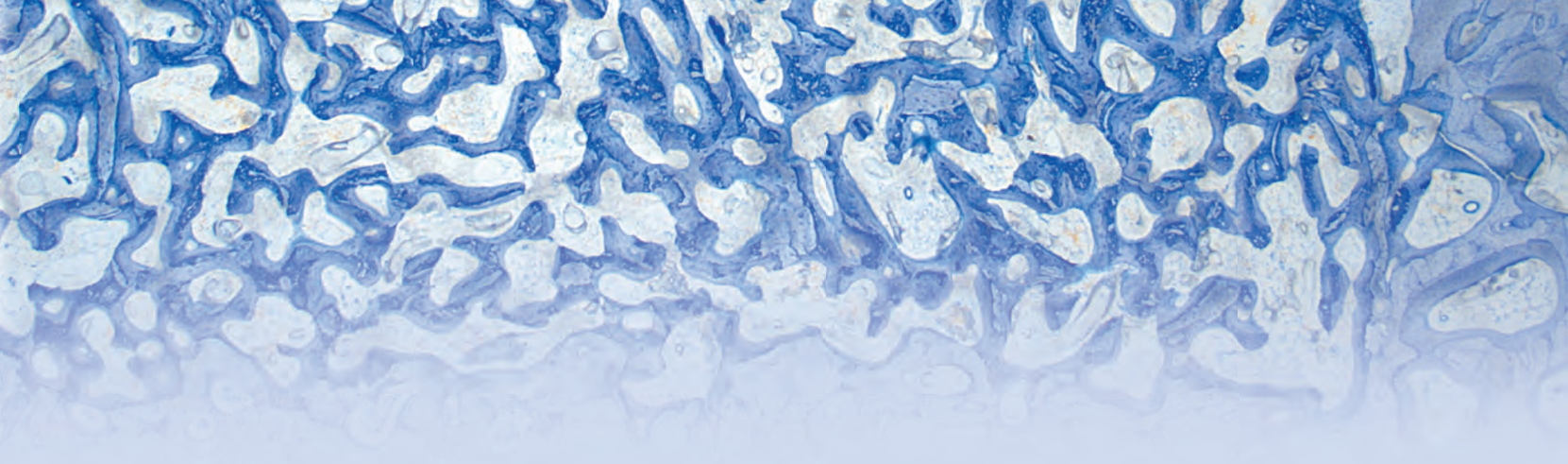
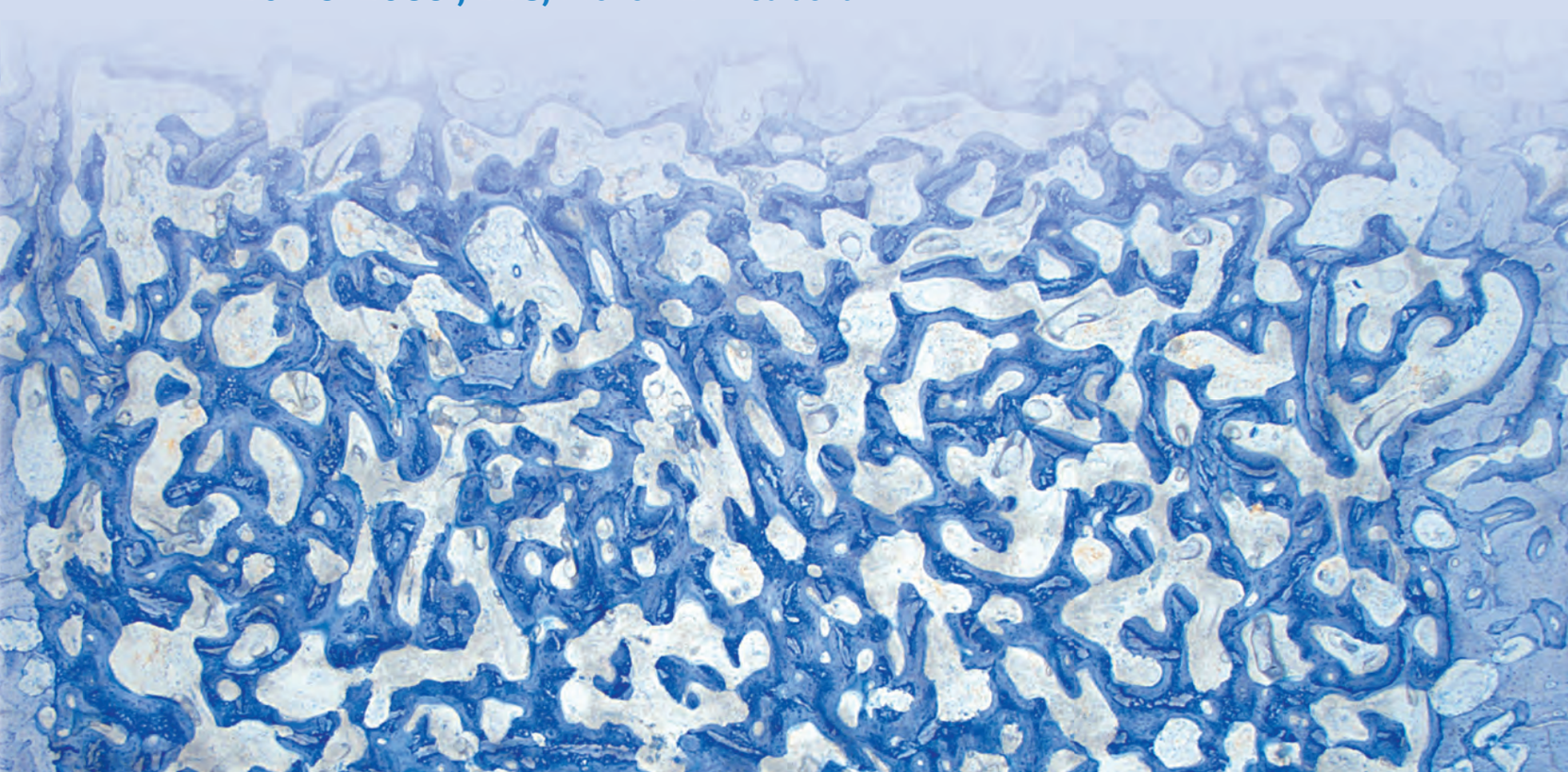


# *30 Years of* Guided Bone Regeneration

THIRD EDITION

*Edited by*

**Daniel Buser, DDS, Prof em Dr med dent**



QUINTESSENCE PUBLISHING

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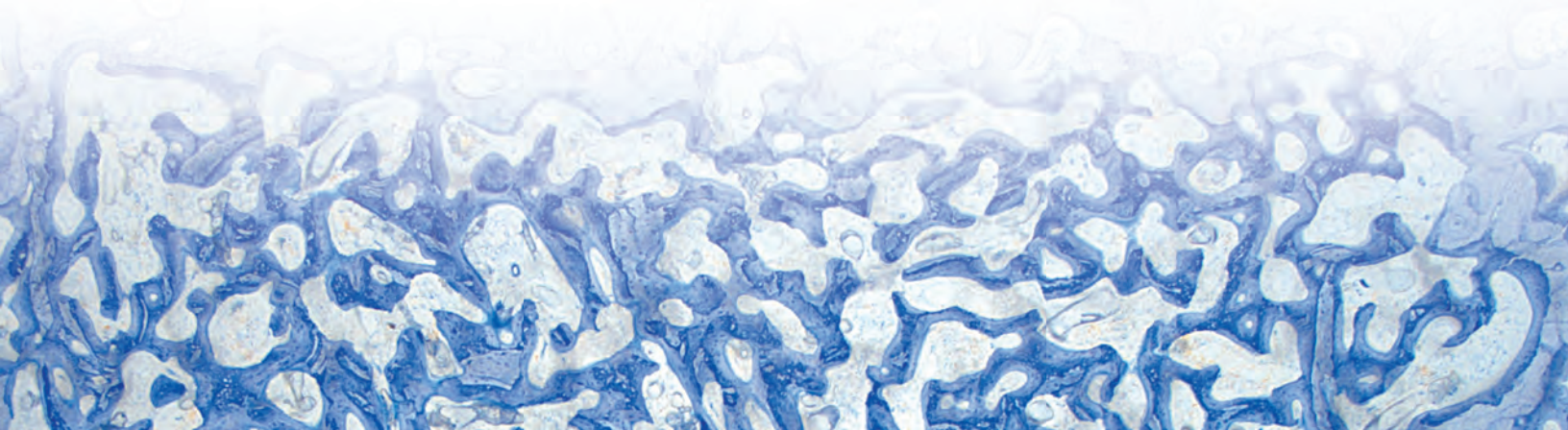

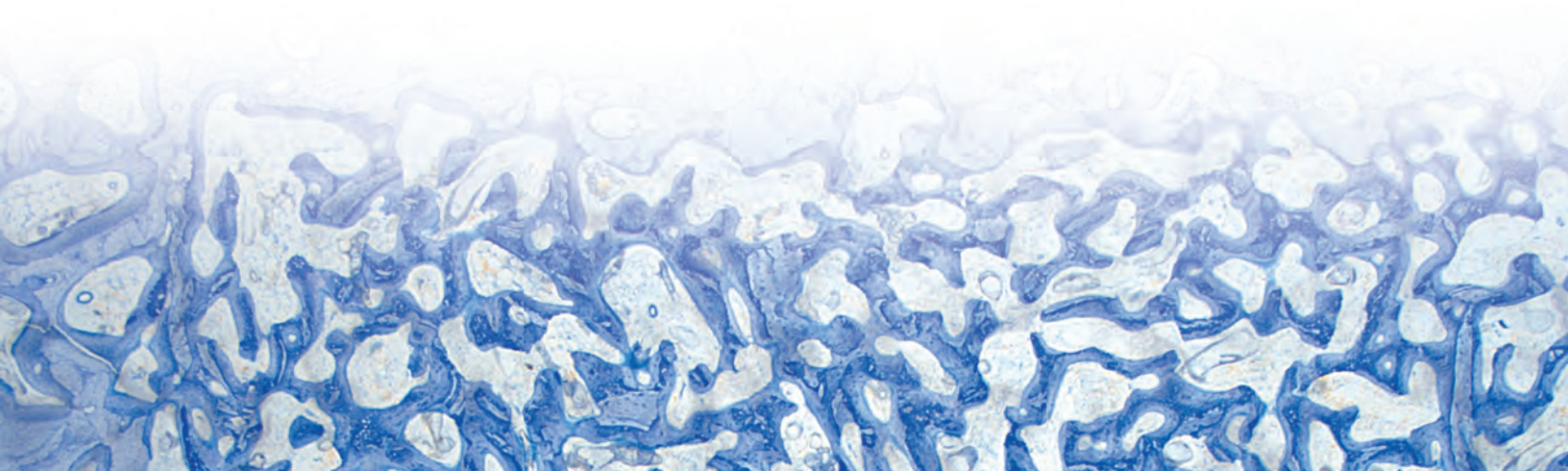

# Foreword

There have already been three decades of scientific documentation and successful clinical experience in the field of GBR—a truly impressive accomplishment! In this third edition of an already well-established textbook, authored and edited under the judicious leadership of Professor Danny Buser, a carefully selected international panel of experts has updated and shed light from all relevant angles on one of the most significant recent achievements of contemporary dental medicine. The text not only surveys 30 years of progress made; it also comprehensively defines the current state of the art in GBR and its tremendous impact, namely on implant dentistry. Clinical protocols aimed at reducing overall treatment complexity and time, as well as diminishing patient morbidity, have been developed and refined during recent years. In addition, based on the remarkable levels of reliability and predictability of GBR, numerous new avenues for clinical application have been opened.

In fact, the knowledge of which techniques and associated biomaterials are recommended today, linked to the indispensable robust scientific documentation, provide the clinician with the basis for target-oriented clinical decision making in view of the subsequent treatment. This includes the consideration of the practitioner's individual state of education and competence. Namely, the SAC concept—which objectively differentiates straightforward, advanced, and complex cases in relation to the difficulty level of a given clinical situation—is of particular importance and has been strongly promoted by the main author for many years.

The current third edition of a textbook that has twice already previously reached the status of a true standard of reference has clearly outperformed its two predecessor issues. Beyond any doubt, oral surgeons, periodontists, prosthodontists, and general practitioners, as well as dental students, will find all the detailed information relevant to successful implementation of GBR in daily practice, ultimately to the benefit of countless patients.

**Urs C. Belser, DMD, Prof em Dr med dent**
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# Dedication

This textbook is dedicated to Robert K. Schenk, Prof Dr med, who was Professor of Anatomy at the University of Bern, Switzerland. He was a world-renowned scientist in the field of bone physiology and bone healing. His instruction on the basics of bone healing was what allowed for the tremendous progress with GBR we made in the 1990s. Dr Schenk's chapter on the basics of bone healing in the first GBR book was a sensation at that time. He was able to illustrate his knowledge with fantastic histologic pictures produced by his lab. Besides his generosity to share his knowledge and wisdom, he was a true friend and mentor.

**Robert K. Schenk, Prof Dr med (1923–2011)**

# Preface

The utilization of barrier membranes for the regeneration of bone defects has significantly changed implant dentistry in the past 30 years and clearly expanded the utilization of dental implants in patients. This principle is called guided bone regeneration (GBR or GBR technique), and was first described in 1959 by Hurley and colleagues for the treatment of experimental spinal fusion. In the 1960s, the research teams of Bassett and Boyne tested Millipore filters for the healing of cortical defects in long bones and osseous facial reconstruction, respectively. The authors utilized these filters to establish a suitable environment for osteogenesis by excluding fibrous connective tissue cells from bone defects. However, these studies did not lead to a clinical application of barrier membranes in patients at that time.

The clinical potential of barrier membranes was picked up in the early 1980s in the field of periodontology by the research team of Nyman and Karring, who systematically examined barrier membranes for periodontal regeneration. A few years later, barrier membranes were also tested for the regeneration of bone defects in experimental studies. The first three studies were done in Gothenburg by Dahlin and Nyman. Based on promising results in these studies, clinical testing of barrier membranes began in implant patients in the late 1980s. After 5 years of intensive experimental and clinical work, the first edition of the textbook *Guided Bone Regeneration in Implant Dentistry* was published in 1994, and it received a high interest by readers in the field of implant dentistry. In 2009, the second edition of the GBR book was published with an update of the scientific knowledge and the surgical techniques being utilized after 20 years of a wide clinical application of GBR.

In the past 12 years, the scientific knowledge and the clinical experience have evolved further. During these years, many fine-tuning efforts have been made for the various surgical techniques to improve the regenerative outcomes, or to reduce the surgical invasiveness for patients. Therefore, it was time to make a new effort to once again analyze the scientific basis of the GBR technique and its clinical applications. The result is in your hands, the third edition of the GBR book, called *30 Years of Guided Bone Regeneration in Implant Dentistry*. This book is again written for the surgical clinician with an interest and experience in implant dentistry.

As an introduction to the topic of the book, chapter 1 discusses the development and fine-tuning phase of the GBR technique over the past 30 years. Chapter 2 covers the biologic basis of bone regeneration and presents a scientific update on bone formation and bone remodeling. The excellent histology utilizing nondecalcified sections is based on more than 30 years of experimental research, and it presents the details of bone regeneration in general and the details of bone formation in membrane-protected defects with bone grafts or bone substitutes in particular. Chapter 3 is completely new and describes the molecular and cellular characteristics of autogenous bone chips, and how they release various growth factors when put in a mixture of blood and physiologic and sterile saline. Chapter 4 is also completely new and describes the hard and soft tissue alterations following tooth extraction. Clinicians need to understand these biologic mechanisms for proper selection of the most suitable treatment option in postextraction implant placement. Chapter 5 is also new and systematically describes the surgical and anatomical factors influencing the regenerative outcome of GBR procedures, including the interesting classifications of defect morphology.

In the clinical section of the book, chapters 6 to 14, clinical procedures associated with different indications of the GBR technique are presented in detail. Each chapter deals with specific indications and describes the criteria for patient selection, the step-by-step surgical procedure, and aspects of postoperative treatment. Emphasis is given to incision technique and flap design; the selection, handling, and placement of barrier membranes; the combination of membranes with autogenous bone grafts and low-substitution bone fillers; and aspects of wound closure. These chapters of the book reflect the immense progress and excellent documentation of GBR in the past 10 to 15 years, and its outstanding importance in daily practice of implant therapy.

## *Acknowledgments*

As editor, I cordially thank all authors and coauthors for their great effort and time to realize this textbook. It has been very intensive work during a pandemic crisis, but a satisfying experience to collaborate with colleagues of such international reputation and high quality. Some of them are long-term personal friends, which makes the pleasure even greater. I also want to share that all authors, including myself, agreed to have the authors' royalties entirely paid into the Buser Implant Foundation, a foundation established in August 2019 right after my retirement as Professor and Chairman at the Department of Oral Surgery and Stomatology, University of Bern, after 20 years of service. The foundation's objectives are the promotion of education and research in the field of implant dentistry by providing personal stipends and junior investigator grants to young colleagues of our profession. The first Buser Foundation Scholarship in Implant Dentistry has been awarded in spring 2021.

I also thank Bernadette Rawyler, who created all the beautiful digital artwork in my chapters. These illustrations have made it much easier to communicate the correct messages and necessary information from the authors to the reader.

Last but not least, I also cordially thank Bryn Grisham and Marieke Zaffron of Quintessence Publishing for their excellent collaboration to realize this book. The quality work and the quality printing of Quintessence was again superb and is highly appreciated. It reflects almost 30 years of close collaboration with Quintessence Publishing, both in Berlin and in Chicago. I thank Horst Wolfgang Haase, Christian W. Haase, as well as Alexander Ammann for this excellent collaboration over so many years, which was based on trust, respect, and friendship.

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# 1

# The Development of Guided Bone Regeneration Over the Past 30 Years

*Daniel Buser, DDS, Prof em Dr med dent*

Modern implant dentistry based on the concept of osseointegration recently celebrated its 50th birthday.[1] The tremendous progress made in the rehabilitation of fully and partially edentulous patients is based on fundamental experimental studies performed by two research teams. One team was located in Sweden and headed by Prof P-I Brånemark from the University of Gothenburg; the other was located in Switzerland and headed by Prof André Schroeder from the University of Bern. In the late 1960s and 1970s, the two research groups independently published landmark papers describing the phenomenon of osseointegrated titanium implants.[2–4] An *osseointegrated implant* was characterized by direct apposition of living bone to the implant surface.[5–7]

In the early phase of this development, several prerequisites were identified for osseointegration to be achieved.[2,3] Some of these have been revised over the past 50 years; others are still considered important. In order to achieve osseointegration, the implant must be placed using a low-trauma surgical technique to avoid overheating the bone during preparation of a precise implant bed, and the implant must be inserted with sufficient primary stability.[5,8] When these clinical guidelines are followed, successful osseointegration will predictably occur for nonsubmerged titanium implants (single-stage procedure) as well as for submerged titanium implants (two-stage procedure), as demonstrated in comparative experimental studies.[9,10]

When clinical testing of osseointegrated implants first began, the majority of treated patients were fully edentulous. Promising results were reported in retrospective studies.[11–13] Encouraged, clinicians increasingly began using osseointegrated implants in partially edentulous patients, and the first reports on this utilization were published in the late 1980s and early 1990s with promising short-term results by various groups.[14–18] As a consequence, single-tooth gaps and distal extension situations have become more and more common indications for implant therapy in daily practice. Today, these practices dominate in many clinical centers.[19–21]

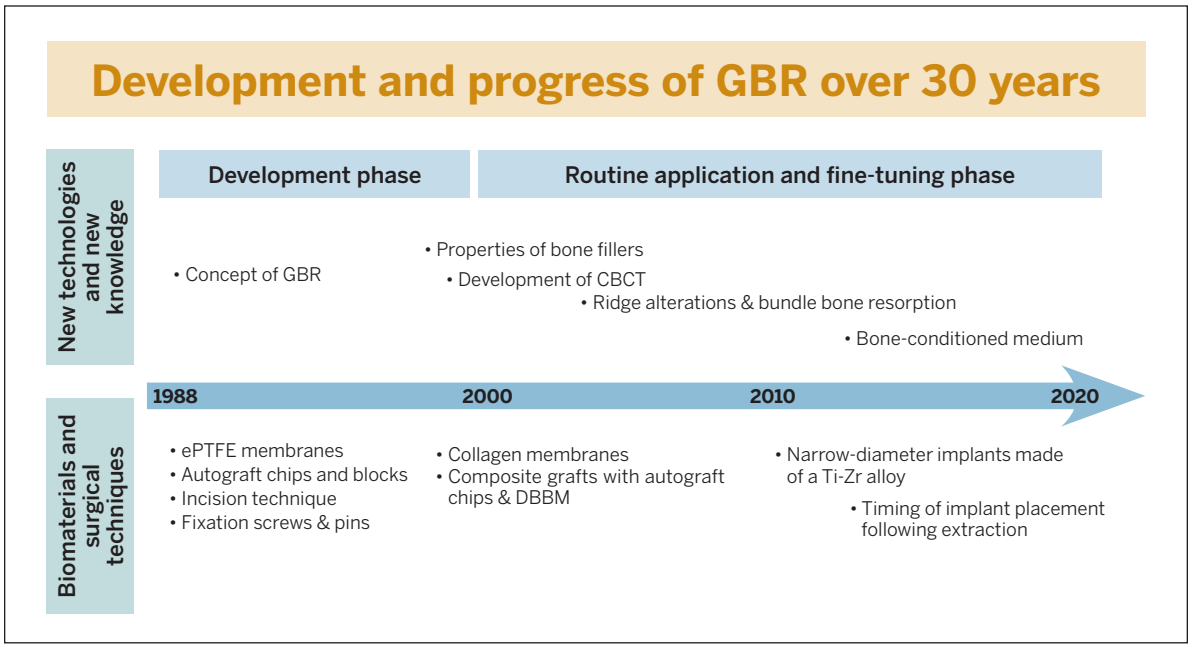


**Fig 1-1** Development of GBR over 30 years since the late 1980s. ePTFE, expanded polytetrafluoroethylene; DBBM, deproteinized bovine bone mineral; Ti-Zr, titanium-zirconium.

One of the most important prerequisites for achieving and maintaining successful osseointegration is the presence of a sufficient volume of healthy bone at the recipient site. This includes not only sufficient bone height to allow the placement of an implant of adequate length, but also a ridge with sufficient crest width. Clinical studies in the 1980s and 1990s showed that osseointegrated implants lacking a buccal bone wall at the time of implant placement had an increased rate of soft tissue complications and/or a compromised long-term prognosis.[22,23] To avoid increased rates of implant complications and failures, these studies suggested that potential implant recipient sites with insufficient bone volume should either be considered local contraindications for implant placement or should be locally augmented with an appropriate surgical procedure to regenerate the local bone deficiency.

During these early decades, several attempts were made to develop new surgical techniques to augment local bone deficiencies in the alveolar ridge in order to overcome these local contraindications for implant therapy. The proposed techniques included vertical ridge augmentation using autogenous block grafts from the iliac crest in extremely atrophic arches,[24,25] sinus floor elevation procedures in the maxilla,[26–28] the application of autogenous onlay grafts for lateral ridge augmentation,[29–31] or split-crest techniques such as alveolar extension plasty.[32–34]

During the same period, in addition to these new surgical techniques, the concept of guided bone regeneration (GBR) with barrier membranes was introduced. Based on case reports and short-term clinical studies, various authors reported first results with this membrane technique for the regeneration of localized bone defects in implant patients.[35–40]

This textbook will provide an update on the biologic basis of the GBR technique and its various clinical applications for implant patients. Clinical experience with GBR in daily practice now spans 30 years. These 30 years can be divided into a development phase and a phase of routine application with extensive efforts to fine-tune the surgical procedure (Fig 1-1). The focus was on improving the surgical technique, expanding the range of applications, improving the predictability for successful outcomes, and reducing morbidity and pain for the patients.

## Development Phase of GBR

The use of barrier membranes for implant patients was certainly triggered by the clinical application of barrier membranes for periodontal regeneration, called *guided tissue regeneration* (GTR). GTR was first developed in the early 1980s by the group led by Nyman et al.[41,42] The initial studies were performed with Millipore filters, which had already been used in experimental studies in the late 1950s and 1960s for the regeneration of bone defects.[43–45] However, these studies had no impact on the development of new surgical techniques to regenerate localized defects in the jaws, because the potential of this membrane application was probably not recognized at that time.

The two papers by Nyman et al[41,42] in the field of GTR, both of which demonstrated successful treatment outcomes of GTR procedures, were received with great interest and led to increased research activities in the mid to late 1980s.[46–49] These studies were already being performed with expanded polytetrafluoroethylene (ePTFE), which is a bioinert membrane and became the standard membrane for GTR and GBR procedures during the development phase of both techniques. The use of ePTFE membranes for bone regeneration was initiated in the mid 1980s by the group of Dahlin et al, who performed a series of preclinical studies.[50–52] These studies confirmed the concept that the application of an ePTFE membrane established a physical barrier that separated the tissues and cells that could potentially participate in the wound healing events inside the secluded space. The barrier membrane promoted the proliferation of angiogenic and osteogenic cells from the marrow space into the bone defect without interference by fibroblasts. These events were nicely demonstrated by Schenk et al[53] in a landmark experimental study in foxhounds. The current biologic understanding of wound healing events in membrane-protected bone defects is presented in detail in chapter 2 of this textbook.

The use of ePTFE membranes for GBR procedures started in the late 1980s. The main objective was to achieve regeneration in peri-implant bone defects in implant sites with local bone deficiencies. The GBR technique has been used with both simultaneous and staged approaches. Implant placement with simultaneous GBR was predominantly used for immediate implant placement in postextraction sites to regenerate peri-implant bone defects[35,36,38] or for implants in sites with crestal dehiscence defects.[40] The staged approach was used in clinical situations with healed ridges but an insufficient crest width. The membrane technique was used to enlarge the crest width with a first surgery, and implant placement took place after 6 to 9 months of healing in a second surgical procedure.[37]

Early on, several complications were observed with both approaches, and modifications of the surgical techniques were proposed to improve the predictability of successful treatment outcomes. One frequent complication was the collapse of the ePTFE membranes, which reduced the volume of the regenerated tissue underneath the membrane. In addition, some of the regenerated sites demonstrated insufficient bone formation and the formation of a periosteum-like tissue underneath the membrane.[37,40] Therefore, bone fillers such as autografts or allografts were recommended by various groups, primarily to support the membrane and reduce the risk of membrane collapse.[54–56] The combination of ePTFE membranes and autogenous bone grafts provided good clinical outcomes for both approaches. Some of these patients are still being followed and documented up to 25 years after surgery (Figs 1-2 to 1-4).

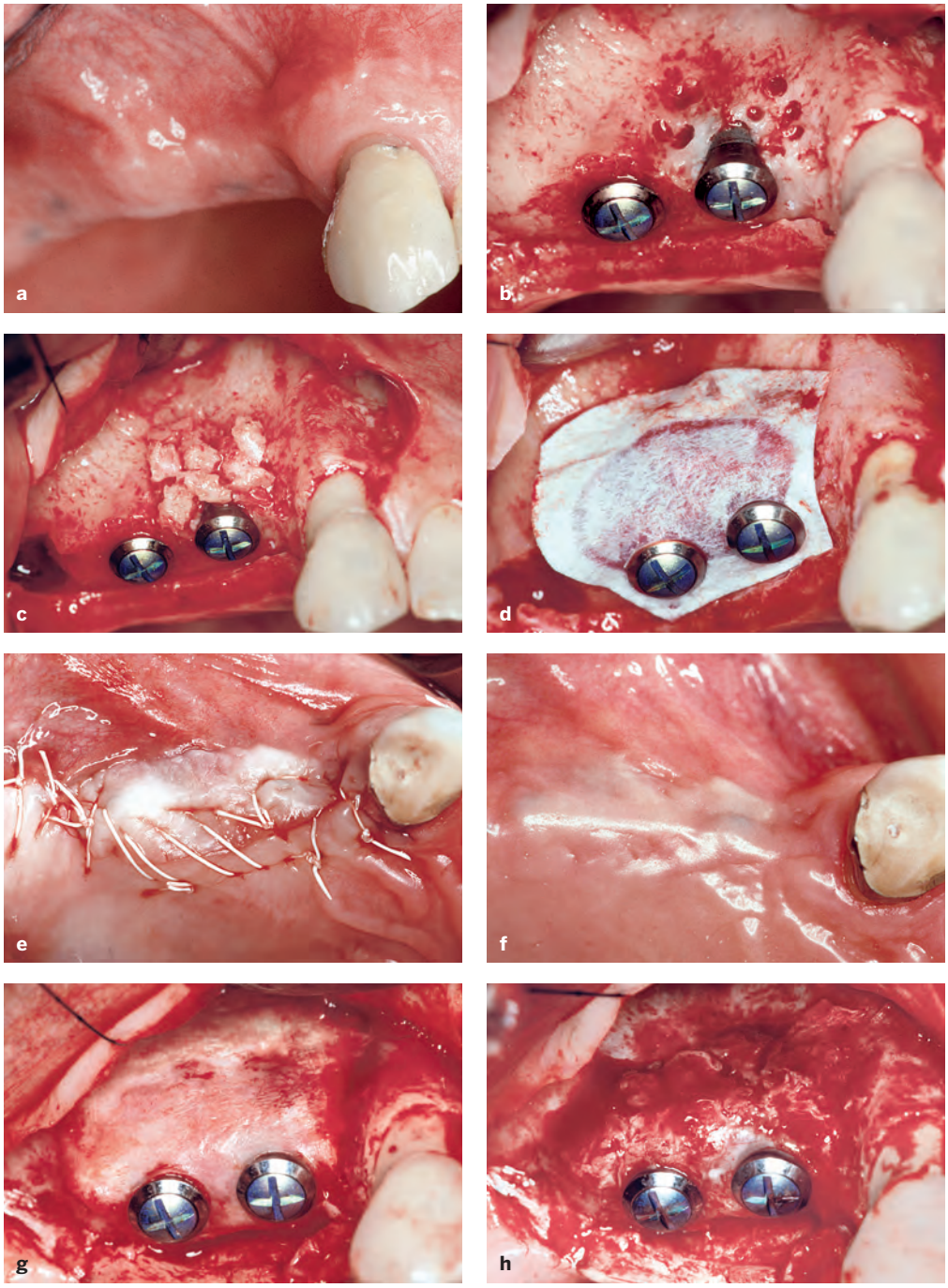


**Fig 1-2 Case 1.** *(a)* Preoperative status (1991). Distal extension situation in the right maxilla of a man with a healed ridge. Two titanium implants were planned to allow a fixed prosthesis. *(b)* Both implants were placed, resulting in a crestal dehiscence defect at the mesial implant. The cortical bone surface was perforated with a small round bur to open the marrow cavity and stimulate bleeding in the defect area. *(c)* Locally harvested bone chips were applied to support the ePTFE membrane and to stimulate new bone formation in the defect area. *(d)* A bioinert ePTFE membrane was applied to function as a physical barrier. The punched membrane was stabilized around the necks of both implants. *(e)* Following incision of the periosteum, the surgery was completed with a tension-free primary wound closure. *(f)* Clinical status 4 months after implant surgery. The wound healing was uneventful. *(g)* Reopening after 4 months of healing. A second surgery was necessary to remove the nonresorbable membrane. *(h)* The clinical status following membrane removal showed successful bone regeneration in the defect area at both implants. →

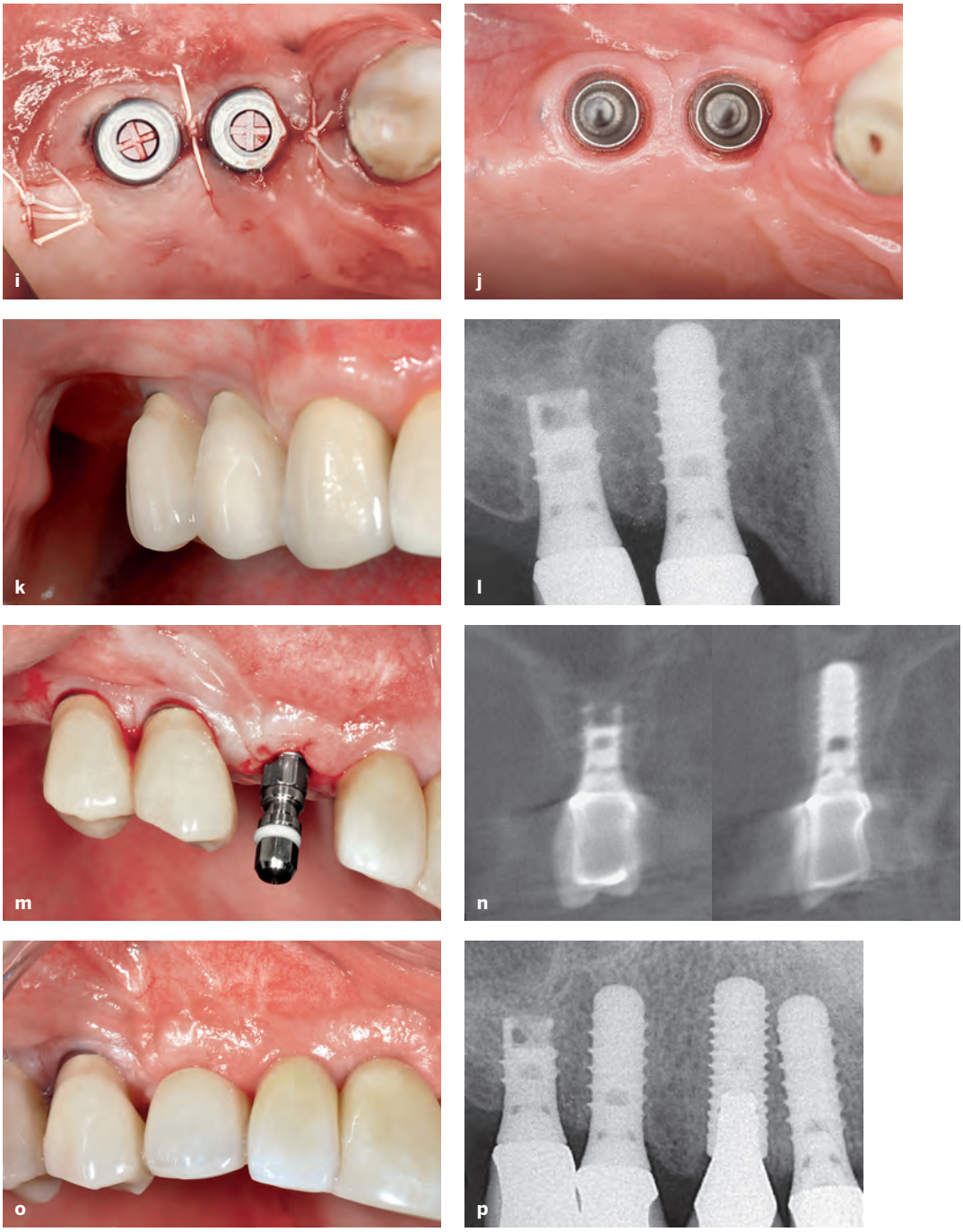


**Fig 1-2 Case 1.** *(cont) (i)* Longer healing caps were applied, and the soft tissue margins were adapted and secured in place with interrupted sutures. *(j)* Two weeks later, the soft tissues had healed, and both implants could be restored with a single crown. *(k)* The clinical status at the 15-year follow-up examination (2006) showed a satisfactory treatment outcome with stable peri-implant soft tissues. *(l)* Radiographic follow-up at 15 years: The bone crest levels were stable around both implants, which are splinted. *(m)* In 2010 (19 years after the initial surgery), an additional implant was placed in the canine site as late implant placement with a flapless approach. The clinical view during surgery showed stable peri-implant soft tissue at both implants in the premolar sites. *(n)* During perioperative examination of the canine implant site, a CBCT scan was taken. The orofacial cuts showed a thick facial bone wall for both premolar implants, which had been in function for 19 years at the time. *(o)* Clinical status after completion of the new single crown at the canine site. The treatment outcome was very satisfactory considering when the GBR procedure was done (1991). *(p)* Periapical radiograph after completion of therapy. The two tissue-level implants in the premolar sites had been in function for 19 years, and both showed stable peri-implant bone crest levels. This was the final follow-up examination, as the patient sadly developed dementia and passed away a few years later.

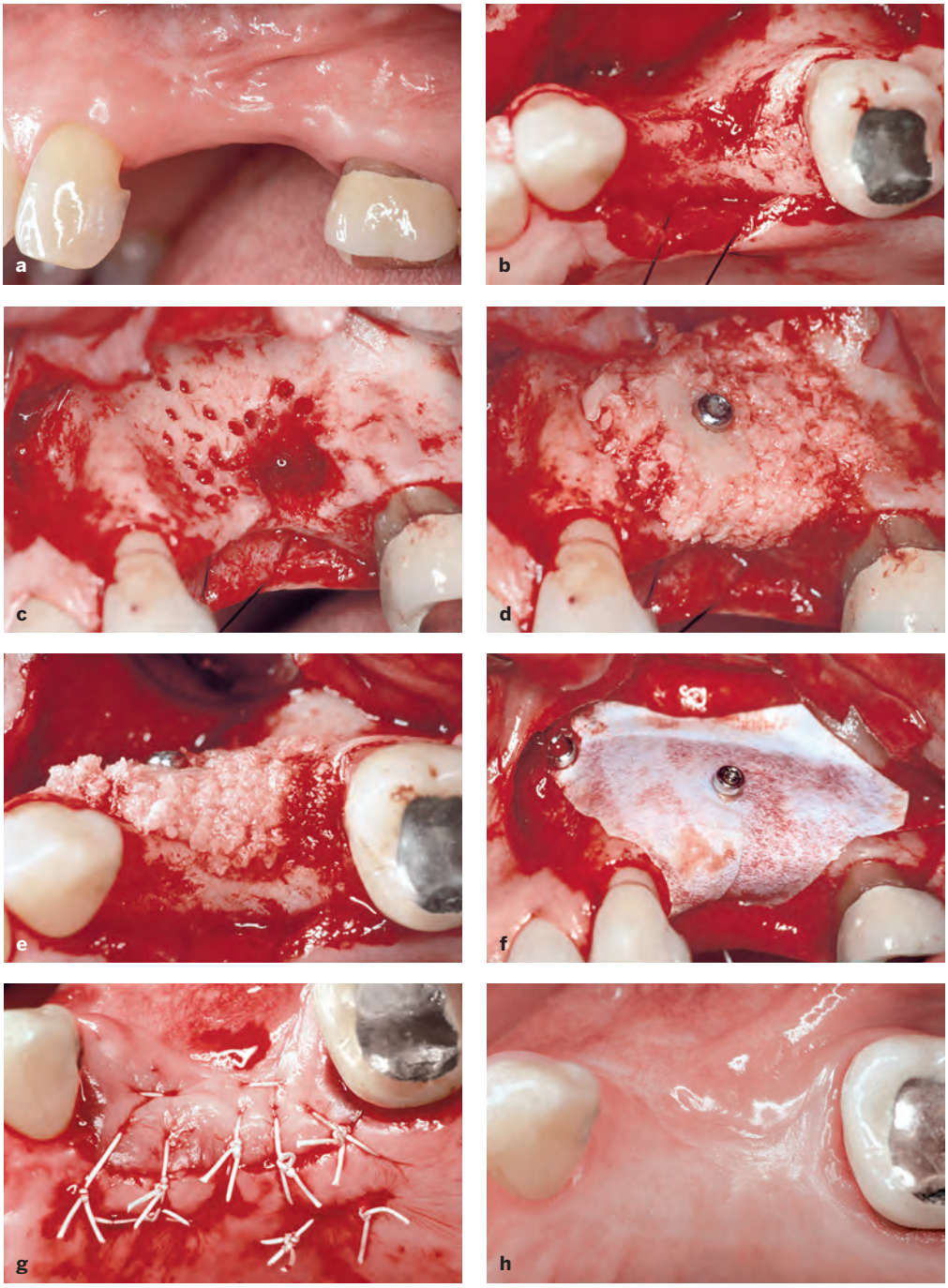


**Fig 1-3 Case 2.** *(a)* Preoperative view (1994). The buccal view of this woman's left maxilla shows two missing premolars. The buccal aspect is flattened. *(b)* The occlusal view during surgery shows a significant buccal flattening and a buccal bone defect in the area of the second premolar. *(c)* Prior to block application, the entire buccal bone surface was perforated to open the marrow cavity. The bone defect was debrided from scar tissues. *(d)* An autogenous block graft harvested from the chin was applied and fixed with a fixation screw. Bone chips were used to augment the entire surrounding area. *(e)* The occlusal view shows the volume of the augmented ridge. *(f)* Buccal view of the applied ePTFE membrane to cover the augmented ridge as a bioinert barrier membrane. *(g)* Primary wound closure was achieved with several mattress and interrupted single sutures using 4-0 and 5-0 ePTFE sutures. *(h)* Six months after ridge augmentation, the clinical status shows healthy soft tissues following a healing period free from complications. →

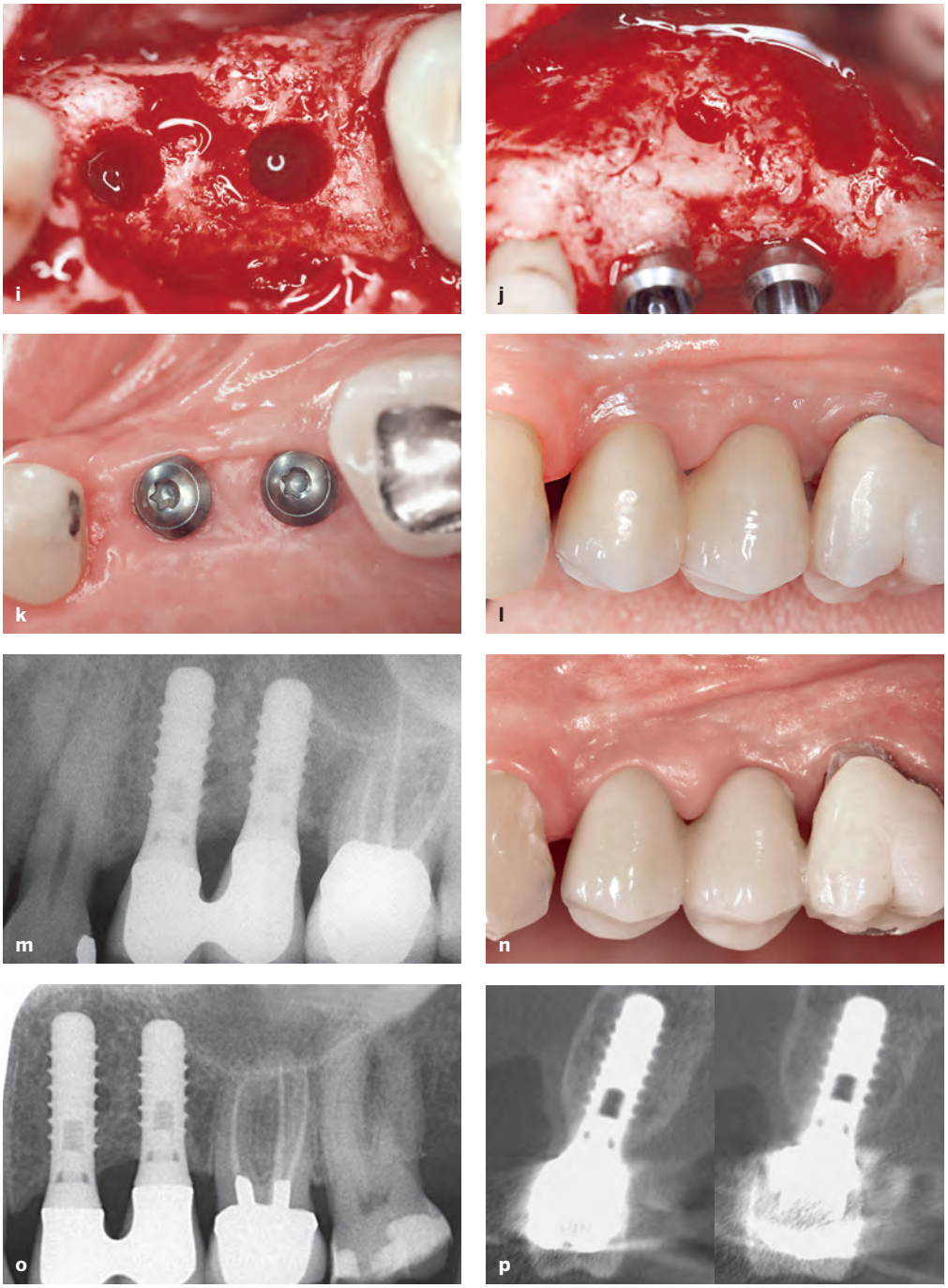


**Fig 1-3 Case 2.** *(cont) (i)* Following flap elevation and membrane removal, the occlusal view demonstrates an excellent ridge volume and thick buccal bone wall following implant bed preparation. *(j)* The buccal view confirms successful ridge augmentation. The block graft can still be recognized, and it is covered in some areas with newly formed bone. *(k)* Clinical status following 3 months of nonsubmerged healing for both implants. The peri-implant mucosa was healthy and included a nice band of keratinized mucosa. *(l)* Clinical status at the 10-year examination (2005) shows the two splinted implant crowns. The peri-implant mucosa was stable with no signs of a peri-implant pathology. *(m)* The periapical radiograph at the 10-year examination confirms stable bone crest levels around the two tissue-level implants with a hybrid design. *(n)* The 25-year follow-up examination (2019) shows the clinical status with quite healthy peri-implant mucosa, although the plaque control is no longer perfect in this elderly patient (age 86). *(o)* The periapical radiograph confirms stable bone crest levels at both tissue-level implants. *(p)* The CBCT scan shows fully intact, thick buccal bone walls for the implants in the first premolar (left) and second premolar (right) sites.

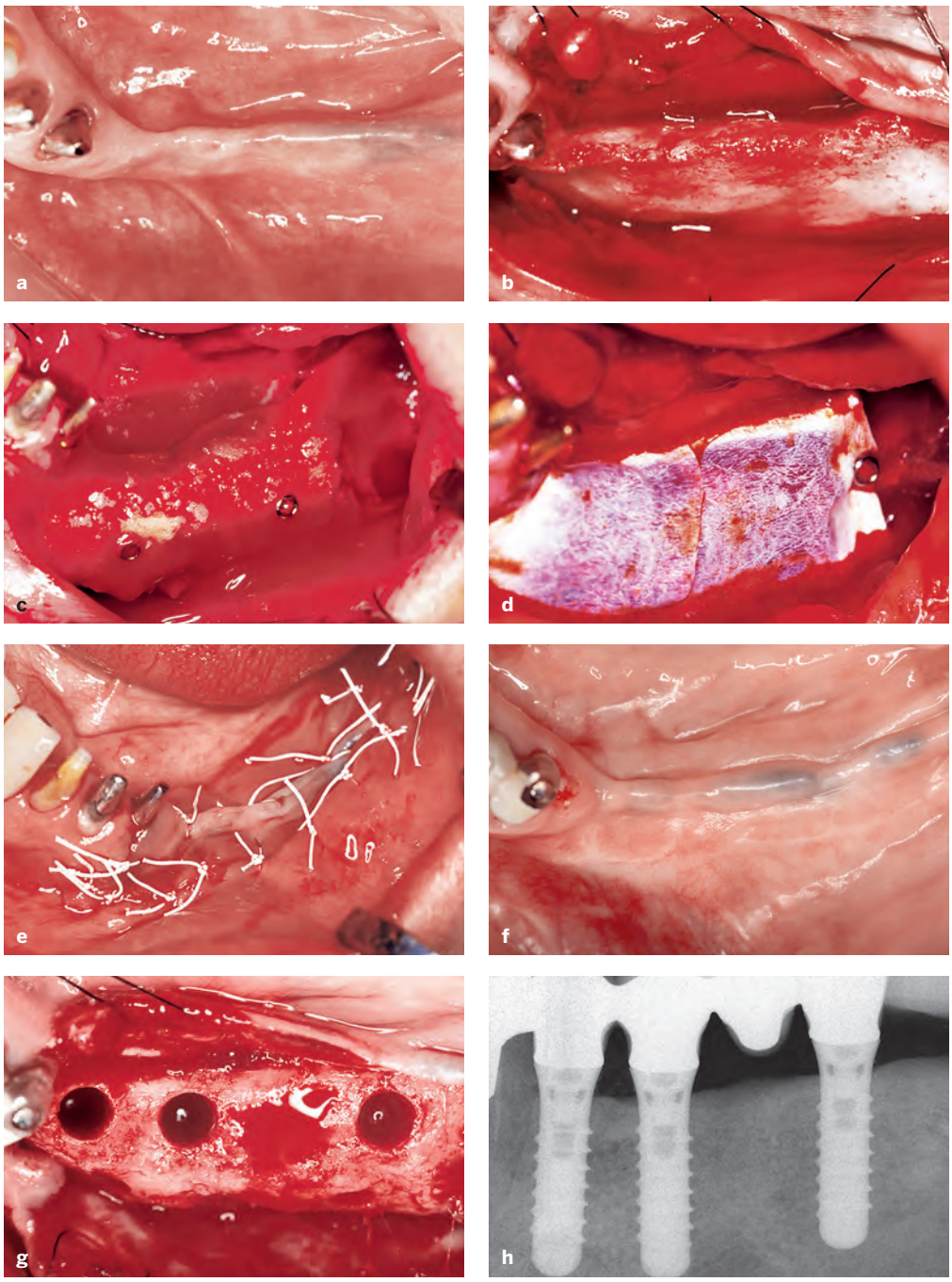


**Fig 1-4 Case 3.** *(a)* Preoperative view (1993). The occlusal view shows a distal extension situation in the left mandible. This woman's healed ridge was atrophic with a severe buccal flattening. *(b)* The intraoperative view shows a crest width of less than 3 mm. *(c)* Status following horizontal ridge augmentation with two block grafts harvested in the third molar area within the same flap. *(d)* The block grafts were covered with an ePTFE membrane. The membrane was stabilized with multiple miniscrews. *(e)* The surgery was completed with a tension-free wound closure with mattress and single sutures to achieve primary wound healing. *(f)* Clinical status after 6 months of healing free from complications. *(g)* Following flap elevation and membrane removal, an excellent augmentation outcome is visible in the areas of the first premolar and first molar, allowing for implants to be placed. *(h)* Following successful restoration, the periapical radiograph at the 1-year examination (1994) shows stable bone crest levels at all three tissue-level implants. →

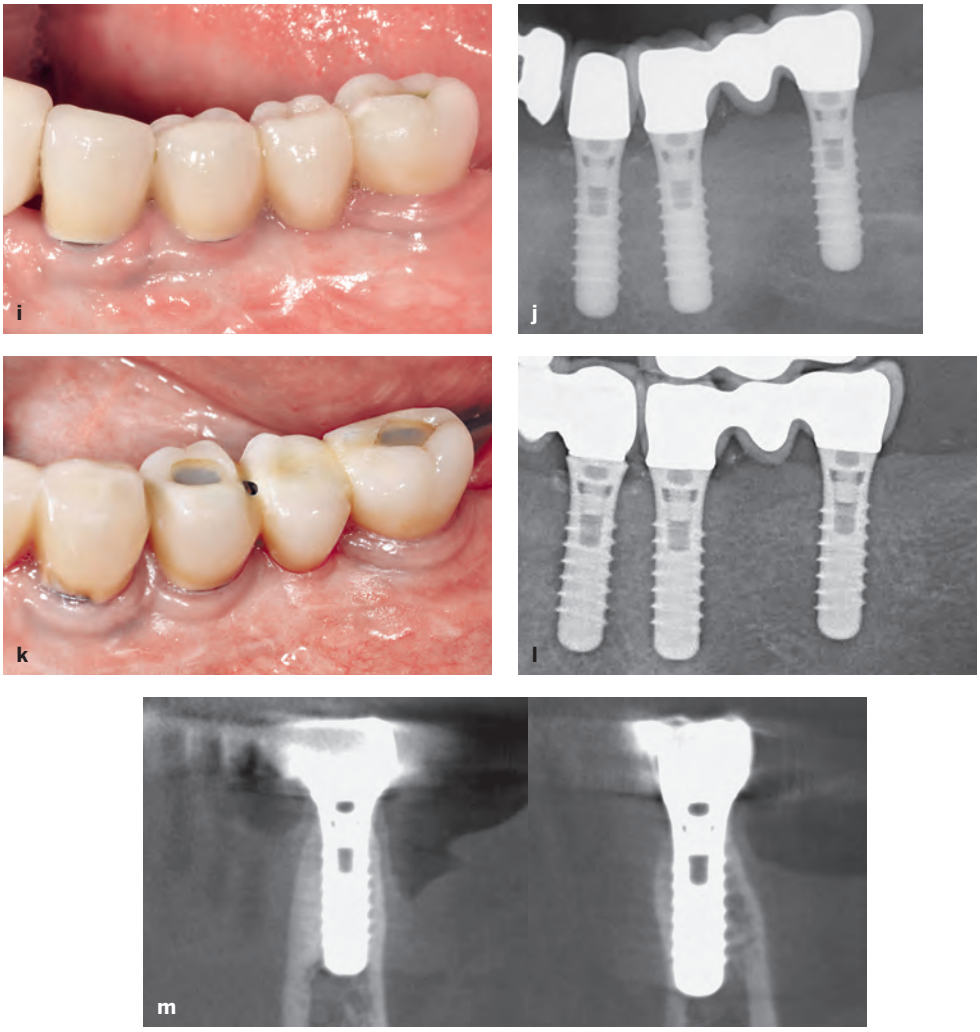


**Fig 1-4 Case 3.** *(cont) (i)* Clinical status at the 15-year examination. The peri-implant mucosa is stable but shows some signs of mucositis. *(j)* The radiograph confirms stable bone crest levels at all three tissue-level implants. *(k)* Clinical view at the 25-year follow-up examination (2019). The patient is now 85 years old, and the plaque control is no longer optimal. The mucosa around the tissue-level implants with a machined implant surface in the neck area shows very stable peri-implant tissues. *(l)* The periapical radiograph confirms stable bone crest levels at all three tissue-level implants after 25 years of function. *(m)* A CBCT scan is taken to examine the peri-implant bone volume. The orofacial cuts demonstrate fully intact buccal bone walls at the two implants in the first premolar and first molar sites, where a block graft augmentation with GBR was done in 1993.


**Fig 1-5** Photo of the expert meeting in 1994 in Arizona with (from the left) Danny Buser, Bill Becker, Sascha Jovanovic, and Massimo Simion.

**Box 1-1** Objectives for improvements of the GBR technique in the mid 1990s

- Improve the predictability of successful outcomes following GBR
- Reduce the rate of complications due to membrane exposure and membrane infections
- Make the GBR technique more user friendly, with easier application of the membrane during surgery
- Make GBR more patient friendly by eliminating a second surgical procedure for membrane removal whenever possible, and by reducing healing periods as much as possible

In 1994, an expert meeting took place in the United States to discuss the potential and the limitations of the GBR technique used in daily practice after 5 years of clinical experience (Fig 1-5). This meeting clearly showed that improvements of the GBR technique were needed to allow more widespread use in implant patients. The experts agreed that the GBR technique—based on the use of ePTFE membranes in combination with bone grafts or bone substitutes—had the following weaknesses and shortcomings:

- A significant rate of membrane exposures due to soft tissue dehiscences, often leading to local infection beneath the membrane and subsequently to a compromised regenerative outcome of the GBR procedure.[57–60]
- Difficult handling of the membrane during surgery due to its hydrophobic properties, requiring stabilization of the membrane with miniscrews or pins.[55,56,61]
- The need for a second surgical procedure to remove the bioinert, nonresorbable membrane, thereby increasing the morbidity and overall treatment time for the patient.

During this meeting, objectives were defined to improve the predictability and attractiveness of GBR procedures both for implant patients and for clinicians (Box 1-1).

It was clear to the participants at this expert meeting that these objectives could only be achieved with the use of a bioresorbable membrane. This trend was again initiated in the field of GTR, with the

introduction of the first bioresorbable membranes in the early 1990s.[62,63] Subsequently, numerous animal studies were performed to examine different bioresorbable membranes for GBR procedures.[64–74] In general, two different groups of bioresorbable membranes were evaluated[75]:

- Polymeric membranes made of polylactic or polyglycolic acid
- Collagen membranes produced from various animal sources

Paralleling these preclinical studies, clinicians started to use bioresorbable membranes in patients. The first published clinical reports predominantly tested collagen membranes,[76–80] and today, collagen membranes are routinely used in daily practice for GBR procedures.

In addition to selecting an appropriate barrier membrane, the selection of appropriate bone fillers for GBR procedures is just as important for the regenerative outcome of GBR procedures. In the early 1990s, autogenous bone chips were primarily used from a mechanical point of view. The role of these filler particles was to support the membrane to avoid a membrane collapse during healing. In the mid 1990s, a first preclinical study in minipigs by Buser et al[81] helped us to understand that bone fillers have different biologic characteristics in terms of their osteogenic potential and rate of filler substitution during bone remodeling.

The various biomaterials used for GBR procedures, such as bone grafts, bone substitutes, and barrier membranes, are also discussed in chapter 2.

## Routine Application and Fine-Tuning Phase of GBR

Around the year 2000, GBR entered a phase of routine application in daily practice. Since then, the GBR technique has been the standard of care for the regeneration of localized bony defects in implant patients. This was confirmed in 2007 in a systematic review by Aghaloo and Moy,[82] who demonstrated that implants placed with the GBR procedure have favorable survival and success rates, and the GBR procedure was the only well-documented surgical technique among various surgical techniques used for localized ridge augmentation. The only other scientifically well-documented surgical technique for bone augmentation at that time was sinus grafting and sinus floor elevation in the posterior maxilla.

Over the past 20 years, however, significant progress has been made with GBR procedures, thanks to new developments in technology and a much better understanding of the tissue and graft biology involved.

The most important improvements are as follows:

- The development of a much better 3D radiographic technique based on CBCT
- Much greater knowledge of tissue biology in postextraction sites
- A much better understanding of the biologic characteristics of bone grafts and bone substitutes
- The development of new narrow-diameter implants

### *CBCT as the new 3D radiographic methodology*

The development of the CBCT technique started in the late 1990s with a first publication by Mozzo et al,[83] and it represents probably one of the most important improvements in implant dentistry in the past 20 years. This new 3D radiographic technique allowed cross-sectional imaging with much better image quality and a clear reduction in radiation exposure when compared with the computed tomography (CT) technology used for dentistry in the 1990s. The CBCT technique allows cross-sectional imaging not only for the preoperative examination of patients, but also for the follow-up documentation of bone augmentation procedures.[84,85] During preoperative examination, CBCT helps to assess the extent of bone deficiencies in potential implant sites, and hence to categorize defect morphologies. These aspects are discussed in detail in chapter 5. In addition, CBCT is also one of the basic techniques necessary for the use of digital technology, including computer-assisted implant surgery (CAIS) in patients.

## *Improved knowledge of tissue biology in postextraction sites*

The progress in this field was initiated around 2004 to 2005 by fundamental studies on bone alterations in postextraction sites performed by the group of Lindhe et al. In the beginning, a series of experimental studies in beagle dogs helped to explain the concept of bundle bone resorption postextraction.[86,87] These studies were followed by a number of clinical studies using the CBCT technique (for review, see Chappuis et al[88]). This new knowledge was fundamental for the definition of selection criteria used in postextraction implant placement. The current knowledge of hard and soft tissue alterations is discussed in detail in chapter 4, and the selection criteria for the different treatment options are presented in chapter 6.

## *Better understanding of the biologic characteristics of bone grafts and bone substitutes*

As mentioned in a previous paragraph, autogenous bone chips had already been utilized with GBR procedures in the late 1980s, but they were used primarily as membrane support to avoid membrane collapse during healing. In the late 1990s, a first preclinical study by Buser et al[81] in minipigs showed that bone fillers have different biologic characteristics. Autogenous bone chips have excellent osteogenic potential, fostering new bone formation during early healing, and have a high substitution rate during bone remodeling. The alternative bone fillers tested were all associated with much slower bone formation during early healing, but one of them showed an interesting low substitution rate. Subsequently, a series of experimental studies with various bone fillers were conducted by Jensen et al,[89–91] confirming the superiority of autogenous bone chips with regard to osteogenic potential in comparison with all other bone fillers tested. In contrast, these studies showed that some bone fillers had very good volume stability with a low substitution rate, such as deproteinized bovine bone mineral (DBBM), a bovine bone filler. This new insight into the biologic properties of bone grafts and bone substitutes increasingly favored the use of two bone fillers as a so-called *composite graft*, which can be used either as a two-layer or a mixed composite graft (see chapter 2).

In the 2010s, the characteristics of autogenous bone chips were further examined in a series of in vitro studies using cell cultures. The studies showed that these bone chips instantly release growth factors (GFs) such as transforming growth factor β1 (TGF-β1) and bone morphogenetic protein 2 (BMP-2) into the surrounding blood, both potent GFs for osteogenesis.[92–95] With this release of GFs, the blood containing them is called *bone-conditioned medium* (BCM). BCM is then able to biologically activate bone fillers and barrier membranes for GBR procedures.[96,97] All these details are presented in this textbook in a completely new chapter 3.

## *Development of new narrow-diameter implants made of a Ti-Zr alloy*

Narrow-diameter implants (NDIs) made of commercially pure titanium (CPTi) were already available in the mid 1990s, but they had limited clinical applications because NDIs showed an increased fracture rate in daily practice due to fatigue fractures.[98] To reduce the risk of fracture, splinting NDIs to other implants was recommended at that time.[8] Around 2010, a new titanium-zirconium (Ti-Zr) alloy called Roxolid (Straumann) was introduced to the market. This new implant material offered much greater strength when compared with CPTi.[99] The stronger implant material was able to reduce the risk of fracture, and hence widened the range of applications in daily practice. In the meantime, NDIs became well documented by clinical studies and systematic reviews.[100–103] In the most recent patient pool analysis, covering 3 years (2014 to 2016) at the University of Bern, the frequency of NDIs clearly increased, to roughly 25%.[21] This means their use has remarkably more than doubled in a 6-year period.[20]

The utilization of NDIs has two advantages in daily practice. First, it allows the clinician to use a standard implant placement protocol without a simultaneous GBR procedure in borderline situations with a crest width of around 6 mm. Second, in case of a local bone defect, it optimizes the defect morphology following implant placement and hence reduces the frequency

of staged approach augmentation procedures. The benefit for patients is obvious, because it reduces not only morbidity, but also costs. These details are discussed in chapter 5 of this textbook.

All these developments have enabled us to fine-tune the GBR technique in the past 20 years, and the details of these aspects are discussed in the clinical chapters of this book.

## Summary

Over the years, significant progress has been made with GBR procedures in implant patients. GBR has not only become the standard of care for the regeneration of localized bone defects in the alveolar ridge of potential implant patients, but it has been an important contributing factor for the rapid expansion of implant therapy in the past 20 years, as well as contributing to significant progress in the field of esthetic implant dentistry.

The procedures recommended in various clinical situations are presented step-by-step in chapters 6 to 13. The reader of this textbook will quickly realize that the recommended surgical techniques are rather conservative, following basic rules of bone augmentation procedures. This offers the clinician the most predictable approach to achieving a successful treatment outcome with a low risk of complications, and thus the ability to become a successful implant surgeon who is able to satisfy the high expectations of today's patients.

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# 2

# Bone Regeneration in Membrane-Protected Defects

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A sufficient amount of living bone is required for both the esthetic outcome and the long-term success of dental implant therapy. In about 50% of implant sites, however, there is a need for a procedure that predictably generates enough bone volume for the placement of a dental implant. There are several options for the enhancement of bone formation, including (*1*) osteoinduction by autogenous bone grafts or the addition of growth factors; (*2*) osteoconduction provided by autogenous bone grafts or bone substitutes that serve as a scaffold for new bone formation; (*3*) transfer of stem cells or progenitor cells that differentiate into osteoblasts; (*4*) distraction osteogenesis; and (*5*) GBR using barrier membranes. Regardless of the method used, there is always an underlying basic biologic mechanism of bone healing.

Bone demonstrates a unique potential for regeneration, which is probably best illustrated by fracture repair. Bone is able to heal fractures or local defects with regenerated tissue of equally high structural organization, without leaving a scar. The mechanism of this healing pattern is often considered as a recapitulation of embryonic osteogenesis and growth. Because bone has a unique spontaneous healing capacity, the trick in reconstructive surgery is to harness this great regenerative potential to enhance bone formation for clinical applications. Thus, adequate bone augmentation or treatment of any bone defect requires a profound understanding of bone development and morphogenesis at the cellular and molecular levels. This chapter summarizes the development, structure, function, and regeneration of bone and discusses the pros and cons of the various biomaterials used for GBR to provide the biologic rationale for selecting appropriate biomaterial combinations for successful bone augmentation around dental implants in the long term.

## Development and Structure of Bone

### *Functions*

Bone certainly represents a great achievement in the evolution of supporting tissues. However, it has many additional functions. These include (*1*) mechanical body support, motion, and locomotion; (*2*) support of teeth for biting and crushing of food;