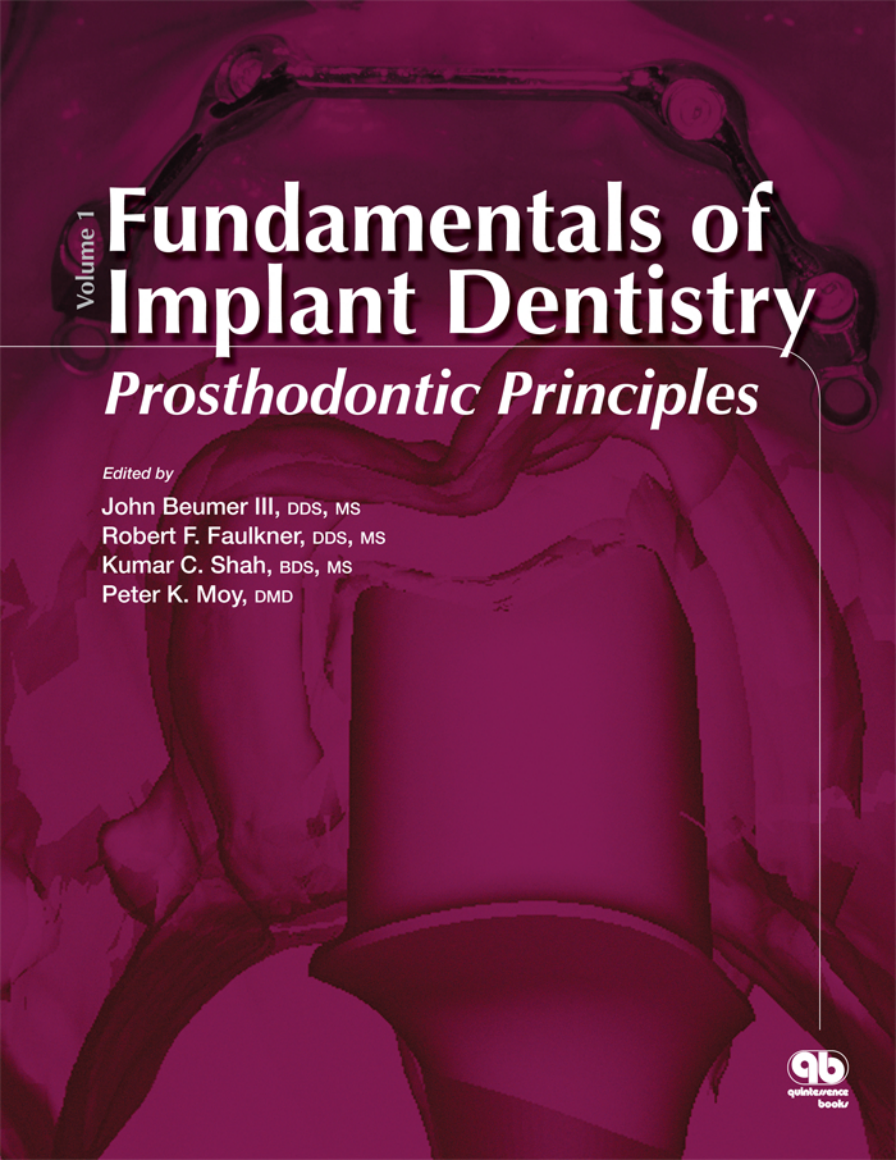
Volume 1
Fundamentals of Implant Dentistry
Prosthodontic Principles
Edited by
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Robert F. Faulkner, DDS, MS
Kumar C. Shah, BDS, MS
Peter K. Moy, DMD
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Fundamentals of Implant Dentistry: Prosthodontic Principles

Volume 1

Fundamentals of Implant Dentistry

Prosthodontic Principles

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Dedication

To Jan, for her continuing love and support.
— John Beumer III

To my wife, Terry, whose continued love, support, and belief in me has made my life's journey truly amazing.
— Robert F. Faulkner

To my entire family for their love and encouragement: to my father (Chimanlal) and mother (Kusum) for always believing in me; to my siblings, Jigar and Hetal, for their unconditional support; to my son, Kiaan, who has inspired me to keep trying no matter what; and last but definitely not least, to my wife, Shreya, for everything she does and her love and support.
— Kumar C. Shah

To my parents and grandparents who, as immigrants, imbued in me a strong work ethic. This has carried me through my professional training and career, instilling the drive to be the best that I can be. For this, I am forever grateful.
— Peter K. Moy

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Contents

Foreword

The recruitment of osseointegrated dental implants in the management of edentulous patients made its North American debut at the 1982 Toronto conference. I was privileged to have organized that event and to subsequently join Per-Ingvar Brånemark and his protégé Tomas Albrektsson in co-authoring the first text on tissue-integrated prostheses, published by Quintessence in 1985. Both seminal events helped usher in osseointegration as a novel development, leading to an exciting era of service, education, and research for the dental profession; and the clinical technique remains an extraordinary example of the merits of scrupulously tested biologic convictions and clinical observations. The Brånemark breakthrough was a far cry from the currently praised, if infrequently achieved, standard of randomized controlled clinical trials. However, it succeeded in changing traditional convictions about the feasibility and desirability of dental implants. Its subsequent worldwide trajectory catalyzed a prosthodontic management revolution in oral rehabilitative dentistry.

The ensuing three decades have seen numerous clinical scientists coloring in novel additional details to the technique, resulting in expansion of its versatility and application. These initiatives have also led to a quasi-panacea treatment status for partially and completely edentulous patients accompanied by a prevailing entrepreneurial spirit and aggressive marketing culture. A virtual implantomania has resulted from the rapidly emerging clinical confidence in osseointegration, which makes this text an opportune and welcome reminder of the importance of prudent and informed clinical judgment in the application of prosthodontic principles for all forms of dental implant therapy.

I am also privileged to have known the lead editor since the inception of the academically driven osseointegration transformation within our discipline. He has excelled at sharing knowledge and innovation in the field as well as surrounding himself with outstanding clinical scholars who contributed immeasurably to developments in implant dentistry. This book—with its stellar cast of contributors and lucid, comprehensive coverage of all that is needed to provide dentists with a synthesis of the best available evidence—is a gift to the dental profession. It is a gratifying reminder of how far the discipline has come since the Brånemark star lit up the sky of our traditional clinical interventions. It has also burnished John Beumer's well-deserved reputation and guarantees him even more recognition for his outstanding clinical scholarship and professional leadership.

George Zarb
Emeritus Professor, University of Toronto
Editor-in-Chief, *International Journal of Prosthodontics*

Preface

Some maintain that the concept of restoring missing dentition with osseointegrated implants has had a greater impact on the practice of dentistry than any new technology introduced during the last half century, and we are inclined to agree. These implant systems enable teams of restorative dentists and surgeons to restore functional and esthetic deficits with a degree of success only dreamed of prior to their introduction. However, in order to achieve this high level of predictability, the implant team must be aware of factors that predispose to their failure as well as a successful outcome. In this text, we have attempted to make the reader aware of the limits of this technology and provide a prescription for the clinician, or a formula if you will, that will ensure the highest degree of success.

In recent years, it has been acknowledged that implant dentistry is driven by the prosthodontic needs of the patient, and so this volume of our two-volume series is dedicated to implant prosthodontics. Although this textbook is devoted to designing and fabricating implant-retained prostheses, we have also attempted to indicate when conventional approaches (tooth-supported fixed partial dentures, removable partial dentures, and the restoration of diseased teeth with endodontic therapy and conventional restorative procedures) should be considered. We have also attempted to provide prosthodontic perspectives of the most commonly employed surgical procedures used to facilitate the bone and soft tissues of the potential implant sites that have evolved during the last 30 years. Even though this text is focused primarily on implant prosthodontics, we hope our colleagues in surgery will find the contents of this book interesting and pertinent to the issues they face in their daily practice. We are well aware that many are asked to provide advice and counsel to their restorative colleagues.

In the early years, osseointegrated implants were used primarily to restore function of edentulous patients experiencing difficulty manipulating mandibular complete dentures. Initial attempts to restore partially edentulous patients were met with frustration and an unacceptable rate of failure. Unfortunately, these frustrations and failures were underreported in the literature. However, with the development of more osteoconductive implant surfaces, and the clinical experience gained from our earlier failures, these implant systems can now be used quite successfully when restoring the partially edentulous patient. Yet restoring partially edentulous patients is considerably more complex and challenging. Issues such as occlusal plane discrepancies, malposed teeth, unfavorable jaw relations, implant biomechanics, and the occlusal scheme to be used, among others, must be carefully addressed when developing plans of treatment.

We strongly believe that the best results are achieved when an interdisciplinary approach is employed, particularly when restoring partially edentulous patients. Some patients present with relatively simple problems and can be handled by a solo practitioner. However, as noted above, many partially edentulous patients present with significant prosthodontic complexities, periodontal compromise of existing dentition, and significant bone and soft tissue defects. Delivery of definitive care for such patients requires the prosthodontist/restorative dentist to have close interaction with oral and maxillofacial surgeons, periodontists, orthodontists, and endodontists as well as dental technicians and staff associated with biomedical modeling centers.

Prosthodontists and restorative dentists placing osseointegrated implants are obligated to understand the basic biologic mechanisms associated with this phenomenon and in particular the factors important to maintaining the long-term health of the peri-implant soft tissues and the anchoring bone. Therefore, the first section of this book is devoted to the biologic processes associated with osseointegration. In order to put these new implant systems in proper perspective, a brief description of implant systems used prior to the introduction of osseointegration is presented, as well as reasons why these systems were unpredictable.

Section two is devoted to the use of these implants in edentulous patients. The basic concepts for restoring these patients have not changed significantly since osseointegrated implants were introduced to the global community over 30 years ago. However, there has been a steady evolution in methods of evaluation, surgical procedures employed, and the methods and materials used to fabricate prostheses for these patients. The rapid development of CAD/CAM technologies has had a particularly significant impact, and we have attempted to put these new technologies in proper perspective. It is also our hope that the reader will realize that conventional complete dentures still remain an effective treatment for most edentulous patients with regard to most outcome measures.

Section three is devoted to restoration of partially edentulous patients with particular emphasis on the esthetic zone. This application has evolved significantly over the years, particularly with the introduction of new means of surgically enhancing the soft tissues and bone of the potential implant sites. The first two chapters of this section place special emphasis on implant biomechanics, particularly when restoring posterior quadrants with linear implant configurations. The last two chapters of the section are largely devoted to restoration of the esthetic zone.

The fourth section of the book addresses special and sometimes controversial topics in implant dentistry, including the use of implants in growing children and in irradiated patients. In addition, chapters are included that discuss the use of implants to facilitate the stability, retention, and support of removable partial dentures and the symbiotic relationship between orthodontics and osseointegration.

Lastly, we have included an illustrated glossary. A new language has evolved with the development of this field, and we recognize the need to provide those just embarking on their careers in this arena with a resource defining the terminology that has evolved.

Acknowledgments

Creating these volumes is a tremendous task, and we would like to thank our many contributors for their tireless and timely efforts. We have made a conscious effort to include as many of our international colleagues as possible in this project.

John Beumer would like to take this opportunity to personally thank his mentors—Dr Sol Silverman, Jr, Distinguished Professor of Oral Medicine, University of California, San Francisco (UCSF); Dr Thomas A. Curtis, Professor of Prosthodontics, UCSF; and Dr F. J. Kratochvil, Professor of Prosthodontics, UCLA. These individuals are rightly considered giants in their respective disciplines. Their commitment to excellence and enthusiasm for their work have been inspiring to me and countless others in our profession. I would also like to thank Dr Henry Cherrick, Professor and Dean Emeritus, UCLA School of Dentistry. His leadership, vision, and support as dean permitted our team at UCLA to build a strong implant program in research, clinical training, and education. Also, his encouragement and support were essential to the development of the Jane and Jerry Weintraub Center for Reconstructive Biotechnology, which could not have been conceived and built without his efforts.

First and foremost, Robert Faulkner dedicates this book to his parents, Bob and Betty Faulkner. My mom's love and encouragement through the years of her life will remain with me and serve as a constant reminder to set goals and to reach for them with all of my being; and my Dad has served as an incredible role model and is truly the man I have always admired and aspired to emulate the most. He has continued to believe in my abilities, even when I doubted myself. To my children, Lauren and Rob, whom God blessed me with, for their love and understanding; I am so proud of the adults they are becoming, and I am honored to be their father. I would also like to acknowledge my co-editors. They have been tireless in their commitment to this book and are a reflection of the level of excellence that we have strived to achieve in our profession of prosthodontics. There are several other individuals who have helped shape my life's journey, and they, too, have given much to develop my path toward the culmination of this book. I would like to express my sincere gratitude to these mentors—Dr Wayne Payne, Professor Emeritus, Ball State University, Department of Health Science and Physiology, whose encouragement allowed the completion of my master's thesis; Dr Julian Woelfel, Professor Emeritus in Prosthodontics, and Dr Wayne Campagni, Professor Emeritus, The Ohio State University, College of Dentistry, both of whom guided my early development in prosthodontics. These two individuals have helped shape many prosthodontists' careers, and it has been my honor to be influenced by their mentorship. Dr Theodore Berg, Jr, Professor Emeritus, UCLA School of Dentistry, remains one of my most cherished mentors in prosthodontics. His careful ways of teaching and encouraging students to excel is unparalleled, and he has

remained an inspiration to me through my years in private practice and continues to be a constant reminder as to the true meaning of being a teacher. Finally, I would like to thank the countless friends and colleagues that have worked with me and have been supportive of my efforts throughout these many years. Without their support, this book would have only been a dream.

Kumar Shah would like to thank his co-editors for the opportunity to engage with them on this enormous task. Their friendship and support have been invaluable. In this process, I have learned a great deal, especially from Dr John Beumer, on what it takes to put something like this together; it is truly a work of passion. Two other individuals have had a big impact on my professional life—Dr Wayne Campagni and Dr Ernest D. Svensson, Professor Emeritus, The Ohio State University. Their dedication to prosthodontic education and their passion had a great influence on my early career. Their exemplary talents and patience have been a motivation for my career in education.

Peter Moy would like to thank two surgical mentors, Dr Bruce Sanders and Dr Jay Weiner, who were instrumental in teaching me the value of preprosthetic surgery to assist our restorative colleagues in managing our edentulous patients. After all, dental implant surgery is an extension of surgical procedures used formerly to prepare our edentulous patients for prosthodontic rehabilitation. To my prosthodontic mentors, I am indebted to Dr John Beumer for first seeing the potential abilities in me as a surgeon and for selecting me as the surgeon to represent the implant team from UCLA to be trained by Professor Brånemark. He has truly been an inspirational leader and an advocate of the team approach to implant dentistry but, most importantly, a trusted friend.

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Introduction and Biologic Basis

I

John Beumer III
Robert F. Faulkner
Kumar C. Shah
Peter K. Moy

History and Biologic Foundations

1

Introduction and Historical Perspectives

It can be argued that osseointegration has had a greater impact on the practice of dentistry than any technology introduced during the last 50 years. Since the introduction of osseointegrated dental implants more than 30 years ago, significant advances have been achieved in implant surface bioreactivity; methods used in diagnosis and treatment planning, particularly three-dimensional (3D) imaging and computer-aided design/computer-assisted manufacture (CAD/CAM) techniques; enhancement of bone and soft tissues of potential implant sites; and prosthodontic approaches and techniques. A degree of predictability with implants has been achieved that was unthinkable a generation ago when the authors of these volumes received their initial dental and surgical training.

When the concept of osseointegration was introduced to the international dental community in the early 1980s, it represented a radically new concept in implant dentistry.[1,2] These implants were made of titanium, and when an implant was placed, bone was deposited on its surface, firmly anchoring the implant in the surrounding bone (Fig 1-1). The phenomenon of osseointegration was discovered by Professor Per-Ingvar Brånemark while he was conducting a series of in vivo animal experiments assessing wound healing in bone. In these experiments, he placed in a rabbit tibia an optical chamber made of titanium that was connected to a microscope (Fig 1-2). When he attempted to remove the chamber from its bone site, he noticed that the bone adhered to the titanium chamber with great tenacity. He recognized the importance of this discovery, and during the next several years he experimented with various sizes and shapes of dental implants, including designs with features of both subperiosteal and endosteal implants. Over 50 designs were tested. He and his colleagues finally settled on a simple screw shape with a hex at the top.

Most of the previous implant systems were made of chrome-cobalt alloys, which were subject to corrosion. Corrosion, with release of metallic ions into the surrounding tissue, precipitated both acute and chronic inflammatory responses, resulting in encapsulation of the implant with fibrous connective tissue. Subsequently, epithelial migration along the interface between the implant and the fibrous capsule led to development of extended peri-implant pockets, and the chronic infections resulting from these pockets led to exposure of the implant framework and its eventual loss (Fig 1-3).

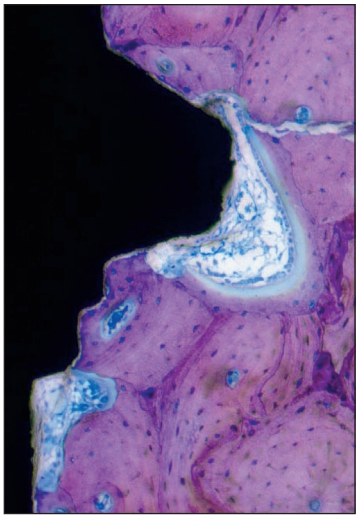


Fig 1-1 Bone is deposited on the surface of the implant, firmly anchoring the implant in bone. (Courtesy of Dr M. Weinlander, Vienna, Austria.)

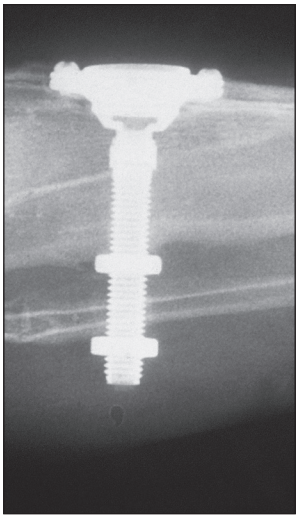


Fig 1-2 A radiograph of the titanium chamber embedded in bone. (Courtesy of Dr P-I. Brånemark, Gothenburg, Sweden.)

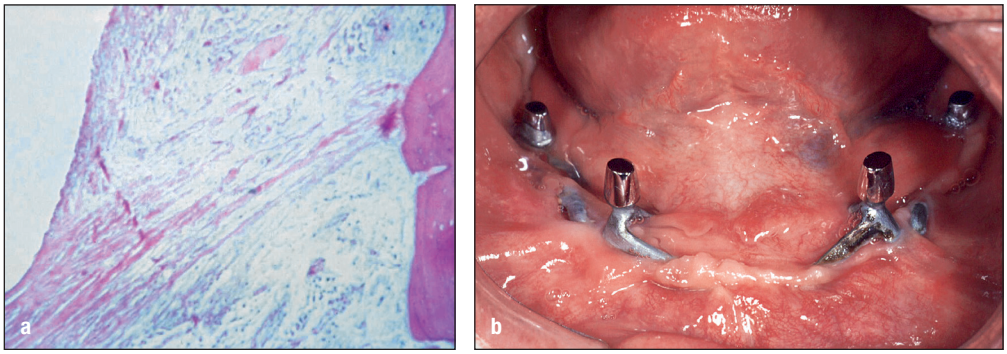


Fig 1-3 *(a)* Subperiosteal implants of chrome-cobalt are enveloped by fibrous connective tissue. (Courtesy of Dr R. James, Loma Linda, California.) *(b)* Epithelial migration led to the formation of extended peri-implant pockets, which in turn developed into chronic infection. The infection led to exposure of the implant struts and eventual loss of the implant.

In general, these implant systems survived for 5 to 7 years before the infections prompted their removal (Table 1-1). The infections were particularly destructive of bone and soft tissue in the maxilla (Fig 1-4).

Most metals are not suitable as implantable biomaterials because of the aforementioned corrosion and continuous release of metal ions into adjacent tissues. The presence of these ions precipitates acute and chronic inflammatory responses, which eventually result in fibrous encapsulation of the offending material. Epithelial migration then follows if the material extends through the skin or mucosa. Titanium, however, is resistant to corrosion and spontaneously forms a coating of titanium dioxide, which is stable and biologically inert and promotes the deposition of a mineralized bone matrix on its surface. In addition, it is strong and easily machined into useful shapes.

Following placement of the implant, a blood clot forms between the surface of the implant and the walls of the osteotomy site.[4] Plasma proteins are attracted to the area, accompanied by platelet activation and the release of cytokines and growth factors.[5–7] Angiogenesis begins, and mesenchymal stem cells migrate via the fibrin scaffold of the clot to the osteotomy site and the surface of the implant. These cells differentiate into osteoblasts and begin to deposit bone on the surface of the implant and the walls of the osteotomy site, eventually leading to anchorage of the implant in bone (the result of contact and distance osteogenesis)[8] (Fig 1-5). The initial events of this process take anywhere from 8 weeks to 4 months, depending on the osteoconductivity (the recruitment of osteogenic cells and their migration to the surface of the implant) of the implant surface.

Table 1-1 Implant survival rates reported in the 1978 Harvard-NIH Implant Consensus Conference[3]

Implant type	Survival rate		Notes
	5 years	10 years	
Subperiosteal	90%	65%	200 patients (5 investigators)
	46%	39%	94 patients (1 investigator)
Staple	95%	NA	Unreliable due to self-reported data
Transosteal	Undetermined		Small sample size
Vitreous carbon	50%–60%	NA	3-year data (2 investigators)
Blade	90%	NA	200 implants (1 investigator)
	65%	NA	70 implants (2 investigators)
	75%	NA	89 patients; full-arch blade implants (self-reported data from 1 investigator)

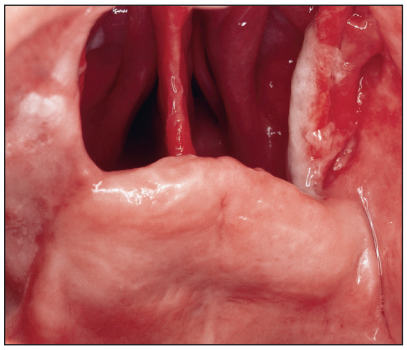


Fig 1-4 Substantial portions of the hard palate were lost secondary to infections caused by a subperiosteal implant.

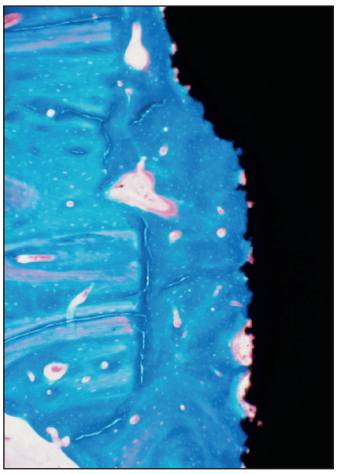


Fig 1-5 The gap between the wall of the osteotomy and the surface of the implant is filled in with bone by means of contact and distance osteogenesis.

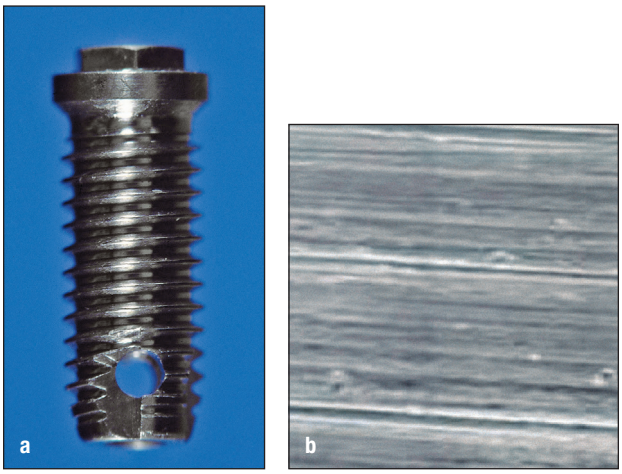


Fig 1-6 *(a)* The original Brånemark machined-surface implant. *(b)* Machined-surface topography.

The original dental implants developed by Professor Brånemark and his colleagues were prepared with a machined surface (Fig 1-6). These machined-surface implants were predictable in bone sites of favorable quantity and quality, such as the mandibular symphysis region, but were problematic when restoring posterior quadrants in partially edentulous patients. Since then, special surface treatments (eg, sandblasting, acid etching, titanium grit blasting, electrolytic processes) designed to change the microtopography of the implant surface have evolved that have significantly improved the osteoconductivity of titanium implants, making these implants highly predictable in less favorable sites, such as when restoring the posterior quadrant of the maxilla in partially edentulous patients (see chapter 8).

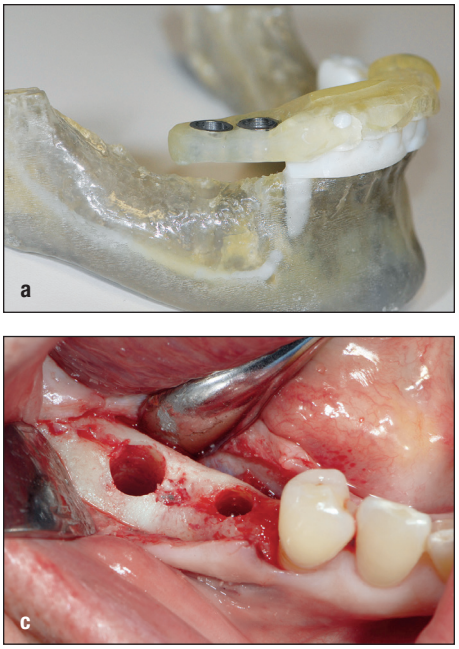


Fig 1-7 *(a)* Surgical drill guide. Note the bushings incorporated with the drill guide. *(b and c)* Osteotomy sites being created. Note the completed osteotomy sites.

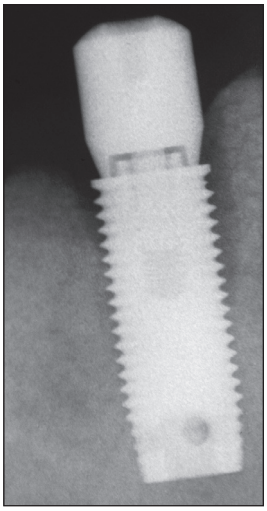


Fig 1-8 The osteotomy site is considerably larger than the implant itself, particularly around the coronal two-thirds of the implant. As a result, this implant will be at increased risk of failure.

Prerequisites for Achieving Osseointegration

Uncontaminated implant surfaces

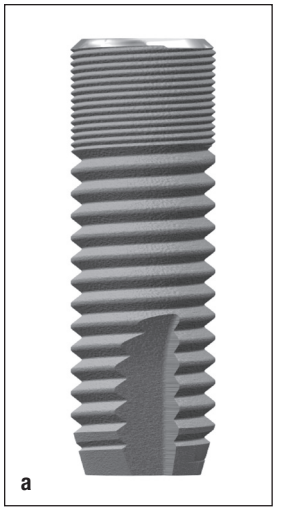
The osteoconductivity of implant surfaces is impaired if they become contaminated with organic molecules. The surface charge is changed from positive to negative, the surface becomes less wettable, and, upon implant placement, adsorption of plasma proteins is inhibited. Recent studies indicate that implant surfaces can be decontaminated by exposure to ultraviolet light.[9,10] Decontaminating implant surfaces with ultraviolet light enhances adsorption of plasma proteins initially after implant placement and promotes more rapid differentiation of mesenchymal stem cells into osteoblasts once they reach the surface of the implant.

Creation of congruent, nontraumatized implant sites

Careful preparation of the implant site is critical to obtaining osseointegration of a titanium implant in bone on a consistent basis (Fig 1-7). In an ideal situation, the gaps between the wall of the osteotomy and the implant are small, the amount of damaged bone created during surgical preparation of the bone site is minimal, and the implant remains immobilized during the period of bone repair. Under these circumstances, the implant becomes osseointegrated a very high percentage of the time (95% or greater with the modern microrough implant surfaces). The smaller the gap between the osteotomy site and the implant surface, the better the chance for osseointegration. In addition, during surgical preparation of the site, excessive bone temperatures should be avoided (above 47ºC), because they result in the creation of a zone of necrotic bone in the wall of the osteotomy site and lead to impaired healing and an increased likelihood of a connective tissue interface forming between the implant and the bone (Fig 1-8).

Primary implant stability

Osseointegration is obtained more consistently when initial primary stability of the implant is achieved in the surrounding bone. This is particularly important when one-stage surgical procedures are employed and is absolutely necessary if the implant is to be immediately placed into function (ie, restored). In attempting to establish initial primary stability, surgeons often underprepare the implant site when the bone is porous or soft. If the implant is not stable in its prepared osteotomy site, many clinicians prefer to replace it with an implant of a slightly larger diameter. This was particularly necessary when machined-surface implants were routinely employed. Today, implant surfaces are considerably more bioreactive, and unstable implants have a reasonable chance of achieving osseointegration as long as the clot remains undisturbed during the initial period of healing (see volume 2, chapter 5).



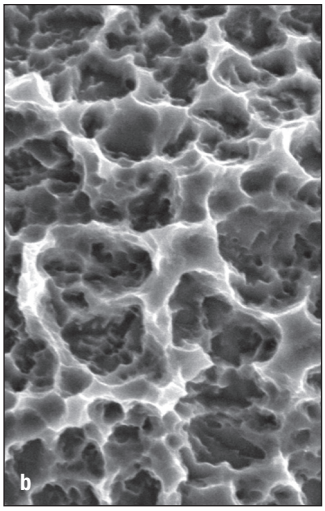
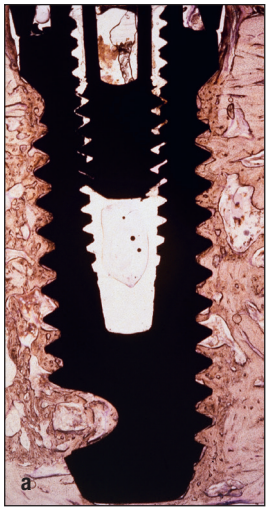


Fig 1-9 *(a and b)* Microrough surface topography. Implant surfaces with similar microsurface topography are more osteoconductive than the original machined-surface implants.



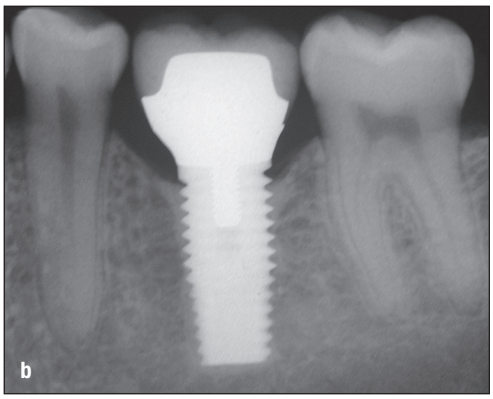


Fig 1-10 *(a)* Following initial healing and when loading forces are favorable, the bone contact area on the surface of the implant continues to increase. *(b)* Note the bone density of the peri-implant bone 7 years following delivery.

No relative movement of the implant during the healing phase

Micromovement of the implant is thought to disturb the tissue and vascular structures necessary for initial bone healing.[11] Excessive micromovement of the implant during healing prevents the fibrin clot from adhering to the implant surface. Eventually, the healing processes are reprogrammed, leading to a connective tissue–implant interface as opposed to a bone-implant interface. These phenomena have clinical significance. For example, immediate loading of dental implants provides a unique challenge. Implants placed into function immediately must be sufficiently stable so as to reduce micromovement to physiologic levels during healing. Otherwise, the implant may fail to osseointegrate. This issue is discussed in detail in the subsequent chapters.

Advances in Implant Surface Osteoconductivity

Implants prepared with a microrough surface topography are considerably more osteoconductive compared with the original machined-surface implants[12,13] (Fig 1-9). There are several reasons why these surfaces are such an improvement over the original machined surfaces. First, the modern implant surfaces with microrough surface topographies retain the fibrin blood clot more effectively than implants with machined surfaces.[14] As a result, the initial critical events (ie, plasma protein adsorption, clot formation, angiogenesis, mesenchymal stem cell migration and attachment, cell differentiation) associated with osseointegration are facilitated.

In addition, mesenchymal stem cells differentiate more rapidly into functioning osteoblasts following attachment to the microrough surfaces as compared with machined surfaces. These surfaces also upregulate and accelerate the expression of genes of the differentiating osteoblasts associated with the osseointegration process.[15] This leads to a different combination of collagenous and noncollagenous proteins making up the bone deposited on the microrough surfaces as compared with the bone deposited on machined-surface topographies. As a result, bone deposited on implant surfaces with microrough surface topography is harder and stiffer than bone deposited on machined surfaces.[16,17]

An active and efficient remodeling apparatus is key to maintaining osseointegration during functional loading of the implants.[18] Osseointegration of the implant with bone continues to occur up to 1 year following delivery of either a provisional or definitive prosthesis.[19] Following initial healing and functional loading within physiologic limits, progressive osteogenesis continues to where the bone-implant contact area approaches almost 90% in favorable sites (Fig 1-10).

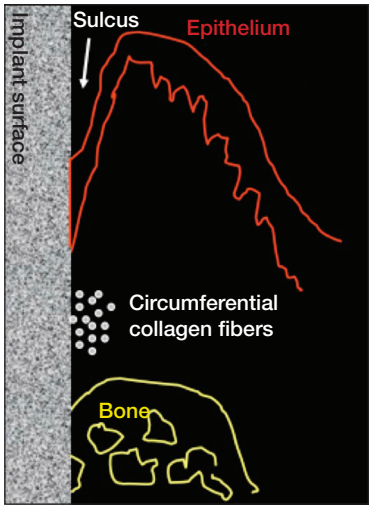


Fig 1-11 Implant–soft tissue interface.

The Implant–Soft Tissue Interface

The peri-implant mucosa is similar to the mucosa circumscribing natural teeth. It is composed of nonkeratinizing epithelium in the sulcus, junctional epithelium, and a supracrestal zone of connective tissue. The connective tissue layer contains a dense zone of circumferential collagen fibers intermingled with fibers extending outward from the alveolar crest. These fibers run parallel to the long axis of the implant. The zone of connective tissue adjacent to the implant is relatively avascular and acelluar and similar to scar tissue histologically. The soft tissue barrier (interface) assumes a minimal dimension during the healing process. If this dimension is less than 2 to 3 mm, bone resorption occurs in order to establish an appropriate biologic dimension of the peri-implant soft tissue barrier.[20]

The titanium–soft tissue interface appears to be similar to but not exactly the same as that seen between gingiva and natural dentition. The epithelial-implant interface is based on the hemidesmosome basal lamina system, similar to that seen between gingiva and teeth. When implants emerge through attached keratinized mucosa, collagen fibers circumferentially configured around the neck of the implant interwoven with collagen fibers running from the crest of the alveolus and the periosteum to the free gingiva hold the epithelium in close proximity to the surface of the implant. The epithelial cells in the sulcus epithelium secrete a sticky substance (a protein network composed of glycoproteins) onto the surface of the implants, enabling the epithelial cells to adhere to the implant surface via hemidesmosomes. The epithelial cuffs that form as a result of the basal lamina hemidesmosomal system and the zone of connective tissue just apical to it effectively seal the bone from oral bacteria (Fig 1-11). However, what differentiates the soft tissues around implants from the gingival tissues around natural teeth is the absence of gingival fibers inserting into a cementumlike tissue. Hence, the soft tissues around implants are much more easily detached from the surfaces of the implant than are the soft tissues surrounding natural teeth. This difference is clinically significant for a number of reasons, especially when cement systems are used for retention of implant prostheses because of the risk of embedding cement subgingivally during cementation of the prosthesis,[21] thereby precipitating peri-implantitis[22] (Fig 1-12).

The phenomenon of biologic width applies not only to the natural dentition but also to the soft tissues around implants. *Biologic width* is defined as the combined length of the supracrestal connective tissue and the zone of junctional epithelium associated with the epithelial attachment. This dimension averages approximately 3 mm around implants[20] and is slightly greater than that associated with the natural dentition. In general, the width of the epithelial component is greater and demonstrates more variability than the width of the connective tissue zone. This phenomenon has particular impact in the esthetic zone, because, as with the natural dentition, the level and contours of the underlying bone primarily determine the contours and level of the overlying soft tissues (Fig 1-13).

The dimension of the biologic width in relation to the nature and topography of the implant surface has been the subject of much debate in recent years. However, there is no clear consensus on whether differences in biologic width exist with respect to the varieties of surface topographies and surface treatments currently in use.[23] Also, the evidence appears to indicate that there are no significant differences in biologic width between one-piece and two-piece implant systems or between one-stage and two-stage surgical procedures.

However, it appears that the nature of the microgap between the abutment and the implant and its position in relation to the bone crest increases the biologic width (see chapter 10). The deeper the implant-abutment connection in relation

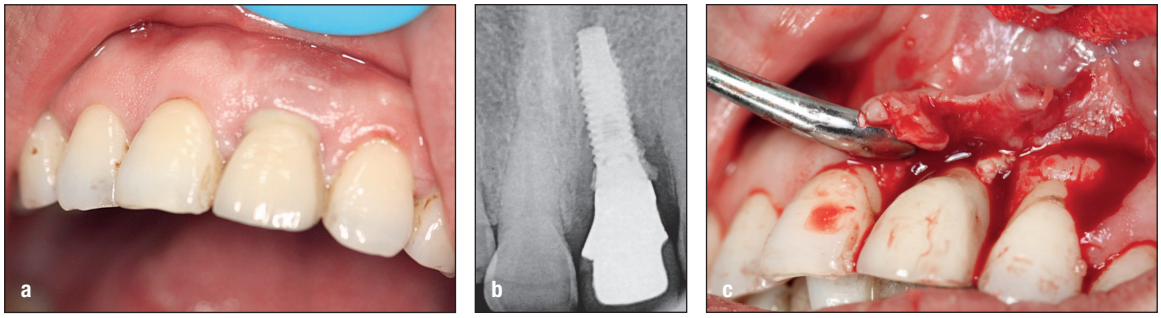


Fig 1-12 *(a)* Patient referred with an infection associated with the soft tissues surrounding the implant crown on the maxillary left central incisor. *(b)* Note the cement retained around the abutment and extending onto the surface of the implant. *(c)* Flap reflected. Note the cement on the distal surface of the implant. (Courtesy of Dr C. Tang, Nanjing, China.)

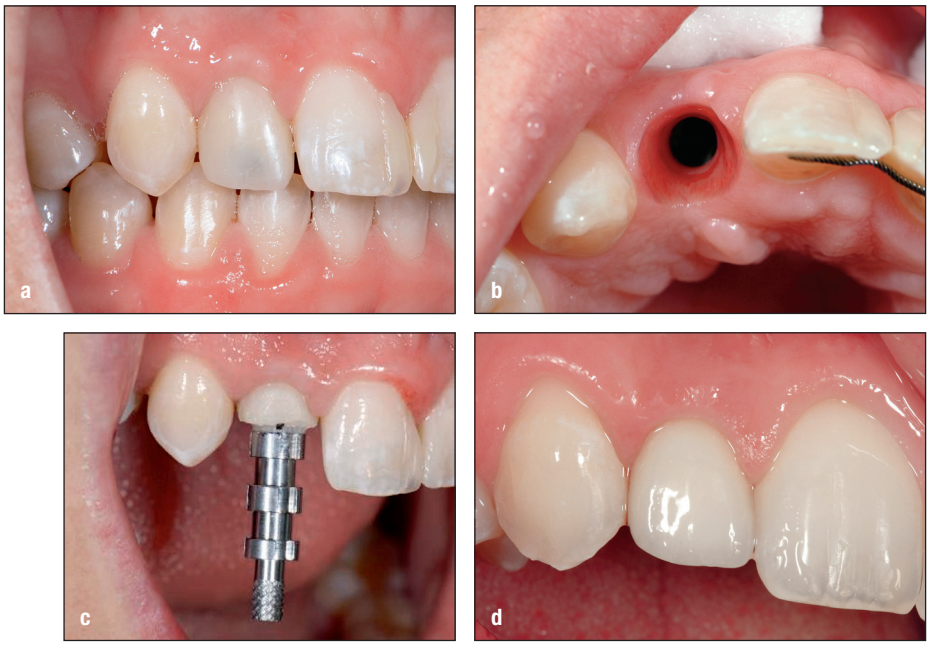


Fig 1-13 *(a and b)* A provisional implant crown. It was delivered at the same time the implant was uncovered, and the soft tissues were adapted to its contours. As a result, the soft tissue contours are idealized. *(c)* A customized impression coping was used to make the final impression. *(d)* The definitive restoration.

to the gingival crest, the greater the biologic width will be, particularly the epithelial component. Multiple abutment manipulations appear to induce an apical migration of the connective tissue–epithelial attachment zone, resulting in marginal bone loss.[24] The lack of stability of the abutment-implant connection may also precipitate an apical migration of the connective tissue–epithelial attachment zone accompanied by marginal bone loss around the neck of the implant, presumably as a result of increased levels of bacterial colonization. The long-term clinical consequences of these findings with respect to implant survival have yet to be determined.

In the esthetic zone, techniques have evolved that idealize the soft tissue contours around the implant prostheses. Provisional restorations are designed to support the soft tissues and develop ideal contours, and these contours can be recorded using customized impression techniques (see Fig 1-13). In addition, surgical procedures have been developed that can be used to enhance bone and soft tissue contours.

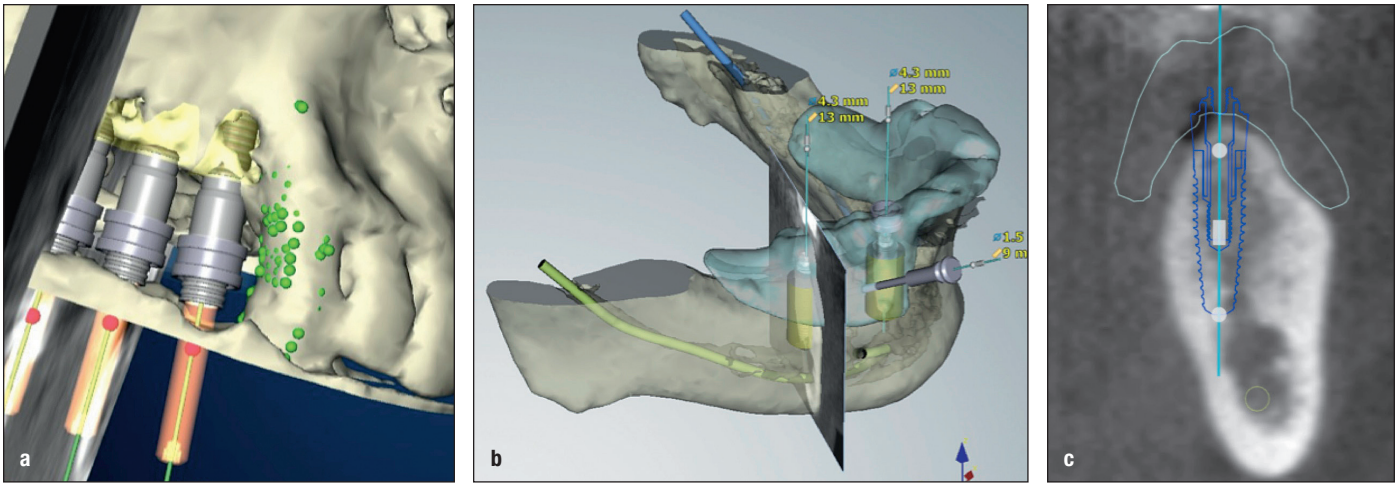


Fig 1-14 *(a to c)* Using scans and CAD/CAM techniques, vital structures can be visualized; bone volumes can be assessed in three dimensions; and implant size, position, and angulation can be determined prior to surgical placement.

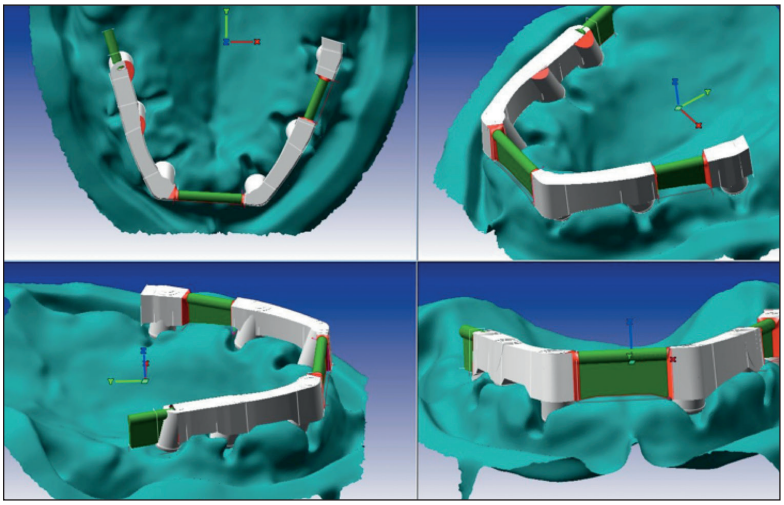


Fig 1-15 An implant-supported connecting bar milled to a 2-degree taper with Hader bar–type attachments can be designed with CAD/CAM techniques.

Impact of 3D Imaging and CAD/CAM on Diagnosis, Treatment Planning, and Prosthesis Fabrication

Computer-based imaging has had an enormous impact on diagnosis and treatment planning. With these tools, clinicians are able to identify vital structures such as the inferior alveolar nerve, determine the 3D nature of the potential implant bone sites, predetermine implant position and angulation with great precision, and fabricate surgical drill guides that allow placement of implants into their intended positions via guided surgery (Fig 1-14; see also Fig 1-7). In addition, CAD software programs allow for the design and manufacture of customized implant connecting bars, custom abutments, provisional restorations, and definitive restorations with great precision (Figs 1-15 to 1-17). It will soon become necessary for all those who practice implant dentistry to become intimately familiar with these emerging technologies. The two volumes of this series describe these new methods and attempt to place them in proper context regarding diagnosis, treatment planning, guided surgery, and fabrication of implant prostheses.

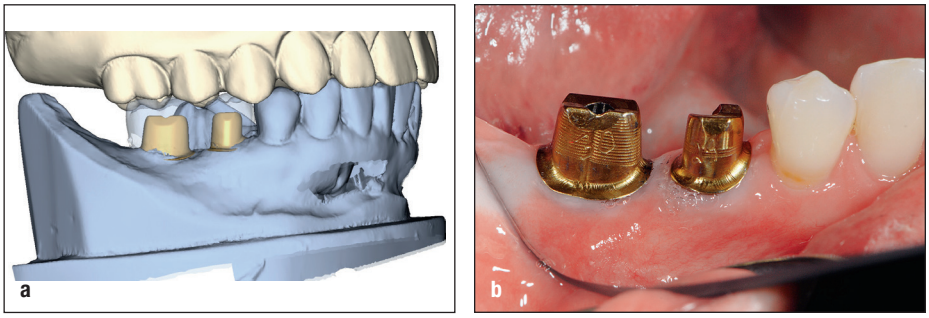


Fig 1-16 *(a and b)* CAD/CAM programs can be used to design and manufacture custom abutments.

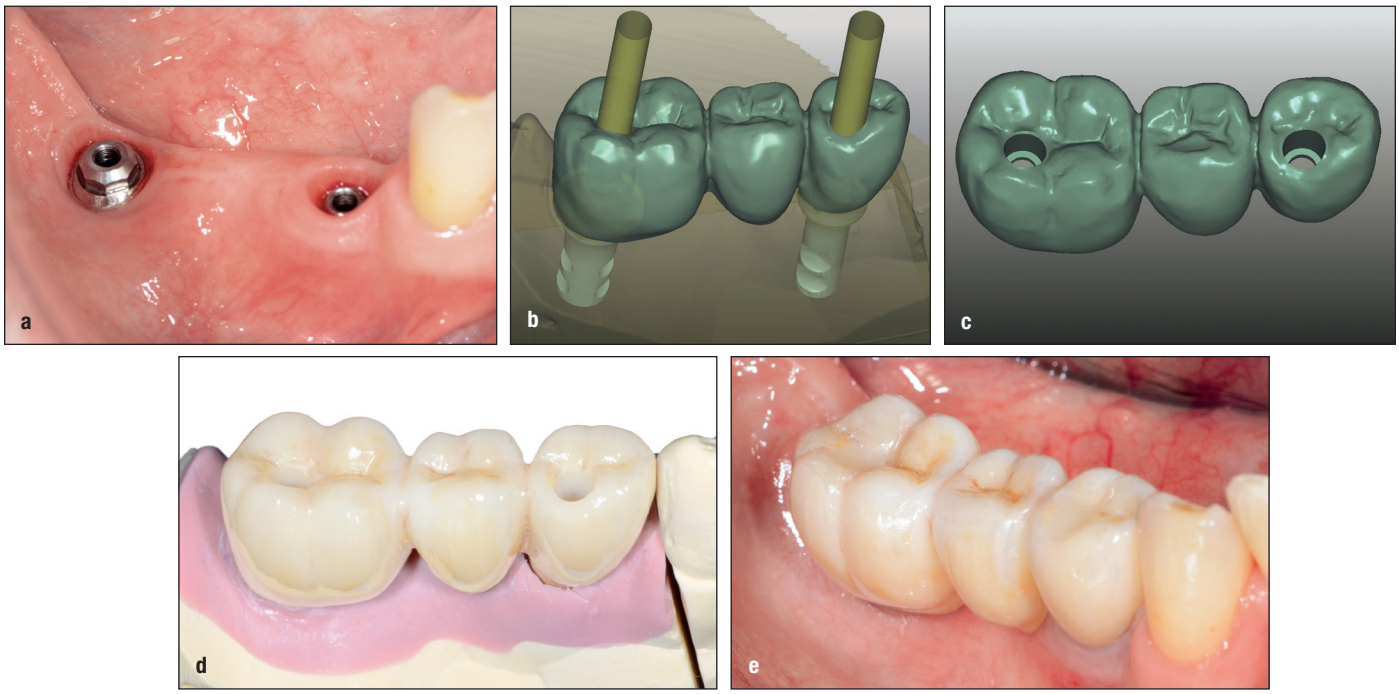


Fig 1-17 *(a)* Two implants have been placed to restore this posterior mandibular defect. *(b and c)* CAD software can be used to design the provisional and/or the definitive prosthesis *(d and e)*. (Courtesy of Dr M. Moscovitch, Montreal, Canada.)

Summary

Osseointegrated implants are highly predictable when used appropriately, and in many situations implant treatment is as predictable or even more predictable than any of the conventional restorative procedures used to restore missing dentition. The key to predictable outcomes when implants are employed is accurate diagnosis and appropriate treatment planning, taking into account significant patient history findings such as parafunction as well as implant biomechanics and the occlusal schemes to minimize undesirable occlusal forces. Successful outcomes are best accomplished in a multidisciplinary setting. The purpose of these volumes is to share with clinicians the approach to patient evaluation and treatment that has enabled the authors to provide these services with a very high degree of success. Indeed, when implant therapy is planned and executed properly, taking into account the basic principles of prosthodontics, it is the authors' expectation that once the implants are osseointegrated, while the prostheses that are retained by the implants may need replacement due to wear or breakage, the implants should last the lifetime of the patient.

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Ichiro Nishimura

Osseointegration and Its Maintenance

2

After the concept of osseointegration was introduced, a high rate of treatment success became a hallmark of dental implant systems. This chapter discusses the biologic sequence of host tissue reactions during the process of implant osseointegration and the pathologic factors that potentially can disturb the maintenance of dental implant systems after they have been placed into function.

Platelet Activation and Fibrin Clot Formation

Cells and biomolecules in blood

The placement of a dental implant requires creation of an osteotomy site, which induces vascular injury and bleeding. Therefore, the first host-derived tissues encountering the implant are circulating cells and biologic factors in blood. The vascular injury immediately activates platelets that adhere to each other and to the injured tissue, resulting in the formation of a platelet plug. Platelets carry surface receptors suitable for attachment to exposed or damaged collagen fibers while secreting internally stored bioactive factors. The platelet-derived factors include a series of enzymes that are essential for the cascade of the coagulation process resulting in fibrin and clot formation. These activated platelets also regulate the subsequent inflammatory response and wound healing processes. The fibrin clot not only works as a temporary "plug" to prevent further bleeding but also serves as an important scaffold for epithelial and mesenchymal cell migration contributing to the wound tissue repair.

Besides the injured collagen fibers and tissues, biomaterials placed in the body can activate platelets at different rates. Platelets are considered to be the first cells to adhere to the implant, and they immediately start secreting bioactive factors and organizing the fibrin clot. It takes only 2 minutes to initiate the fibrin clot formation on titanium (Ti) surfaces.[1] Platelet adhesion and activation on different biomaterials and material surfaces have become subject to intense investigation because the resulting fibrin clot scaffold is thought to determine inflammation behavior and subsequent wound healing around the biomaterial.

Hong et al[2] reported that there was much less platelet activation on the surface of stainless steel plates than on Ti plates. When used as an endosseous implant, stainless steel is surrounded by a sustained inflammatory reaction, resulting in minimal, if any, direct bone contact.[3] Therefore, the ability to activate platelets and form the fibrin clot may be an important first step in osseointegration.

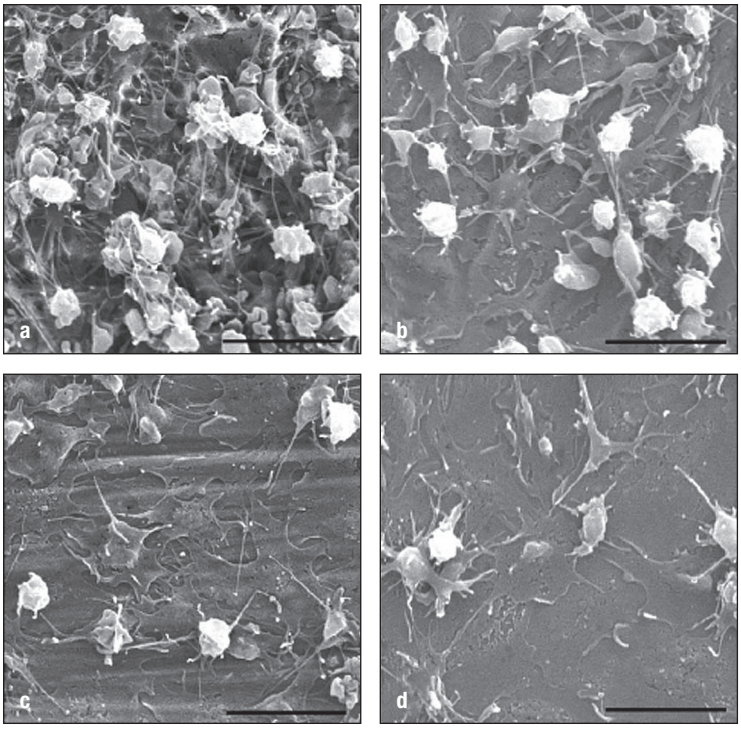


Fig 2-1 Scanning electron micrographs (SEMs) of platelet-rich plasma contact (for 30 minutes) with commercially pure Ti: *(a)* double acid-etched; *(b)* 320-grit abraded; *(c)* machined; *(d)* polished. The platelet aggregation and fibrin clot formation were more significant on roughened Ti surfaces. (Reprinted from Park et al[4] with permission.)

Effect of implant surface modifications on fibrin clot formation

Recent research and development efforts have been directed toward creating more bioactive Ti surfaces suitable for increased platelet adhesion. Moderately rough surface topography has been shown to increase platelet activation prepared by various methods: double acid etching[4] (Fig 2-1), fluoride ion–modified grit blasting,[5] sandblasting, and acid etching.[6]

Interestingly, in the field of vascular stent development, research efforts have been directed toward decreasing the adhesion of platelets and thus minimizing thrombosis formation. In fact, the micrometer to nanometer surface topography created on the Ti vascular stent[7] or polymer materials[8] was shown to decrease the platelet adhesion. The stark contrast in the observations regarding endosseous implants and vascular stents that both carry moderately rough Ti surface topography may suggest that not only the surface roughness but also other factors might determine the initial host response.

Complex surface topography is generally associated with increased hydrophobicity, which prevents the adhesion of platelets and other cells. Acid etching used to create microtopography increases the surface precipitation of titanium dioxide (TiO_2),[4] whereas alkali treatment results in the formation of charged TiO_2 on the Ti surface.[9] These surface modifications involving TiO_2 have been postulated to control platelet adhesion and activation. TiO_2, or *titania*, is a stable and relatively bioinert material that is largely responsible for the biocompatibility of Ti implants. However, the therapeutic role of TiO_2 has not been well characterized. The zeta potential or electron charge of the surface of TiO_2 is influenced by pH levels and the presence of various ions such as Ca^{2+}. Both acidic (low pH) and alkali (high pH) treatments are known to change the zeta potential of TiO_2, contributing to the modulated cell and protein adhesion behavior. Recent studies suggest that the proprietary SLActive preparation (Straumann) or postfabrication ultraviolet light treatments could increase surface hydrophilicity or surface charge of Ti implants. Characterization of their effect on the platelet behavior and fibrin clot formation has just begun,[10] which may present an important clue to understanding the role of surface reactivity and zeta potential on osseointegration.

It must be noted that hydroxyapatite (HA) surfaces show somewhat different platelet adhesion and activation properties as compared with Ti surfaces. The HA surface disproportionately increases complement activation in the fibrin clot[5] and increases adsorption of serum proteins.[11] Therefore, new surface modifications employing a hybrid of TiO_2 and HA[12–16] may present a unique opportunity to expand the available armamentaria for better optimization of platelet activation and fibrin clot formation relevant to osseointegration.

Platelet activation occurs at the tissue injury site and on the surface of biomaterials. However, the tissue injury site activates fibrin clot formation much more efficiently than do Ti materials.[6] Experimentally, the periodontal ligament on the freshly

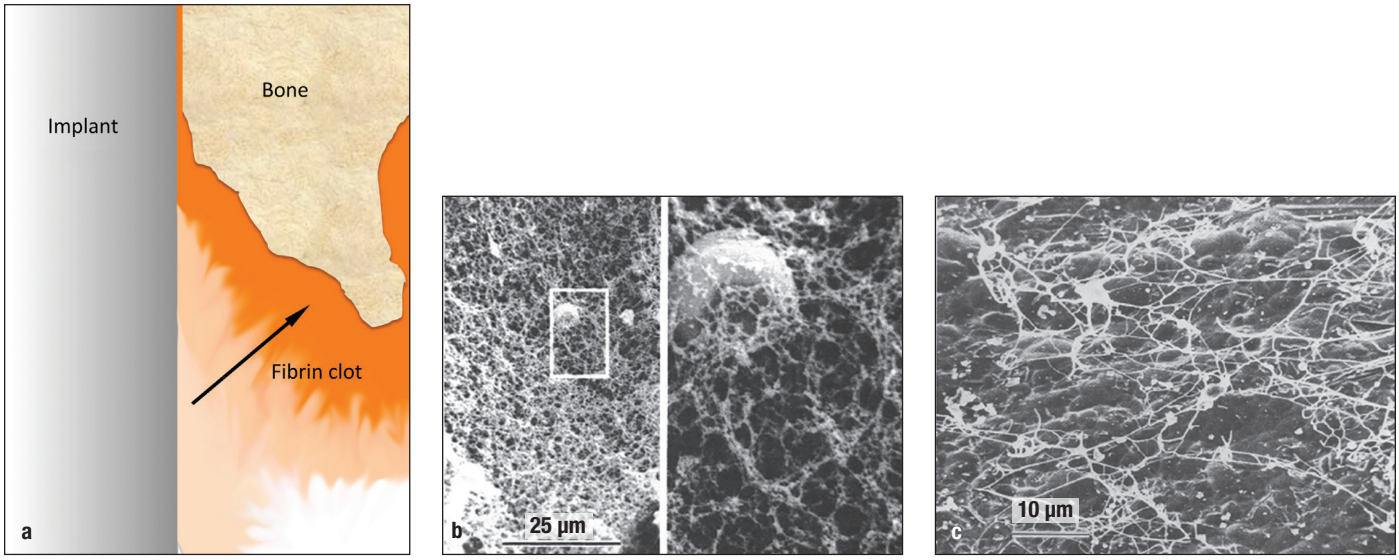


Fig 2-2 *(a)* Diagram of fibrin clot organization around an implant immediately after placement in the osteotomy site. Platelet activation is significantly more efficient on the exposed collagen from the injured tissue than on the Ti surface. As a result, a gradient of fibrin clot *(arrow)* is organized from the implant surface to the bone surface. *(b)* A cleaned extracted human tooth with remaining periodontal ligament was dipped in a fresh extraction socket for 60 seconds, and the surface was examined by SEM. A dense fibrin clot was already formed and organized (magnification: *left*, ×880; *right*, ×4,400). (Reprinted from Steinberg and Willey[17] with permission.) *(c)* A similar experiment was performed with a Ti plate. A Ti plate was dipped in a fresh extraction socket for 60 seconds. The fibrin clot formed a different architecture. (Reprinted from Steinberg et al[1] with permission.)

extracted tooth induced significantly more active clot formation than any artificial materials tested.[17] Therefore, there may be a gradient of fibrin clot network around the implant that is more organized and matured on the osteotomy-wounded bone surface than on the implant surface (Fig 2-2).

Fibrin Remodeling and Bone Formation

Fibrin scaffold network and macrophage infiltration

The wound-induced fibrin clot formation results in the organization of a fibrin scaffold network necessary for the succeeding tissue repair. Although the structure of fibrin networks is determined by multiple factors such as pH, clotting rate, and coagulation factor concentrations, polymerization of fibrin molecules generally occurs within the first 24 hours of wounding. The organized fibrin network is further modified by the incorporation of fibronectin molecules, which serve as the critical factor influencing bone formation in the fibrin scaffold. A recent study suggested the presence of macrophages within the fibrin clot adjacent to a dental implant within 12 to 24 hours.[18] The early and transient expression of CXCR4 (a cell surface receptor of monocytes/macrophages) in this study supports the involvement of macrophages in the process of osseointegration as well as the process of clearing the tissue debris (Fig 2-3).

Macrophages are classically described as proinflammatory phagocytic cells (M1 macrophages) that clear tissue debris and eliminate bacterial infection. It has been demonstrated that there are alternative differentiation pathways generating M2 macrophages that are capable of resolving inflammation and actively inducing angiogenesis for tissue repair.[19] It must be noted that the study by Omar et al[18] further suggested that macrophages infiltrating the fibrin scaffold around the implant were recognized by the CD163 cell surface marker. A subset of macrophages carrying CD163 are thought to express the M2 phenotype and are considered *myeloid-derived suppressor cells (MDSCs)*. MDSCs originate in bone marrow and resolve inflammatory reactions by suppressing T-cell activities. In addition, MDSCs induce angiogenesis and secrete a set of growth factors that support rapid wound healing.[20] Therefore, the presence of macrophages and MDSCs is critical for establishing a tissue repair environment for wound healing and bone formation.

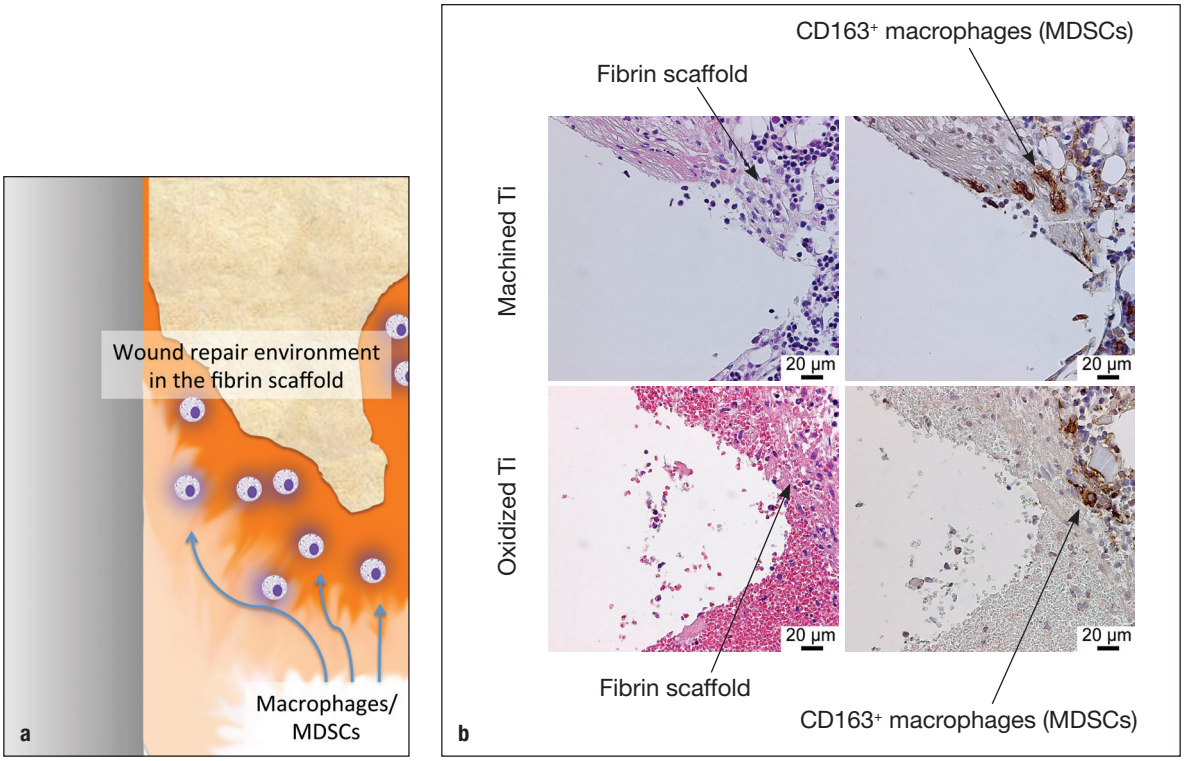


Fig 2-3 A diagram of bone formation around an implant. *(a)* Immediately after the fibrin clot scaffold is formed, bone marrow–derived myeloid cells called *myeloid-derived suppressor cells (MDSCs)* migrate into the mature fibrin clot and organize the local environment for wound repair. MDSCs stimulate new vascular formation and suppress wound-induced inflammation. *(b)* After 24 hours of implantation, the fibrin clot scaffold is already organized on the implant surface. Immunohistologic evaluation revealed the infiltration of CD163+ macrophages (or MDSCs) stained in brown in the fibrin scaffold. (Reprinted from Omar et al[18] with permission.)

Distance osteogenesis and contact osteogenesis

As seen in wound healing following tooth extraction, initial bone formation occurs in the bottom of the socket, suggesting the establishment of a tissue repair environment in the mature fibrin network (Fig 2-4). *Fibronectin* is a large glycoprotein with active binding sites not only to fibrin but also to other extracellular matrix (ECM) molecules and integrin-expressing cells. Incorporation of fibronectin in the fibrin network has been shown to be important for supporting macrophage function. The earliest bone formation should occur in the matured fibrin network adjacent to the osteotomy-exposed alveolar bone. An experimental implant model in mice demonstrated the early sequence of bone formation within the well-organized fibrin network that was more apparent on the bone surface.[21] This study further demonstrated the highly localized fibronectin molecules associated with the bone surface fibrin network. Bone tissue formation away from the implant is called *distance osteogenesis*,[22] which involves an ordinary sequence of bone wound healing as often seen in the tooth extraction socket or in the bone marrow ablation site.

During this period, the implant surface is still associated with a less organized fibrin scaffold network. However, the implant surface fibrin network is rapidly remodeled with the incorporation of fibronectin and provides the scaffold for bone formation. Distance osteogenesis may now approach in close proximity to the implant surface, while the new bone formation can occur within the now-matured fibrin network surrounding the implant. *Contact osteogenesis* describes this bone formation near the implant surface, which may be significantly affected by the different environment influenced by the implant material.[22] The gap between regenerating bone and the implant surface may be completely filled as early as 7 days after surgery, establishing the histologic osseointegration.

Fibrin clot formation and remodeling take place rapidly at the tissue injury site, where distance osteogenesis should be initiated immediately. Slow fibrin network maturation on the implant surface may cause delayed bone formation. In other words, contact osteogenesis around the implant occurs in a sequence, and the bone-to-implant contact (BIC) is established during the last stage of bone remodeling (Fig 2-5). There is a small but distinct time lag between distance osteogenesis and contact osteogenesis. However, active implant surface modifications may significantly accelerate contact osteogenesis.

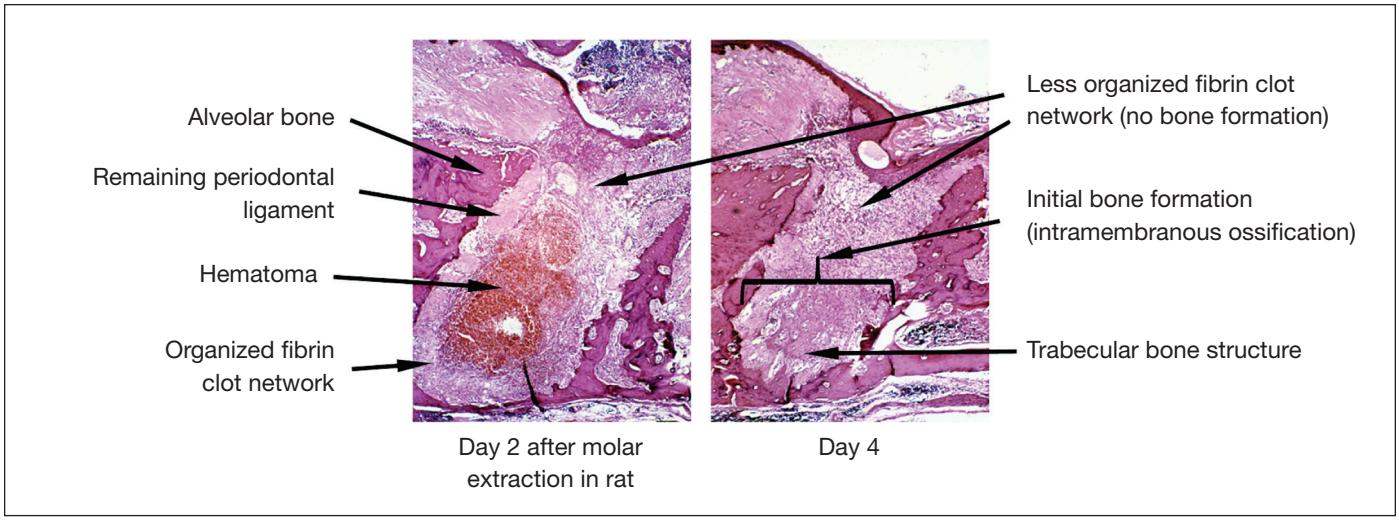


Fig 2-4 After rat molar extraction, the fibrin clot is organized at the bottom of the extraction socket *(left)*. The bone remodeling first occurs within the fibrin clot scaffold *(right)*. The cervical region where the initial fibrin clot formed is less organized and appears to delay the bone formation.

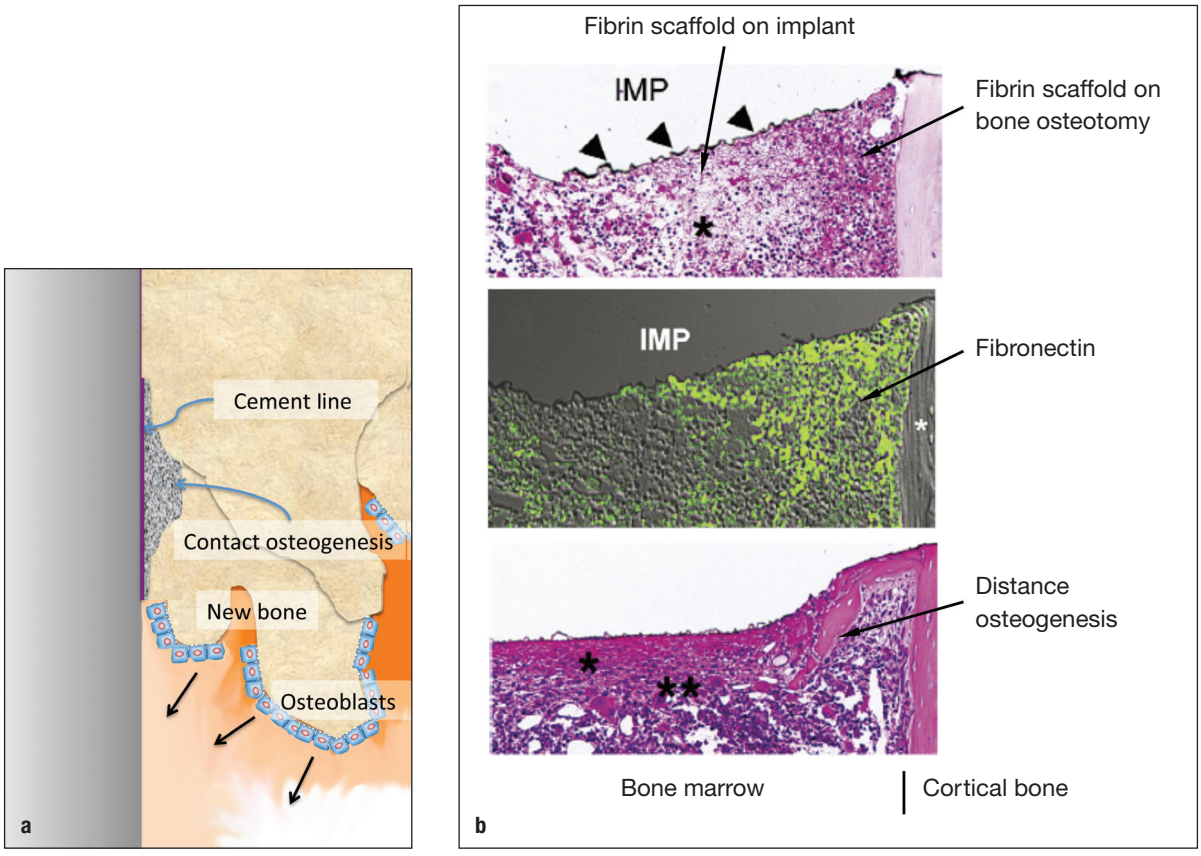


Fig 2-5 *(a)* The first bone formation occurs within the fibrin scaffold associated with the bone tissue exposed by osteotomy. Along with the delayed organization of the fibrin scaffold on the implant surface, bone formation catches up and eventually establishes BIC. *(b)* An experimental implant (IMP: Ti-coated *[arrowheads]* plastic implant) was placed in an osteotomy site of a mouse femur. Fibrin clots were organized 1 day after implant placement *(top)*. The fibrin scaffold associated with the bone osteotomy site and cortical bone (*) appeared to be more organized than that on the implant surface. Fibronectin *(green)* was found in the organized fibrin scaffold close to the bone osteotomy site *(middle)*. Two days after implant placement, the initial bone formation was detected within the organized fibrin clot containing fibronectin, while the fibrin network (*) on the implant surface appeared to be still immature. (Reprinted from Jimbo et al[21] with permission.)

Characteristics of Peri-implant Bone

Peri-implant bone, which is formed in close proximity to the implant surface, plays a central role in the sustained support of the implant. Peri-implant bone is formed within the fibrin scaffold surrounding the implant and is likely to be influenced by the implant surface topography, chemistry, and charged energy. These factors may affect the unique characteristics of the bone deposited onto the surface of the implant, which could directly or indirectly contribute to the maintenance of osseointegration. This section discusses the biomechanical characteristics, the shear strength at the bone-implant interface, and the long-term stability of peri-implant bone.

Biomechanical characteristics of peri-implant bone

Ideally, the intrinsic biomechanical properties of peri-implant bone should be capable of withstanding functional forces. It has been shown that hardness and stiffness of peri-implant bone may be associated with certain implant surface modifications. Butz et al employed nano-indentation assays to measure the hardness and Young modulus of peri-implant bone associated with a relatively smooth machined or double acid-etched Ti implant in a rat model.[23] The hardness of peri-implant bone associated with a relatively smooth (machined) implant was progressively increased from 2 weeks to 4 weeks after the surgical implant placement and reached the equivalent hardness of trabecular bone. The bone hardness associated with a moderately rough (double acid-etched) implant similarly underwent the progressive increase; ultimately, however, it was found to be much harder and reached the equivalent hardness of cortical bone. Recently, a similar experiment in a rabbit model revealed that the hardness of peri-implant bone almost doubled when a moderately rough (sandblasted/acid-etched) implant surface was further modified with a nano-HA coating.[24]

Once osseointegration is established, the intrinsic biomechanical properties of peri-implant bone should greatly contribute to the load-bearing function. It is intriguing that peri-implant bone may reach the hardness of cortical bone around implants with moderately rough and more complex surfaces. The primary mechanism determining the bone hardness and stiffness has been debated. A positive correlation between the stiffness and bone mineral density was demonstrated in bovine cortical bone[25] and porcine mandibular condyles.[26]

Bone is a composite tissue of collagen-based fibers and crystalline HA. The bone mineral content is regulated by the organic collagen matrix, which is largely composed of type I collagen. Fragile bone is the primary phenotype of a group of genetic disorders called *osteogenesis imperfecta*. Patients with these disorders experience bone fractures even during normal physical activity. A number of mutations have been discovered in type I collagen genes; however, the most severe form of osteogenesis imperfecta is associated with the genetic mutations in enzymes that control collagen cross-linking, such as prolyl-3-hydroxylase (P3H)[27] and cartilage-associated protein (CRTAP).[28] In addition, prolyl-4-hydroxylase (P4H) is also involved in collagen cross-linking, and collectively these enzymes are critical in determining the intrinsic bone mechanical properties. In vitro biomimetic mineralization on collagen films using a polymer-induced liquid-precursor mineralization process further supports the notion that increased collagen cross-linking significantly stimulates mineralization and increased intrinsic mechanical properties.[29]

With the use of genetic characterization methods, the increased expression of P4H and CRTAP has been reported in the peri-implant tissue during the early stages of osseointegration.[30,31] While type I collagen gene expression is not significantly affected by the presence of implant materials, the increased presence of collagen cross-linking enzymes associated with the implant is thought to contribute to the formation of stronger peri-implant bone[32] (Fig 2-6).

Bone-to-implant contact and interfacial shear strength

Direct bone attachment to the implant surface is the hallmark of osseointegration. Therefore, histologic assessment of osseointegration commonly uses the percent area of BIC. Higher failure rates in the posterior maxilla have been attributed to its relatively poor trabecular structure leading to decreased BIC. Traditionally, nondecalcified histologic ground specimens have been used to determine BIC. Significant intrasample variations in BIC have been found,[33] and a small but critical discrepancy has also been reported between histologic specimens and three-dimensional (3D) images reconstructed through microcomputed tomography (microCT).[34] Therefore, the data analysis of BIC may require careful interpretation.

Recently, an increasing number of studies report that BIC does not correlate with mechanical withstanding load. When the implant push-in test and microCT-based 3D BIC were used in a rat model, the moderately rough implant (due to double acid etching) showed three times higher shear strength than the relatively smooth machined implant.[35] Because the 3D BIC was not different between these tested implants, the increased interfacial shear strength was due to the increased bone bonding to the implant surface. The mechanical interlocking mechanism for roughened implants may contribute to the increased withstanding load. However, this study indicated that epoxy resin–embedded implants showed only a small increase in the withstanding load, suggesting that biologic bone bonding may play the central role. The discrepancy between the BIC measurement and the mechanical withstanding load assay suggests that while bone formation around the implant must be a prerequisite, the development of osseointegration may rely on the actual bonding between the bone and the implant surface.

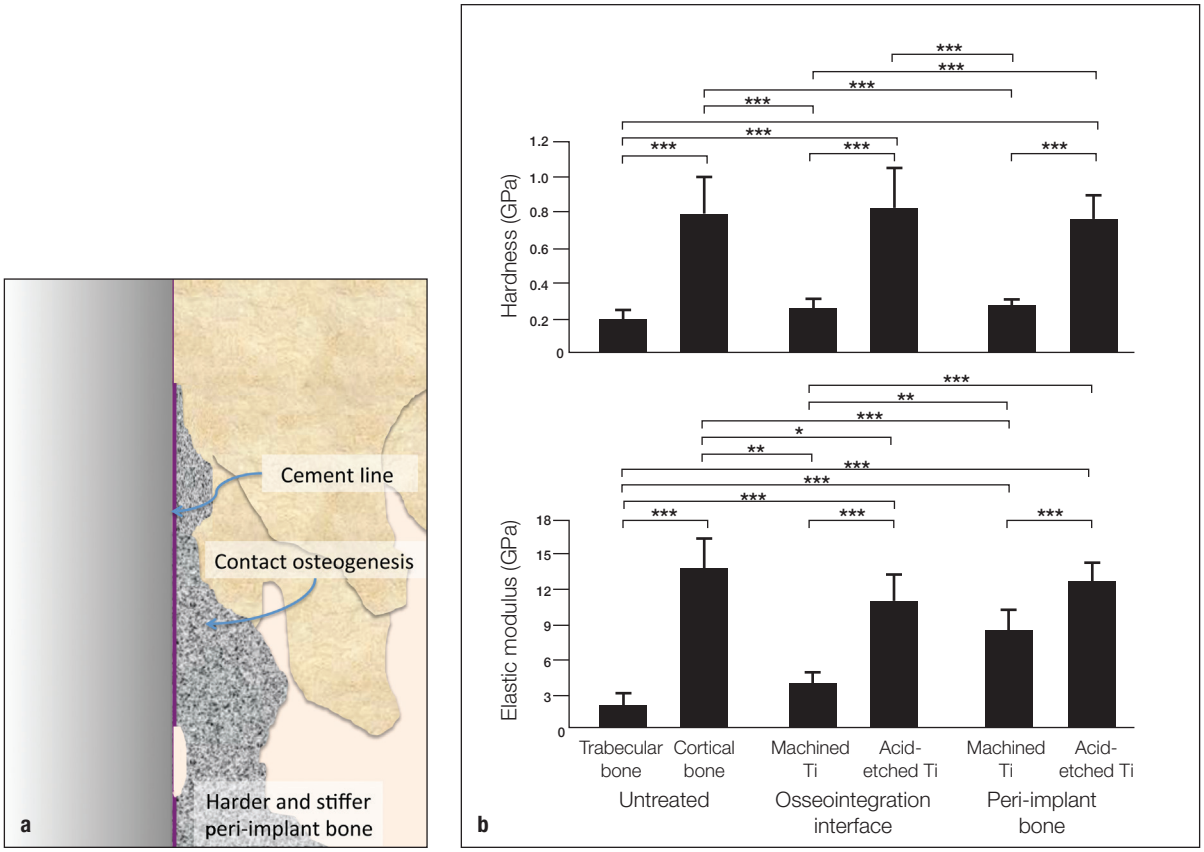


Fig 2-6 *(a)* Responding to a Ti implant, peri-implant bone synthesized through contact osteogenesis acquires a unique biomechanical property. *(b)* Hardness and stiffness of bone formed around an implant with a machined or a double acid-etched surface were measured by a nano-indentation assay. Peri-implant bone of the roughened implant was much harder and stiffer than trabecular bone, and its biomechanical properties nearly resembled that of cortical bone. Peri-implant bone deposited on the smooth, machined implant was not as hard; however, it had increased stiffness. *$P < .05$; **$P < .01$; ***$P < .001$. (Reprinted from Butz et al[23] with permission.)

For many years, the existence of a thin layer of tissue between the bone and the implant surface has been reported in electron microscopy observations. This tissue layer is generally described as comprising an electron-dense zone 20 to 50 nm thick[3,36] and a 100 to 200 nm–thick zone without typical collagen fibers,[37] followed by the collagen-rich bone tissue. However, considerable structural variations of this interface tissue have been pointed out, possibly due in part to sample preparation artifacts. Davies proposed that the electron-dense layer might be comprised of "globular accretions" that are highly mineralized.[38] Cross sections of globular accretions may result in the reported variation in thickness of the interface tissue layer or so-called cement line (Fig 2-7). A study using a Ti-coated polystyrene cell culture plate revealed a globular accretion–like electron-dense structure abutting the Ti layer.[39] The globular accretion–like interface layer was found to contain crystalline calcium phosphates similar to HA and the previously unreported thin collagen fibers. The precise molecular composition of the interface tissue has not been elucidated. However, it is postulated that molecules comprising the interface tissue between bone and the implant surface should hold the key to the mechanical withstanding force of osseointegrated implants.

It has been reported that this interface zone contains proteoglycans (PGs),[40] although the amount of PGs has been debated.[41,42] PGs are associated with glycosaminoglycan (GAG) side chains, which provide a sticky consistency, and therefore it has been postulated that PG-GAG in the interface zone may play a role in the bonding between bone and implant. The adhesion of in vitro mineralized tissue to a Ti disk was moderately attenuated by the treatment of GAG degrading enzymes such as chondroitinase AC, chondroitinase B, and keratinase.[43] Although this study suggested a functional role of PG-GAG for bone adhesion to the implant surface, the impact of chemical degradation of PG-GAG was surprisingly small. Therefore, the shear strength of osseointegrated implants to withstand occlusal load appears to involve more complex mechanisms.

The interface tissue (also known as the *cement line*) contains osteopontin (OPN).[44] OPN is a noncollagenous ECM molecule in bone. It has an integrin-binding sequence, suggesting cell adhesion functions. In addition, because OPN has been found

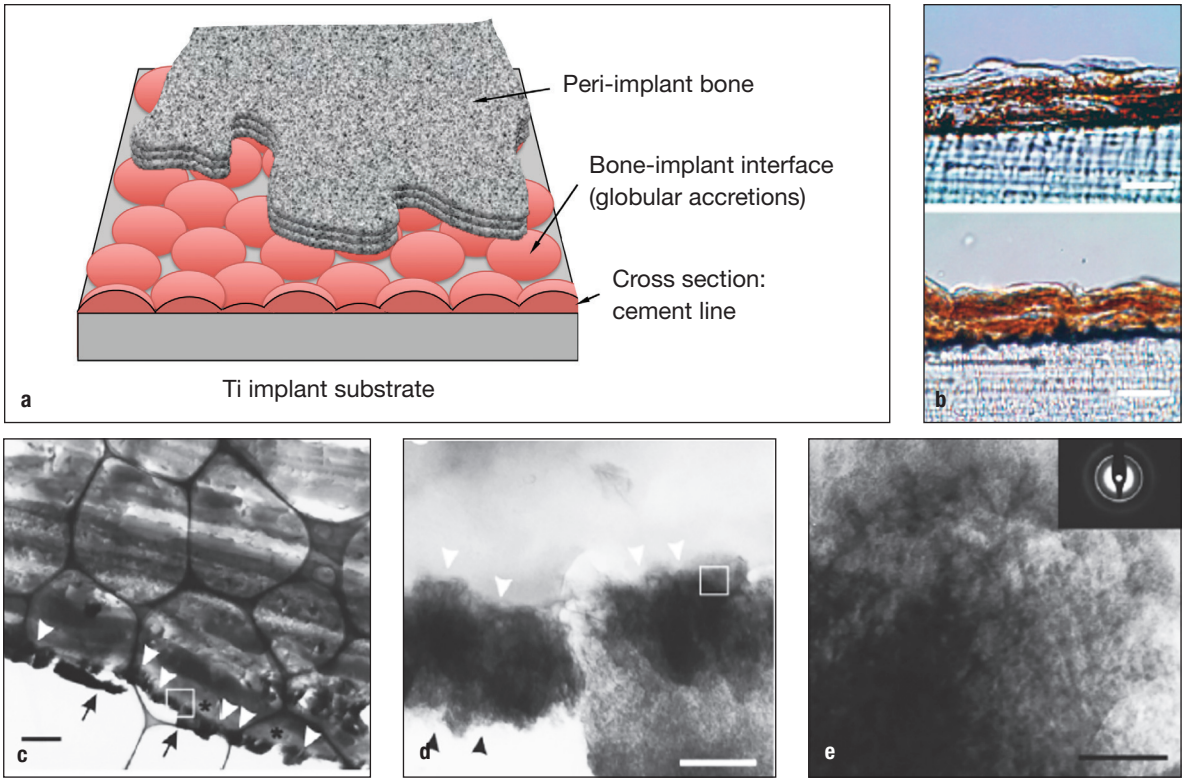


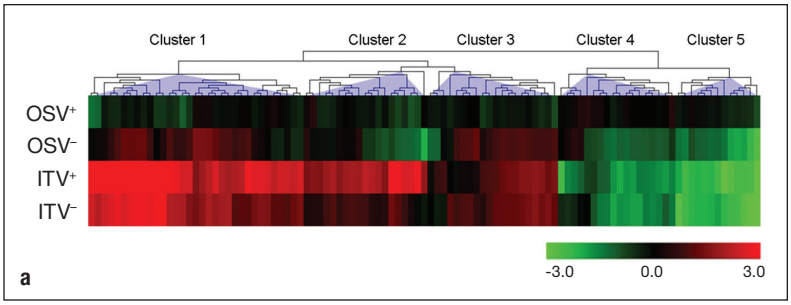
Fig 2-7 *(a)* Diagram of the implant and the bone interface. There is a thin layer of interface zone between the peri-implant bone and the implant surface, which is thought to be composed of globular accretions. The cross section of a cluster of globular accretions may be equivalent to the zone of tissue of the so-called cement line. It has been proposed that the molecular composition of this interface structure plays a key role in the function of osseointegration. *(b)* A recent in vitro study revealed that the osteogenic cells precipitated more mineralized tissue on the Ti-coated polystyrene cell culture plate *(bottom)* than on the control polystyrene surface *(top)*. *(c)* Transmission electron microscopy suggested an electron-dense zone of globular accretions *(white arrowheads)* on the Ti coating *(arrows)*. The globular accretion–like structures were interposed between the titanium coating and poorly mineralized bone (*). *(d)* A high magnification of the square in *c* demonstrated the mineral content *(arrowheads)* as well as thin fibrous structures. *(e)* A close-up of the square in *d*. The mineral content showed a crystalline structure consistent with hydroxyapatite. (Reprinted from Saruwatari et al[39] with permission.)

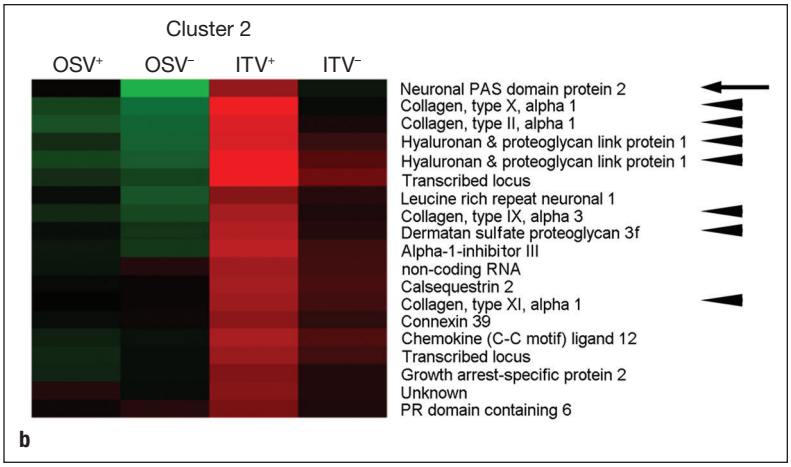
in high levels in mineralized tissue of bone and teeth, its postulated functions include regulation of bone remodeling. However, genetically modified mice lacking OPN were surprisingly normal, and their skeletal tissues developed without any complications.[45] The cement line of OPN-deficient mice was also found to exhibit the normal structure. Recently, a re-evaluation of OPN-deficient mouse bone revealed that there was a 30% decrease in bone fracture toughness, while the bone mass remained unaffected.[46] The nano-indentation assay showed that the stiffness, not the hardness, was significantly decreased. Although this conclusion is highly speculative, the high OPN content in the cement line may contribute to the increase in stiffness of the mineralized interface tissue between the bone and the implant surface, which could contribute to an increase in mechanical withstanding shear strength.

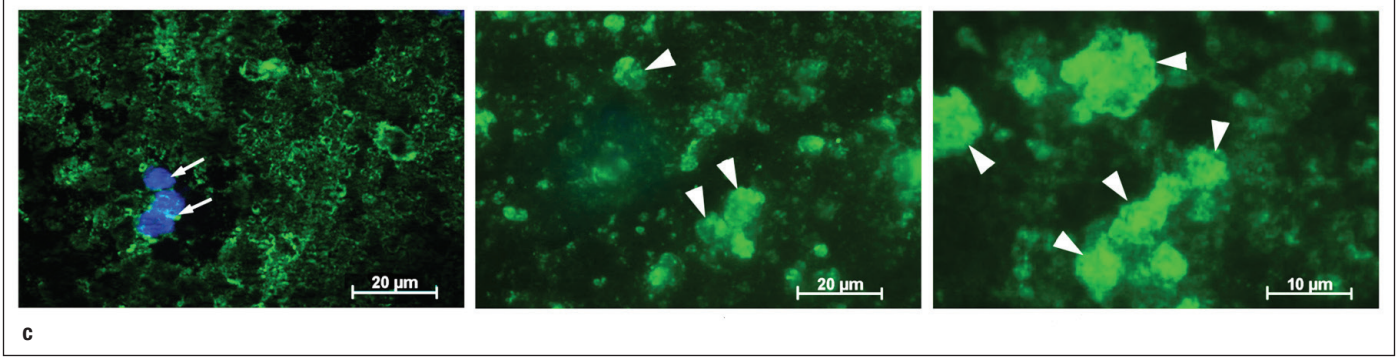
The large shear strength is due to the bone insertion sites of the ligament and tendon. Characterization of this interface zone of ligament insertion to bone repeatedly found the presence of types II, IX, and X collagen[47,48] that are commonly found in cartilage tissue. In particular, type X collagen is expressed by hypertrophic chondrocytes during endochondral ossification. In the growing bone, type X collagen is co-localized with PGs and appears on the longitudinal septa of hypertrophic cartilage when the bone starts to bear the body weight.[49] Type X collagen forms a network of hexagonal mesh and, when embedded in a mineralized tissue, enforces its intrinsic mechanical property. Therefore, type X collagen in the developing bone and the bone insertion sites of the ligament and tendon is thought to generate the significant shear strength to resist gravity and physical activities.

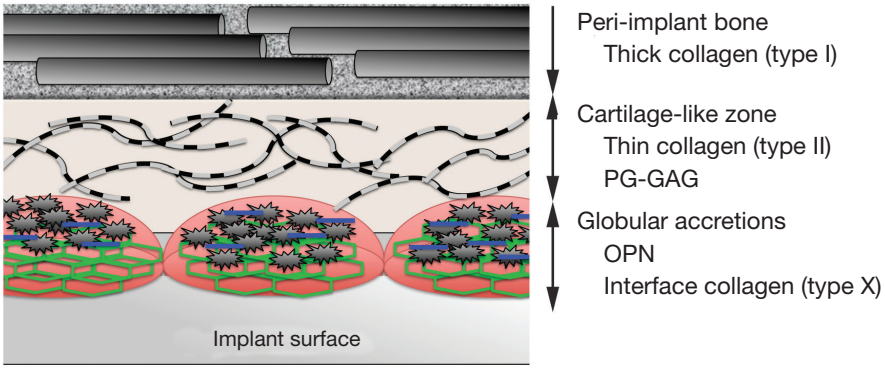
Studies involving DNA microarray reported a puzzling observation: The gene expression profile of peri-implant tissues contained not only bone-related genes but also other genes that were notably of the cartilage molecules.[50–53] Those cartilage-related molecules include PGs; types II, IX, X, and XI collagen; and hyaluronan and PG link protein.[54] In other words, the presence of an implant during the healing following osteotomy surgery may create a mixture of bone- and cartilage-related molecules in peri-implant bone. Recently, type X collagen was identified in the interface tissue between bone and implant.[50] It may be postulated that cartilage-related molecules such as PGs and type X collagen may be involved in the interface layer between implant and bone, potentially contributing to the shear strength of implant bonding to bone (Fig 2-8).

Fig 2-8 *(a)* The entire genome microarray gene expression of peri-implant tissue. A hierarchical cluster analysis revealed that there were five major gene groups, of which Cluster 2 exhibited the genes most sensitively associated with implant osseointegration. *(b)* Cluster 2 included cartilage-related ECM genes *(arrowheads)*. *(c)* Among cartilage-related genes, type X collagen *(green, arrowheads)* was identified within the interface zone between the bone and the implant surface. *(blue)* Bone marrow mesenchymal cells. (Parts *a* to *c* reprinted from Mengatto et al[50] with permission.) *(d)* Hypothetical structure and molecular components of the bone-implant interface tissue. The so-called cement line is composed of crystalline calcium phosphate particles *(gray sunbursts)* in globular accretions containing OPN *(blue bars)* and type X collagen *(green hexagonal mesh)*. These molecules may increase the stiffness and shear strength of the cement line. There is a less mineralized and relatively amorphous zone resembling cartilage tissue containing thin and sparsely arranged type II collagen fibers. The cartilage-like zone may also contain PG-GAG molecules, possibly contributing to the shock-absorbing function.









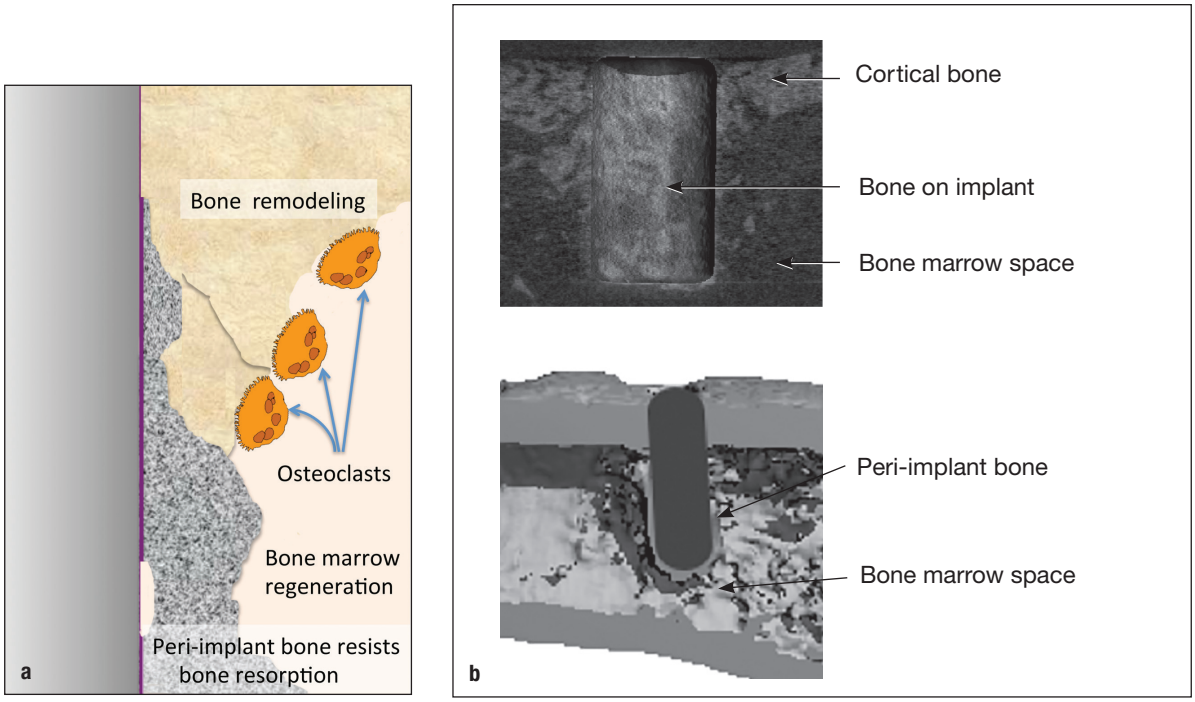


Fig 2-9 *(a)* A diagram of bone marrow ablation healing around an implant. The newly formed bone around the implant is subjected to osteoclastic bone resorption, regenerating the bone marrow space. It has been noted that peri-implant bone resists bone resorption activity. *(b)* MicroCT-reconstructed 3D picture depicting the persistent presence of peri-implant bone, with the surrounding bone marrow having lost its trabecular structure, in an experimental animal model using rats.

Long-term stability of peri-implant bone

The osteotomy procedure used to prepare an implant placement site creates an ablation wound in the bone marrow. Intramembranous ossification occurs during the healing of bone marrow ablation[55] and tooth extraction wounds,[56] thus leading to the formation of woven bone trabeculae in the marrow space. The trabecular bone formed in response to ablation wounding is then subjected to intensive remodeling and largely resorbed to create fatty bone marrow (Fig 2-9). Uniquely, bone tissue formed in the vicinity of implant surfaces appears to resist this catabolic bone remodeling and thus maintains the osseointegration for an extended period.[57] Trabecular bone derived from distance osteogenesis around the implant may be relatively unstable and can disappear due to physiologic bone remodeling. On the contrary, peri-implant bone derived from contact osteogenesis appears to escape from the bone marrow remodeling and remains around the implant for the long term (see Fig 2-9).

The rapid formation of bone marrow trabecular bone, perhaps with the woven bone characteristics, after the implant placement may occur in 1 to 2 weeks and may potentially contribute to the immediate implant stability. Whether the early woven bone can support the occlusal load has not been established. While the majority of woven bone may be resorbed, the remaining bone structures continue to mature. During the transition stage from resorption of a large volume of new woven bone to the maturation of the small but well-organized trabecular bone, there may be a vulnerable period in which the degree of implant integration may temporarily drop. This phenomenon has been observed in an animal model (Nishimura et al, unpublished data); however, its clinical significance has not been established.

Bone resorption is facilitated by osteoclasts. Osteoclasts are formed by fusion of monocytes under a combination of chemical cues including receptor activator of nuclear factor κB (RANK) ligand, or RANKL. During the developmental stage, RANKL is secreted from osteoblasts and hypertrophic chondrocytes. However, when bone is matured, RANKL is primarily secreted from osteocytes embedded in bone, which sensitively respond to mechanical stimuli.[58] The occlusal load applied to the implant should be sensed by osteocytes in the implant-supporting bone. As discussed previously, the mechanical property of peri-implant bone may be harder than that of surrounding trabecular bone. It is conceivable that the increased mechanical properties of peri-implant bone may insulate the embedded osteocytes, which may not secrete RANKL under the normal occlusal force. There must be an increased threshold for loading for peri-implant bone osteocytes; however, implant overloading beyond this threshold can stimulate the osteocytes to initiate the secretion of RANKL, resulting in osteoclast formation and bone resorption.

Osteoclasts strongly adhere to bone surface and form a ringlike apparatus, referred to as the *sealing zone*. Osteoclasts create an acidic milieu within the sealing zone and secrete proteinases such as cathepsin K to degenerate the organic matrix of bone. As a result, bone mineral HA and collagen matrix are removed. The osteoclast adhesion to the bone surface is required for this bone resorption process. It has been reported that the adhesion of osteoclasts is influenced by the bone surface topography. When mouse osteoclasts were cultured on Ti disks with different surface roughness ranging from 1 to 4.5 μ Ra, the sealing zone formation was shown to be disturbed by microtopographic obstacles.[59] There was an inverse correlation between the stability of the osteoclast ring (ie, the structural integrity and sealing zone translocation rate of osteoclasts) and the increasing microtopography.

Because the adhesion of osteoclasts appears to be less effective on a rough surface, it may be postulated that the surface topography of peri-implant bone may be rougher than that of surrounding trabecular bone. The placement of an implant appears to influence biochemical compositions of peri-implant bone. Cartilage and bone comprise the major skeletal system, and both contain ECM such as collagen. There are distinct differences in the composition of ECM molecules; ie, types I and V collagen are predominant in bone, whereas types II, IX, X, and XI collagen are in cartilage. However, recent studies indicate that peri-implant bone may be composed of a mixture of bone and cartilage ECM. In a mouse model lacking type IX collagen, one of the cartilage ECM molecules was shown to develop an age-related osteoporosis-like phenotype.[60] Type IX collagen maintains the space between the adjacent collagen fibers and has been shown to exist in a small amount in bone. The lack of type IX collagen appeared to manifest as a dense bone collagen network, resulting in the smoother bone surface. Osteoclasts were found to adhere widely to this mutant bone surface. Although highly speculative, the reduced susceptibility of peri-implant bone to osteoclastic bone resorption may in part be facilitated by its different biochemical compositions, such as increased type IX collagen, and bone surface topography.

Summary

Ti materials have long been considered to be bioinert. Therefore, it has been believed that the presence of a Ti implant in an osteotomy site should not influence the wound healing process. While the mechanistic elucidation is not complete, it is increasingly clear that osseointegration is not achieved only via bone formation. Recent observations and experimental evaluations indicate that there are distinct molecular and cellular behaviors that appear to be unique to peri-implant tissue. Some of these characteristics contribute to the mechanical advantage and long-term stability of osseointegrated implants. In addition, peri-implant bone may not undergo the same biologic and pathologic sequences as tooth-bearing alveolar bone. The maintenance of osseointegration may require special consideration.

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