. 2.

The cellular cascade associated with generalized wound healing. Neutrophils are the first leukocytes to migrate into the wound site, followed by macrophages. Neovascularization not only brings these cells and a nutrient supply into the site, but also pericytes, or perivascular cells, which are tissue-resident mesenchymal stem cells that can differentiate into the connective tissue lineages, depending on local environmental cues. In the soft-tissue example illustrated, these cells differentiate into fibroblasts, but in an endosseous site, osteogenic cells would enter the wound site. Reproduced from Anderson JM. The Cellular Cascades of Wound Healing. In: Davies JM (ed). Bone Engineering, Toronto: em2 Inc., 2000:81-93.

Figs. 3a-b.

(A) An SEM photomicrograph of the cement line, which forms a distinct anatomical boundary between new and old bone at remodeling sites. (B) The stages of *de novo* bone formation, including the cement line (Davies 1998).

The degree of primary stability of endosseous dental implants is believed mainly to depend upon bone type, implant design, patient characteristics, and surgical technique.⁹

After several weeks of healing, primary stability is followed by a biological, or secondary, stability.¹⁰ Biological stability is achieved by contact osteogenesis, the direct deposition of bone tissue on the implant surface. This is

the product of a complex cascade of events that characterize early peri-implant healing, in which osteoconduction and *de novo* bone formation are the key mechanisms.¹¹

The cascade starts at the instant of injury with an acute inflammatory response that lasts from two to five days. Within nanoseconds after implant placement, ionic exchange between the plasma of the extravasated blood

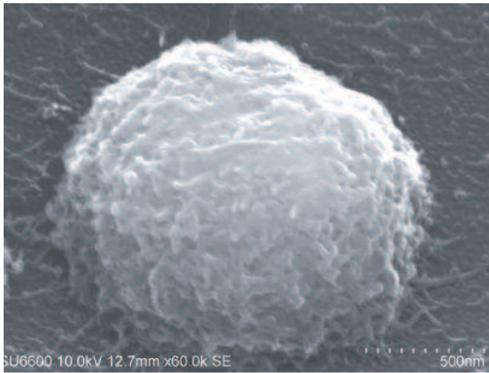


Fig. 3c

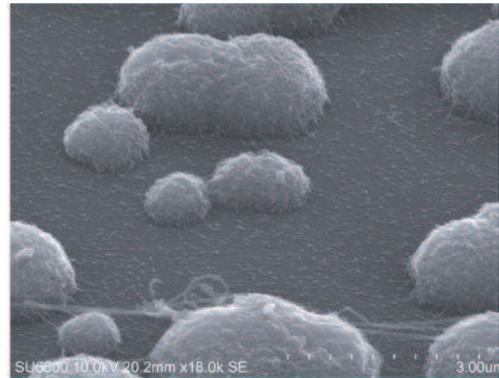


Fig. 3d

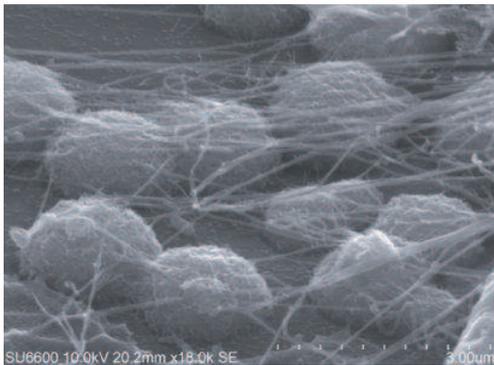


Fig. 3e

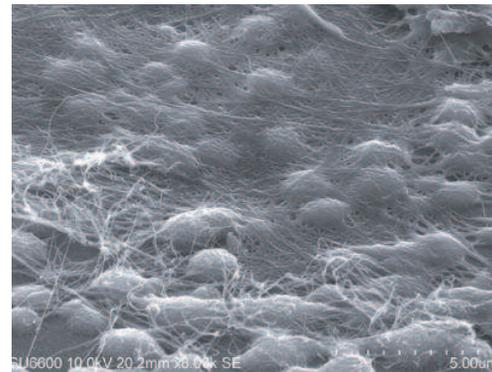


Fig. 3f

and the implant surface occurs. Competitive plasma protein adsorption to the implant surface follows within milliseconds and initial cell contact within seconds. Since the majority of cells in blood are red blood cells and platelets, it is these cells that contact the implant surface first, with leukocytes (particularly neutrophils and macrophages) following soon afterwards (Fig. 2). Platelets, once activated, play a crucial role in peri-implant healing.

As tissue healing progresses, coagulating blood not only serves as a reservoir of growth factors but also as a provisional scaffold in which osteogenic mesenchymal cells can migrate. In this context, implant surface topography is of utmost importance for maintaining the blood-clot structure. Microtopographically complex implant surfaces have peaks and valleys that foster increased fibrin adhesion and a higher resistance to

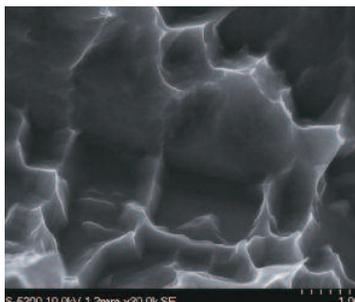


Fig. 4a

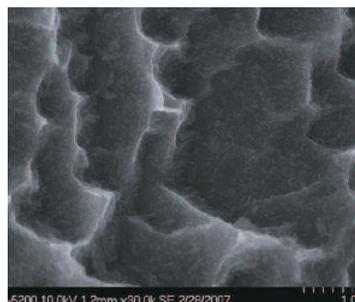


Fig. 4b

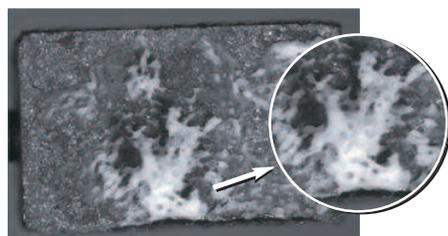


Fig. 5

Figs. 3c-f.

SEM photomicrographs showing the earliest stages of *de novo* bone formation *in vitro* [Courtesy of James Ko, Bone Interface Group, University of Toronto] (c & d). Globular, mineralized, non-collagenous matrix composed mainly of osteopontin, bone sialoprotein, and two proteoglycans (e & f). Further stages of bone matrix deposition, in which a collagenous extracellular matrix has been elaborated, by mature osteoblasts and assembled as fibers on the cement-line matrix.

Figs. 4a-b.

Field emission scanning electron micrograph (FE-SEM) of cpTi DAE (a) and cpTi DAE-DCD (b) implant surfaces. Both surfaces present identical microtopographies due to the initial dual acid etch treatment, but the latter surface has discrete nanocrystals of calcium phosphate (20-100nm in size), which enhance the surface complexity at a nanometer-scale level. Such features can only be observed at very high magnifications but have been shown to have profound biological effects.

Fig. 5.

Photograph of a retrieved DAE-DCD custom-made rectangular implant (4mm x 2.5mm x 1.4mm). This implant was placed in the distal aspect of the rat femur for nine days and subjected to mechanical (tensile) testing. After sample disruption, interfacial bone bonding was observed (see enlargement) as a result of the mechanical interlock between the bone matrix and the DCD nanofeatures.

detachment. A strong mechanical interlock to the implant surface stabilizes the fibrin clot during osteogenic cell migration and guarantees that these cells will reach the implant for subsequent bone deposition directly on its surface (see animations at www.ecf.utoronto.ca/~bonehead/).

Formation of granulation tissue starts approximately on the fourth day after implant placement and may last until

the third week post-injury. During this period, osteogenic cells are stimulated and bone deposition commences. In the immediate loading scenario, the rupture of the fibrin clot and vascular network due to excessive micro-movement of the implant body will negatively affect osteogenesis. The tolerable level of implant micromotion under immediate loading during healing has been reported to range from 50 to 150µm.⁸

Once migrating osteogenic cells reach the implant surface, they start secreting the first organic matrix, devoid of collagen and composed of osteopontin, bone sialoprotein, and proteoglycans. This first layer, analogous to the cement line formed during normal bone remodeling (Figs. 3a-b), provides nucleation sites for calcium phosphate, which subsequently grow within the organic matrix. After the deposition of the cement-line matrix, the osteogenic cells differentiate into osteoblasts that elaborate the collagenous extracellular matrix assembled as fibers. Finally, the collagenous fibers undergo calcification and are separated from the underlying substratum by a calcified non-collagenous matrix.¹¹ This stage is named *de novo* bone formation (Figs. 3c-f).

Osteogenesis in a peri-implant environment results from two distinct mechanisms. *Distance* osteogenesis occurs when bone matrix is deposited from the host bone towards the implant surface. *Contact* osteogenesis occurs when bone matrix is deposited from the implant surface to the host bone (see animations at www.ecf.utoronto.ca/~bonehead/). The anatomical location and surface topographical design of the implant influence both phenomena. However, while osteoconduction is influenced by and dependent upon the implant surface, the process of bone formation itself is independent of the surface material. This explains why bone has been shown to form on almost any non-toxic surface from Teflon™ to titanium alloy. Bone grows both appositionally and through a matrix; the former process is slower (0.6-1 μm/day) than the latter (30-50 μm/day).¹² However, when osteoconduction results in bone growth along a material surface, there is the possibility that the bone may bond to the implant surface, a phenomenon known as bone bonding.

Three theories of bone bonding have emerged in the literature: the “physico-chemical” (often abbreviated to “chemical”), the “micro-mechanical,” and the “biochemical.” Speculation that a variety of chemical interactions drove the Bone Bonding® Process was first advanced by Hench et al in 1971.¹³ While the authors undertook no experiments to address their speculations, this paper enormously influenced the subsequent literature. The chemical theory was adopted by Jarcho,¹⁴ and a similar approach was employed by Tracy and Doremus¹⁵ and Bonfield and Luklinska.¹⁶ This focus on

chemistry has also been adopted by the most recent so-called “biochemical” theory of bone bonding. However, the latter is neither based upon experiment nor any biochemistry; it is solely a speculation on the importance of small atomic percentages of dopant ions in metal-oxide surfaces without any consideration of very significant differences in microtopography of the materials examined.¹⁷ Of the three theories of the mechanism of bone bonding, only one is based on robust experimental evidence. The “micro-mechanical” theory has evolved from an understanding of how new bone bonds to old bone in the natural process of bone remodeling, and has been substantiated by evidence from both *in vitro* and *in vivo* experimentation.¹⁸

Implant Surface Design

The first generation of endosseous root-form implants introduced by Brånemark was characterized by a relatively smooth surface obtained by machining titanium. Subsequently, various techniques were developed to modify the implant surface topography, using both additive and subtractive processes. The additive approach typically employs deposition methods such as titanium or hydroxyapatite plasma spraying. The subtractive approach uses techniques such as sandblasting or acid etching.

As discussed above, the characteristics of the implant surface play a major role in the early events of endosseous healing and contribute to improved secondary implant stability. *In vivo* studies employing implants with a complex surface topography have shown increased shear strength and removal resistance after healing. A higher percentage of bone-implant contact (BIC) has been demonstrated on implants with microtopographically complex surface designs in comparison to those of originally smoother surfaces.¹⁹

Recent research has focused on understanding the role of implant surface nanotopography on the mechanisms of peri-implant healing.²⁰ By definition, nanotopographic features range in size between 1-100nm. Changes to the implant surface topographic design at the nanometer level have been shown to affect tissue response positively during healing and consequently enhance osteogenesis.^{21,22} Various technologies have been developed to create nanotopographical features on endosseous implant surfaces with successful experimental outcomes.²² One such



approach involves the discrete crystalline deposition (DCD) of calcium phosphate (CAP) (20-100nm) on the titanium surface by means of a sol-gel process.²³ The resulting nanocrystals cover an area of about 50-60% of the implant surface and enhance its complexity on a nanometer scale without altering its original microtopography (Fig. 4). The CAP nanoparticles have been shown to adhere strongly to the surface of DAE commercially pure titanium (cpTi) and titanium alloy (Ti6Al4V) implants, and the ability of the nanotopographically complex DCD implant surface to enhance early healing (osteoconduction) has been evaluated using bone-ingrowth chambers fabricated of either cpTi or Ti6Al4V. The internal walls of the chambers were treated by the DAE or DAE-DCD method and implanted in rat femora. Harvested samples were resin-embedded in blocks, which were ground and backscatter-electron-imaged (BSEI) numerous times at different planes of the chamber height. BIC was measured from 1087 micrographs. The results showed that the DCD nanotopography enhanced osteoconduction significantly on both cpTi and Ti6Al4V implant surfaces.²¹

The question of whether the DCD nanofeatures render metallic surfaces a Bone Bonding®* Surface (i.e. NanoTite™ Implant Surface, BIOMET 3i) has also been investigated. The bone bonding phenomenon is characterized by a strong micromechanical interlock between the bone matrix and the implant surface. When DAE and DAE-DCD cpTi and

Ti6Al4V implants implanted in rat femora were subjected to a disruption test in an Instron machine, the results revealed that the DCD treatment rendered all metallic implant surfaces bone bonding (Fig. 5), and significantly higher force values were required to disrupt them.²³

Clinical studies employing implants with the DAE-DCD surface have also been conducted.^{24,25} When custom-made test implants (2 × 9.5mm) of either DAE or DAE-DCD surfaces were inserted in the posterior maxillae of patients for four and eight weeks, in a double-blind randomized trial, the results showed significantly greater percentages of BIC around DCD-treated implants in comparison to DAE implants.²⁴ Histological findings at four weeks showed predominant signs of contact osteogenesis for DCD groups, whereas distance osteogenesis was observed in the DAE groups.

A recent prospective, multicenter clinical trial has been published with one-year follow-up of DCD implants placed under an immediate loading protocol.²⁵ The cases were selected for rehabilitation of fixed partial prostheses and single-tooth restorations (STR), which are considered as clinical challenges for this type of approach. Following surgical placement of the implants, the prostheses were inserted within 48 hours. A total of 335 implants were provisionalized (128 STR and 88 multiple-unit fixed prostheses) under the same protocol, which was followed by the participating 15 study centers located worldwide. This one-year interim report showed a cumulative survival rate of 94.4%, which the authors consider as good performance in comparison to other studies employing different implant topographical designs under stricter inclusion criteria.

Clinical Relevance

Primary stability of the implant is critical for successful osseointegration. While employment of the most refined nano-scale implant surfaces can only be founded on sound treatment planning and expert surgical technique in placing implants that have appropriate three-dimensional forms and microtopography, within this strict clinical framework, peri-implant osteogenesis can be enhanced by implant surface topographical design. Implants with nanotopographically complex surface designs are emerging as the next generation of endosseous dental implants.

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*Bone Bonding® is the interlocking of the newly formed cement-line matrix of bone with the implant surface.

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John E. Davies, BDS, PhD, DSc



Dr. Davies received his Doctor of Science degree from the University of London and is Professor of Dentistry and Biomaterials at the University of Toronto, Toronto, Ontario, Canada, specializing in research on peri-implant bone healing, bone-tissue engineering, and mesenchymal stem-cell biology. He is also a member of the Institute of Biomaterials and Biomedical Engineering, with cross appointments in the Faculty of Applied Science and Engineering and the Faculty of Medicine at the University of Toronto.