

# Implant Materials, Designs, and Surface Topographies: Their Effect on Osseointegration. A Literature Review

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*The aim of this article was to review the literature on materials, designs, and surface topographies of endosseous dental implants. The different categories of dental implants and the parameters of their design were analyzed in relation to their effect and significance in the process of osseointegration. The events that immediately follow implantation were described, emphasizing the factors that play a role in the development of the bone-implant interface. In addition, the methods and techniques that allow qualitative and quantitative evaluation of the interfacial zone were reviewed and their clinical correlation was assessed. (INT J ORAL MAXILLOFAC IMPLANTS 2000;15:675-690)*

**Key words:** dental implants, dental materials, histomorphometry, laboratory techniques and procedures, osseointegration, surface properties

Missing teeth and the various attempts to replace them have presented a treatment challenge throughout human history.<sup>1,2</sup> Becker<sup>3</sup> reviewed the simple and naïve ancient artificial anchoring of dental units in the maxilla and mandible, which indicated the constant need for restoring function and esthetics by any means. However, it was not until the 1960s that the scientific foundation of modern implant dentistry was set. At that time, vital microscopic studies of osseous wound healing initiated by Brånemark and

colleagues using the titanium chamber gave rise to the concept of osseointegration.<sup>4</sup> Osseointegration was initially defined on the light microscopic level as “a direct structural and functional connection between ordered, living bone and the surface of a load-carrying implant”<sup>5</sup> (Fig 1). A short time later, osseointegration was given a more clinical definition as a process in which clinically asymptomatic rigid fixation of alloplastic materials is achieved and maintained in bone during functional loading.<sup>6</sup> Additionally, objective criteria for determining implant success have been proposed.<sup>7,8</sup>

Currently, endosseous implants are a well accepted treatment modality for oral and craniofacial reconstruction, serving as transmucosal structures to support single teeth,<sup>9</sup> fixed partial dentures,<sup>10</sup> complete-arch reconstructions,<sup>11</sup> and complete removable dentures<sup>12</sup> or to reconstruct maxillofacial defects.<sup>13-18</sup> Implant technology is continually evolving as new research findings provide a better understanding of the biologic principles that govern the development of a dynamic interface between the living tissue and an artificial structure.

This paper provides a review of the materials, designs, and surface topographies of endosseous dental implants currently in use, emphasizing the association of the reported variables with the biologic outcome. The focus is on the initial events

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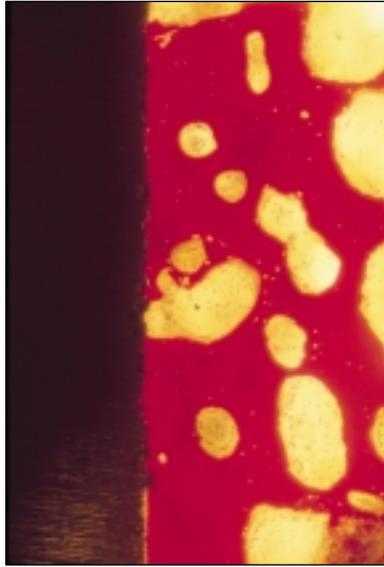
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**Fig 1** Developed bone-implant interface characterized as "osseointegrated" (Stevenel's blue and van Gieson picrofuchsin stain; original magnification  $\times 100$ ).

that immediately follow implantation in an attempt to explain the mechanisms and interfacial dynamics that lead to osseointegration. The last section of this review describes the methods and techniques that allow qualitative and quantitative evaluation of the bone-implant interface.

## IMPLANT MATERIALS

Materials used for the fabrication of dental implants can be categorized in 2 different ways. From a fundamental chemical point of view, dental implants fall into 1 of the following 3 primary groups: (1) metals, (2) ceramics, and (3) polymers. In addition, biomaterials can be classified based on the type of biologic response they elicit when implanted and the long-term interaction that develops with the host tissue. Three major types of biodynamic activity have been reported: (1) biotolerant, (2) bioinert, and (3) bioactive<sup>19,20</sup> (Table 1). The different levels of biocompatibility emphasize the fact that no material is completely accepted by the biologic environment. To optimize biologic performance, artificial structures should be selected to minimize the negative biologic response while ensuring adequate function.

Biotolerant materials are those that are not necessarily rejected when implanted into living tissue, but are surrounded by a fibrous layer in the form of

a capsule. Bioinert materials allow close apposition of bone on their surface, leading to contact osteogenesis. Bioactive materials also allow the formation of new bone onto their surface, but ion exchange with host tissue leads to the formation of a chemical bond along the interface (bonding osteogenesis). Bioinert and bioactive materials are also called *osteoconductive*, meaning that they can act as scaffolds allowing bone growth on their surfaces. *Osteoconductive* should not be confused with *osteoinductive* materials, such as recombinant human bone morphogenetic protein 2 (rhBMP-2), which refers to the capacity to induce bone formation de novo. Biotolerant, bioinert, and bioactive materials are all biocompatible by definition and result in a predictable host response in specific application.<sup>21</sup> *Biomimetics* are tissue-engineered materials designed to mimic specific biologic processes and help optimize the healing/regenerative response of the host microenvironment. Biomimetic materials can be any combination of the chemical and biodynamic activity categories, depending on the therapeutic strategy and the type of host tissue.<sup>22,23</sup>

## Metals

Metals for implants have been selected based on a number of factors: their biomechanical properties; previous experience with processing, treating, machining, and finishing; and suitability for common sterilization procedures. Occasionally, various metals and metal alloys used for the fabrication of dental implants have produced adverse tissue reactions, and their low success rates undermined long-term clinical application. Many of the metals and alloys (gold, stainless steel, cobalt-chromium) are now obsolete within the oral implant industry. Titanium (Ti) and its alloys (mainly Ti-6Al-4V) have become the metals of choice for endosseous parts of currently available dental implants. However, prosthetic components, including abutment screws, abutments, cylinders, prosthetic screws, and various attachments, are still made from gold alloys, stainless steel, and cobalt-chromium and nickel-chromium alloys. Consequently, there is the potential for galvanic action developing between dissimilar metallic surfaces, with possible effects on electrochemical corrosion, oxidation, and triggering of pain.<sup>24</sup>

Titanium interacts with biologic fluids through its stable oxide layer, which forms the basis for its exceptional biocompatibility.<sup>25,26</sup> When exposed to air, Ti forms an oxide layer immediately ( $10^{-9}$  sec) that reaches a thickness of 2 to 10 nm by 1 sec and provides corrosion resistance.<sup>27,28</sup> Because of the high passivity, controlled thickness, rapid formation, ability to repair itself instantaneously if damaged,

**Table 1** Classification of Dental Implant Materials

| Biodynamic activity | Chemical composition                                                                  |                                                                                                                                                                                    |                                                                                                |
|---------------------|---------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------|
|                     | Metals                                                                                | Ceramics                                                                                                                                                                           | Polymers                                                                                       |
| Biotolerant         | Gold<br>Cobalt-chromium alloys<br>Stainless steel<br>Zirconium<br>Niobium<br>Tantalum |                                                                                                                                                                                    | Polyethylene<br>Polyamide<br>Polymethylmethacrylate<br>Polytetrafluoroethylene<br>Polyurethane |
| Bioinert            | Commercially pure titanium<br>Titanium alloy (Ti-6Al-4V)                              | Aluminum oxide<br>Zirconium oxide                                                                                                                                                  |                                                                                                |
| Bioactive           |                                                                                       | Hydroxyapatite<br>Tricalcium phosphate<br>Tetracalcium phosphate<br>Calcium pyrophosphate<br>Fluorapatite<br>Brushite<br>Carbon: vitreous, pyrolytic<br>Carbon-silicon<br>Bioglass |                                                                                                |

resistance to chemical attack, catalytic activity for a number of chemical reactions, and modulus of elasticity compatible with that of bone of titanium oxide, Ti is the material of choice for intrasosseous applications.<sup>29,30</sup> The stoichiometric composition of commercially pure titanium (cpTi) allows its classification into 4 grades that vary mainly in oxygen content, with grade 4 having the most (0.4%) and grade 1 the least (0.18%).<sup>31</sup> Although oxide properties are not affected, mechanical differences exist between the different grades primarily because of the contaminants that are present in minute quantities.<sup>31</sup> Traces of other elements such as nitrogen, carbon, hydrogen, and iron have also been detected and added for stability or improvement of the mechanical and physicochemical properties. Iron is added for corrosion resistance and aluminum is added for increased strength and decreased density, while vanadium acts as an aluminum scavenger to prevent corrosion.<sup>32,33</sup> The condition of the oxide layer, namely its chemical purity and surface cleanliness, is of paramount importance for the biologic outcome of osseointegration.<sup>34,35</sup> Nevertheless, the effect of contamination of the implant surface on cellular response and cellular morphology has been reported in the literature as a result of the production process or sterilization procedures.<sup>36-39</sup> Further discussion of Ti-Ti alloys can be found in the work of Han and colleagues<sup>40</sup> and Johansson and coworkers.<sup>41</sup>

### Ceramics

Ceramic materials used in the field of oral and maxillofacial implants are listed in Table 1 and

are either bioinert or bioactive. Hydroxyapatite ( $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ ) (HA), tricalcium phosphate ( $\text{Ca}_3(\text{PO}_4)_2$ ), and bioglasses are some of the more commonly used bioactive ceramics, which possibly develop a chemical bond of a cohesive nature with bone.<sup>42-44</sup> Ceramics can make up the entire implant, or they can be applied in the form of a coating onto a metallic core. Low flexural strength and various degrees of dissolution/solubility of an all-ceramic implant make coating the application of choice in the field of implant dentistry. Coatings can be dense or porous, depending on the chemical composition of the parent material and the coating method that is employed. The goal is to achieve strong adherence between the coating and the metallic core, which is able to withstand functional loading and avoid fragmentation. Hot isostatic pressing ( $P = 1,000$  bar,  $T = 750^\circ\text{C}$ ) results in the formation of highly dense HA coatings with a surface roughness ( $R_a$ ) of  $0.7 \mu\text{m}$  and bond strength  $> 62$  MPa.<sup>45</sup> Surface-induced mineralization (SIM) results in the same surface characteristics as the plasma-sprayed technique but may provide a stronger bond between the coating and substrate.<sup>46</sup>

Crystallinity is also affected by the heat and pressure conditions of the coating environment. Lacey<sup>43</sup> reported that plasma-sprayed HA has a crystallinity of 60% to 70%, which can increase with heat treatment, although values of 30% to 66% for the crystalline nature have been observed.<sup>47</sup> Crystallinity relates directly to the rate of dissolution, with denser and more crystalline coatings being least dissolvable.<sup>48</sup> Hydroxyapatite coatings consist of 2

phases: the amorphous phase and the crystalline phase. Gross and colleagues<sup>49</sup> evaluated the crystalline phase of HA coatings on 5 commercially available dental implants and found that differences depended on several factors. Heat dissipation of the molten particles through the metal core of the implant affected the thickness of both the amorphous and crystalline phase, as well as the shape and location of the crystalline areas. The macroscopic design of the implant also plays a role in the thickness and quality of the crystalline phase, with the threads and collar region exhibiting 75% to 80% crystallinity, whereas apical portions related to apical holes reached a level of 100% crystalline phase. The temperature of the spray process and the chemical composition of the melt are factors equally important to the end result.<sup>50</sup> Distance from the gun, the nature of the carrier gas, and possible contamination by the nozzle<sup>43</sup> are additional variables that may influence the quality of the coating layer among different vendors.<sup>49,51,52</sup> Variations in the ratio of the amorphous/crystalline phase and the actual composition of the coating may necessitate the description of the applied bioceramic as a calcium phosphate coating rather than an HA coating.<sup>53,54</sup> Coating thickness is usually 50 to 70  $\mu\text{m}$ <sup>49,52,55</sup> with the plasma-spraying technology but can range from 1 to 100  $\mu\text{m}$  depending on the coating method.<sup>43</sup>

Some of the concerns associated with HA-coated implants were reviewed by Biesbrock and Edgerton<sup>56</sup> and included microbial adhesion, osseous breakdown, and coating failure. However, the authors suggested that in cases where more rapid and enhanced bone-implant contact is needed, such as in type IV bone, grafted bone sites, or when short implants are indicated, HA-coated implants may be preferable. Caulier and coworkers<sup>57</sup> found improved performance with threaded calcium phosphate-coated implants placed in less mineralized trabecular bone, although the thickness of the coating decreased over time.

While the clinical success of HA-coated implants has been reported to be 97.8% at 6 years,<sup>58</sup> various concerns are associated with their use.<sup>59</sup> The degradation of ceramic coatings has been a point of controversy,<sup>60</sup> and concerns have been expressed about their long-term stability and success.<sup>61,62</sup> In a comparative study by Vercaigne and coworkers,<sup>63</sup> it was found that the chemical composition of the HA coating has a more profound influence on the bone reaction than does the implant's surface roughness, although signs of coating degradation were observed. The glassy phase of HA coatings remains unaffected after implantation while crystallization progresses within the mass of the crystal phase.<sup>64</sup> During this process, stress accumulation may affect the coating/substrate

interface and result in fragmental delamination. Loading of HA-coated implants has been shown to affect the resorption rate and pattern of the coating. Overgaard and colleagues<sup>65</sup> demonstrated that the surface area and volume of the HA coating on immobilized implants were reduced by 53% and 67%, respectively, at 16 weeks, whereas the corresponding values for loaded implants were 83% and 87%.

## Polymers

A variety of polymers, including ultrahigh molecular weight polyurethane, polyamide fibers, polymethylmethacrylate resin, polytetrafluoroethylene, and polyurethane, have been used as dental implant materials.<sup>66-68</sup> It was hoped that their flexibility would mimic the micromovement of the periodontal ligament and possibly allow connection with natural teeth.<sup>69,70</sup> However, the ability of flexible implants to transfer stress more favorably to bone was compared to rigid implants, and no statistical differences were found.<sup>71</sup> Inferior mechanical properties, lack of adhesion to living tissues, and adverse immunologic reactions have eliminated the application of these materials as a coating layer.<sup>66,72</sup> Today, polymeric materials are limited to the manufacturing of shock-absorbing components incorporated into the suprastructures supported by implants.<sup>73</sup>

## IMPLANT DESIGN

Implant design refers to the 3-dimensional structure of the implant, with all the elements and characteristics that compose it. *Form, shape, configuration, surface macrostructure, and macro-irregularities* are terms that have been used in the literature to describe aspects of the 3-dimensional structure. The authors believe that implant design is an inclusive term with direct association to what is represented.

Endosseous dental implants exist in a wide variety of designs,<sup>74</sup> with the main objective in every instance being the long-term success of the osseointegrated interface and uncomplicated function of the prosthetic replacement (Figs 2 and 3). The type of prosthetic interface, the presence or absence of threads, additional macro-irregularities, and the shape/outline of the implant are considered some of the most important aspects of implant design. The prosthetic interface, that is, the level at which the suprastructure or the abutment connects to the implant body, can be either external or internal. The most common external connection is the hexagonal ("hex") type; variations in height and width affect tactile perception and the stability (most often, antirotational) of the prosthesis. The



**Fig 2** Threaded dental implants.



**Fig 3** Non-threaded cylindric dental implants.

octagonal top (“octa”) and the “spline” interface (Sulzer Calcitek, Carlsbad, CA), with its interdigitating projections and slots, are also external connections. The category of internal connection includes the Morse Taper interface (ITI, Straumann, Waldenburg, Switzerland), the internal hexagon, and internal octagon.

Dental implants are also categorized into threaded and non-threaded cylindric or “press-fit.” Although surgical fit and primary stability are very important for the fixation and long-term success of the implant, cylindric (non-threaded) implants have not been followed with regard to maintaining an average, steady-state bone level in the literature. Ivanoff and

coworkers<sup>75</sup> studied the influence of initial implant stability on the process of osseointegration by comparing stable, rotation-mobile, and totally mobile threaded implants. After 12 weeks of healing, although all implants appeared clinically stable, significantly less bone-implant contact and bone fill within the implant threads were found for the totally mobile implants. Yet initial rotation-mobility did not lead to inferior osseointegration. Manufacturing tolerances, operative technique, surgical conditions, and bone quality affect the dimensions of the osteotomy site and determine the magnitude of discrepancies in the surgical fit. Carlsson and colleagues<sup>76</sup> investigated the interfacial reaction of cylindrical Ti implants with perfect fit and initial gap distances of 0.35 mm and 0.85 mm in rabbits. They found that 0.35 mm is the critical size gap beyond which no direct implant-bone contact can be achieved. Other investigators have suggested that larger gaps (up to 2 mm) still fall within the natural ability of bone to bridge the defect.<sup>77-79</sup> Various studies have indicated that calcium phosphate-coated implants may enhance fixation in the presence of initial gaps,<sup>80-82</sup> provided that stability is maintained and any possible micromotion is kept to a minimum (< 150  $\mu\text{m}$ ).<sup>83-85</sup> Only excessive micromotion can be detrimental to osseointegration in cases of early loading, but the critical threshold varies with implant design and initial stability.<sup>86-88</sup> At the same time, surface changes of HA-coated implants may occur as a result of increased torsional forces generated in situations of undersized and untapped osteotomy sites.<sup>89</sup>

Threads are used to maximize initial contact,<sup>90</sup> improve initial stability,<sup>91,92</sup> enlarge implant surface area, and favor dissipation of interfacial stress.<sup>93,94</sup> Thread depth, thread thickness, thread pitch, thread face angle, and thread helix angle are varying geometric parameters that determine the functional thread surface and affect the biomechanical load distribution of the implant.<sup>95</sup> Thread thickness and thread face angle determine the shape of the thread, which can be V-shape, square, or a reverse buttress thread.<sup>95,96</sup> Recently, some manufacturers (Nobel Biocare, Göteborg, Sweden, and Paragon, Encino, CA) have introduced the concept of double-threaded or triple-threaded implants, which are faster to thread into the osteotomy site, generate less heat upon placement, provide increased initial stability, and require more torque for placement (and thus tighter contact with bone). These are indicated primarily for Type IV (cancellous) bone.

A plethora of additional features have been employed by implant companies to accentuate or replace the effect of threads. These include perforations of various shapes and dimensions, vents,

ledges, grooves, flutes, and indentations. The implant can be solid or hollow, with a parallel, tapered/conical, or stepped shape/outline and a flat, round, or pointed apical end.

## SURFACE TOPOGRAPHY

The quality of the implant surface is one of the 6 factors described by Albrektsson et al<sup>34</sup> that influence wound healing at the implantation site and subsequently affect osseointegration. For the purpose of this review, *implant surface* will refer to the descriptive parameters of surface roughness.

### Smooth

Wennerberg and coworkers<sup>97,98</sup> have suggested that *smooth* be used to describe abutments, whereas the terms *minimally rough* (0.5 to 1  $\mu\text{m}$ ), *intermediately rough* (1 to 2  $\mu\text{m}$ ), and *rough* (2 to 3  $\mu\text{m}$ ) be used (apart from porous surfaces for implanted surfaces). However, in the majority of literature reports, based on the average surface roughness ( $S_a$ ), surfaces with an  $S_a \leq 1 \mu\text{m}$  are considered smooth, and those with  $S_a > 1 \mu\text{m}$  are described as rough. Machined (turned) cpTi is a smooth surface with an  $S_a$  value of 0.53 to 0.96  $\mu\text{m}$ ,<sup>99,100</sup> depending on the manufacturing protocols, grade of the material, and shape and sharpness of the cutting tools. Circumferential parallel lines of 0.1  $\mu\text{m}$  in depth/width, perpendicular to the long axis of the implant, are a common finding in machined surfaces. Surface topography can produce orientation and guide locomotion of specific cell types and has the ability to directly affect cell shape and cell function.<sup>101-104</sup>

### Rough

Plasma spray-coating is one of the most common methods for surface modification. Plasma-spraying is used for the application of both Ti or HA on metallic cores with a coating thickness of 10 to 40  $\mu\text{m}$  for Ti<sup>105</sup> and 50 to 70  $\mu\text{m}$  for HA. Thickness depends on particle size, speed and time of impact, temperature, and distance from the nozzle tip to the implant surface area. The surface roughness value ( $R_a$ ) for Ti plasma spray is 1.82  $\mu\text{m}$ , and for HA plasma spray,  $R_a = 1.59$  to 2.94  $\mu\text{m}$ .<sup>100</sup>

Blasting with particles of various diameters is another frequently used method of surface alteration. In this approach, the implant surface is bombarded with particles of aluminum oxide ( $\text{Al}_2\text{O}_3$ ) or titanium oxide ( $\text{TiO}_2$ ), and by abrasion, a rough surface is produced with irregular pits and depressions. Roughness depends on particle size, time of blasting, pressure, and distance from the source of parti-

cles to the implant surface. There seems to be a strong tendency for surface roughness to increase as the particle size increases. Blasting a smooth Ti surface with  $\text{Al}_2\text{O}_3$  particles of 25  $\mu\text{m}$ , 75  $\mu\text{m}$ , or 250  $\mu\text{m}$  produces surfaces with roughness values of 1.16 to 1.20, 1.43, and 1.94 to 2.20, respectively.<sup>99,106</sup>

Chemical etching is another process by which surface roughness can be increased. The metallic implant is immersed into an acidic solution, which erodes its surface, creating pits of specific dimensions and shape. Concentration of the acidic solution, time, and temperature are factors determining the result of chemical attack and microstructure of the surface. In 1996, an implant was marketed that had its surface etched with a mixture of hydrochloric acid/sulfuric acid ( $\text{HCl-H}_2\text{SO}_4$ ) solution (Osseotite, Implant Innovations, Palm Beach Gardens, FL). Resistance to torque removal was found to be 4 times greater with this acid-etched surface when compared to a machined surface,<sup>107</sup> and in a prospective multicenter study, where implants were loaded for 0 to 36 months, the total success rate was 93.7%.<sup>108</sup>

Recently, a new surface was introduced that was sandblasted with large grit and acid-etched (SLA, Straumann).<sup>109</sup> This surface is produced by a large-grit (250 to 500  $\mu\text{m}$ ) blasting process, followed by etching with hydrochloric-sulfuric acid.<sup>110</sup> The average  $R_a$  for the acid-etched surface is 1.3  $\mu\text{m}$ , and for the sandblasted and acid-etched surface,  $R_a = 2.0$   $\mu\text{m}$ .<sup>109</sup> Increased removal torque values of the sandblasted and acid-etched surface, as compared to the acid-etched surface,<sup>109</sup> and bone-implant contact values of 60% to 70%<sup>111</sup> provide the basis for a 6-week healing period protocol for the former surface type, which is currently being tested.

### Porous

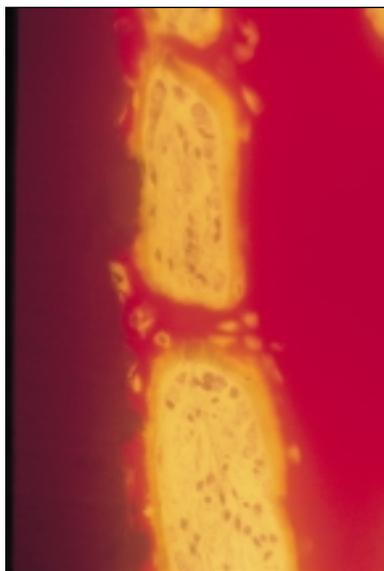
Porous sintered surfaces are produced when spherical powders of metallic or ceramic material become a coherent mass with the metallic core of the implant body. Lack of sharp edges is what distinguishes these from rough surfaces. Porous surfaces are characterized by pore size, pore shape, pore volume, and pore depth, which are affected by the size of spherical particles and the temperature and pressure conditions of the sintering chamber.<sup>112</sup> Pore depth depends on the size of the particles (44 to 150  $\mu\text{m}$ ) and their concentration per unit area, as well as on the thickness of the applied coating (usually 3,000  $\mu\text{m}$ ). A pore depth of 150 to 300  $\mu\text{m}$  appears to be the optimal size for bone ingrowth and maximum contact with the walls of the pore.<sup>113,114</sup> Pore shape does not seem to influence the biologic result, whereas pore volume (% porosity) needs to critically balance the metal contact points (strength of coating) with the opportunity for bone

ingrowth.<sup>115</sup> Story and coworkers<sup>116</sup> reported that a decrease of 9% in porosity resulted in a 12% decrease in bone ingrowth at 12 weeks after implantation in the canine mandible, and implant topology together with porous distribution can influence trabecular bone adaptation.<sup>117</sup> Clinical trials of porous-coated implants demonstrated a survival rate of 95% at 4 years and reported advantages of the implant design, which included the ability to use shorter endosseous lengths because of the threefold increase in the surface area compared to a machined implant.<sup>118</sup> In the future, porous-coated implants could be impregnated with growth factors and act as delivery vehicles because of increased surface volume.<sup>119</sup>

## OSSEOINTEGRATION

Endosseous dental implants are introduced as artificial structures into a site that is surgically created within mature tissues, and a sequence of cellular and molecular events is initiated as a response to trauma that includes inflammation, repair, and remodeling.<sup>120</sup> Invasion of mature bone by surgical instrumentation to create an implant site results in vascular trauma and bony discontinuity. The osteotomy site is almost instantly filled with blood, and subsequent dental implant placement forces this bioliquid to escape, saturating the implant surface along the entire length.<sup>121</sup> Proteins, lipids, or other biomolecules may be absorbed on the implant surface, and interfacial interactions develop in space and time in a series of well-orchestrated events that can be described according to the level of observation.<sup>122</sup> As a general rule, cells do not bind directly to the implant but rather to extracellular glycoproteins that are adsorbed to the surface. Numerous reports have demonstrated that there is an amorphous layer of proteoglycans and unmineralized collagen between the bone and implant surface varying in thickness between 40 and 400 nm.<sup>123-129</sup> A large number of adhesive proteins have been found to be involved in the cell adhesion mechanism. Fibronectin, vitronectin, osteopontin, thrombospondin, fibrinogen, and von Willebrand factor all contain the tripeptide arginine-glycine-aspartic acid (RGD), which is recognized by receptors (integrins) on the cell surface.<sup>130,131</sup> Many authors have demonstrated that a number of cellular properties, including growth gene expression and secretory production, are affected by cell shape, which in turn is determined by the 3-dimensional conformation of the cytoskeleton.<sup>132-135</sup>

Cooper and coworkers<sup>136</sup> studied the effect of surface topography on the ability of osteoblast cultures to produce a mineralizing matrix and concluded that



**Fig 4** Photomicrograph of bone modeling adjacent to a cpTi dental implant. Osteoblasts are depositing bone against the implant surface and the osteotomy wall (Stevenel's blue and van Gieson micro-fuchsin stain; original magnification  $\times 800$ ).

titanium plasma-sprayed, TiO<sub>2</sub> grit-blasted, or machined surfaces modulated cell differentiation and cell responses in various aspects. Along the same line of evidence, Gronowicz and McCarthy<sup>137</sup> concluded that the type of substrate determines the type of cell adhesion mechanism and affects production of extracellular matrix proteins. In the case of osseointegration, if the implant surface is less than optimal, cells will be unable to produce the local factors that allow control and guidance of the various cellular and populations along the proper pathways.<sup>138,139</sup> The initial reaction at the bone-implant interface will involve the release of blood cells and vasoactive amines, fibrin clot formation, debridement by macrophages, and organization and replacement of the hematoma by granulation tissue, which is subsequently replaced by fibrous (woven) callus and later by primary bony callus or osteoid.<sup>140-142</sup>

There is a debate in the literature as to whether bone grows from the osteotomy walls toward the implant surface or along the implant material as well (Fig 4). Schwartz and coworkers<sup>143</sup> and Roberts<sup>141</sup> agreed that new bone grows from periosteal and endosteal osteogenic tissue toward the implant surface, whereas Davies<sup>144</sup> supported the opinion that distance and contact osteogenesis can both take place. Differences in implant designs

may affect the pattern of healing response. Porous-coated implants provide the space and volume for cell migration and attachment and thus support contact osteogenesis. In the case of threaded implants, where a tight fit does not allow colonization of its surface by osteogenic cells, osseointegration will proceed from the newly created osteotomy walls.<sup>145</sup> Regardless of the order in which bone is produced, when healing is completed and the implant becomes stably anchored in bone, the mature interface exhibits certain characteristics that can be evaluated clinically and histologically.<sup>146</sup>

## EVALUATION OF THE INTERFACE

In their detailed and inclusive reviews, Masuda and coworkers<sup>147</sup> and Cooper and colleagues<sup>148</sup> described a plethora of *in vivo* and *in vitro* studies designed to offer insight into the process of osseointegration and detailed information about the structure of the developed interface. Two of the methods most often employed to assess the quality of the osseointegrated interface are the biomechanical test and the histomorphometric analysis. The literature is replete with reports on the aforementioned analyses that attempt to evaluate the bone-implant interface quantitatively and qualitatively. For the purpose of this paper, several studies are reviewed to allow the identification of those factors and parameters that influence the numerical value of the results. There are generally 3 types of biomechanical tests: pull-out, push-out, and torque measurement (Table 2).

### Pull-out Tests

Cook and colleagues<sup>149</sup> tested the interfacial attachment strength of HA-coated cylindrical implants with 4 different designs (grooved, threaded, dimpled, and smooth) in both axial pull-out and torsion. Implants were  $4 \times 10$  mm and were implanted in canine mandibles for 15 weeks. Reported stress values were estimated by dividing the failure load by the total implant surface area and ranged from 4.61 to 6.85 MPa. In a similar study, Block and coworkers<sup>150</sup> recorded interfacial strength values of 130 to 282 MPa. It is important to mention that in this study, longer and wider implants exhibited the highest absolute pull-out force but the lowest force per unit area. Kraut and coworkers<sup>151</sup> performed a pull-out test on titanium plasma-sprayed cylindrical,  $4 \times 11$  mm implants that were placed for various periods ranging from 2 to 24 weeks. The authors reported pull-out forces of 50 to 1,000 N with the observation of a time-dependent increase in force.

**Table 2** Biomechanical Studies of the Bone-Implant Interface

| Model                                      | Implant type                                               | Observation time    | Biomechanical result | Biomechanical test |
|--------------------------------------------|------------------------------------------------------------|---------------------|----------------------|--------------------|
| Goat mandible and maxilla <sup>151</sup>   | Cylindric 4 × 1 1-mm TPS                                   | 2 to 24 wk          | 50 to 1,000 N        | Pull-out           |
| Canine mandible <sup>150</sup>             | Cylindric 3/3.3/4 × 4/8/15-mm HA                           | 15 wk               | 130 to 282 MPa       | Pull-out           |
| Canine mandible <sup>149</sup>             | Threaded/cylindric 4 × 10-mm HA                            | 15 wk               | 4.61 to 6.85 MPa     | Pull-out           |
| Rat tibia <sup>177</sup>                   | Threaded 2 × 2-mm cpTi                                     | 8 wk                | 10 to 32 MPa         | Pull-out           |
| Rabbit femur <sup>178</sup>                | Cylindric 2 × 12-mm cpTi, HA-glass                         | 3, 6, and 9 wk      | 4.5 to 27 MPa        | Pull-out           |
| Canine femur <sup>179</sup>                | Cylindric 4.7 × 12-mm Ti alloy, HA-coated                  | 12 and 24 wk        | 14 to 16 MPa         | Pull-out           |
| Canine mandible <sup>153</sup>             | Threaded 4 × 14-mm cpTi                                    | 0 and 3 mo          | 813 to 1,194 N       | Push-out           |
| Canine femur <sup>154</sup>                | Cylindric 6 × 13-mm Ti alloy, HA                           | 4 and 12 mo         | 0.1 to 11.7 MPa      | Push-out           |
| Canine femur <sup>155</sup>                | Cylindric 4 × 15-mm carbon, HA, Ti alloy                   | 8 wk                | 1.59 to 8.71 MPa     | Push-out           |
| Rabbit femur <sup>157</sup>                | Cylindric 2.8 × 6-mm HA, Al <sub>2</sub> O <sub>3</sub>    | 3 mo                | 3 to 15 MPa          | Push-out           |
| Canine femur <sup>156</sup>                | Cylindric 10 × 10-mm HA, glass-ceramic                     | 12 wk               | 0.24 to 3.84 MPa     | Push-out           |
| Goat tibia <sup>180</sup>                  | Cylindric 4 × 10-mm Ti alloy, TPS                          | 3 mo                | 2.9 to 12.9 MPa      | Push-out           |
| Canine humerus <sup>181</sup>              | Cylindric 6 × 10-mm Ti alloy, HA, TPS                      | 6 wk                | 0.31 to 3.4 MPa      | Push-out           |
| Rabbit tibia and femur <sup>160</sup>      | Threaded 3.75 × 6-mm cpTi, blasted                         | 12 wk               | 9 to 65 Ncm          | Torque             |
| Rabbit tibia and femur <sup>159</sup>      | Threaded 3.75 × 4-mm cpTi                                  | 6 wk and 3 and 6 mo | 20 to 37 Ncm         | Torque             |
| Rabbit tibia <sup>161</sup>                | Threaded, cylindric 3.5 × 10-mm cpTi machined, blasted, HA | 3 and 12 wk         | 20 to 117 Ncm        | Torque             |
| Rabbit femur <sup>107</sup>                | Threaded 3.25 × 4 mm cpTi, machined, acid-etched           | 2 mo                | 1.8 to 36.1 Ncm      | Torque             |
| Miniature pig maxilla <sup>109</sup>       | Threaded 3.75 × 10-mm, 4 × 8-mm TPS, acid-etched           | 4, 8, and 12 wk     | 46 to 227 Ncm        | Torque             |
| Rabbit femur and tibia <sup>98</sup>       | Threaded 3.75 × 6-mm cpTi, machined, blasted               | 12 wk               | 10 to 60 Ncm         | Torque             |
| Canine mandible <sup>182</sup>             | Threaded, cylindric 3.5 × 10-mm cpTi, machined, blasted    | 12 wk               | 22 to 150 Ncm        | Torque             |
| Baboon mandible and maxilla <sup>183</sup> | Threaded 3.8 × 10-mm cpTi, Ti alloy, HA                    | 3 to 4 mo           | 65 to 168 Ncm        | Torque             |
| Rabbit tibia <sup>40</sup>                 | Threaded 3.75 × 6-mm cpTi, Ti alloy                        | 3 mo                | 18 to 86 Ncm         | Torque             |

TPS = plasma-sprayed titanium; HA = hydroxyapatite; cpTi = commercially pure titanium; wk = weeks; mo = months.

### Push-out Tests

With push-out tests, both the coronal and apical ends of the implant must be free of bone contacts. The coronal portion accepts the applied push-out force, and the apical end must be exposed to allow smooth and free extrusion of the implant. Dhert and colleagues<sup>152</sup> described the proper conditions and the biomechanical characteristics of the push-out model and emphasized that clearance of the hole in the support jig, Young's modulus of the implant, cortical thickness, and implant diameter are 4 parameters that influence the interface stress distribution. However, Brosh and coworkers<sup>153</sup> performed a push-out test of 4 × 10-mm threaded implants with significant thread depth and without any apical clearance. It is evident that the high forces observed

(813 to 1,194 N) resulted in part from the compressive resistance of the bone structure between the threads and at the apical end of the implant. Push-out tests of HA-coated implants ranged from 3.21 to 15 MPa, depending on implant dimensions, bone quality and configuration, and crystallinity of the HA coating.<sup>154–157</sup> In a study by Wong and colleagues<sup>158</sup> in which various implant surface structures were tested, it was found that push-out failure load was correlated with average surface roughness. Hydroxyapatite-coated implants exhibited higher surface coverage by bone and increased failure loads. Push-out and pull-out tests are indicated by cylindric or press-fit implants, whereas threaded implants are more effectively tested with the counter-torque or reverse-torque test.

**Table 3** Histomorphometric Studies of the Bone-Implant Interface

| Model                                      | Implant type          | Observation time     | Bone-implant contact (%) |
|--------------------------------------------|-----------------------|----------------------|--------------------------|
| Canine mandible <sup>167</sup>             | Threaded Ti           | 5 to 24 mo           | 50 to 65                 |
|                                            | Threaded ceramic      |                      | 41                       |
| Rabbit tibia <sup>162</sup>                | Threaded Ti           | 4 wk                 | 20 to 36                 |
| Sheep tibia <sup>184</sup>                 | Threaded cpTi         | 6 mo                 | 56 to 60                 |
| Canine mandible <sup>185</sup>             | Threaded cpTi         | 4 mo                 | 42 to 70                 |
| Baboon mandible and maxilla <sup>186</sup> | Threaded cpTi, alloy  | 3 mo                 | 40                       |
|                                            | Threaded HA           |                      | 62                       |
| Baboon mandible <sup>187</sup>             | Cylindric HA          | 6 mo                 | 67                       |
| Rabbit knee and tibia <sup>159</sup>       | Threaded cpTi         | 6 wk, 3 mo, and 6 mo | 21 to 58                 |
| Canine mandible <sup>164</sup>             | Cylindric TPS         | 3 mo                 | 48                       |
| Canine mandible <sup>165</sup>             | Threaded Ti           | 3 mo                 | 46                       |
|                                            | Cylindric TPS         |                      | 55                       |
|                                            | Cylindric HA          |                      | 71                       |
| Rhesus monkey mandible <sup>169</sup>      | Porous                | 74 mo                | 64 to 67                 |
| Human biopsies <sup>188</sup>              | Threaded cpTi         | 1 to 16 y            | 43 to 100                |
| Canine mandible and maxilla <sup>189</sup> | Threaded cpTi         | 5 mo                 | 46 to 60                 |
| Ewe femur <sup>163</sup>                   | Threaded cpTi         | 12 wk                | 61 to 68                 |
| Human biopsies <sup>168</sup>              | Threaded cpTi         | 8 to 20 mo           | 34 to 93                 |
| Human biopsies <sup>166</sup>              | Threaded hollow cpTi  | 23 to 36 mo          | 18 to 74                 |
|                                            | Cylindric hollow cpTi |                      |                          |
| Canine mandible <sup>190</sup>             | Threaded hollow cpTi  | 3, 6, and 15 mo      | 52 to 78                 |
| Rabbit tibia <sup>40</sup>                 | Threaded cpTi, alloy  | 3 mo                 | 21 to 46                 |
| Human biopsies <sup>191</sup>              | Threaded cpTi         | 24 mo                | 61 to 69                 |
| Canine mandible <sup>192</sup>             | Cylindric cpTi        | 12 wk                | 2 to 100                 |
| Human biopsies <sup>193</sup>              | Threaded hollow cpTi  | 6 mo                 | 17 to 72                 |
| Monkey mandible <sup>194</sup>             | Threaded cpTi         | 18 mo                | 11 to 73                 |

Ti = titanium; cpTi = commercially pure titanium; TPS = plasma-sprayed titanium; HA = hydroxyapatite; wk = weeks; mo = months; y = years.

## Torque

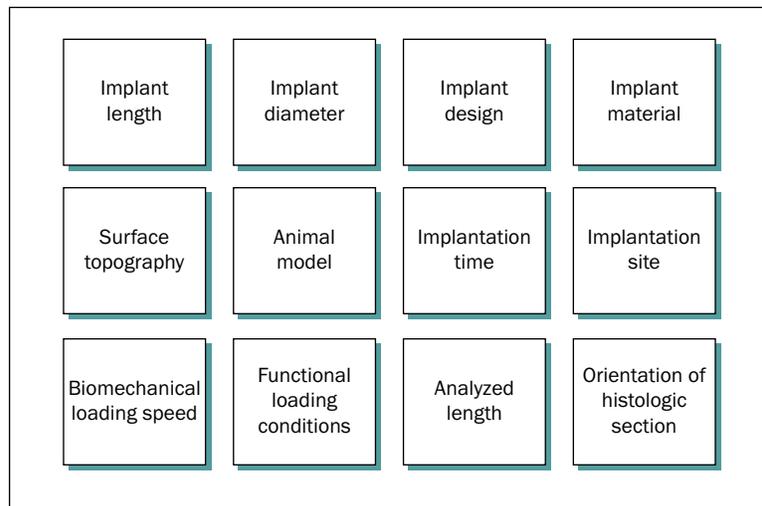
In a torque removal study in the femur of the rabbit, Klokkevold and coworkers<sup>107</sup> reported removal torque values (RTV) of 20.5 Ncm for a chemically etched surface versus 4.95 Ncm for machined  $3.25 \times 4$ -mm Ti implants. In a similar study, Sennerby et al<sup>159</sup> reported an RTV of 35.6 Ncm for  $3.75 \times 4$ -mm screw-shaped machined implants that were implanted for 6 months. Grit-blasting of machined  $6 \times 3.75$ -mm threaded implants with  $25\text{-}\mu\text{m}$   $\text{Al}_2\text{O}_3$  or  $\text{TiO}_2$  resulted in RTV of 24.9 to 26.5 Ncm in the tibia of the rabbit.<sup>160</sup> Gotfredsen and colleagues<sup>161</sup> compared 2 implant designs and 3 surface treatments and found increased RTV with time. Specifically, at 12 weeks the RTV for threaded HA-coated,  $\text{TiO}_2$ -blasted, and machined implants were 117, 45, and 32 Ncm, respectively. In a recent study, Buser and coworkers<sup>109</sup> compared the acid-etched surface with the sandblasted and acid-etched surface at 4, 8, and 12 weeks of healing. Results revealed a corresponding RTV for the acid-etched surface of 62.5, 87.6, and 95.7 Ncm at the aforementioned healing periods, whereas RTV for the sandblasted/acid-etched surface were 109.6, 196.7, and 186.8 Ncm, respectively.

## Histomorphometry

Histomorphometric analyses of the bone-implant interface can be done in different ways, considering various parameters; this has resulted in a wide spectrum of reported values (Table 3). Investigators often present bone-implant contact as a percentage of the total implant length and as a percentage of the 3 consecutive "best threads" length.<sup>162</sup> Depending on bone quality, the ratio of cortical versus cancellous bone, and the length of the implant, significant differences may exist between "total length" and "three best threads" results.<sup>159</sup> Implant design (threaded vs cylinder<sup>163,164</sup> or solid vs hollow<sup>165,166</sup>), implant material,<sup>167</sup> surface treatment,<sup>168,169</sup> healing time, and loading conditions are some of the parameters influencing the analytic approach. Thread volume fill and number of cells in contact with the implant surface are 2 other variables frequently reported in histomorphometric studies.<sup>159,160,170</sup>

It is evident from the aforementioned that data from the histologic and biomechanical evaluation of dental implants can represent the combined/additive effect of many variables and can be presented in many different ways. Reporting the biomechanical results

**Fig 5** Parameters affecting histologic/bio-mechanical data.



of implants with various lengths and diameters in various units (N, MPa, Ncm, Nm) and in absolute force values or stress values (absolute force value divided by the implant surface) creates confusion for comparative evaluation of literature reports (Fig 5). For this reason, complete description and identification of the test/study conditions should accompany any data reports, and critical judgment must be exercised when fair comparisons are attempted.

### Clinical Correlation

As extremely important and necessary as these studies appear to be for the ultrastructural evaluation of the bone-implant interfacial zone, they offer very little help for the clinical judgment of successful osseointegration. Differences between healing rates in animal models and humans, variance of bony sites and implant parameters, and variability of biomechanical tests and conditions prevent direct correlation of these histomorphometric and biomechanical results to the prediction of clinical results. For this reason, in addition to the criteria for success proposed by Zarb and Albrektsson,<sup>8</sup> other non-invasive methods have been developed that allow objective assessment of the osseointegration process. Radiographic evaluation,<sup>171</sup> tapping the implant with a metallic instrument and assessing the emitted sound,<sup>172</sup> resonance frequency measurements,<sup>173</sup> stability measurement with the Periotest instrument<sup>174</sup> or rotational stiffness produced upon impact,<sup>175</sup> and reverse torque application<sup>176</sup> are suggested clinical methods for monitoring successful implant placement and osseointegration.

### CONCLUSIONS

The wide variety and constant evolution of dental implant designs, driven by scientific findings and research studies, reflect the attempts of investigators to successfully incorporate an artificial structure within a biologic system. Clinicians must have knowledge of the cellular and molecular events that lead to osseointegration, because such knowledge is essential to relate clinical findings with basic mechanisms. It is evident that implants should be carefully selected, balancing the research information on their properties with the intended treatment plan. Clinical judgment of bone quality and quantity, implantation site, as well as biomechanics of the implant and type of final restoration, are important considerations in evaluating the properties and features of an implant system. The significant evidence presented in this review illustrates the difficulty in comparing various implant systems. In the future, better understanding of molecular biology and biomaterials science will generate dental implants with properties and features that will provide an enhanced biologic response.

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