On Factors Influencing the Outcome of Various Methods Using Endosseous Implants for Reconstruction of the Atrophic Edentulous and Partially Dentate Maxilla

by

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This PhD thesis represents number 33 in a series of investigations on implants, hard tissue and the locomotor apparatus originating from the Department of Biomaterials/Handicap Research, Institute for Clinical Sciences at Sahlgrenska Akademy, Göteborg University, Sweden.

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ABSTRACT

Surgical reconstruction of the severely resorbed edentulous maxilla often requires a combination of bone grafts and dental implants. Different methods have been used during the years where donor site, type of bone graft, healing period, timing of implant placement and implant surface have varied. The overall objective of this research work is to evaluate the clinical outcome of such methods when used on a routine basis at one oral & maxillofacial surgery clinic at a county hospital in Sweden. The purpose is also to evaluate the influence of various factors on implant failure.

In Paper I, one group of 64 grafted patients with 437 implants and one group of 118 non-grafted patients with 683 implants were retrospectively evaluated and compared with regard to implant and prosthesis survival. The former patients had received bone grafts from the iliac crest with simultaneous or delayed (6 months) placement of dental implants with a minimally rough surface (machined/turned). More implant losses were seen in grafted than in non-grafted patients after a mean follow-up of 5 to 6 years, 25% versus 16%, respectively. Most of the implants were lost before loading. There was no difference in prosthesis survival rate. A correlation between the bone volume of the residual jaw bone prior to bone grafting and implant failure rate was seen in the anterior maxilla. There was no difference in implant failure rate between one-stage and two-stage bone grafting and implant placement procedures.

The influence of the type of occlusal support on early implant failure in grafted maxillae was evaluated in Paper II. Ninety (90) patients previously treated with bone grafts from the iliac crest and 643 machined/turned implants were included in the retrospective study. The total failure rate was 18%. In comparison, few failures (6.2%) were seen in patients with a removable mandibular denture and the highest failure rate (43.8%) was seen in patients with unilateral occlusal support.

Sixteen patients previously treated with 31 zygomatic implants and 74 regular implants in the anterior maxilla as an alternative to bone grafting of the atrophic maxilla were evaluated in Paper III. All implants had a minimally rough surface. Three (4.1%) regular implants were lost and three (9.7%) zygomatic implants had to be removed due to recurrent sinusitis after a mean follow up period of 4 years. All patients received and maintained a fixed bridge.

Paper IV evaluated 17 patients subjected to maxillary sinus floor augmentation with blocks of bone from the iliac creast and simultaneous or delayed (6 months) placement of 69 machined/turned implants. After a mean follow up period of 4 years, 8.7% of the implants had been lost. All failures occurred prior to loading of the fixed prostheses. More implants were lost in grafted (10.4%) than in non-grafted (4.8%) areas. Less implants were lost when using a two-stage approach than when using a one-stage technique, 6% versus 18%, respectively.

In a prospective study including 61 patients (Paper V), the use of particlated mandibular bone for maxillary sinus floor augmentation and delayed placement of three types of surface modified implants (oxidized, blasted, blasted+acid etched) was evaluated. The majority of patients were treated under local anaesthesia. Two of 180 implants were lost from placement to delivery of the final prosthesis.

It is concluded that more implant failures occur in grafted than in non-grafted maxillae. The bone volume of the residual anterior crest and the occlusal support depending on the type of mandibular occlusion seems to influence the outcome of grafting procedures in the edentulous maxilla. Delayed placement of dental implants in bone grafts seems preferable, at least in partially dentate patients. The use of surface modified implants and particulated mandibular bone may be one way to further improve the results of sinus grafting procedures. The use of zygomatic implants is a viable alternative to bone grafting in the treatment of the severely resorbed maxilla.

Keywords: clinical studies, dental implants, maxilla, bone grafting, zygomatic implants

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LIST OF PAPERS

I. **Becktor JP, Isaksson S, Sennerby L.** Survival Analysis of Endosseous Implants in Grafted and Nongrafted Edentulous Maxillae.
Int J Oral Maxillofac Implants 2004;19(1):107–115.

II. **Becktor JP, Eckert SE, Isaksson S, Keller EE.**The Influence of Mandibular Dentition on Implant failures in Bone-grafted Edentulous Maxillae.
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III. **Becktor JP, Isaksson S, Abrahamsson P, Sennerby L.** Evaluation of 31 Zygomatic Implants and 74 Regular Dental Implants Used in 16 Patients for Prosthetic Reconstruction of the Atrophic Maxilla with Cross-Arch Fixed Bridges
Clin Implant Dent Relat Res 2005;7(3):159-65.

IV. **Becktor JP, Isaksson S, Sennerby L.** Endosseous Implants and Bone Augmentation in the Partially Dentate Maxilla:
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V. **Becktor JP, Hallström H, Isaksson S, Sennerby L.** A prospective clinical and radiographic analysis of 180 implants placed in partially dentate maxilla after maxillary sinus floor augmentation with particulated autogenous bone from the mandibular ramus/corpus.
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INTRODUCTION

Audit and quality assessment

New public management (NPM) has been introduced to the world of public health lately. The ideas are coming from the cooperate world and are modified to fit the establishments of public health (Hood and Dunleavy, 1994). The idea is to be capable of evaluating the different structures at a hospital, such as cultural/ social, institutional/organizational and down to the individual level. The hospitals should regulate themselves by systematic compulsory training, education and collegial discipline (Starr and Immergut, 1987). One of the ingredients of NPM is quality assessment, audit, which should provide a way of measuring and describing the public health from a quality point of view. ”We have always been working with quality in our department, we just did not have the tools and knowledge to systemize it”.

In the ”Audit bill” which was passed in Sweden in 1997,(Socialstyrelsen 1996-00-116, Stockholm, 1996) it was required that ”right things will be done the right way” to acquire productivity and efficiency in the organization.

The material in the present thesis has been collected throughout the daily work at the Department of Oral and Maxillofacial Surgery, Maxillofacial Unit, at the County Hospital, Halmstad, Sweden. One may consider the present thesis as representative of one form of NPM, where the audit of treatment is evaluated and thereby leading to a research based improved development.

Background

Total or partial edentulism of the maxilla can be of different aetiologies; agenesis, periodontal disease, infections, caries, malignancies or trauma. Despite of the different aetiologies, oral rehabilitation of these patients currently involves installation of endosseous implants and good long-term clinical results have been demonstrated (Adell *et al.*, 1990a; Jemt and Lekholm, 1995; Tolman and Laney, 1992).

Conventional removable prostheses retained by remaining teeth and/or the residual alveolar crest and a tooth supported dental bridge with cantilevers in the edentulous regions have been the treatment of choice for many years. In cases of low patient acceptability and risk for prosthetic mechanical failures, the use of endosseous implants is currently well documented and considered a routine treatment for prosthetic reconstruction of the edentulous and partially

dentate maxilla (Branemark *et al.*, 1977; Owall and Cronstrom, 2000; Randow *et al.*, 1986). The use of titanium implants for rehabilitation of edentulism was first introduced by Brånemark *et al.* (1969) and later by Schroeder *et al.*(1976). Acceptable long-term implant survival rates with minimal marginal bone loss have been presented in patients with sufficient jaw bone volumes (Adell *et al.*, 1990a; Henry *et al.*, 1996; Jemt and Lekholm, 1993; Roos *et al.*, 1997; Tolman, 1995). However, an adequate amount of jaw bone to allow sufficient numbers and sizes of implants seems to be a requirement for achieving good results. Moreover, the quality/density of the jaw bone is an important factor for implant survival (Friberg *et al.*, 1991; Sennerby and Roos, 1998; van Steenberghe *et al.*, 1990).

In subjects with insufficient jaw bone volume the problem may be solved by using shortand/or thin implants or by tilting the implants into regions where bone is present. However, this approach may sometimes result in difficulties of managing the prosthetic treatment (Aparicio *et al.*, 2001; Krekmanov, 2000; Mattsson *et al.*, 1999).

The insertion of specially designed long implants, zygomatic implants, has also been used to overcome problems with insufficient bone volume in the posterior maxilla. The placement of dental implants in the zygomatic bone is well known from preprosthetic surgery following ablative tumour surgery (Higuchi, 2000; Parel *et al.*, 2001) and has also been used in conjunction with regular implants in patients with severe atrophy and resorption of the posterior maxilla as an alternative to bone augmentation (Bedrossian *et al.*, 2002; Branemark *et al.*, 2004; Higuchi, 2000; Hirsch *et al.*, 2004; Malevez *et al.*, 2004). (Table 1) Another technique is the pterygomaxillary implant that was first described by Tulasne (1992). This implant is placed in the maxillary tuberosity region, and is supposed to involve the pterygoid plate to gain acceptable implant stability (Bahat, 1992; Balshi *et al.*, 1999; Tulasne, 1992). Reviews of the literature reveal an increased implant failure rate in situations with inadequate bone volume and the insertion of either zygomatic or pterygomaxillary implants could thus be an alternative treatment (Esposito *et al.*, 1998a; Esposito *et al.*, 1998b; Tong *et al.*, 1998).

The atrophied maxilla constitutes a challenging therapeutic problem and bone augmentation is often essential to enable placement of sufficient number and sizes of implants. Bone augmentation is required when the width and the vertical height of the residual alveolar ridge in the edentulous or partially dentate patient is insufficient for placing implants with acceptable size, which is necessary for optimal functional and aesthetic prosthetic reconstruction. The use of

autogenous bone grafts is still the most recognized method of augmentation. Different methods for grafting the maxilla and/or mandible have been developed during the last 25 years (Adell *et al.*, 1990b; Boyne and James, 1980; Breine and Branemark, 1980; Isaksson and Alberius, 1992; Jensen *et al.*, 1994; Keller *et al.*, 1994; Kent and Block, 1989; Lundgren *et al.*, 1997; Misch, 1999).The techniques have been used with different modifications both with regard to donor site, form of the bone graft and timing for grafting and implant placement. The surgeon frequently focuses on bone volume, bone density and space conditions, whereas the prosthodontist is concerned about creating a stable occlusion and acceptable aesthetics. Prior to installation of endosseous implants in the maxilla, all possible factors influencing treatment outcome should be evaluated, therefore patients who are in need of extensive oral rehabilitation benefits from treatment carried out by a multidisciplinary team.

In the following, different factors influencing the success rate for implant installation and bone augmentation in the maxilla will be presented.

Table 1. Summary of clinical follow-up studies on zygomatic implants.

Study	Patients (no.)	Follow -up (years)	Zygomatic implants		Additional implants		Sinusitis	Soft tissue infection
			placed	failed	placed	failed		
Hirsch et al. (2004)	66	1	124	3 (2%)	?	?	8 (?)	8 (?)
Malevez et al.(2004)	55	0.5-4	103	0	194	16 (8%)	5	?
Brånemark et al. (2004)	28	5-10	52	3 (6%)	116	29 (27%)	4	2 (?)
Becktor et al.(2005)	16	1-6	31	3 (10%)	3	74 (4%)	6	9
Farzad et al. (2006)	11	1.5-4	22	0	42	1 (2%)	3	7 (?)
Ahlgren et al.(2006)	13	1-4	25	0	46(?)	0	?	?
Aparicio et al. (2006)	69	0.5-5	131	0	304	2 (1%)	3	8

Bone biology and implant integration

Bone biology

A characteristic of all bones is a dense outer sheet of compact bone and a central medullary cavity. The cavity is filled with bone marrow, which is interrupted by a network of bone trabeculae. Mature bone, irrespective if cortical or cancellous, is histologically identical, in that it consists of microscopic layers or lamellae. Three distinct types of layering are recognised: circumferential, concentric and interstitial. Circumferential lamellae (i) enclose the entire adult bone, forming its outer perimeter. Concentric lamellae (ii) make the bulk of compact bone, and represent the basic metabolic unit of bone, the osteon. The osteon is a cylinder of bone, with a central Haversian canal, lined by layers of bone cells that cover the bone surface; each canal houses minimally one capillary. Haversian canals are interconnected by Volkmann canals, channels that also contain blood vessels, thus creating a rich vascular network through cortical bone. Interstitial lamellae (iii) are interspersed between adjacent concentric lamella and fill the spaces between them.

The periosteum is surrounding the outer aspect of every compact bone and the internal surfaces of compact and trabecular bone is covered by the endosteum. In general the periosteum is more active in bone formation than the endosteum, particularly in young individuals.

Bone formation occurs by three main mechanisms: endochondral, intramembranous and sutural. Endochondral bone formation takes place when cartilage is replaced by bone, intramembranous bone formation occurs directly within the mesenchyme and sutural growth takes place at the sutural margins.

Bone cells

Two cell lineages are present in bone: (i); osteogenic cells, which form and maintain bone and (ii); osteoclasts which resorb bone. Osteogenic cells (i) include osteoprogenitors, preosteoblasts, osteoblasts, osteocytes and bonelining cells. Osteoblasts synthesize collagenous and noncollagenous bone matrix proteins that may accumulate as an uncalcified matrix called osteoid that acts as a scaffold for the deposition of apatite crystals of bone. They arise from pluripotent stem cells, which are of mesenchymal origin. In addition to osteoid, ostoblasts secrete a variety of cytokines that regulates cell metabolism. Osteoblasts produce several different forms of bone morphogenetic proteins (BMP). Although the interaction between these growth factors is very complex,

they increase the rapidity of bone formation and bone healing. Hormones are also a important factor for bone metabolism.

Transformation of an osteoblast into an osteocytes occurs when the osteoblast stops synthesising matrix (osteoid) and it becomes buried within the calcified tissues. Woven bone have more osteocytes than lamellar bone. Adjacent osteocytes maintain contact through channels called canaliculi, that also connect with nearby capillaries. Osteoclasts are large multinucleated cells that resorb bone and their origin is hematopoietic. Recruitment of bone forming cells and bone resorbing cells is of great importance during bone growth and bone healing. Osteoblasts and osteocytes, although of opposing fractions, act as coupled cells, i.e. their actions are dependent of one another.

Intramembranous and endochondral bone formation

Intramembranous bone formation occurs directly within the mesenchyme, the mesenchymal cells proliferate and condense simultaneously with an increase in vascularity at these sites of condensed mesenchyme where osteoblasts differentiate and begin to produce osteoid. The interval between osteoid deposition and mineralization in woven bone is 1-3 days. Once begun, intramembranous bone formation proceeds rapidly, and the first deposited bone is termed woven bone. A continual process occurs where woven bone is transformed into lamellar bone. Consequently, woven bone is seen during early bone formation during growth and healing whereas lamellar bone is the more mature bone characterized by tightly packed osteons.

The formation of endochondral bone takes place through the differentiation of the mesenchymal cells into cartilage producing cells, forming a cartilage template of the future bone. The cartilage template will become hypotrophic, calcify, and then be replaced by bone tissue. The initially produced bone has a primitive and irregular appearance which also is the case for intramembranous woven bone, before it remodels into lamellar bone (Alberius *et al.*, 1992; Rabie *et al.*, 1996; Zins and Whitaker, 1983)

Bone turnover

Bone remodelling is a substitution of the bone tissue without changing its architecture in contrast to surface modelling that changes the shape of bone due to resorption and/or appositional growth. Remodelling occurs

throughout life by the coordinated action by osteoclasts and osteoblasts, in a healthy individual, this turnover is in steady state, i.e. the amount of lost bone is balanced by bone formation.

Bone healing

Jaw bone healing, e.g. after a fracture or implant placement, occurs in two phases, initial repair and secondary remodelling (Schenk *et al.*, 1994). Initially, as a result of vascular disruption, a haematoma forms between and around the bone segments. The haematoma is converted into a clot and bony necrosis occurs at the end of the fracture segments. Ingrowth of vasoformative cells and capillaries for the restoration of blood supply, angiogenesis, followed by migration of granulocytes, monocytes, lymphocytes and pluripotent stem cells occur in the traumatized area. After 1-3 days the clot is replaced by granulation tissue, which consists of inflammatory cells, fibroblasts, collagen and invading capillaries. The granulation tissue is converted into a collagen matrix with continuous ingrowths of capillaries. Woven bone is rapidly formed by osteoblasts, which have either been differentiated from mesenchymal stem cells or activated lining cells. Because of poor mineralization and organization of this bone, its biomechanical properties are poor. The second phase, secondary remodelling, consists of replacement of the woven bone with ordered lamellar bone, which is directed by osteoblastic and osteoclastic activities. A complete regeneration of a wound, where all areas of woven bone have been replaced by lamellar bone is seldom seen in adults. Incomplete healing occurs with ingrowth of fibrous tissue. This can be due to lack of sufficient blood supply, pressure and instability (Schenk *et al.*, 1994). Stability of the immature bone is important in the early stage of wound healing, if this is not established the mesenchymal stem cells may differentiate into fibroblasts instead of osteoblasts (Hjørting-Hansen *et al.*, 1990; Phillips and Rahn, 1988).

Osteoinduction and osteoconduction

Osteoinduction is when primitive undifferentiated and pluripotent cells are stimulated by an inductive agent to develop into bone-forming cells and osteogenesis is induced. Osteoconduction is when bone grows in a matrix or on a surface. An osteoconductive surface permits bone growth on its surface and down into pits and pores and it is suggested that the bone is conformed to a materials surface (Albrektsson and Johansson, 2001).

Osseointegration and implants

Per-Ingvar Brånemark placed his first clinical oral implant in 1965 and the term osseointegration was established in 1977 (Brånemark *et al.* 1977). Although early trials with the Brånemark system of osseointegration were unsuccessful, significant improvements and thorough documentation of the clinical outcome led to their general acceptance of the osseointegration technique (Brånemark *et al.*, 1977). Osseointegration is histologically defined in *Dorland's Illustrated Medical Dictionary* as the direct anchorage of an implant by the formation of bony tissue around the implant without the growth of fibrous tissue at the bone-implant interface.

Different dental implant systems are available on the market. Jokstad et al. reported 220 different implant brands produced by about 80 manufactures. The implants vary in shape, material, dimension and surface structure (Jokstad *et al.*, 2003). In the past, the most common implants where produced either with a machine turned technique resulting in a minimally rough surface (machined/turned) or with a plasma spraying approach producing a rough surface. Today, the market is dominated by implants with moderate surface roughness, i.e. blasted, acid-etched, oxidized, plasma-sprayed and hydroxylapatite coated ones, which have been developed to allegedly improve the clinical performance.

The importance of implant surface properties for successful osseointegration has been known for some time (Albrektsson *et al.*, 1981). However, the exact role of the surface properties of titanium implants during the formation of osseointegration is still under discussion (Albrektsson, 1983; Wennerberg, 1996). Interests in the surface oxide properties of titanium implants have increased with the development of methods to characterize such surfaces. Moreover, the influence of surface modification of titanium implants on the tissue responses is an important and common topic in implant research. Implants with rough surfaces are claimed to promote faster and earlier bone healing and thereby be more suitable for earlier loading than has previously been the standard for many years. Ivanoff *et al.*(2003) evaluated the human bone tissue response to two surfaces (oxidized and turned) implants on twenty patients who received one test and one control micro-implant each during implant surgery. Surface roughness and enlargement were greater for the oxidized implants than for the turned implants. Histomorphometric evaluations demonstrated significantly higher bone-to-implant contact and bone density in the threaded region for the oxidized implants (Ivanoff *et al.*, 2003). However, rougher surfaces may have theoretical clinical drawbacks such as being more prone to marginal bone

resorption and/or increased ion release, which has been found in bone tissue in the surrounding area of titanium implants and it has been hypothesized that this could be damaging to osteogenesis (Osborn *et al.*, 1990; Tsutsui *et al.*, 1999). However, Wennerberg *et al.* (2004) showed no correlation between increasing roughness and ion release, neither in vitro nor in vivo.

In the contact zone between implant and bone, the ”tissues” have no direct contact to the bulk titanium, but rather to a thin oxide layer of the metal. This thin oxide layer was shown to be in ’contact’ with remodelled mineralized bone (Sennerby *et al.*, 1992). Studies of implants that have been retrieved from patients have demonstrated that both the thickness and the nature of the thin oxide layer changed during implantation. Successfully osseointegrated titanium implants showed an increase in oxide thickness of up to 200 nm (Sundgren *et al.*, 1985). However, in the case of failed titanium implants that were retrieved from patients, there were no changes in the oxide thickness or oxide composition during a period of function of up to eight years (Esposito *et al.*, 1999).

It is likely that the surface of a transmucosal implant part should have a smooth surface in order to establish a mucosal seal and to avoid soft tissue reactions (Sawase *et al.*, 2000). Previous publications have indicated that abutment surface roughness is positively correlated with increased accumulation of subgingival plaque (Quirynen *et al.*, 1990). Experimental studies have shown that plaque accumulation may lead to inflammatory lesions in the adjacent mucosa and bone resorption, with subsequent risk of implant failure (Abrahamsson *et al.*, 1998; Lindhe *et al.*, 1992). However, Wennerberg et al. (2003) presented a statistically significant difference only between patients regarding the amount of accumulated plaque on the abutment surfaces and inflammatory cells, but no difference between the surface modifications in relation to plaque accumulation or number of inflammatory cells, although their studies were limited to a healed situation and a follow up time of only one month (Wennerberg *et al.*, 2003).

Influence of maxillary growth and anatomy on implant installation

Maxillary growth

The facial skeleton is formed by intramembranous ossification and comprises six different anatomical bones: Maxillary bone, Palatine bone, Zygomatic bone, Vomer, Ethmoid bone and Nasal bone. Vomer is a single bone and the remaining five bones are pairs. The maxilla consists of four processes: Processus frontalis, processus zygomaticus, processus palatinus and processus alveolaris. The four processes meet the facial skeleton in different sutures from where vertical and sagittal growth displacement of the maxilla occurs. Growth of the alveolar process occurs sagitally, vertically and transversely by eruption of the dentition and additionally there is apposition posteriorly to the maxillary tuberosity. The maxilla also increases in height by relocation of the nasal floor and transversely by differentiated growth of the midpalatine suture (Bjork 1964; Bjork and Skieller, 1977).

Congenital maxillary edentulism

In areas of the maxilla with multiple missing teeth, growth of the alveolar process will not occur. Accordingly, sufficient bone for implant installation will not be present. Unfavourable anatomy of the maxillary sinus may further decrease the amount of jaw bone and thereby complicate implant installation in the congenital fully or partially edentulous maxilla.

Due to the fact that implants are osseointegrated, they will not take part in the growth mechanism of the alveolar process, it has been recommended not to place implants in growing individuals (Thilander *et al.*, 2001). The continuously erupting dentition in growing individuals will lead to infraocclusion of the implants.

Acquired maxillary edentulism

Acquired maxillary edentulism shows morphological alteration of the jawbone anatomy and reduces the mastication capability with time. Resorption of the alveolar process and the maxillary basal bone (Cawood and Howell, 1988; Tallgren, 1972) and pneumatization of the maxillary sinus, lead to an unfavourable anatomy and thereby constituting a therapeutic problem. The same morphological alteration of the jaw bone anatomy is also present in the partially dentate patient, and it is most likely that future demands for implant-based reconstructions will

come from partially edentulous patients, of whom a number will need bone augmentation (Meskin and Brown, 1988; Weintraub *et al.*, 1985).

Bone grafting to the maxilla and implant installation

Historical review

In the 19th century, Ollier (1867) considered the periosteum of major importance for successful bone grafting and accepted only autogenous bone grafts for clinical use, because this was the only type of graft that survived transplantation. Barth (1895) questioned the conclusions made by Ollier and reported that the periosteum seldom survived transplantation. The important factor for regeneration of a bone defect was suggested to be the osteogenic property of the host bone. He also believed that the transplanted bone always was resorbed and replaced by the host. Accordingly, there should be no difference between autogenous, allogenous and xenogenous bone grafts (Barth, 1895). Bull (1928) supported Barth´s theory, but concluded that the replacement phase was shortest for the autogenous graft. Baschkirzew & Petrov (1912) experimented by inserting different types of bone into muscular tissue and noticed that neither the periosteum nor the osteocytes were necessary for bone formation. In vital bone, without periosteum or marrow and transplanted into muscular tissue, osteocytes were differentiated from the surrounded connective tissue cells (Baschkirzew and Petrov, 1912).

Several reviews have been published (Albreksson, 1979; Chase and Herndon, 1955; Puranen, 1966; Ray, 1956; Urist, 1960) based on the above mentioned basic principles. Today, it is generally accepted that autogenous bone is the best grafting material and that osteogenic cells from periosteum, endosteum and bone marrow, all may take part in the process of bone graft incorporation and healing.

Numerous surgical procedures for implanting allogenous materials to compensate for loss bone and teeth, such as subperiosteal and blade implants were used for many years, if with dubious results. The first scientifically documented rehabilitation of edentulism with osseointegrated implants was described by Brånemark *et al.* (1969). Today, when following the same principles, the use of osseointegrated oral implants is considered to be a well documented, safe procedure with predictable outcomes.

Free autogenic bone grafts

The process of healing and incorporation of free autogenic bone is of utmost importance for clinical success. Due to osteoinductive and osteoconductive capacities, they are superior to both allografts and xenografts. Osteoinduction is described as a process where mesenchymal cells within the donor tissue has the potential to initiate new bone formation under influence of BMP (Urist, 1960). Osteoconduction is a three dimensional process, where the donor tissue acts as a scaffold for ingrowth of capillaries, perivascular tissue and osteoprogenitor cells from the recipient bed into the donor tissue (Urist, 1960).

Abundant factors and biological processes have to take place before an autogenic transplant is successfully incorporated in the recipient bed. Primarily, the surgical technique has an important influence on the success rate. Furthermore, the level of incorporation depends on biologic factors associated with the graft and on factors associated with the recipient site. The important factors for healing are similar in all the different types of autogenous grafts to the maxilla such as; sinus inlays, alveolar/maxillary onlays, block and/or particulated bone and vascularized bone grafts.

Biologic factors

Revascularization is crucial for graft healing and is characterised by microvascularisation initially occurring in a layer of about one mm of the graft surface, which is in direct contact with the recipient bed. Microanastomoses may restore circulation and are responsible for survival of osteoprogenitor cells in the graft. The revascularization process differs between cortical and cancellous bone grafts due to different morphologies. Cortical bone is densely packed and cancellous bone porous with marrow tissue in between the bone trabeculae, because of this difference, vascular ingrowth has been demonstrated to occur 30% more rapidly into cancellous compared to cortical bone grafts (Albrektsson, 1980).

In the osteoinductive graft preosteoblasts may survive transplantation and these proliferating cells will form a bridge between the surface of the donor and the recipient site, which in turn will enhance the amount and pace of remodelling. Furthermore growth factors and proteins will influence the osteoinductive process during healing of the autogenic bone graft. BMP has demonstrated to enhance bone healing (Urist, 1960; Urist, 1965) and autogenic bone enriched with BMP

and BMP alone will lead to enhanced bone regeneration (Marukawa *et al.*, 2001). Another factor that has been demonstrated to have an osteoinductive influence on bone grafting, is autogenic bone enriched with platelet-rich plasma (PRP) which is suggested to increase bone regeneration (Wiltfang *et al.*, 2004).

Embryology

The embryological origin of the bone graft has been suggested to play a role in the success of the bone augmentation procedure. It has been proposed based on animal studies, that intramembranous bone block grafts have a better resistance towards volumetric bone block graft resorption compared to endochondral bone grafts (Smith and Abramson, 1974; Zins and Whitaker, 1983). Alberius *et al.* (1992) showed in an animal study that intramembranous bone grafts healed better compared to endochondral grafts and indicated that a biological difference exists between the two types of bone grafts. Rabie *et al.*(1996) reported that intramembranous bone grafts healed through an osteogenic ossification route where preosteoblasts, osteoblasts, and osteocytes were observed with no cartilage intermediate stage, while in endochondral bone grafts, chondroblasts and chondrocytes were observed and healing occurred through an endochondral ossification route. Kusiak *et al.* (1985) suggested in an animal study that intramembranous onlay bone grafts become earlier revascularized than endochondral grafts and thereby maintain volume and viability to a greater extent. Sullivan & Szwajkun (1991) found that endochondral grafts had quantitatively greater revascularization than intramembranous grafts. Differences in graft architecture were theorized to account for the difference in revascularization in endochondral and membranous bone grafts.

Chen *et al.* (1994) demonstrated that calvarial bone grafts maintained volume better than iliac bone grafts. The osteoclastic activity and revascularization were greater in the cancellous portion of calvarial and iliac bone grafts. Because calvarial bone grafts contain more cortical bone, their superior volume maintenance can be understood by the architectural influence on revascularization and resorption. The revascularization process differs between cortical and cancellous bone grafts because of the different morphologies. Cortical bone is densely packed and cancellous bone porous, with marrow tissue in between the bone trabeculae.

Donor sites

Autogenous grafts are often used due to their osteoconductive and osteoinductive capacities (Urist, 1980). They can be harvested from different sites in the body e.g.: the iliac crest, the calvaria, the ribs, the mandible (Kondell *et al.*, 1996; Loukota *et al.*, 1992; Lundgren *et al.*, 1996). The most appropriate procedure to use depends on the amount of bone needed and surgical preference.

To harvest large amounts of bone, extra oral sites such as the iliac crest has often been used. Postoperative morbidity as bruising, swelling, pain and functional problems at the donor site is more often seen using extra- than intra-oral donor sites. The extra oral approach will also produce a permanent cutaneous scar, and usually involves general anaesthesia with days of hospitalization (Beirne, 1986; Cricchio and Lundgren, 2003; Raghoebar *et al.*, 1999).

Harvesting of bone from intra oral sites such as mandibular ramus/body or symphysis shows acceptable donor site morbidity (Hirsch and Ericsson, 1991; Misch, 1999; Nkenke *et al.*, 2001; Nkenke *et al.*, 2002). More over, the procedure can be made in local anaesthesia and no hospitalization is needed.

Inlay bone grafts

Boyne et al.(Boyne and James, 1980) described a procedure whereby particulated cancellous bone and bone marrow harvested from the iliac crest, was grafted to the floor of the maxillary sinuses below the mucous membrane through a fenestration of the lateral maxillary sinus wall. This method has sine then been frequently used, either with particulated bone or bone blocks and immediate or delayed implant placement with or without the combination of onlay (Blomqvist *et al.*, 1996; Jensen *et al.*, 1994; Johansson *et al.*, 1999; Raghoebar *et al.*, 2001b)(Table 2a & b).

The use of interpositional bone blocks in conjunction with a Le Fort I procedure was originally described by Keller *et al.* (1987) and by Sailer (1989). This approach has shown to have advantages when used in combination with correction of class III malocclusions (Isaksson, 1994).

It has been suggested that a delayed approach, where the bone graft is allowed to heal prior to implant placement, ought to result in higher implant survival (Lundgren *et al.*, 1997; Rasmusson *et al.*, 1999). However, clinical

Table 2a. Summary of clinical follow-up studies of bone grafting and implants in the totally edentulous maxilla.

	N pat.	Graft	Bone graft technique				Implant survival			Failures		Follow-up
Literature:		Donor site	Onlay: block / particulated	Inlay: block / particulated	Implant surface	1-stage / 2-stage	falures/placed/survival rate			Before loading	After loading	Years (mean)
(Adell *et al.*, 1990b)	23	Iliac crest	Block	no	BS turned	1-stage	33	124	74%	?	?	2-9
(Isaksson and Alberius, 1992)	8	Iliac crest	block	no	BS turned	1-stage	8	46	83%	75%	25%	2-3
(Donovan *et al.*, 1994)	10	calvarial	Block	no	BS turned	both	1	44	98%	?	?	1.5
(Jemt and Lekholm, 1995)	16	Iliac crest	block	no	BS turned	1-stage	16	83	82%	?	?	5
(Astrand *et al.*, 1996)	17	Iliac crest	Block	no	BS turned	1-stage	23	92	75%	?	?	3
(Kondell *et al.*, 1996)	14	rib	Block	no	BS turned	1-stage	20	75	74%	80%	20%	4-6
(van Steenberghe *et al.*, 1997)	13	Iliac crest	block	block	BS turned	1-stage	12	93	87%	?	?	10
(Lundgren *et al.*, 1997)	20	Iliac crest	Block	Block	BS turned	2-stage	23	136	83%	35%	65%	2
(Kondell *et al.*, 1996)	14	rib	Block	no	BS turned	1-stage	20	75	74%	80%	20%	4-6
(Nystrom *et al.*, 2002)	30	Iliac crest	Block	no	BS turned	1-stage	45	177	75%	69%	31%	5
(Johansson *et al.*, 1999)	39	Iliac(n=28) chin(n=11)	no	block	BS turned	1-stage	47	254	81%	68%	32%	3
(Wannfors *et al.*, 2000)	20	Iliac crest	no	block	BS turned	1-stage	20	148	86%	65%	35%	1
(Wannfors *et al.*, 2000)	20	Iliac crest	no	particulated	BS turned	2-stage	10	140	93%	80%	20%	1
(Widmark *et al.*, 2001)	16	Iliac crest	block	block	BS turned	1&2-stage	25	101	75%	56%	44%	5
(Raghoebar *et al.*, 2001b)	75	Iliac crest	no	block	BS turned	1&2-stage	30	326	91%	67%	33%	1-10
(Becktor *et al.*, 2004)	40	Iliac crest	block	block	BS turned	1-stage	63	260	76%	92%	8%	2-9
(Becktor *et al.*, 2004)	24	Iliac crest	block	block	BS turned	2-stage	45	177	75%	93%	7%	2-9
(Sjostrom *et al.*, 2005)	29	Iliac crest	block	block	BS turned	2-stage	17	222	92%	76%	24%	1
(Thor *et al.*, 2005)	19	Iliac crest	Block / particulated	particulated	TiUnite	2-stage	2	152	99%	100%	0%	1

follow-up studies have shown similar results as compared with a simultaneous approach (Lekholm *et al.*, 1999; Schliephake *et al.*, 1997).

Onlay bone grafts

Adell *et al.* (Adell *et al.*, 1990b) presented five-year follow-up results with an onlay bone grafting technique using iliac bone, of the shape of a horseshoe, and simultaneous placement of implants. They reported a survival rate of approximately 72%. Isaksson *et al.* (1992) presented a study, where management of the atrophic maxilla was accomplished by using two segments of onlay iliac bone blocks, constructed to meet in the midline and fixed to maxilla with immediate implant insertion. The implants were followed for 32-64 months and had a survival rate of 83% was observed. Both studies are consistent with the findings of other authors using similar techniques (Albrektsson, 1988; Keller *et al.*, 1999; Lekholm *et al.*, 1999; Nystrom *et al.*, 2004). (Table 2a & b)

Block and/or particulated bone

In 1980, Breine & Brånemark (Breine and Branemark, 1980) reported two different reconstructive procedures for patients with severe jaw atrophy:
1; Reconstruction of 14 maxillas and 4 mandibles with placement of 5-6 implants and packing of autogenic onlay grafts, consisting of chips of cancellous bone and marrow from the upper tibial metaphysis, to form a new alveolar bone. Only about 25% of the the originally installed implants remained integrated.
2; Reconstruction of 8 maxillas and one mandible, with autogenic grafts from the proximal tibial metaphysis, containing two incorporated implants in each graft, and fixed with one additional implant in each graft, providing permanent support for bridge constructions with an implant survival of approximately 60%.
In a study with a split-mouth design, Thor *et al.* (2005) placed particulated bone mixed with PRP on one side in the anterior maxilla and onlay block grafts on the other side. Implants were placed in the grafted bone after 6 months of healing. The two sides were evaluated and compared after one year of loading. No implants were lost, the marginal bone level showed no significant differences; a resonance frequency analysis (RFA) revealed higher implant stability in the particulated bone mixed with PRP. Although there were no obvious positive effects of PRP on bone graft healing, the handling of the particulated bone grafts was improved (Thor *et al.*, 2005). Johansson *et al.* (2001) evaluated the volumetric changes of onlay block bone grafts and bilateral particulate bone

Table 2b. Summary of clinical follow-up studies of bone grafting and implants in the edentulous maxilla.

	N pat.		graft technique posterior				Implant survival			Failures		Follow-up
		Donor site	Onlay: block / particulated	Inlay: block / particulated	1-stage / 2-stage	Implant surface	lost/placed/survival			Before loading	After loading	Years (mean)
Donovan *et al.* (1994)	14	calvarium	block	no	both	BS turned	7	49	86%	49	86%	1.5
Raghoebar *et al.* (2001b)	24	mandible & iliac crest	block	particulated & block	1 & 2-stage	BS turned	2	66	97%	?	?	1-10
Cordaro *et a*l. (2002)	10	mandible	block	no	2-stage	iti	0	24	100	?	?	1
Brechter *et al.* (2005)	14	mandible	block	particulated	2-stage	TiUnite	1	32	97%	0%	100%	2
Becktor *et al.* (2006a)	5	iliac crest	no	block	1-stage	BS turned	3	17	82%	100%	0%	7
Becktor *et al.* (2006a)	12	iliac crest	no	block	2-stage	BS turned	3	52	94%	100%	0%	3
Becktor *et al.* (2006b)	61	mandible	block	particulated	2-stage	SLA/TiUnite/ tioblast	2	180	99%	100%		to loading

grafts to the maxillary sinus of the severely atrophic edentulous maxilla over 6 months. The area of each graft was measured and the volume calculated with the help of computerized tomography. The volume of the inlay and onlay grafts was reduced by an average of 49.5 and 47%, respectively, of the initial volume. The same author, measured cutting torques during the placement of self-tapping dental implants in non-grafted bone and in bone grafts, in 2-stages, either as blocks or in a milled particulate form, in 40 edentulous maxillae. Significantly lower cutting torque values were assessed in grafted regions than in non-grafted regions, irrespective of grafting technique. Lower values were also seen for implants placed in block grafts compared with implants placed grafts in particulate form (Johansson *et al.*, 2004). (Table 2a & b)

Vascularised bone grafts

Vascularised bone flap methods are mostly used in management and reconstruction of oral malignancies and have resulted in improvements of the treatment results (Urken *et al.*, 1991; Vaughan *et al.*, 1992). Surgical ablation of oral tissues, radiotherapy and microvascular tissue reconstruction often precedes the oral rehabilitation. Occlusal rehabilitation often includes fixed or removal prostheses supported by dental implants. However, management in the head

and neck cancer patient is demanding both surgically and prosthodontically. Factors contributing to the failure of oral implants include medical compromise, smoking, bone quality, use of bone grafts, radiation therapy, and poor oral hygiene (Esposito *et al.*, 1998c).

Different opinions regarding irradiated bone and implant treatment exist. Irradiated jaw bone has been regarded as a contraindication to implant treatment (Gurlek *et al.*, 1998; Kluth *et al.*, 1988). The use of hyperbaric oxygen therapy in irradiated tissues in conjunction with implantat treatment has been recommended (Granstrom *et al.*, 1993; Ueda *et al.*, 1993). On the contrary, other studies report acceptable implant survival results in irradiated bone without hyperbaric oxygen therapy (Eckert *et al.*, 1996; Niimi *et al.*, 1998). Some authors state that implants placed before radiotherapy will osseointegrate more successfully than after radiotherapy (Urken *et al.*, 1989), whereas others believe that the bone perfusion has recovered sufficiently 12 months after radiotherapy (Keller, 1997). The greater success of implant placement in native bone or vascularized bone flaps rather than free bone grafts has also been discussed in the literature (Foster *et al.*, 1999). In an animal study, showed histologically that new bone formation and bone union was observed and completed after 8-12 weeks in the vascularized tibial grafts and bone formation was clearly delayed in non-vascularized tibial grafts. Dental implants in vascularized tibial graft seemed not to have any negative effect on revascularization (Kobayashi *et al.*, 2005).

Shaw *et al.* (2005) presented data from 386 implants in 81 patients who received microvascular free flap reconstruction after surgical ablation of oral squamous cell carcinoma. The patients lost 15% of the implants after a median follow-up of four years. Radiotherapy did not seem to jeopardize implant survival, and hyperbaric oxygen had no demonstrable benefit. Despite some persistent soft tissue problems and implant loss, most patients reached a successful prosthetic and functional outcome (Shaw *et al.*, 2005).

Allogenic and xenogenic bone grafts

Allograft is by definition a bone graft containing living cells, derived from an individual of the same species. They are hardly recommended because they initiate a cell mediated immune response: an allograft may only survive if the donor is a parent or a sibling (Urist, 1980). A substitute to an allograft is an allo-implant which is bone tissue derived of an individual of the same species and which contains no viable cells. Allo-implants are prepared by freezing, freeze drying, irradiation or sterilization of the tissue. Autolysed antigen –extracted

allogenic (AAA) bone will incorporate better than freeze-dried or irradiated bone. The principles for incorporation of allo-implants and autografts are similar, since both osteoinductive and osteoconductive responses have been described, even if several other reports also describe the alloimplant to lack osteoinductive properties and to show very modest osteoconductive responses (Pinholt *et al.*, 1994; Solheim *et al.*, 2001; Urist, 1980).

Although autografts are superior to allografts, allografts are used to some extent in oral and maxillofacial reconstruction but commonly so in orthopaedic surgery. In subjects with large bone defects, autographs are either not available in sufficient quantities or their use accompanied by high morbidity at the donor site (Gocke, 2005; Simion *et al.*, 2001).

Xenografts are defined as bone derived from living tissue from another species whereas xeno-implants are bone grafts where all living cells and proteins has been extracted. Consequently a xeno-implant can only be osteoconductive and is replaced by new bone very slowly or to a small extent only (Jensen *et al.*, 1996).

Recently, Hallman et al reported an implant survival rate of 86%, for implants placed in grafted areas after three years of prosthetic loading. They used a mixture of deproteinized bovine bone and autogenous bone in patients for maxillary sinus inlay augmentation (Hallman *et al.*, 2005). Accordingly cadaveric bone allo-implant and bone substitutes are inferior to autogenous bone graft due to lacking of osteogenic cells and a significant amount of osteoinductive growth factors. The combination of autologous cancellous bone marrow and AAA bone is called a composite bone graft. The use of these grafts is often mandatory in small children with insufficient iliac crest and tibia bone. Their success depends on absolute, uninterrupted internal fixation.

Healing period

Early occlusal rehabilitation evolved from the concept of balanced articulation, which can be defined as bilateral, simultaneous, anterior and posterior occlusal contacts of the teeth in centric and eccentric positions. Bilateral articulation, or balance, as the occlusal scheme of choice has a long history in complete denture construction (Kurth, 1954).

Repeated trauma to the implant and/or local bone during the healing period is considered to be a causative factor for implant failure (Brunski, 1993; Esposito *et al.*, 1999; Pilliar *et al.*, 1986). This trauma could be induced by the use of a prosthesis that transmits forces to the underlying bone (Atwood, 1971). A

combination syndrome has been described, in which the anterior maxilla undergoes residual ridge resorption in response to trauma from retained mandibular anterior teeth with a lack of stable posterior mandibular occlusion (Kelly, 1972). A provisional maxillary denture opposed by a mandibular dentition that creates force concentration rather than force distribution could induce further trauma to the reconstructed maxilla. Force concentration is likely to occur when occlusal instability is likely such as the presence of unilateral edentulism or retained anterior teeth only. Conversely, an intact mandibular arch, completely restored dentition or any other distribution of teeth that allows a broad distribution of forces should prove more favorable to the maxilla. Uhthoff *et al.* (1973) described that premature loading of an implant may result in a permanent soft tissue encapsulation and Albreksson *et al.* (1981) recommended a minimum healing period before loading of 3-4 months (Uhthoff, 1973). A literature review by Esposito *et al.* (1998a) reported a pooled failure rate of 15% after three years of loading in grafted edentulous and partially edentulous patients. Most of the implant failures occurred during the healing period, at the second stage surgery and the period immediately prior to connection of the permanent prosthesis (Esposito *et al.*, 1998a). Trauma could be induced by the use of a prosthesis during the healing period that transmits forces to the underlying bone (Atwood, 1971). The reasons for this concern is mostly depending on the absence of a periodontal ligament supporting the implants and the observation that non-axial forces will create areas of high stress concentration instead of uniform compression along the implant to bone interface. The non-axial loading of a mechanical device assembled with screw joints, such as dental implants, will induce more mechanical failures (Rangert *et al.*, 1989). However, evidence is lacking, regarding the effect of non-axial load or overload on the osseointegrated interface between bone and implant. The implant shape and surface texture indicate that the load will be transferred to bone by compression in some areas and as tension and shear in other areas (Jemt *et al.*, 2000). The load of occlusion is seldom vertical and mastication distributes both non-axial and axial loading and the damaging effects of bruxism are created through lateral friction between the occlusal surfaces of maxilla and mandible. Thus, the resultant forces are not vertical. There is limited evidence available and it does not demonstrate that non-axial loading is unfavourable to the osseointegrated interface (Asikainen *et al.*, 1997).

The proprioception of the periodontal ligament is missing when the natural teeth are lost and could be an important consideration in the replacement of

natural teeth with dental implants. The perception has been demonstrated to be extraordinarily different between natural teeth and implants (average 3.8-g pressure for natural teeth tested horizontally vs. 580-g horizontal force for implants in the anterior mandible) (Mericske-Stern *et al.*, 1993). Despite these findings, patients with extensive implant-supported restorations seem, to function well without the benefit of periodontal proprioceptive nerve endings. The presence of proprioceptive nerve endings in periosteum, muscles of mastication, oral mucosa, and the temporomandibular joints may to some extent compensate for those lost from the missing periodontal ligament (Van Loven *et al.*, 2000).

Surgeon's experience

When a new method is described the difficulties in the beginning are commonly addressed by excluding the first cases in the results, claiming a "learning curve", the latter cases showing better but also more realistic results (Adell *et al.*, 1990b; Nystrom *et al.*, 2002). It has been demonstrated that a gentle surgical technique with a minimal trauma to the graft, will lead to a faster remodelling and revascularization. In addition, the degree of stability of the graft is important. Bone is heat sensitive and a temperature of more than 47ºC combined with an exposure time of more than 1 minute has been shown to result in an impaired bone healing (Eriksson and Albrektsson, 1983). To minimize increased temperature in the bone due to drilling, intense cooling with saline solution, a graded series of drills and well sharpened instruments have been recommended (Eriksson, 1984). The integration of titanium implants in autogenous free bone grafts is dependent on the state of the bone graft. Revascularization of the bone graft is very important for its incorporation and remodelling (Albreksson, 1979). This is dependent on gentle surgery, minimal trauma to the donor and recipient sites and the preservation of as much blood supply as possible (Bell, 1969; Eriksson, 1984). The potential of the bone graft to respond to the surgical trauma from installation of the implant will most likely influence the quality of osseointegration and the stability of the implant. The degree of osseointegration, (bone to implant contact) is supposed to increase when the implant is installed six months after the bone graft procedure compared with simultaneous implant installation (Lundgren *et al.*, 1999). These findings support the notion of the importance of a well vascularized and incorporated bone graft to an optimal bone to implant contact.

Lambert *et al.* (1997) defined a learning curve for dental implant placement. Implants placed by inexperienced surgeons failed twice as often as those placed by experienced surgeons. It was suggested that surgeons with little or no previous

experience must expect a definite learning curve (Lambert *et al.*, 1997). However, another study reported no differences in implant survival rate as a function of the level of training of the resident surgeon (Melo *et al.*, 2006).

Albrektsson emphasized the importance of surgical skill of the surgeon when analyzing the reasons for implant success and failure (Albrektsson, 2001).

AIMS

- To analyze and compare the survival rate of endosseous implants placed in the maxilla of patients (i) subjected to bone augmentation procedures prior to or in conjunction with implant placement and (ii) in routine patients without bone augmentation.

- To analyze the influence of the mandibular dentition on implant performance in the maxilla prior to attachment of the definitive prosthesis when reconstruction is possible only with the use of autogenous bone-grafting techniques.

- To evaluate the clinical outcome of zygomatic implant treatment and discuss whether the treatment with zygomatic implants could be an alternative to the bone grafting and implant procedures in patients with edentulous maxillae.

- To analyze the survival rate of endosseous implants placed in the partially dentate maxilla treated with sinus inlay block bone-grafts harvested from the iliac crest.

- To describe the surgical technique when using particulated bone from the mandible for maxillary sinus floor augmentation prior to the placement of surface modified implants. The purpose was also to report on the clinical outcome from bone grafting to delivery of the final prosthesis

MATERIALS AND METHODS

Subjects

Paper I

The study included 216 consecutively treated patients with edentulous maxillae, rehabilitated with minimally rough (machined/turned) endosseous implants (Brånemark System, Nobel Biocare AB, Gothenburg, Sweden) with or without bone augmentation. Of a total of 216 patients and 1357 implants, 34 patients with 237 implants were withdrawn as described below.

The patient material were divided into two retrospective patient groups: (i) the Graft Group included 64 patients with 437 implants and (ii) the Non-Graft Group included 118 patients with 683 implants, that had been consecutively treated during a period from 1990 to 1996 (Table 3). In addition, the retrospective patient groups were also prospectively followed using a standardized clinical and radiographic study-design. Routine implant treatment was commenced if the remaining bone volume was evaluated as adequate. The Graft Group, included 64 patients, 22 male and 42 female. Because of advanced horizontal and vertical bone loss of the alveolar processes as well as extensive pneumatization of the maxillary sinuses, the patients were considered to have insufficient bone volume for routine implant treatment. A one-stage grafting technique was used from 1990 to 1994 and a two-stage grafting technique was used from 1994 to 1996.The Non-Graft Group included 118 patients, 72 male and 46 female, were judged from clinical and radiographic examinations to have sufficient bone volume for implant treatment.

Table 3. Paper I. Distribution of Placed Implants With Regard to Number, Length and Diameter. Corrected values on gray background.

Paper II

The present study was conducted as a retrospective investigation of consecutively treated patients from two oral and maxillofacial surgery departments. A total of 101 consecutively treated patients were included, all with edentulous maxillae that underwent treatment planning to receive endosseous implants in conjunction with autogenous bone grafting. All patients had insufficient bone volume and autogenous bone augmentation was required. The group of patients was treated from 1990 to 1996.
Of a total of 101 patients, 11 subjects were excluded. The remaining 90 patients (31 men, 59 women) with 643 implants(Brånemark System, Nobel Biocare AB, Gothenburg, Sweden) were examined retrospectively according to the study protocol.

Paper III

The study included 16 patients, 6 males and 10 females with edentulous maxillae, consecutively treated with 74 endosseous dental implants (Brånemark Implant System, Nobel Biocare AB, Gothenburg, Sweden, or Astra Tech Implant Dental System, Astratech AB, Gothenburg, Sweden) and 31 zygomatic implants (Brånemark System, Nobel Biocare AB, Gothenburg, Sweden) from 1998 to 2002. The patients were retrospectively evaluated and prospectively followed, using a standardized clinical and radiographic study-design. Because of advanced horizontal and vertical bone loss of the alveolar processes as well as extensive pneumatization of the maxillary sinuses, the patients were considered to have insufficient bone volume for routine implant treatment. The patients were treated with zygomatic implants as an alternative bone grafting.

Paper IV

A number of 17 partially dentate patients, 4 males and 13 females, were subjected to bone augmentation procedures prior to or in conjunction with implant placement. Bone volumes were regarded as insufficient for implant treatment unless a bone grafting procedure was performed. A total of 69 implants (Brånemark System, Nobel Biocare AB, Gothenburg, Sweden) were placed in the patients. All patients were consecutive admissions treated from 1990 to 1996. The retrospective patient group was also prospectively followed using a standardized clinical and radiographic study-design.

Paper V

The study group included 61 patients, 23 males and 38 females. All patients were partially dentate. Because of advanced horizontal and vertical bone loss of the alveolar processes and/or extensive pneumatization of the maxillary sinuses, the patients were considered to have insufficient bone volume for routine implant treatment. All patients were consecutive admissions treated from 1998 to 2004. The patients were subjected to a bone augmentation procedure using autogenous bone grafts and implant treatment using 180 surface modified implants: 119 Straumann implants with blasted/acid-etched surface (SLA, Straumann AG, Basel Switzerland) 38 Brånemark System implants with oxidized surface (TiUnite, Nobel Biocare AB, Gothenburg, Sweden) and 23 Astra Tech implants with blasted surface (TioBlast, AstraTech AB, Gothenburg, Sweden) were placed.The patient group was prospectively followed using a standardized clinical and radiographic study-design.

Drop-outs

In paper I, a total of 34 patients (15.7%) with 237 implants (17.5%) were drop-outs. In the Graft Group, 19 patients with 133 implants were withdrawn as a result of; (i) combined infection and dehiscence of the wound related to the use of a non resorbable membrane (n=3), (ii) patients had moved from the area (n=7), (iii) reduced health (n=3) or (iv) patients had deceased (n=6). In the Non-Graft Group, 15 patients with 104 implants were withdrawn because, (i) patients had moved from the area (n=6), (ii) reduced health (n=7) or (iii) patients had deceased (n=2).

In paper II, 11 of 110 subjects (10,9%) were drop-outs; (i) three patients with combined infection and dehiscence of the wound due to the use of a non resorbable membrane, (ii) two patients with maxillary discontinuity due to gun shot wounds and resection of malignancy, (iii) three patients who moved before treatment was completed and (iv) three patients were deceased.

In paper III, sixteen patients received zygomatic implant treatment and were included in the study. All patients were contacted for a further prospective follow-up examination. Of 16 patients, 14 presented, one patient was deceased, and another patient was hospitalized in another city. Subsequently, 14 patients underwent clinical and radiographic examination according to the prospective follow-up protocol.

There were no drop-outs in paper IV and V.

Surgery

Papers I, II and IV

Bone augmentation was performed in a hospital operating room setting under general anaesthesia with nasal endotracheal intubation supplemented with infiltration of local anaesthetic agents and a vasoconstrictor for haemostasis. Patients were preoperatively given benzylpenicillin (3g) and metronidazole (0.5g) preoperatively on a routine basis. All patients in paper I, II and IV received autogenous corticocancellous bone blocks harvested from the iliac crest. At the recipient site, different surgical augmentation techniques were performed (Figure 1). In Paper I, segmental bone block onlay and maxillary sinus bone block inlay techniques were performed. In Paper II segmental bone block onlay, full-arch bone block onlay (horseshoe-shaped) or nasal bone block inlay and maxillary sinus bone block inlay was used. In paper IV, maxillary sinus bone block inlay grafts were used only. In papers I, II and IV both 1-stage surgery, with the bone graft and implants placed simultaneously, and 2-stage surgery, with a healing period between bone grafting and implant placement, were utilized. Postoperatively, the patients were prescribed antibiotics for one week. Brånemark System implants (Nobel Biocare AB, Gothenburg, Sweden) with a minimally rough turned surface were used in all these papers.

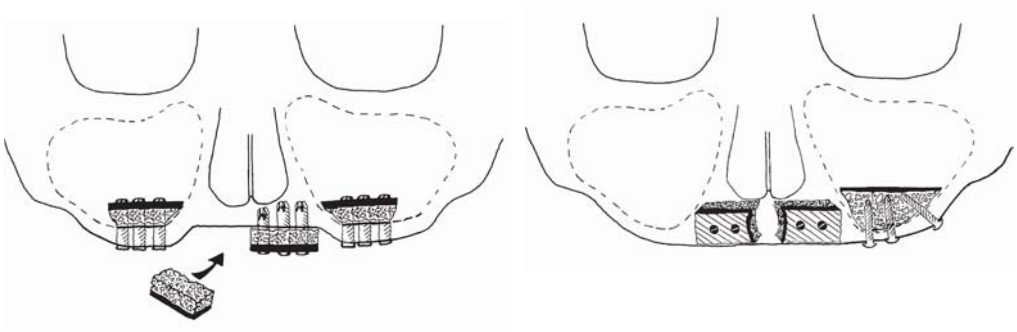

Figure 1. Schematics of one- and two stage grafting procedures.

Paper III

Surgery was performed under general anaesthesia with nasal endotracheal intubation supplemented with infiltration of local anaesthetic agents with a vasoconstrictor for haemostasis. Patients were preoperatively given bensylpenicillin (3g) and metronidazole (0.5g) preoperatively on a routine basis. A crestal incision was made extending from the second molar bilaterally. A vestibular releasing incision was made at the posterior extent of the incision in the maxillary second molar region. A muco-periosteal elevation revealed the nasal apertures and the piriform rim to the inferior aspect of the infraorbital foramina and laterally of the buttress and body of the zygoma, bilaterally.

A round bur was then used to create a lateral window, 5 x 10, mm in the lateral wall of the maxillary sinus. The sinus mucosa was then carefully reflected and protected through the preparation of the zygomatic implant site. A retractor was placed over the superior aspect of the zygomatic arch to enable a correct orientation of the implant site preparation. The zygomatic implants head were placed palatal and as close as possible to the alveolar crest, in the region of the second premolar and first molar. After penetrating the maxillary bone into the maxillary sinus, the preparation went through the cortical layer of the anterior-superior part of the zygomatic bone. The implant sites were then enlarged. Implant size was decided and final placement of the implant was accomplished using the standard protocol. The zygomatic implant was placed using low speed until the tip of the implant engaged the zygomatict bone and finalized manually until the implant was optimally seated. All 31 zygomatic implants had a stable and ridgid primary stability at the installation and were dressed with a cover screw.

Patients obtained simultaneous placement of additional endosseous implants in the anterior region of the maxilla (Brånemark Implant System, Nobel Biocare AB, Gothenburg, Sweden, or Astra Tech Implant Dental System, Astratech AB, Gothenburg, Sweden).(Branemark, 1985) The wound was closed with a continuous, absorbable 4-0 sutures. Postoperatively, the patients were prescribed antibiotics for one week.

Paper V

In the first three patients of paper V, the bone augmentation was performed under general anaesthesia with nasal endotracheal intubation supplemented with infiltration of local anaesthetic agents. The majority of the remaining patients were treated in local anesthesia, using Lidocain / Adrenalin

2% in combination with Bupivacain / Adrenalin 5% with or without per oral sedation with flunitrazepam (0.5 – 1.0 g) one hour preoperatively.

From the retromolar to the second or first molar area a 20-30 mm incision was made in the facial vestibule on the external oblique ridge of the mandible. The lateral aspect of the mandible was exposed and the localization of the osteotomy was marked with a 1mm fissure bur. The osteotomy was started anterior to the coronoid process, cutting along the anterior border of the ramus, medially to the external oblique ridge, finishing in the mandibular body in the molar region. The length of the anterior and posterior vertical cuts was determined by the size of the graft required. The inferior osteotomy, which connects the vertical cuts, was made with a diamond disc that creates a 2-mm depth in the cortical bone. With adequate osteotomies through the cortical layer, the splitting of the bone block was done with careful bending movements using a chisel. Following removal of the bone, sharp edges around the ramus/body were smoothed off with a round burr. The wound was rinsed with saline solution, haemostatic dressing (collagen) was placed into the donor area and the wound was sutured using resorbable sutures. In all 61 patients the harvested bone was kept in saline solution or blood until it was particulated with a surgical bone mill. In eight out of the 61 patients, a part of the harvested bone was kept as a bone block and trimmed and used as onlay bone graft.

The approach for the posterior maxilla was made by a crestal incision along the alveolar process. The alveolar crest was subsequently exposed by raising a buccal pedicled mucoperiosteal flap and a bony window was established on the lateral aspect of the maxillary sinus. The sinus membrane was carefully elevated and the particulated bone was positioned in contact with the floor of the maxillary sinus. In eight cases the alveolar crest had to be widened and some of the harvested bone was then used as a block. The bone block was trimmed and fixed with titanium osteosynthesis screws (7 to 15mm in length and 2mm in diameter) on the lateral aspect of the alveolar crest. After a healing period of five to 21 months (mean 7.2) the implant placement was carried out. In total, 180 implants were placed. Three different implant systems with moderately rough surfaces were used, 119 Straumann implants with blasted/ acid-etched surface (SLA, Straumann AG, Basel Switzerland) 38 Brånemark System implants with oxidized surface(TiUnite, Nobel Biocare AB, Gothenburg, Sweden) and 23 Astra Tech implants with blasted surface (TioBlast, AstraTech AB, Gothenburg, Sweden) were placed. The implants were in lengths from 8 to 15 mm (mean: 11.5mm) and in diameters from 3.3 to 4.8 mm (mean: 3.9mm).

Effort was made not to perforate into the maxillary sinus with the drills or the implants, assuring that the implants were covered with grafted bone at the apical part. A non-submerged technique was used for Straumann implants and a submerged technique for the other implant systems. The implants were allowed to heal for 3 to 6 months prior to abutment connection and prosthetic treatment.

Prosthodontics

In papers I, II and III, conventional dentures were relined 1 to 3 weeks after bone grafting and /or implant surgery and at abutment connection. No dentures were used in papers IV and V. Fabrication of gold-acrylic fixed prostheses, and in cases with overdenture therapy using a bar and clips, followed the standard procedures for the different implant systems.

Examinations and Follow-up

In papers I, III and IV, data were collected from the time of bone augmentation or implant treatment until the last follow-up and retrospectively analyzed according to a research protocol. All patients were contacted for a prospective follow-up examination and subsequently underwent clinical and radiographic examination according to the prospective follow-up protocol.

All available data in paper II, such as clinical records and radiographs, were documented from the time of bone augmentation or implant treatment until the last follow-up. This material was retrospectively analyzed according to a study protocol to confirm understanding of the material.

In paper IV, data were collected from the time of bone augmentation till the day of delivery of definitive prosthesis and was prospectively analyzed according to a research protocol.

Radiographic Examination

The retrospective radiographic examinations had not been consistently performed at the time of the abutment connection surgery and at the annual controls in papers I, II, III and IV. Radiographs used in papers I and IV were taken at the prospective follow up examination. An intraoral radiographic paralleling technique (Hollender and Rockler, 1980) was utilized at the time of the prospective patient follow-up. The distance from the implant-abutment junction to the marginal bone at mesial and distal surfaces of each implant was recorded. Linear measurements were performed to the closest one mm.

In paper III, preoperatively, panoramic images supplemented with intra oral radiographs were used to evaluate the bone volume of the maxilla. Computed tomograms were used to determine whether the anatomy would allow installation of zygomatic implants and to eliminate the risk of undiagnosed pathological lesions.

Preoperative classification according to Cawood & Howell(Cawood and Howell, 1991), was performed in all papers, retrospectively with the help of lateral and panoramic radiographs. The lateral radiographs were used to determine the height in the anterior maxilla. The panoramic radiographs were used for the classification in the region of the posterior maxilla where 5mm or less of bone in height corresponded to class V and VI, 6mm – 12mm to class III-IV and 12mm or more to Class I-II.

The radiographic evaluation in paper IV consisted of one pre-surgical panoramic radiograph and one post-surgical panoramic radiograph, taken after the bone grafting and implant installation.A standardized natural head position was used while obtaining panoramic radiographs. The radiographs were taken with the same equipment at the radiographic department, and the same film/focus distance was used. All radiographs were taken at optimal exposure and anatomical landmarks were clearly visualized. All radiographs were hand-traced on acetate paper by one examiner. Reference lines were drawn through structures like top of the alveolar crest, nasal bones and the floor of the maxillary sinus directly on the pre-surgical radiograph with a sharp soft pencil. The post-surgical radiograph was superimposed on anatomical structures and the implant sites were evaluated pre- and post-surgically with regards to implant position and its vertical bone volume including grafted and residual bone.

Statistics

In papers I, II and IV life table analyses were performed to calculate the cumulative implant survival rate (CSR). The Wilcoxon rank sum test was used in paper II, to test differences in implant survival rates between the Non-Graft Group and the Graft Group, with the relative frequency of implant loss in each patient as the calculation unit and to test the difference between the groups in specific regions (incisor, canine, premolar and molar) with the implant as the unit. The Pearson Chi-Square test was used to compare the Non-Graft Group and the Graft Group with respect to a variety of explanatory variables. The level of statistical significance was set at the 5% level.

In paper II the experimental unit in the analysis was an individual implant, of which there were several within each patient. The outcome of interest was the occurrences of implant failure at any time during the healing period, including second-stage surgery, up until the time of prosthesis attachment. Various risk factors were evaluated for their association with failure. The association between each risk factor and failure was summarized using an odds ratio (OR) and corresponding 95% confidence interval (CI). An OR of 1 indicates no association between a risk factor and the occurrence of an implant failure. The binary response (failure versus no failure) was modelled using a logistic regression model. Robust estimates of the ORs and corresponding tests of significance were obtained based on generalized estimating equation methods to account for the correlation between implants within a patient. The correlations among the outcomes for each patient were modelled as exchangeable correlations. The SAS procedure PROC GENMOD (SAS Institute, Cary, NC) was used to perform the analysis.33 All calculated P values were 2-sided, and P values less than .05 were considered statistically significant.

In paper IV, the test between groups were performed with Fisher's exact text for dichotomous variables, Chi-square test for non-ordered categorical variables and Mantel Haenszel's test for ordered categorical variables. All tests were two-tailed and conducted at 5% significance level

RESULTS

Paper I

Implant and Bone Graft Stability

Graft Group

Sixty-five (14.9 %) of 437 implants placed were lost through the healing period including the abutment connection surgery. Seventeen (3.9%) failed before abutment connection surgery. Between abutment connection surgery and definitive prosthetic loading, another 35 implant were lost. Five patients lost all their implants within 4 months after abutment connection surgery. At the time of prosthetic loading the total number of lost implants were 100 (22.9%). During the first year of loading, 3 further implants were lost and another 6 implants were lost until the end of the study, giving a cumulative survival rate (CSR) of 75.1 % after a mean follow-up period of 68.9 months. All bone grafts were stable (Table 4a).

The study material showed no statistical difference between the one stage and the two stage grafting groups. The two groups have therefore been treated as one in subsequent statistical analyses (Table 5).

Non-Graft Group

Fifty-five (8.1%) of 683 implants were lost through the healing period including the abutment connection surgery. Three patients lost all their implants within 4 months after abutment connection. At the time of prosthetic loading the total number of lost implants was 95 (13.9 %). After 1 year of loading with fixed prostheses or overdentures another 4 implants had been lost. After a mean follow-up period of 75.8 months the CSR was 84.0 % (Tables 4b).

The material revealed a statistically significant difference (p=0.007) of the relative frequency of implant loss per patient between the Non-Graft Group and the Graft Group. Statistically, the two groups were comparable according to the majority of variables. The variables gender, implant-position and diameter were not comparable, even if differences were small, their importance cannot be fully ignored.

Implant Position and Implant Length

The implant failure rate was evaluated in relation to implant position and type of bone in both groups. Implants placed in onlay grafts showed a

Table 4a Paper I. Distribution of Failed Implants in the Graft Group.

				Observation period after loading of prosthesis							
Graft Group	Before abutment surgery	At abutment surgery	Before loading of prosthesis	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8
No. implants surveyed	437	420	373	338	313	296	256	238	187	89	17
No. implant failed in interval	17	48	35	3	2	2	2	0	0	0	0
Interval failure rate (%)	3.9	11.4	9.4	0.9	0.6	0.7	0.8	0	0	0	0
Cumulative failure rate (%)	3.9	14.9	22.9	23.6	24.0	24.5	24.9	24.9	24.9	24.9	24.9

Table 4b Paper I. Distribution of Failed Implants in the Non-Graft Group.

				Observation period after loading of prosthesis								
Non-Graft Group	Before abutment surgery	At abutment surgery	Before loading of prosthesis	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9
No. implants surveyed	683	680	628	588	584	562	514	472	370	209	101	29
No. implant failed in interval	3	52	40	4	6	1	1	2	0	0	0	0
Interval failure rate (%)	0.4	7.6	6.4	0.7	1.0	0.2	0.2	0.4	0.0	0.0	0.0	0.0
Cumulative failure rate (%)	0.4	8.1	13.9	14.5	15.5	15.6	15.7	16.0	16.0	16.0	16.0	16.0

Table 5. Paper I. Distribution of Failed Implants / Inserted Implants in the Graft Group With Regard to Placement in Type of Bone and Tooth Region. Corrected values on gray background.

Graft Group			Tooth region			
		Total	Incisor	Canine	Premolar	Molar
one-stage	Total	64 / 260	12 / 60	16 / 62	22 / 94	63 / 260
		(24.6)	(20)	(25.8)	(23.4)	(24.2)
	in inlay graft	42 / 146	0 / 0	7 / 16	21 / 86	41 / 146
		(28.8)		(43.4)	(24.4)	(28.1)
	in onlay graft	4 / 7	2 / 5	2 / 2	0 / 0	0 / 0
		(57.1)	(40)	(100)		
	in residual bone	18 / 107	10 / 55	7 / 44	1 / 8	0 / 0
		(16.8)	(18.2)	(15.9)	(12.5)	
two-stage	Total	45 / 177	19 / 52	10 / 51	12 / 64	4 / 10
		(25.4)	(36.5)	(19.6)	(18.8)	(40)
	in inlay graft	20 / 105	0 / 0	4 / 29	12 / 64	4 / 10
		(19.1)		(13.8)	(18.8)	(40)
	in onlay graft and residual bone	26 / 72	20 / 53	6 / 18	0 / 0	0 / 0
		(36.1)	(37.7)	(33.3)		
Graft Group total		109 /437	32 / 113	26 / 105	34 / 165	17 / 54
		(24.9)	(28.3)	(24.8)	(20.6)	(31.5)

Table 6. Paper I.Distribution of Failed Implants / Inserted Implants in the Non-Graft Group With Regard to Tooth Region. Corrected values on gray background.

Non-Graft Group		Tooth region			
	Total	Incisor	Canine	Premolar	Molar
Non-Graft Group total	109 /683	44 / 307	31 / 212	34 / 163	0 / 1
	(16)	(14.3)	(14.6)	(20.9)	(0)

higher failure rate (37.0 %) compared with implants placed in inlay grafts (24.9 %). Implants placed in non-grafted sites showed small differences in failure rate between the groups, 16.0 % and 16.8 % for the Graft Group and Non-Graft Group respectively (Table 6). Implants placed in inlay grafts in the premolar region had a failure rate of 22.1 %, which was similar to the implants in the same region of the Non-Graft Group in (20.6%). There was a tendency of a lower failure rate for longer implants in both groups.

Jaw Bone Shape

The outcome of implant treatment in the anterior edentulous maxillae could be related to the original jaw bone volume (Table 7a). The results in the posterior region shows a higher implant failure rate for class III-VI in the Non-Graft Group compared with class V-IV in the Graft Group (Table 7b).

Prosthesis Stability

All patients wore temporary complete dentures during the implant-healing phases.

Graft group

Of 64 patients included, 46 (71.8%) received a fixed prosthesis. Two patients were treated with an overdenture and four patients with a complete denture. The remaining 12 patients were treated with additional implant surgery and 10 obtained fixed prostheses, one overdenture and one complete denture. Of the 56 (87.5%) patients who received a full arch prosthesis, all (100%) were stable throughout their observation periods.

Non-Graft Group

Of 118 patients included, 89 (75.4%) received a fixed prosthesis, 20 an overdenture and four a complete denture. The remaining 5 patients were treated with additional implant surgery and subsequently after 4 obtained fixed prostheses and one received an overdenture. Finally, 93 (78.8%) of the patients received fixed prostheses of which all (100%) were stable at the end of the study period.

Table 7a. Paper I.Distribution of Failed Implants / Inserted Implants With Regard to Jaw Bone Shape and Tooth Region in the Anterior Maxilla. Corrected values on gray background.

Classification according to Cawood &Howell[25] in the Anterior Maxilla			Tooth region	
		Total	Incisor	Canine
Graft Group	class I–II	0 / 0	0 / 0	0 / 0
	class III-IV	10 / 75	7 / 36	3 / 39
		(13.3)	(19.4)	(7.7)
	class V–IV	48 / 139	25 / 75	23 / 64
		(34.5)	(33.3)	(35.9)
Non-Graft Group	class I–II	5 / 111	1 / 70	4 /41
		(4.5)	(1.4)	(9.8)
	class III-IV	52 / 337	34 / 200	18 / 137
		(15.4)	(17.0)	(13.1)
	class V–IV	18 / 46	9 / 24	9 / 22
		(39.1)	(37.5)	(40.9)

Table 7b. Paper I. Distribution of Failed Implants / Inserted Implants With Regard to Jaw Bone Shape and Tooth Region in the Posterior Maxilla. Corrected values on gray background.

Classification according to Cawood & Howell[25] in the Posterior Maxilla			Tooth region	
		Total	Premolar	Molar
Graft Group	class I–II	0 / 0	0 / 0	0 / 0
	class III-IV	0 / 0	0 / 0	0 / 0
	class V–IV	51 / 219	34 / 165	17 / 54
		(23.3)	(20.6)	(31.5)
Non-Graft Group	class I–II	0 / 22	0 / 21	0 / 1
		(0)	(0)	(0)
	class III-IV	34 / 142	34 / 142	0 / 0
		(23.9)	(23.9)	(0.0)
	class V–IV	0 / 0	0 / 0	0 / 0

Paper II

Implant and Bone Graft Stability

Of the 643 consecutively placed implants in 90 patients, 81 implants (12.6%) were lost during the period from implant placement until and including abutment connection surgery. At the time of definitive prosthesis placement, an additional 37 implants were lost, resulting in a total of 118 lost implants (18.4%). During the first year of functional loading with the definitive prosthesis, an additional 2 implants failed to maintain osseointegration, and 8 implants were lost subsequent to that time. The overall mean patient follow-up was 64.2 months. All bone grafts were stable. The follow-up period ranged from 22 to 105 months, with a mean of 64.2 months.

Mandibular Dentition

The type of mandibular dentition was significantly associated with implant failure during the period from implant placement until the time of definitive prosthesis placement (Figure 2)(Table 8 a-c). In the unilateral occlusal support group, 28 of 64 implants were lost, indicating the highest rate of implant failure (43.8%). Among the implants placed opposing limited occlusal support, 14 of 70 were lost (20.0%). Patients with stable occlusal contact, defined as mandibular bilateral occlusal support or an implant supported fixed prosthesis, demonstrated implant failure rates of 16.9% (62 of 366) and 14.3% (10 of 70), respectively. The lowest implant failure rate was observed in the patients who wore a mandibular removable denture, with a failure rate of 6.2% (4 of 65 implants failed). No failures were observed in the no dentition group, which consisted of 1 patient with 8 implants.

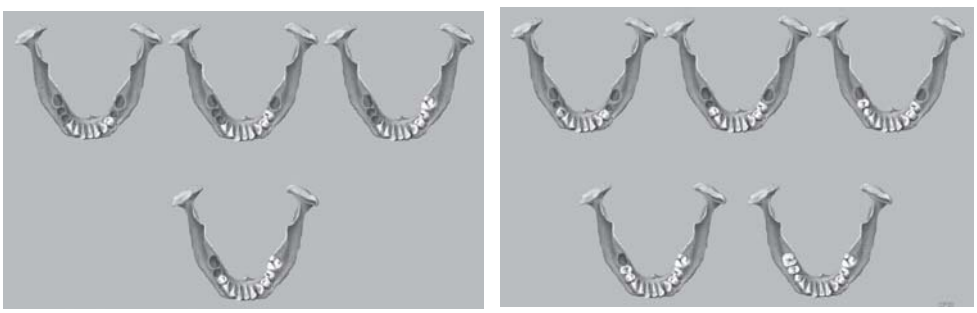

Figure 2. Showing examples of different unilateral (left) and bilateral (right) occlusal support in the mandible.

Table 8a. Paper II. Distribution of Lost Implants.

				Observation period after loading of prosthesis							
	Before Stage-2 surgery	At Stage-2 surgery	Before Prosthesis attachment	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8
No. implants still at risk for failure	643	625	562	523	463	387	293	194	117	24	7
No. implant failed in interval	18	63	37	2	4	2	2	0	0	0	0
Interval failure rate(%)	2,8	10,1	6,6	0,4	0,9	0,5	0,7	0,0	0,0	0,0	0,0
Cumulative failure rate(%)	2,8	12,6	18,4	18,7	19,3	19,7	20,2	20,2	20,2	20,2	20,2

Table 8b. Paper II. Distribution of Lost Implants / Inserted Implants with Regard to Mandibular Dentition and Time for Failure.

Mandibular Dentition	Total	Before Second-Stage	At Second- Stage	Between Second and Prosthesis Attachment
No Mandibular Dentition	0 / 8 (0%)	0	0	0
Removable Denture	4 / 65 (6.2%)	0	3	1
Limited Occlusal Support	14 / 70 (20.0%)	1	8	5
Unilateral Occlusal Support	28 / 64 (43.8%)	7	12	9
Bilateral Occlusal Support	62 / 366 (16.9%)	6	35	21
Implant Fixed Prosthesis Support	10 / 70 (14.3%)	4	5	1
Total	118 / 643 (18.4%)	18	63	37

Table 8c. Paper II. Distribution of Lost Implants / Inserted Implants With Regard to Graft Placement and Tooth Region.

		Tooth region			
Graft	Total	Incisor region	Canine region	Premolar region	Molar region
Implanted in Onlay Block	2 / 65 (3.1 %)	0 / 20	0 / 18	1 / 24	1 / 3
Implanted in Segmental Onlay	26 / 80 (32.5%)	21 / 59	5 / 20	0 / 1	0 / 0
Implanted in Nasal Inlay	4 / 24 (16.7%)	2 / 18	2 / 6	0 / 0	0 / 0
Implanted in Sinus Inlay	67 / 329 (20.4%)	0 / 1	11 / 42	34 / 193	22 / 93
Implanted in Non-Graft	19 / 145 (13.1%)	10 / 65	8 / 63	1 / 16	0 / 1
Total	118 / 643 (18.4%)	33 / 163 (20.3%)	26 / 149 (17.5%)	36 / 234 (15.4%)	23 / 97 (23.7%)

Paper III

Implant Stability

Three zygomatic implants in three different patients were removed, after the prosthetic loading (Table 9). Recurrent acute and chronic sinusitis occurred and despite monthly long treatment of local infection of the sites of the zygomatic implants, they had to be removed. Three (4.1%) of the 74 additional dental implants were lost between the abutment connection surgery and definitive prosthetic loading. After a mean follow-up period of 46.4 months (3 years and 10 months) the overall percentage of functioning implants, including the zygomatic implants, was 94.3 % (99/105).

Implant Position and Implant Length

All 31 zygomatic implants were installed in the second premolar/ first molar region. The palatal location, of the zygomatic implants, was measured with the distance from the nearest buccal cusp on the prosthesis to the centre of the gold screw with a mean distance of 11.2 mm (range: 4-15). The zygomatic interimplant distance was on average 21.7 mm (range: 13-29). The length of the zygomatic implants varied between the patients.

The additional 74 dental implants were all distributed in the anterior region of the maxilla.

Complications

There were no records of any complications during the implant surgery, during implant healing phase or at the abutment connection surgery.

After the abutment connection surgery, 10 of 16 patients had problems with oral hygiene at the zygomatic implant site. After professional help from a dental hygienist, 7 patients had improved their hygiene and three patients are still in this phase. Gingivitis was registered in nine patients and five of these patients presented with fistulas and local infections around their zygomatic implant and four of these five patients had fistulas bilaterally. The local infection was treated with antibiotics and in some cases excision of the fistulas. Sinusitis was a problem for six patients. Three patients had sinusitis bilaterally and another three unilaterally. This occurred both early and later in the period after the abutment connection surgery. They were treated by an ear, nose, and throat-specialist, with antibiotics and sinus rinses. Three patients had one zygomatic implant removed due to recurrent infections in the maxillary sinus. One patient was in treatment of her sinusitis throughout the observation periods.

Table9. Paper III. Summary of patients and results

Pat.	Sex	Age (Yrs)	Zyg. impl. length right/left (mm)	Follow-up (mo.)	Distance between zyg, implants, (mm)	Distance bucc. cusp to zyg. impl. right/left (mm)	Dental implant type	Dent. impl. placed/ failed	Poor oral hygiene at zyg. impl. in time period (mo.)	Local infection at the zyg. impl. in time period (mo.)	Sinusitis symptoms in time period (mo.)	Pal. periimpl. probe at right / left zyg. impl. with antral communication at the last follow up
1	M	71	45/45	65	13	10/10	BS	4/0	NO	YES 5-6	NO	YES / YES
2	F	76	45/45	69	21	10/12	AS	5/0	YES 0-1	YES 16-	NO	NO / NO
3	F	62	45/40	62	-	-/10	BS	4/1	YES 0-16	YES 2-14	YES	- / YES
4	M	44	45/45	63	24	5/7	BS	4/0	YES 0-12	YES 3-19	NO	NO / NO
5	F	68	40/30	57	18	15/9	BS	5/1	YES 0-	NO	NO	NO / YES
6	M	57	45/40	58	-	8/-	BS	4/0	NO	NO	YES 33-37	YES / -
7	M	77	45/45	45	24	12/10	BS	4/0	NO	NO	NO	YES / NO
8	M	59	50/45	55	25	4/8	BS	4/0	NO	NO	NO	NO / NO
9	F	63	40/40	48	24	10/8	AS	4/1	NO	NO	YES 1-6	YES / YES
10	F	56	50/45	50	19	9/6	AS	4/0	YES 0-	YES 4-10	NO	NO / NO
11	M	76	40/40	38	-	-/-	BS	4/0	YES 0-12	YES 1-12	NO	- / -
12	F	75	40/40	28	24	9/8	AS	6/0	YES 0-10	NO	NO	NO / NO
13	F	49	40/40	34	29	9/7	AS + BS	5/0	YES 0-3	YES 1-4	YES1-6	NO / NO
14	F	29	40/40	28	-	6/-	BS	4/0	YES 1-2	YES 1-2	YES 1-6	NO / -
15	F	59	45/-	9	-	-/	BS	6/0	YES 0-	YES 1-6	NO	- / -
16	F	56	40/35	34	18	9/12	BS	4/0	NO	NO	YES 18-	NO / NO

Prosthesis Stability

All patients wore temporary complete dentures during the implant-healing phase (6-8 months). All 16 patients received a fixed prosthesis that was stable throughout the observation period.

Paper IV

Implant and Bone Graft Stability

Six (8.7 %), of the 69 implants placed were lost. All implant failures occurred during the period from abutment connection surgery to delivery of the definitive prosthesis. No implants failed during prosthetic loading, giving a CSR of 91.3% after a mean follow-up period of 53.1 months (Table 10a).

The study showed better implant survival rate in the two-stage grafting group (49/52, 94%) compared to the one-stage grafting group (14/17, 82%).All bone grafts were stable and supported 48 implants of which five implants failed (10.4%). In the residual bone, 21 implants were installed of which one failed (4.8%)(Table 10b).

Prosthesis Stability

All patients received fixed prostheses, which were all stable throughout the observation periods.

Radiographic Examination

The marginal bone level was on average 2.2 mm (SD: 1.01) from the reference point after a mean follow up of 53.1 months. All (17) patients were found to belong to class V and VI in the posterior part of the maxillae, using the Cawood and Howell classification(Cawood and Howell, 1988).

Table 10a. Paper IV. Life Table of failed Implants.

				Observation period after loading of prosthesis								
	Before abutment surgery	At abutment surgery	Before loading of prosthesis	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9
No. implants surveyed	69	68	63	61	48	28	18	14	8	6	6	3
No. implant failed in interval	0	1	5	0	0	0	0	0	0	0	0	0
Cumulative failure rate (%)	0.0	1.4	8.7	8.7	8.7	8.7	8.7	8.7	8.7	8.7	8.7	8.7

Table 10 b. Paper IV. Distribution of failed implants with regards to type of bone and tooth region

		Tooth region			
	Total	Incisor	Canine	Premolar	Molar
Total	6 / 69	0 / 13	3 / 14	3 / 32	0 / 10
	(8.7)	(0)	(21.4)	(9.4)	(0)
in inlay graft	5 / 48	0 / 0	2 / 6	3 / 32	0 / 10
	(10.4)	(0)	(33.3)	(9.4)	(0)
in residual bone	1 / 21	0 / 13	1 / 8	0 / 0	0 / 0
	(4.8)	(0)	(12.5)	(0)	(0)

Paper V

Implant and Bone Graft Stability

The 61 patients received 52 unilateral and 9 bilateral sinus inlay bone grafts. Eight patients also received an onlay bone graft in addition to the sinus inlay bone graft. All bone grafts, were stable and supported 146 implants of which two implants failed (1.4%) giving an early survival rate of 98.6%. The implant failures were in the canine and premolar position, both engaged in grafted sinus inlay bone. In the residual bone, 34 implants were installed of which no implants failed. Only two (1.1%), one Straumann implant and one Brånemark implant, of the 180 implants placed were lost resulting in an implant survival rate of 98.9%.

Prosthesis Stability

All patients received a fixed prostheses after an implant healing period of 2 to 17 months (mean 5.7).

Radiographic Examinations

The radiographic examinations showed an average residual vertical bone height of 6.5mm (37 implants) in first premolar region, 3.8mm (56 implants) in the second premolar region, 3.5mm (46 implants) in the first molar region, and 2.6 mm (7 implants) in the second molar region. The average implant length was 12 mm in the first premolar region and 11 mm in the second premolar, first and second molar regions (Figure 3).

Complications

The postoperative symptoms at the donor site were similar to the symptoms after surgical removal of teeth. Paraesthesia of the inferior alveolar nerve was seen in one patient, who completely recovered after less then 2 months. There were no records of injured teeth, heavy bruising, bleeding or swelling from either the donor or the recipient site. At the recipient site three patients had local postoperative infections with shallow fistulas. This was managed with antibiotics and was cured after 2-3 weeks and had no negative effect on bone graft or implant survival. It was noted, in three patients, during the implants installation, that the new bone was softer than the residual bone. However, this had no negative influence on implant primary stability but one out of ten implants installed in soft bone, failed.

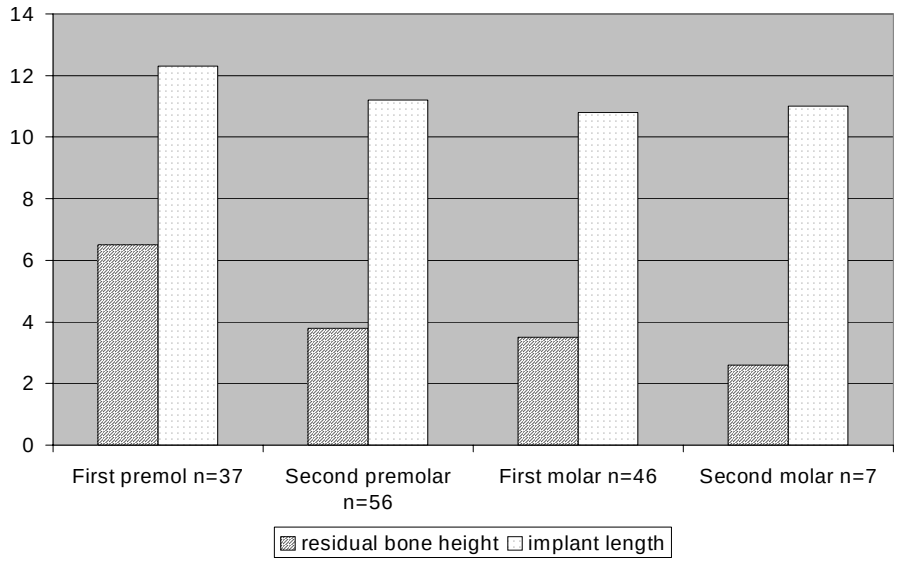

Figure 3. Paper V. Distribution of residual bone height before bone grafting and implant lengths after implant placement in different regions of the posterior maxilla.

Additional analysis of learning curve

The 64 grafted patients in Paper I was divided in two groups with regard to if a one- (n =24) or a two-stage (n=40) procedure had been used. The two groups were further divided in three depending on when the treatment had been perfomed. For the one-stage patients, more failures occurred with time as the first 13 cases had a failure rate of about 16% compared with 21% and 33% for the more recently treated groups comprising 14 and 13 patients, respectively. For the two-stage patients, the trend was decreased number of failures with time since the first 7 cases had a failure rate of 25%, followed by 38% and 7% for the following groups including 8 and 7 patients, respectively.

DISCUSSION

Bone grafting technique

In papers I and IV, edentulous and partially dentate patients were treated with bone block grafts using the iliac crest as the donor site. In paper I, approximately 25 % (109 / 437) of the implants placed in the Graft Group failed whilst 16 % (109 / 683) of the implants placed in the Nongraft Group were lost after a mean follow-up of 68.9 and 75.8 months respectively. The difference in implant failure rate was statistically significant. A failure rate of 17 % was seen in implants placed in the residual bone in the Graft Group (18 / 107) comparable to the implant failures in the Nongraft Group of 16 % (109 / 683). In paper IV, approximately 10 % (5/48) of the implants placed in augmented bone failed whilst 5 % (1/21) of the implants placed in residual bone were lost. In paper I, the inlay bone grafting technique, showed comparable implant survival rate in the premolar region as in the same region in the Non-Graft Group. Analysis of the patient material suggested that the more jaw bone volume present in anterior regions at the start of treatment, the better the implant survival rates in both groups.

In paper V, the possibility of achieving improved results compared to papers I and IV, by using a combination of particulated mandibular bone for augmentation and delayed placement of surface modified implants was demonstrated. The survival rate was 98.9% (2/180) for all implants and 98.6% (2/148) for implants placed in grafted areas after a mean follow-up of 12.8 months, which was until the delivery of fixed prostheses. A previous study, carried out in the same clinic, comparing implant survival in grafted and in residual bone, showed an implant survival rate of 96% in 76 partially dentate patients treated during the same time period as paper I and IV of the present thesis, but without bone augmentation procedures and with a mean follow-up of 53,9 months (Johansson and Ekfeldt 2003).

Different outcomes may be expected when comparing edentulous and dentate jaws as discussed by Ragoebar *et al.* (2001b), who found a 97% versus 90.8% survival rate in dentate and edentulous patients respectively. (Table 2a & b) This is in line with our experiences where an overall implant survival rate of 91.3% was found in 17 partially dentate patients in paper IV, which indicated a better clinical outcome with bone grafting procedures in the partially dentate patient compared with totally edentulous cases as in paper I. Interestingly, in both paper I and IV, implant failure occurred mainly from abutment connection to delivery of the final prosthesis. This indicates that many implants were not

well integrated and/or were sensitive to repeated manipulation and trauma from attaching and de-attaching abutments and impression copings and provisional prostheses during the prosthetic phase. Another negative factor could be the short healing periods of the grafts, which were on average 4.9 months in paper I and 4,8 months in paper IV, possibly leading to an immature quality of the bone graft and thereby impaired osseointegration of the implants.

It was noted in paper IV, that more implants failed when placed simultaneously with the bone graft than if a two-stage procedure was used. This was not seen in paper I. However, two-stage implants showed a lower survival rate in inlays but higher in onlay bone grafts and vice versa, which suggests that the results were not conclusive. Wannfors et al. reported a doubled risk for implant failure when using a one-stage technique compared with a two-stage approach (Wannfors *et al.*, 2000). (Table 2 & 3)

Biologically, a two-stage surgery is preferable, since revascularization, maturation and incorporation of the grafted bone are accomplished before the implants are inserted (Lundgren *et al.*, 1999). If the residual bone height beneath the maxillary sinus is 4 to 5 mm and of good quality, initial stability of the implants can probably be achieved using both approaches. However, in cases with insufficient bone volume where primary implant stability can not be achieved, delayed implant placement is preferred (Block and Kent, 1997; Lundgren *et al.*, 1999). On the other hand, simultaneous placement is less invasive, more cost-effective, and more time-efficient.

An analysis of implant failure rates in the grafted patients in Paper I, revealed more failures with time for one-stage procedures and less failures with time for two-stage procedures. Thus, a learning curve, which may be expected for complex surgery like bone grafting, could be seen only for the two-stage procedures. The increasing failure rate with time for the one-stage procedures may relate to a higher degree of cautiousness in the first cases.

Bone graft origin and donor site

In papers I and IV, endochondral bone from the iliac crest was used as bone grafts. There were no graft failures reported and the implant survival was 75.1 (Graft Group) in the edentulous cases and 91,3 % in the partial dentate cases. In paper V, intramembranous bone from the mandibular ramus/corpus was used as bone graft. There were no graft failures reported and the implant survival was 98.9 % in the partially dentate cases.

The embryological origin of the bone graft has been suggested to play a role in the success of the bone augmentation procedure. It has been

proposed, that intramembranous bone, has a better resistance towards bone resorption, shows better incorporation, becomes earlier revascularized and hence maintain volume and viability to a greater extent than endocondral bone (Alberius *et al.*, 1992; Rabie *et al.*, 1996; Smith and Abramson, 1974; Zins and Whitaker, 1983). On the other hand, it has been suggested that the revascularization process would be better in endochondral bone due to the difference in graft architecture. The endochondral bone graft consists mostly of cancellous porous bone, with marrow tissue in between the bone trabeculae in which the revascularisation easier can take part, while intramembranous bone consists of more densely packed cortical bone (Albrektsson, 1980; Sullivan and Szwajkun, 1991).

In papers I, II and IV, the majority of implant failures were early losses, since more than 90 % of the failed implants occurred before loading, which most likely could be related to the bone graft inability to integrate the implants. This may be explained by the biomechanical properties of the endochondral bone grafts as well as the healing capacity of the bone. Another negative factor could be the short healing period of the bone graft leading to an immature quality of the bone graft and thereby impaired osseointegration.

In papers I, II and IV, all bone grafted patients were treated with bone grafts from the iliac crest. It is possible to harvest large amounts of bone from the iliac crest, but postoperative morbidity with bruising, swelling, pain and functional problems from the donor site are occasionally seen. This approach may also produce a permanent cutaneous scar and the procedure usually involves general anaesthesia with days of hospitalization (Beirne, 1986; Cricchio and Lundgren, 2003; Raghoebar *et al.*, 1999).

The advantages of intra oral sitesfor bone harvesting, such as the mandibular ramus/body h, which was used in paper V, are the use of local anaesthesia, reduced operating time, no need for postoperative hospitalization and less morbidity at the donor sites (Clavero and Lundgren, 2003; Hirsch and Ericsson, 1991; Raghoebar *et al.*, 2001a).

Recent reports have been focusing on the morbidity after harvesting of bone from the mandibular symphysis region. Problems that include superficial sensory impairment with hyper and hypoesthesia and teeth that lost their pulp sensitivity have been described. These studies and others suggested that the morbidity when harvesting bone from the mandibular symphysis is more advanced than harvesting from the retromolar region (Hallman *et al.*, 2002; Hallman *et al.*, 2005; Nkenke *et al.*, 2001; Nkenke *et al.*, 2002; Raghoebar *et al.*, 2001a). According to earlier findings (Paper V), very few complications with

intra-oral bone harvesting occurred at the lateral ramus/corpus of the mandible. Paraesthesia of the inferior alveolar nerve was seen in one patient, who completely recovered after less then 2 months. There were no records of heavy bruising, bleeding or swelling from either the donor or the recipient site.

Different kinds of grafting material have been evaluated for maxillary sinus floor augmentation (Hallman *et al.*, 2005; Wiltfang *et al.*, 2003). Recently, Hallman *et al.* (2005) reported an implant survival rate of 86%, for implants placed in grafted areas after three years of prosthetic loading using a mixture of deproteinized bovine bone and autogenous bone in patients subjected to maxillary sinus inlay augmentation. One obvious advantage of using an allografts or xenografts in combination with or instead of autogenous bone is that a minor/no donor site is needed, since morbidity after bone harvesting, for instance on the iliac crest and chin, is not negligible. Paper V describes a bone grafting method that produces sufficient volume of bone with a minimum of per- and post-operative discomfort. Recently, several bone-collecting instruments have come on the market. The ”Bone Trap” is connected on the suction and bone chips created while drilling are collected (Widmark and Ivanoff, 2000). A so-called ”Safe Scraper” is a device that shaves the outer surface of the cortical bone at the recipient site or at the donor site and thereby creates a bone chips that can be used as graft material.

Lundgren *et al.* demonstrated bone formation in the maxillary sinus by creating a secluded compartment by elevating the sinus membrane, placing implants and replacing the bone window of the entrance through thelateral sinus wall according to the principle of guided tissue regeneration (Lundgren *et al.*, 2004; Palma *et al.*, 2006; Zuccati and Bocchieri, 2003). The studies showed that the maxillary sinus has agreat potential for healing and bone formation without the use of additional bone grafts or bone substitutes. The method revealed to be a predictable technique for bone augmentation of the maxillary sinus floor.

With an increasing demand for bone augmentation procedures it is important that uncomplicated techniques which results in a minimum of morbidity and predictable outcomes are developed and tested (Meskin and Brown, 1988; Weintraub *et al.*, 1985).

Implant surface and integration

Implants with rough surface are claimed to promote faster and earlier bone healing and thereby supposed to be more suitable for earlier loading than has been the standard for many years. Ivanoff *et al.* (2003), evaluated the human bone tissue response to two implant surfaces (oxidized or turned) (TiUnite,

Brånemark System). Surface roughness and enlargement were greater for the oxidized implants than for the turned implants. Histomorphometric evaluation demonstrated significantly higher bone-to-implant contact and bone response for the oxidized implants, placed in the maxilla or in the mandible and significantly more bone was found inside the threaded area for the oxidized implants placed both in the mandible and maxilla. The implants used in papers I, II and IV had all machined turned and minimally rough surfaces, which may also have contributed to the higher failure rate in grafted bone compared to the surface modified dental implant survival outcome in paper V. One could speculate that the longer implant healing periods in paper I and IV (mean: 8.8 and 7.2, respectively) were be appropriate since machined turned implants were used.

Histology of micro-implants has demonstrated a stronger bone response to surface modified implants as compared with turned implants (Ivanoff *et al.*, 2001; Ivanoff *et al.*, 2003) which confirms the findings from numerous animal investigations (Wennerberg, 1996). Brechter *et al.* (2005) evaluated 200 surface modified implants used in various bone reconstruction procedures. Of the 200 implants, 199 were considered osseointegrated at the time of abutment surgery. At the 12-month post-loading follow-up, another two implants were considered not stable. Thus, three implants (1.5%) were considered as failures. The same team had previously reported on a failure rate of 8% when using turned implants (Sjöström *et al.* 2005), which may indicate a better outcome with surface modified implants (Brechter *et al.*, 2005). Also the results in paper V, showed a similar low failure rate, which is different to the high early failure rates reported in papers I, II and III. However, comparative clinical trials are needed to statistically establish possible differences.

Nevertheless, rougher surfaces may have theoretical clinical drawbacks such as being more prone to marginal bone resorption and/or increased ion release which has been found in bone tissue in the surrounding area of titanium implants (Osborn JF, 1990) and it has been hypothesized that this could be damaging to osteogenesis (Tsutsui *et al.*, 1999).

The healing period

In paper I and II the majority of implant failures were early losses, since more than 90 % of the failed implants were lost before loading, which most likely could be related to the bone grafts inability to integrate the implants. Another factor for early implant failure in bone-grafted patients might be the poor bone to implant interface and its sensitiveness to trauma. It is thought, that

trauma interferes with early integration, a situation that is exacerbated due to a limited amount of bone at the interface of the implant and the host bone (Esposito *et al.*, 1999; Nystrom *et al.*, 1993). A heterogeneous interface with areas of highly vascularized connective tissue and portions of bone were described. Where bone was present, there was always evidence of bone detachment from the implant surface by erythrocytes due to bleeding. This could indicate that manipulation of the implants at the abutment surgery and during the restorative treatment phase, might cause bleeding due to mechanical disruption of the bone/implant interface (Aspenberg and Herbertsson, 1996). ”Reosseointegration” of implants with rotation mobility may be possible, if the implants are kept unloaded for a longer healing period but this situation is likely subject to further atraumatic healing (Aspenberg and Herbertsson, 1996; Ivanoff *et al.*, 1997).

Szmukler-Moncler *et al.* (Szmukler-Moncler *et al.*, 1998) reported that the critical level of micromotion on the implant was not zero as generally interpreted, instead, the tolerated micromotion threshold was found to lie somewhere between 50 and 150 microns. Above this level, healing would undergo fibrous repair rather than the desired osseous regeneration. However, in immediate functional loading, the implant survival is believed to be successful due to that a large number of implants are spread out, which creates a stiff and inflexible prosthesis that controls the forces applied to the bone-implant interface (Balshi *et al.*, 2005).

In paper II, aII patients were using a removable prosthesis in the maxilla during the healing period after the bone graft procedure and implant surgery prior to definitive prosthesis attachment. The results from this paper, suggest that the type of mandibular dentition, occlusion and bite force might be of significance for early implant failures. Occlusal loading during the healing period could result in inadequate tissue healing and thereby impaired osseointegration. Furthermore, according to a parallel study, it was revealed that also in edentulous maxillae without bone graft, the type of mandibular dentition, might be of significance to early implant failures (Abrahamsson *et al.*, 2003).

In a study with similar bone grafting and implant treatment procedures as used in our studies, the final survival rate was 88 % when special care was taken to minimize the occlusal trauma to the edentulous maxillae during the healing periods, by not using prostheses in the maxillae (Jensen *et al.*, 1994). In another study, a special splint was fabricated to prevent occlusal trauma to the anterior graft site during the first 2 –3 months of the healing period, and after

this a new removable prostheses was handed out, revealing a 80 to 90 % implant survival (Lundgren *et al.*, 1997).

The higher survival rate forthe grafted partially dentate patients in paper IV as compared with the edentulous patients in paper I, may be due to that no removable dentures were used in study IV. Moreover, in partially dentate patients occlusal forces on the definitive prosthetic construction are reduced and merely transferred to the natural dentition.

It has been suggested that fixed prostheses create a favourable force distribution to dental implants (Barzilay *et al.*, 1996; Randow *et al.*, 1999; Tarnow *et al.*, 1997). Applying this hypothesis to the edentulous maxilla, it may be prudent to consider fixed immediate loading of transitional implants in the labile bone of an autogenous graft rather than allowing force transmission through a provisional prosthesis that depends on the soft tissue of the residual ridge and the hard palate for retention, support and stability of the prosthesis. Further studies will be necessary before this routinely can be used clinically.

The correlation between bite force and implant failure during the healing period is not well described in the literature. It is known that the maximal bite force is greater with implant supported prostheses increases than with removable dentures. Carr and Laney (1987) reported a significant improvement of bite force in patients whom changed from conventional dentures to implant supported prostheses in the mandibular arch. The mean maximal bite force was 59.6 N in the case of conventional removable dentures and 112.9 N for the patients who had received a mandibular implant fixed prosthesis. These findings, together with the results of paper II, suggest that-the unfavourable concentration of forces and/or the magnitude of force could jeopardize the integration process of implants. Future studies addressing these issues may help to determine if there is an association between bite force and implant failures.

According to the findings of paper II, it seems reasonable to suggest that one causative factor for early implant failure might be the traumatic influence from the opposing arch during the healing period of bone-grafts and implants. The trauma caused by a provisional maxillary denture opposed by a mandibular dentition that creates force concentration rather than force distribution could induce further trauma to the maxilla.

Based on the observation that implant failure is higher when the opposing occlusion is not well distributed, it may be suggested that patients subjected to bone grafting and implant placement should refrain from wearing dentures during the healing period. Especially, if the mandibular dentition reveals a limited or unilateral occlusion. Another suggestion is to restore the mandible

to bilateral occlusion prior to bone grafting and implant treatment in the edentulous maxilla. This may ensure a broad distribution of teeth and stable occlusion, which should distribute forces favourably to the maxilla and thereby encourage implant survival. However, It is impossible to attribute the failure rates to the effect of mandibular dentition alone, as more uncontrolled and unknown parameters very well may play an additional role in implant failure.

Different outcomes may be expected when comparing edentulous and dentate jaws as discussed by Raghoebar *et al.* (2001b), who found a 97% survival rate in dentate and 90.8% survival in edentulous patients respectively. This is in line with paper IV, where an overall implant survival rate of 91.3% was found in 17 partially dentate patients, which indicated a better clinical outcome with bone grafting procedures in the partially dentate patient compared with totally edentulous cases as previously reported. Interestingly, in both paper I and IV, implant failure occurred mainly from abutment connection to delivery of the final prosthesis. This indicates that the implants were not well integrated and were sensitive to repeated manipulation when attaching and de-attaching abutments and impression copings during the prosthetic phase

It may be wise to place the implant deeper within the graft in an effort to avoid trauma to the implant from the provisional prosthesis. However, this will create a reduced cortical bone/implant contact with less favorable primary stability. It is possible that an internal space screw during the healing period, instead of the conventional cover screw, might have minimized the risk of trauma to the implant.

Alternative treatments to bone grafting

The use of alternative implant sites and tilted implants have been advocated to reduce the necessity of bone grafting procedures. The placement of dental implants in the zygomatic bone has been used in conjunction with regular implants in patients with severe resorption of the maxilla (Bedrossian *et al.*, 2002; Branemark *et al.*, 2004; Higuchi, 2000; Hirsch *et al.*, 2004; Malevez *et al.*, 2004). However, few studies include long-term evaluation of the soft and bone tissue reactions to zygomatic implants. In paper III, six out of 16 patients had been treated for recurrent sinusitis. Three of these patients had one zygomatic implant removed due to the infection in the maxillary sinus. Another alternative technique for bone grafting is the pterygomaxillary implant (Bahat, 1992; Balshi *et al.*, 1999; Tulasne, 1992). Sorni *et al.* (2005) reported, in a

review of the literature, a survival rate from 86.3% to 97.2 for the pterygomaxillary implant and reported of no major complications during implant surgery.

The objective of paper III was to evaluate the clinical outcome of zygomatic implant treatment in the severely atrophied maxilla as an alternative to bone grafting procedures in patients with edentulous maxillae. There were no adverse complications associated with the zygomatic implant surgery and all patients had an uneventful healing period after the implant placement until the abutment connection surgery, similar to conventional implant surgery. After the abutment connection surgery, the complications were at an unacceptable level. However, oral hygiene was a problem at the zygomatic abutment only. With help and instructions from a dental hygienist, most of the patients improved their oral hygiene. It seems that the posterior, palatal localization of the zygomatic implant creates difficulties in upholding hygiene and extra professional assistance may be required. Even though effort was made to place the zygomatic implant as close as possible to the alveolar crest, this was not possible to accomplish in this material due to the anatomy and degree of atrophy. The distance from the nearest buccal cusp on the prosthesis to the zygomatic implant, was measured with a mean distance of 11.2 mm and the zygomatic interimplant distance had an average of 21.7 mm. An optimal dental implant placement is often considered to result in a screw hole in the center of the prosthetic crown, which would mean 2-4 mm from the buccal cusp. Considering the localization of the zygomatic implant in this study, one can understand the difficulties, managing an optimal oral hygiene.

All zygomatic implants became osseointegrated and a survival rate of 100% would have been the case if not three zygomatic implants had been removed because of recurrent sinusitis. Nine (9/16) patients had problems with local infections at the periimplant site of their zygomatic implants with mucositis and/or fistulae, which is in line with the findings of other researchers (Table 1). The reason for the sinusitis observed in this study can be attributed to several factors. The internal threaded abutment screw chamber of the zygomatic implant seems to create a communication from the oral cavity into the maxillary sinus, which may result in sinusitis. Another causative factor may be the lack of osseointegration, bone-to-implant contact, at the marginal level in the palatal area and the functional loading, resulting in transversal mobility of the long coronal part of the zygomatic implant. This could implicate a higher risk of communication between the maxillary sinus and the oral cavity and thereby causing sinusitis. The prosthetic survival rate of 100% in this clinical report is encouraging for the treatment of this patient population. Treatment with the zygomatic implant in

extensive maxillary defects looks very promising and could, in some cases, be the only treatment solution (Parel *et al.*, 2001; Reichert, 1999; Schmidt *et al.*, 2004). However, the risk of soft tissue problems and sinusitis should not be underestimated, especially if other treatment options are at hand. Further prospective long-term clinical studies are required focusing on the health of the maxillary sinus. Zygomatic implant treatment is promising and has some advantages over bone grafting procedures. However, the frequent soft tissue complications at the abutment level and the development of sinusitis call for more studies.

In growing individuals who are lacking development of the alveolar process due to either trauma, congenital missing teeth, infra occluded teeth or other pathological conditions, autotransplantation to the affected region often is a very reliable treatment option in order to prevent extensive bone augmentation later. If the treatment is successful, the autotransplantated tooth, in connection with tooth eruption, will lead to continue development of the alveolar process (Zachrisson *et al.*, 2004). Furthermore in adults with loss of vertical bone height as a result of periodontal disease hard tissue grafting can be difficult to overcome. In subjects where the failing teeth or failed tooth is still present, an alternative method can be utilized to generate vertical bone height. Pre-implant orthodontic extrusion can be exerted on the hopeless tooth and thereby induce bone and soft tissue formation in the future implant site (Salama and Salama, 1993; Zuccati and Bocchieri, 2003).The same principle can also be used by moving remaining teeth into an atrophied alveolar crest, whereby new bone is formed behind the orthodontically translated tooth. Behind the translated tooth there often will be sufficient bone for implant installation without additional bone augmentation. This treatment approach is often indicated if the patient besides lacking teeth, also has a malocclusion

Reconstruction of the maxilla with distraction osteogenesis is a treatment option of choice. The method is new and the distraction osteogenesis devices are mostly very costly and are still under development. Case reports have shown promising results, however, the morbidity, cost, and time required for the treatment must be weighed against the benefits of alternative approaches (Jensen *et al.*, 2004; Laster *et al.*, 2005).

The placement of short implants could be one therapeutic option that reduces the need for augmentation therapy in the maxilla. In a retrospective study, it was demonstrated that the use of short implants may be considered for prosthetic rehabilitation of the severely resorbed maxilla as an alternative to more complicated surgical techniques (Renouard and Nisand, 2005).

Diagnostic imaging has grown in recent years and a specialized technique has become available for the preoperative planning of oral implant placement with the help of computer tomography. This imaging technology provides 3D and cross-sectional views of the jaws. This will provide us with information to plan a case more accurate and thereby decide in what degree bone grafting is needed (Guerrero *et al.*, 2006).

CONCLUSIONS

- There is a lower overall implant survival rate in grafted than in non-grafted maxillae after a mean follow-up period of 5 to 6 years. The majority of implant failures occur before prosthetic loading. It seems that the more jaw bone volume present in anterior regions at the start of treatment, the better the implant survival rates in both groups. Moreover, the implant survival rate is similar in grafted posterior edentulous maxillae of class V-IV and in non-grafted posterior edentulous maxillae of class III-IV.

- The type of mandibular dentition has an influence on the outcome of reconstructive surgery using endosseous implants and bone grafting in the edentulous maxilla. An unfavourable concentration of forces in the maxilla, such as in cases of an unilateral occlusal support, may contribute to the increased risk of implant failure. If grafting is required in the edentulous maxilla, every effort should be made to create a favourable occlusion in the mandible, with attention being paid to broad distribution of occlusal contacts.

- The zygomatic implant, when placed in conjunction with premaxillary implants, shows an acceptable outcome with regard to implant and prosthetic survival rates. However, other complications, such as sinusitis, not related to implant and prosthesis stability, may lead to the removal of zygomatic implants.

- The use of endosseous implants and sinus inlay block bone-grafts harvested from the iliac crest for reconstruction of the partially dentate maxilla results in a satisfactory clinical outcome after a mean follow-up of more than 4 years.

- The use of particulated manibular bone grafts for maxillary floor augmentation and delayed placement of surface modified dental implants results in low morbidity and few implant failures from placement to delvery of the final prosthesis.

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