

CLINICAL OUTCOMES OF THE NOBEL ACTIVE DENTAL IMPLANT SYSTEM  
AFTER ONE YEAR OF LOADING: A RETROSPECTIVE MULTICENTRE  
ANALYSIS

by

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## ABSTRACT

**Objective:** A retrospective review of charts was conducted to assess the survival rate and marginal bone loss around Nobel Active implants after one year of loading.

**Methods:** The study included 124 NobelActive dental implants that were placed by experienced practitioners in two private clinics and by senior Graduate Periodontics residents at the University of British Columbia. The effect of patient, medical condition, site, implant, surgeon's experience and timing related risk factors on implant survival and marginal bone loss was evaluated. Implant failure was defined as the loss or removal of an implant. Radiographic measurements of marginal bone loss (mm) were made using Image J 1.42 software and Planmeca Romexis 2.2.7R software. Bivariate analyses were used to identify variables associated with implant failure and marginal bone loss. Risk factors that were shown to be significant ( $p < 0.05$ ) or thought to be relevant in previous studies were included in stepwise linear multiple regression and logistic regression analyses.

**Results:** NobelActive implants demonstrated a survival rate of 94.4% with 7 of the 64 patients experiencing one failure. Variables considered risk factors did not have a statistically significant effect on failure. The average mean marginal bone loss of the mesial and distal measurements was  $0.89 \pm (0.95)$  mm during the follow up period of 12.9 months (range of 4-27 months). The bivariate analysis revealed smoking, insertion torque, anatomic location, previous bone augmentation and immediate loading as significant predictors of marginal bone loss. Significant correlations were observed between insertion torque and bone quality and insertion torque and anatomic location in terms of marginal bone loss. The multiple regression analyses identified predictors that had the largest impact on marginal bone loss, these included diabetes, smoking, anatomic location, immediate placement and immediate loading.

**Conclusions:** The short-term clinical outcomes of survival rate and marginal bone loss for NobelActive implants are similar to those reported in literature for currently validated implant systems. Variables considered risk factors did not have a statistically significant effect on implant failure, however diabetes, smoking, anatomic location, immediate placement and immediate loading did have a significant impact on marginal bone loss.

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## LIST OF ABBREVIATIONS

BIC	Bone-to-implant contact
CI	Confidence interval
CT	Computerized tomography
GBR	Guided bone regeneration
HA	Hydroxyapatite
HU	Hounsfield units
ISQ	Implant stability quotient
ITI	International team for implantology
OR	Odds ratio
PTV	Periotest value
RCT	Randomized controlled trial
RFA	Resonance frequency analysis
RR	Relative risk
SLA	Sandblasted, large-grit, acid-etched
TPS	Titanium plasma-sprayed



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## 1. INTRODUCTION

Since their introduction in 1965, implant supported dental prostheses have been shown to be a predictable and reliable treatment option for the rehabilitation of both partial and completely edentulous sites. Prospective long-term studies have demonstrated survival and success rates for several commercially available implant systems clearly exceeding 90% after five and ten years of function (Bornstein *et al*, 2008).

Unfortunately, despite the predictability of dental implants, a small but significant number of patients continue to experience implant failure (Moy *et al.*, 2005). As a result, the development of dental implants has been an evolving process based on scientific research, contribution by clinicians, and manufacturers' ingenuity. Implant designs with enhanced macroscopic and microscopic features are continually researched in order to achieve more predictable osseointegration and to shorter healing periods.

One new addition to the dental implant armamentarium, the NobelActive implant (Nobel Biocare, Zurich, Switzerland) was introduced by approximately two years ago with numerous reported advantageous properties due to its unique design features. It has a tapered body and a double-lead thread pattern with deep and widely spaced 35-degree threads emanating from a pair of sharp cutting blades at the apex (Appendix A). These properties enable the implant to cut through bone and actively change direction during insertion to obtain an optimal restorative orientation (NA Clinical Story, [www.nobelbiocare.com](http://www.nobelbiocare.com)). The tapered body design behaves like a threaded osteotome through the condensation of the surrounding bone during placement, a feature that is purported by the manufacturer to be beneficial to achieving higher primary stability in reduced bone conditions. Moreover, an inward tapered collar and built-in platform

shifting design should allow for marginal bone maintenance and soft tissue stabilization (Appendix B). Although the NobelActive implant can be used in most clinical situations, its key design characteristics allows for high levels of initial stability even in situations with low density or compromised bone, making it a good implant choice for immediate implant placement, and immediate load cases, as well as cases with less-than-ideal qualities and quantities of bone. These advantages should be beneficial for patients, however, clinical data regarding this novel implant system is lacking. This retrospective multi-centre analysis evaluates the clinical outcome of the novel NobelActive implant after one year of function. The impact of multiple patient, medical condition, site and implant design related factors on implant survival rate and marginal bone loss was evaluated. The success of implant therapy in terms of immediate placement and immediate loading was also examined. This article discusses the characteristics of the NobelActive implant in detail and employs case presentations to illustrate its clinical use.

## **2. REVIEW OF THE LITERATURE**

### ***2.1 Patient-related risk factors***

#### **2.1.1 Age**

The effect of age on implant success is of particular interest since a large majority of patients who receive implant treatment are older. A mean age of greater than 50 years has been consistently reported (Bornstein *et al*, 2008; Garcia-Bellosta *et al*, 2010; Lemmerman & Lemmerman, 2005). With age, alterations in mineral composition, collagen, bone morphogenic protein content, and bone conformation take place and may effect healing and implant success. In fact, delayed fracture healing and less tissue regeneration have been shown in the elderly (Hwang & Wang, 2007). Bone remodeling has been shown to be less efficient in older populations and older individuals were more likely to be completely edentulous, which was associated with lower implant success (Brocard *et al.*, 2000). A retrospective study, evaluating implant failures and associated risk factors for 1140 patients over a 21-year period using various implant systems reported that patients older than 60 years of age were twice as likely to have adverse outcomes (Moy *et al.*, 2005). A prospective report assessing implant treatment outcomes in 1022 Straumann implants over a period of seven years demonstrated that younger patient groups (<40 years and 40-60 years) had greater implant success rates than older groups (>60 years) (Brocard *et al.*, 2000).

Conversely, large retrospective studies have reported no statistically significant effect of age on implant failures after adjustment for other factors (Bornstein *et al.*, 2008; DeLuca *et al.*, 2006; Garcia-Bellosta *et al.*, 2010; Lemmerman & Lemmerman, 2005). Garcia-Bellosta *et al.* (2010) assessed 980 Astra Tech implants for 323 patients treated between 1994 and 2005; Bornstein *et al.* (2008) evaluated 1206 patients who received

1817 Straumann dental implants from 2001 to 2004 and DeLuca *et al.* (2006) assessed 464 consecutively treated patients with a total of 1852 implants placed between 1979 and 1999. Finally, Lemmerman and Lemmerman (2005), reviewed 1003 implants of various brands placed between 1987 and 2002 and followed them until 2003. Results of these retrospective studies were in agreement that age did not have a significant effect on implant survival.

A large majority of publications suggests that age does not have a significant effect on implant treatment outcomes. It's possible that age has been implicated in some studies because older individuals may have a greater tendency to experience significant systemic disease (osteoporosis, diabetes), higher incidence of periodontitis, and greater ridge resorption, which necessitates more complex bone grafting and prosthetic procedures in addition to implant placement. All of these factors may negatively impact implant treatment outcomes, and it may not be possible to separate age from these predictors due to their close association. With the refinement of implant designs, surface modifications and surgical techniques, the effect of older age on implant survival appears to be insignificant.

On the other hand, when placing implants in adolescents, one should be aware that because of the intimate bone apposition (osseointegration), which resembles ankylosis, these implants do not follow the spontaneous and continuous eruption of the natural dentition. Such implants may even disturb normal development of the jawbones (Hwang & Wang, 2007). In order not to interfere with the growth of the jawbones, and to prevent unfavourable final implant position if continued growth appears, installation of an implant should generally be postponed until cessation of growth. The most ideal

method of assessing growth status is not by chronological or even dental age, but by comparison of a skeletal film over time (hand-wrist or lateral cephalometric) (Hwang & Wang, 2007). Generally speaking, it is prudent to wait until the completion of skeletal maturation before implantation to avoid imperfect fixture positioning or stunted alveolar expansion that may occur if an implant is placed prematurely.

### **2.1.2 Gender**

Numerous large publications with long observation periods in addition to review papers have concluded that gender does not have a significant effect on implant success (Blanes *et al.*, 2007; Bornstein *et al.*, 2008; DeLuca *et al.*, 2006; Garcia-Bellosta *et al.*, 2010; Lemmerman & Lemmerman, 2005; Levin *et al.*, 2006; Moy *et al.*, 2005). An exception may occur in the case of post-menopausal women who have been found to have lower success rates, especially in the maxillary arch, an observation that may be attributed to bone density and osteoporosis (Moy *et al.*, 2005). However, evidence delivered by clinical studies pertaining to the association between implant survival and osteoporosis in post-menopausal women is equivocal. Some reports have demonstrated increased failure rates for implants placed in the maxilla of osteoporotic postmenopausal women without estrogen supplementation compared to pre-menopausal women (August *et al.*, 2001, Moy *et al.*, 2005), while other studies have demonstrated no difference in survival rates (Amorim *et al.*, 2007, Mellado-Valero *et al.*, 2010). The presence of osteoporosis in post-menopausal women does not preclude implant placement, however, the difference in bone metabolism and possible increased failure risk should be explained to the patient prior to treatment.

### 2.1.3 Diabetes

The replacement of missing teeth with endosseous implants for the rehabilitation of edentulous and partially edentulous jaws has become a standard of care in the last few decades. As a result, clinicians must consider medical conditions that affect bone metabolism or any aspect affecting the patients' capacity to heal normally. A more detailed analysis will be offered for diabetes, a frequently evaluated medical condition potentially affecting osseointegration, and for which implant therapy is not generally considered an absolute contraindication. Diabetes mellitus represents a heterogeneous group of metabolic disorders characterized by elevated blood glucose levels (Salvi *et al.*, 2008). Destructive autoimmune processes of the pancreatic B cells leading to insufficient insulin secretion are the main features of type I diabetes, whereas resistance of tissues to circulating insulin is the main feature of type II diabetes (American Diabetes Association, 2005). Type II diabetes may be preceded by the “metabolic syndrome” consisting of six parameters including obesity, dyslipidemia, insulin resistance, high blood pressure, and a pro-inflammatory and pro-thrombotic status (American Diabetes Association, 2005). Major systemic complications of diabetes such as retinopathy, nephropathy, neuropathy micro and macrovascular disease, and altered wound healing represent the result of a prolonged hyperglycemic state (Beikler & Flemmig, 2003). Mechanisms proposed for the influence of diabetes on biological responses to implant placement include impairment of bone healing response, reduction of vascular supply due to microangiopathies, decrease of host defense, formation of advanced glycation end-products (AGEs), reduction of collagen production, and increased collagenase activity (Fiorellini & Nevins, 2000; Kotsovilis *et al.*, 2006). In the oral cavity, diabetes mellitus is associated with xerostomia, increased levels of salivary glucose, caries and

periodontitis (Bornstein *et al.*, 2008).

A review of eleven experimental studies concluded that diabetic animals have an impaired bone healing response to implant placement as compared with non-diabetic controls, both quantitatively and qualitatively (Kotsovilis *et al.*, 2006). More specifically, animal studies have demonstrated that diabetes may be associated with less mature bone formation, a delayed healing response, and lower bone-to-implant contact (BIC) around implants (Gerritsen *et al.*, 2000; Giglio *et al.*, 2000). BIC was reported to be significantly lower in diabetic than in non-diabetic rats. However, twelve weeks after implant placement, the difference between diabetic and non-diabetic rats no longer reached statistical significance (Gerritsen *et al.*, 2000). In light of these findings, it may be reasonable to hypothesize that although the healing process in diabetic subjects may be delayed when osseointegration has been accomplished, BIC reaches comparable levels between diabetic and non-diabetic animals. Insulin therapy has been shown to upregulate the formation of bone around implants placed in diabetic rats, however, histometric parameters indicated that there was significantly less BIC in the insulin controlled diabetic group as compared to normal, non-diabetic controls (Fiorellini *et al.*, 1999). This report suggests that insulin therapy may reduce the retarding effects of diabetes on bone healing around implants in rats. It is noteworthy that Kotsovilis *et al.* (2006) cautioned the extrapolation of these findings to human populations prior to further clinical research.

In a systematic review, Bornstein *et al.* (2009) evaluated 18 articles related to the effects of diabetes on implant survival. Due to the heterogeneous nature of the data, a meta-analysis could not be performed, but the following trends were recognized: i) more



failures in diabetic patients occurred early ii) the percentage of diabetic patients experiencing failures seemed to be relatively high, but the percentage of failing implants appeared to be in the normal range. Diabetic patients generally had well-controlled blood glucose levels, at least before and immediately after implant therapy. No unequivocal overall tendency emerged for subjects with diabetes to have higher failure rates (Bornstein *et al.*, 2009). However, it is noteworthy that the largest study included, a retrospective cohort analysis by Moy *et al.*, indicated a statistically significant relative risk of 2.75 for increased implant failure in diabetes. They included 48 diabetic and 1092 non-diabetic patients treated over 21 years (Moy *et al.*, 2005). It is interesting to note that studies finding greater failures in diabetics were generally associated with the uncovering of implants and the early phase of loading (Bornstein *et al.*, 2008; Fiorellini & Nevins, 2000). These findings are supported by animal studies that demonstrated initial delayed healing and lower BIC in diabetic, versus non-diabetic rats, a difference that was no longer statistically significant at twelve weeks (Gerritsen *et al.*, 2000; Giglio *et al.*, 2000). It is possible that the microvascular disease leading to a diminished immune response and reduced bone turnover might be a contributing factor to implant failure (Olson *et al.*, 2000).

Conversely, a large retrospective analysis in which 2004 subjects were treated with 6946 implants demonstrated diabetes had no apparent influence on 252 implant failures that occurred in 178 patients (Alsaadi *et al.*, 2007). Unfortunately, very few reports include information on complications associated with diabetic patients. In a cross-sectional study of 212 subjects with 578 implants, Ferriera *et al.* (2006) analyzed the risk factors associated with peri-implant disease. In diabetic patients (n=29), peri-

implant mucositis was diagnosed in 59% of cases and peri-implantitis in 24%. In subjects with no diabetes, the prevalence of mucositis was similar (66%), but peri-implantitis was significantly lower (7%). Poor metabolic control in diabetic subjects did not present a statistically significant association with peri-implant mucositis; however, these subjects did present a higher risk of developing peri-implantitis. (Ferreira *et al.*, 2006). These results indicate that diabetics may be more prone to greater marginal bone loss. These patients should therefore be informed of the greater risk of peri-implant complications with implant treatment. A regiment of good oral hygiene must be implemented prior to, and following placement of dental implants in order to minimize the risk of developing peri-implant disease in diabetic patients.

In their review article, Beikler and Flemmig (2003) outline some considerations for diabetic patients undergoing implant therapy: i) glycemic control should be reassessed and optimized prior to implant surgery ii) the practitioner should be experienced in managing possible peri- and post-operative complications iii) chlorhexidine digluconate (0.12%) should be used peri-and post-operatively iv) antibiotics should be prescribed with the first dose given preoperatively. The American Diabetes Association recommends an HbA1C level of approximately 7.0% in patients with type II diabetes (American Diabetes Association, 2005). The efficacy of chlorhexidine rinse has been well documented in literature. Rinsing with chlorhexidine after implant placement improved survival rate by 9.1% (13.5% to 4.4%) in type II diabetic patients as compared to 2.5% in non-diabetic controls (Morris *et al.* 2000). Furthermore, pre-surgical antibiotic treatment improved survival rates by 10.5% in diabetic patients as compared to only 4.5% in control groups (Morris *et al.*, 2000).

Literature regarding the effect of diabetes on implant failure is inconclusive, however, some studies have shown a greater tendency towards more early failures in diabetic patients (Bornstein *et al.*, 2008; Fiorellini & Nevins, 2000). These findings are in agreement with animal studies that demonstrated significantly delayed initial healing and lower BIC in diabetic, versus non-diabetic rats; a difference that was no longer significant at twelve weeks (Gerritsen *et al.*, 2000; Giglio *et al.*, 2000). In addition, a greater risk of peri-implant complications in diabetic patients has been reported (Ferreira *et al.*, 2006). Since diabetic patients may be at greater risk for implant failure during the osseointegration phase, precautions should be taken by the practitioner to limit this risk by ensuring that patients are well-controlled, and that post-operative infection is minimized. Patients should be made aware of current literature results so that control of the disease and oral hygiene are maintained at an optimal level to limit the risk of peri-mucositis and peri-implantitis.

#### **2.1.4 Smoking**

The deleterious effect of smoking on wound healing, rate of tooth loss, alveolar ridge resorption, bone quality, and periodontal disease has been well documented (Levin & Schwartz-Arad, 2005; van Steenberghe *et al.*, 2002). Heat as well as toxic by-products of cigarette smoking, such as nicotine, carbon monoxide, and hydrogen cyanide, have been implicated as risk factors for impaired healing (Levin & Schwartz-Arad, 2005). The vasoconstrictive action of nicotine, increased platelet aggregation and adhesiveness, increased levels of fibrinogen and blood viscosity, and decreased polymorphonuclear neutrophil function are all possible mechanisms leading to impaired wound healing (van

Steenberghe *et al.*, 2002). Smoking has also been shown to adversely affect bone mineral density (Porter & Hanley, 2001).

Jones and Triplett (1992) first documented an association between smoking and implant failures. The following year, Bain and Moy (1993) reported that smoking is a risk factor for osseointegrated implant failure. The overall failure rate of 5.92% was consistent with other studies, however, when patients were subdivided into smokers and nonsmokers, it was demonstrated that a significantly greater percentage of failures occurred in smokers (11.28%) than in nonsmokers (4.76%). Three systematic reviews evaluating the effects of smoking on implant survival found smoking to be a significant predictor of implant failure. A meta-analysis of 19 studies revealed a significant increased risk for implant failure among smokers compared to non-smokers (OR=2.17) (Hinode *et al.*, 2006). In another systematic review that combined the results of 29 studies in a meta-analysis, a significantly increased risk of implant failure was reported among smokers, both for implant-related (OR 2.29) and patient-related (OR 2.64) data compared to non-smokers. Furthermore, smokers receiving implants with accompanying bone augmentation procedures also had an increased risk of failure compared to non-smokers (OR 3.61) (Strietzel *et al.*, 2007). Finally, a meta-analysis of 14 articles revealed a pooled estimate of 89.7% for implant survival in smokers as compared to 93.3% in non-smokers. The pooled estimate for implant success was 77.0% in smokers as compared to 91% in non-smokers (Klokkevold & Han, 2007). A greater implant survival was reported for non-smokers than for smokers with implants placed in soft bone (7.43% difference). The authors concluded that the effect of smoking on implant survival seems more pronounced in soft bone (Klokkevold & Han, 2007). It is noteworthy that

the majority of studies included implants with turned or moderately rough surfaces. Moy *et al.* (2005) retrospectively evaluated 4680 implants over a 20-year period (1982-2003) and found smoking to be a significant predictor of implant failure with a relative risk of 1.56. Smokers had a failure rate of 20% with most failures occurring within the first year (Moy *et al.*, 2005).

Early failure rates, prior to loading, were evaluated by De Bruyn and Collaert, who reported early implant failure of 9% in smokers versus 1% in nonsmokers when evaluating 462 Branemark fixtures. All failures occurred in the maxilla and in 31% of the smokers, despite reports of excellent bone quality, long fixture length, or good initial stability (De Bruyn & Collaert, 1994). Van Steenberghe *et al.* (2002) also reported significantly more early failures in smokers compared to non-smokers. A large prospective study showed no influence of smoking on early implant failure (placement to uncovering), but found more failures in smokers in the time between uncovering of the implant and before insertion of the prosthesis (Lambert *et al.*, 2000). It was suggested that smoking is not associated with an inability to attain osseointegration, but rather an inability to maintain it (DeLuca *et al.*, 2006).

It has also been demonstrated that the maxilla may be more susceptible to cigarette smoke than the mandible (De Bruyn & Collaert, 1994; Klokkevold & Han, 2007; Lambert *et al.*, 2000). One study found that in smokers, maxillary implants failed 1.6 times more often than mandibular implants; it was postulated that this was not the result of poor healing or osseointegration, but rather a result of peri-implant tissue exposure to tobacco smoke (Lambert *et al.*, 2000). Following evaluation of 1263 Branemark implants, lower success rates were demonstrated in the posterior maxilla

(91.4%) as compared to the anterior maxilla (97%), posterior mandible (96.3%), and in the anterior mandible (97.9%) (van Steenberghe *et al.*, 2002). Moreover, implants placed within the maxilla experienced almost twice the failure rates as those in the mandible, with the anterior mandible having the lowest failure rate (Moy *et al.*, 2005). Bain *et al.* (1993) indicated that the prevalence of Type IV bone was twice as high among heavy smokers as compared to nonsmokers or even light smokers. This view was supported by a systematic review that demonstrated a statistically significant increase in implant failure in the maxillary arch (OR 2.06) in smokers as compared with non-smokers; the mandibular arch did not show any difference (OR 1.32) (Hinode *et al.*, 2006). Factors contributing to higher implant failure rates in the maxillary arch are not well understood, however, the findings do suggest that bone density may have some effect on the unfavourable outcomes. Aside from reported lower density in the posterior maxilla, tissues in this area may be more susceptible to the local influence of tobacco smoke than in the mandible, which is protected by the tongue.

The quantity and duration of cigarette smoking has been associated with a significantly higher incidence of implant complications and failure rates (Bain & Moy, 1993; DeLuca *et al.*, 2006; Levin & Schwartz-Arad, 2005; Mundt *et al.*, 2006). A dose-response effect between the duration of smoking and implant failure has been demonstrated with 15.0% failures in screw-type tapered implants among current smokers, 9.6% among former smokers, and 3.6% among non-smokers (Mundt *et al.*, 2006). Higher failure rates for former smokers and a dose-response effect suggested that permanent tissue damage from smoking may occur in addition to immediate local and systemic effects. Van Steenberghe *et al.*, (2002) found nearly 30% of early implant

failures occurring in patients who smoked, with one out of five patients smoking greater than ten cigarettes a day.

It appears that the implementation of smoking cessation programs may improve implant survival rates in smokers. A cessation protocol introduced by Bain in 1996, dictated complete cessation for one week before and eight weeks after initial implant placement. Smokers had 1.69 times higher incidence of early implant failures compared to patients who had never smoked or who had stopped smoking at least one week prior to and eight weeks following implant surgery (Bain, 1996). It is noteworthy that numerous patients in the cessation program never resumed smoking, therefore the results of this study may be misrepresented.

Although numerous reports have indicated smoking as a risk factor for implant failure, several studies have shown no significant differences between smokers and non-smokers (Alsaadi *et al.*, 2008; Bain *et al.*, 2002; Blanes *et al.*, 2007; Brocard *et al.*, 2000; Grunder *et al.*, 1999; Lambert *et al.*, 2000; Lemmerman & Lemmerman, 2005; Machtei *et al.*, 2006; Schwartz-Arad *et al.*, 2002; Sverzut *et al.*, 2008). The improvement is likely attributed to the surface-modifications on the dental implants, which render them less susceptible to the effects of smoking. Feldman *et al.* (2004) reported a 9% difference in five-year survival rate in the maxilla between machined-surfaced short-length (86.8%) and dual acid-etched short-length implants (95.8%). Balshe *et al.* (2008) evaluated the effects of smoking on smooth and rough surface implants and only found a significant association with failures in smooth-surface implants. In addition, anatomic location only affected the implant survival among smokers with smooth-surface implants. Implant survival was the poorest when placed in the maxillary posterior areas of smokers (Balshe

*et al.*, 2008). A systematic review by Bain *et al.* demonstrated that in smokers, the success rate was 93.5% with smooth surface implants and 98.7% with rough surface implants. There were no significant differences in implant failure rates among smokers and non-smokers (Bain *et al.*, 2002). This view has been challenged by Hinode *et al.* (2006) who claims that if the data is evaluated using the synthesized odds ratio estimates, a significant risk of implant failure does exist for smokers (OR=2.17).

Despite the fact that the effect of smoking on implant failures is discordant, its association with implant complications appears undisputed. Increased peri-implant marginal bone loss (Cochran *et al.*, 2009; Heitz-Mayfield & Huynh-Ba, 2009; Kan *et al.*, 2002; Levin & Schwartz-Arad, 2005; Nitzan *et al.*, 2005; Strietzel *et al.*, 2007) and reduced success rates of bone grafts (Kan *et al.*, 2002; Strietzel *et al.*, 2007) have been documented in smokers. In a recent consensus statement, it was stated that strong evidence exists for smoking as a risk factor for adverse implant outcomes. Smokers were reported to have an increased risk of peri-implantitis (OR 3.6-4.6) and radiographic marginal bone loss (OR 2.2-10) compared to non-smokers (Cochran *et al.*, 2009). A review article demonstrated that of 22 studies evaluating marginal bone loss, 18 reported a statistically significantly greater risk of bone loss over time in patients who smoked. Odds ratios for progressive bone loss ranged from 1.95 to 10 in smokers over a period of 1-24 years (Heitz-Mayfield & Huynh-Ba, 2009). Levin and Schwartz-Arad (2005) reported that in the maxilla, heavy smokers (> ten cigarettes/day) had the highest amount of marginal bone loss, followed by light smokers (< ten cigarettes/day) and non-smokers. In the mandible, there was no distinction between heavy and mild smokers, and both had higher marginal bone loss than non-smokers (Levin & Schwartz-Arad, 2005). Studies on



guided bone regeneration (GBR) have shown a significantly enhanced risk of implant failure in grafted sites (Strietzel *et al.*, 2007) and greater complications associated with graft or barrier membrane exposures requiring partial or complete graft or membrane removal in smokers (Levin & Schwartz-Arad, 2005). A meta-analysis assessing the effects of smoking on implants placed in bone augmentation sites, found a significantly greater risk of implant failure in smokers versus non-smokers (OR 3.61 vs 2.15 respectively) (Strietzel *et al.*, 2007). Moreover, complications following lateral window sinus augmentation procedures occurred in 23.2% of smokers versus 6% of non-smokers (Levin & Schwartz-Arad, 2005).

The negative effects of smoking on immediate placement and immediate loading protocols have also been demonstrated. Schwartz-Arad *et al.* (2002) evaluated the effect of smoking in patients who received immediate and delayed implant placement (288 and 671 implants, respectively). More complications were reported in smokers than in non-smokers, regardless of the time of implant placement, and a significantly higher incidence of complications were found among smokers who received immediate implants as compared with smokers who received delayed implants. Sanna *et al.* (2007) evaluated flapless implant placement and immediate loading of the edentulous jaws with fixed complete dentures over a five-year period. Lower implant survival rate and greater marginal bone loss was reported in smokers (defined as > ten cigarettes per day) as compared to non-smokers. The cumulative survival rate (CSR) was 98.9% for smokers and 81.2% for non-smokers. The mean marginal bone resorption was 2.6 mm and 1.2 mm in smokers and non-smokers, respectively (Sanna *et al.*, 2007).

While cigarette smoking is not an absolute contraindication for implant placement, smokers should be informed that there is an increased risk of complications with grafting procedures and peri-implantitis. The diminished wound healing in smokers cannot be disregarded, but studies have demonstrated improved survival rates for smokers when rough-surfaced implants are placed in good quality bone and when good oral hygiene practices are maintained. A smoking cessation protocol should be recommended prior to treatment and a strict recall regime maintained to ensure early detection of negative changes of peri-implant tissues or implant failure.

## **2.2 Implant design-related factors**

### **2.2.1 Macroscopic design features**

The macroscopic design of an endosseous implant refers to its three dimensional structure, with all the elements and characteristics that compose it. The shape or outline of the implant, the presence or absence of threads, additional micro and macro-irregularities, and the prosthetic interface are considered some of the most important aspects of implant design (Steigenga *et al.*, 2003). Endosseous implants can be categorized into cylindric, press-fit or screw-shaped, with threaded or non-threaded designs. They can be hollow or solid, with a parallel, tapered, or conical shapes and have flat, round or pointed apical portions (Sykaras *et al.*, 2000). Implant companies have been using a plethora of additional features such as vents, grooves, flutes, indentations, and perforations to accentuate or replace the effect of threads (Sykaras *et al.*, 2000). The shape of the implant determines the surface area available for stress transfer and governs the initial stability of the implant (Misch *et al.*, 2004b; Steigenga *et al.*, 2004). Although

microscopic surface features allow for greater BIC percentage during initial healing, the functional surface area over which loads are effectively dissipated to the surrounding bone during long-term loading is most dependent on the macroscopic design (Misch, 2006a).

The original Branemark endosseous implant, introduced in 1965, had a machined, threaded screw shape (Branemark *et al.*, 1977). This design has been modified over the years to allow for more efficient placement, better load distribution and greater BIC (Steigenga *et al.*, 2003). In the 1970s, the International team for implantology (ITI) introduced cylindrical implants, which have evolved through generations of implant designs ranging from symmetrical hollow cylinder, hollow screws, and the latest most commonly installed implant, the full-body screw (Karoussis *et al.*, 2004). Initially, it was thought that the hollow geometry would confer greater BIC and favour in growth of bone to offer additional fixation (Karoussis *et al.*, 2004). High initial rates of success were noted with cylinder implants, however, after five to ten years of loading, reports indicated significantly lower survival rates and higher incidence of biological complications with the hollow cylinders versus the hollow screws. The ten-year survival rates were 85.7% and 95.4% for hollow cylinders and hollow screw implants respectively (Karoussis *et al.*, 2004). Other long-term studies on over 1000 ITI implants have demonstrated similar trends with greater survival rates for solid-screw implants versus hollow screws and cylinders (Brocard *et al.*, 2000; Buser *et al.*, 1997).

Currently, most implant companies seem to have some variation of a screw-shaped, threaded implant. Threads are used to maximize initial contact, improve initial stability, enlarge implant surface area and facilitate dissipation of loads at the bone-

implant interface (Huang *et al.*, 2007; Strong *et al.*, 1998). The implant design has a greater impact on functional surface area than implant size (Strong *et al.*, 1998). Thread depth, thickness, pitch, face angle and helix angle are some of the varying geometric patterns that determine the functional thread surface and that affect the biomechanical load distribution of the implant (Misch, 2006a). Cylinder implants were shown to provide 50% less surface area than a conventional threaded implant of the same length and width (Strong *et al.*, 1998). Moreover, a threaded implant with ten threads per ten mm in length has more surface area than one with five threads (Strong *et al.*, 1998). Finally, a thread depth of 0.2 mm provides less surface area than an implant with 0.4 mm thread depth. Hence, one threaded implant may have more than 2 times the overall functional surface area, when compared with other implants of similar length and width (Strong *et al.*, 1998). Therefore, it appears that a greater number and depth of the threads is proportional to a greater functional surface area. Watzak *et al.* (2005) evaluated screw-shaped and cylinder implants histologically and found a higher BIC and more organized trabecular pattern for threaded implants as compared to cylindrical implants in the maxilla.

It has been hypothesized that implant design may play a role for the preservation of peri-implant marginal bone (Rieger *et al.*, 1989). Finite-element studies have demonstrated that cylindrical, stepped, tapered and screw-shaped implant designs yield variations in stress distribution *in vitro*, and greater strain concentrations at the implant neck may be associated with greater crestal bone resorption (Rieger *et al.*, 1989). Bone is strongest in compressive and weakest in shear loading; its been shown that compressive forces decrease the microstrain to the bone implant interface as compared to shear force

type transfers (Steigenga *et al.*, 2004). Besides providing an increased surface area, threaded implants have also been shown to convert occlusal loads into more favourable compressive loads at the bone interface as compared to less favourable shear forces around cylindrical implants (Steigenga *et al.*, 2004). For cylindrical implants, horizontal loading induced maximum strain in the crestal aspects, while for screw-shaped implants, maximum strain is concentrated in the regions below the uppermost threads (Rieger *et al.*, 1989; Rieger *et al.*, 1990). Furthermore, a tapered implant design can decrease stress by up to 32% in the cortical region and 17% in the trabecular region (Huang *et al.*, 2007). In addition to decreasing crestal strain, tapered implants have the additional advantages of placement in narrower apical sites and decreased risk of apical bone fenestrations (Huang *et al.*, 2007).

Platform shifting is another method devised to preserve the peri-implant marginal bone around endosseous implants. Following the abutment connection, crestal bone may move 1.3 mm to 1.4 mm away from the microgap in a horizontal direction (Tarnow *et al.*, 2000). It has been demonstrated that placing an abutment with a smaller diameter on wider diameter platforms, a concept called platform shifting, can defer the microgap from the crestal bone and confer beneficial effects on the bone remodeling around the implant (Gardner, 2005; Vela-Nebot *et al.*, 2006). By altering the horizontal position of the microgap, platform switching can be used to reduce bone loss after abutment placement (Gardner, 2005). Platform shifting may reduce the risk of soft tissue recession often seen around dental implants (Rompen *et al.*, 2007). Two different mechanisms have been hypothesized to contribute to the success of platform shifting: 1) the increased length of the soft tissue-to-implant interface stabilizes the connective tissue adhesion and, in turn,

the marginal bone (Rompen *et al.*, 2007) and 2) crestal bone height is stabilized by increasing the distance between the abutment-implant interface and the bone-implant interface. This defers the microgap biofilm away from the bone-implant interface, thereby reducing the risk of local inflammation when comparing implants restored conventionally with prosthetic components with matching diameters (Gardner, 2005; Lazzara & Porter, 2006). A three-dimensional finite element analysis has indicated that platform-shifting has the biomechanical advantage of shifting the stress concentration area away from the cervical bone-implant interface (Maeda *et al.*, 2007). Unfortunately, it also has the disadvantage of increasing stress in the abutment or abutment screw (Maeda *et al.*, 2007).

### **2.2.2 Microscopic design features**

Dental implant surface technology has been evolving rapidly with the aim of achieving a more rapid bone formation on the implant surface and to increase the predictability of expedited implant therapy. Implant surface microtopography can influence wound healing, the rate of lamellar bone formation, and the percentage of bone contact (Misch *et al.*, 2004b; Sykaras *et al.*, 2000). The excellent biocompatibility of titanium (most commercially pure titanium (cpTi) and Ti-6Al-4V alloy) is attributed to the stable oxide layer (TiO<sub>2</sub>), that spontaneously forms when titanium is exposed to oxygen (Puleo & Thomas, 2006). This layer increases calcium deposition and the consequent primary adsorption of adhesive proteins (ie: glycosaminoglycans or albumin), one of the most important events of the initial phase of osseointegration (Avila *et al.*,

Traditionally, the term ‘machined’ has been used to describe turned, milled or

polished surfaces (Puleo & Thomas, 2006). These surfaces were most popular in the 90's with Branemark implants (Nobel Biocare, Zurich, Switzerland). With careful selection of patients and anatomical sites, meticulous surgical technique and delayed loading, this system has shown excellent survival rates. In the mandible, success at five to eight years exceeded 99% and was approximately 85% in the maxilla (Albrektsson, 1998). Although Branemark implants have been documented to perform well in humans, implants with different surface characteristics continue to be developed in attempts to increase the degree and rate of osseointegration, to allow early and immediate loading, and to promote integration in anatomic sites with poor bone quality or insufficient bone quantity for conventional implants.

Roughened surfaces have been shown to demonstrate a number of advantages over machined, including increased surface area for bone-to-implant contact to offer increased mechanical stability at insertion, retention of the blood clot after placement, stimulation of the wound healing process, and a faster rate and higher degree of bone formation (Morand & Irinakis, 2007). Roughened surfaces are also associated with increased interfacial strength, measured by reverse (or removal) torque testing, as compared to traditional smooth titanium surfaces (Gotfredsen *et al.*, 2000). Methods for altering surface texture to produce a 'rough' surface can be classified as either ablative, which removes material from the surface (grit-blasting, acid-etching) or additive (plasma-spraying, hydroxyapatite) (Puleo & Thomas, 2006). Puleo and Thomas described the surface preparation of some of the most commonly used implant systems available. The TiUnite surface (Nobel Biocare, Zurich, Switzerland), formed by anodically oxidizing titanium in a proprietary electrolytic solution, results in an increased thickness of the

oxide layer and a porous surface topography that provides increased surface area (Puleo & Thomas, 2006). Dual acid-etching (DAE) of titanium in a solution of hydrochloric acid and sulfuric acid results in microrough surfaces, a technique used with the Osseotite Implant System (Implant Innovations, Inc. (3i)). The sandblasted, large-grit, acid-etched (SLA) surface of implants from Institut Straumann (Basel, Switzerland) depict a macroroughness from sandblasting onto which acid etching superimposes microroughness. The recently developed SLActive surface uses the same initial manufacturing process as SLA, but is then conditioned in nitrogen and immediately preserved in an isotonic saline solution. SLActive surface is hydrophilic, and is purported to quickly attract blood and proteins, potentially promoting the process of bone formation around the implant and giving it increased early stability (Bornstein *et al.*, 2008).

Titanium plasma-sprayed (TPS) implants are prepared by first heating the titanium particles to a nearly molten state and then spraying them at the substrate via an inert gas plasma. The resultant surface texture is quite irregular and rough with relatively greater void volume into which bone can grow. By coating implants with hydroxyapatite (HA) through the method of plasma spraying, both the roughness and surface chemistry are altered. The surface chemistry is dramatically changed from TiO<sub>2</sub> to a bone-like ceramic with the potential for chemically bonding to bone (Puleo & Thomas, 2006).

In a Cochrane systematic review, a meta-analysis demonstrated no evidence of any particular type of rough surface implant having better long-term success (Esposito, *et al.*, 2005). Other studies, however, have shown cause for concern with TPS implants because titanium particles have been detected in peri-implant tissues, which have been associated with greater peri-implantitis (Franchi *et al.*, 2004). An eight-year retrospective



study that compared implant survival of TPS implants (889) versus HA-coated implants (313) (Wheeler, 1996). Cumulative survival rates were 92.7% and 77.8% for TPS and HA-coated systems, respectively. HA implants favor an early chemical interaction between the implant surface and bone, but these implants were associated with greater ‘late’ failures, presumably due to resorption of the material and detachment of the implant; as a result they are not commonly used anymore (Wheeler, 1996).

The increase in surface area may be the most valuable factor of altered surface topographies, since the opportunity for osseointegration at the bone-implant interface is greatly increased. Such an increase in area may compensate for the use of shorter or narrow diameter implants in areas where conventional implants are impossible to place (Morand & Irinakis, 2007). Numerous studies demonstrate greater survival rates with rough implants as compared to those with machined surfaces (Bain *et al.*, 2002; Balshe *et al.*, 2008; Balshe *et al.*, 2009; Misch, 2006a; Rocci *et al.*, 2003b). Considering the patient as the unit for the analysis, there was no statistically significant difference for early failures between the implants with turned and roughened surfaces, though trends clearly favoured implants with roughened surfaces. (Esposito *et al.*, 2005). There is limited evidence, however, for decreased incidence of peri-implantitis around smooth (ie, machined) implants compared to implants with rougher surfaces. Rough surfaces, particularly TPS surfaces exposed to the oral environment, can favor the accumulation of plaque, which can lead to peri-implantitis (van Steenberghe *et al.*, 1999). A meta-analysis evaluating the presence of peri-implantitis between turned and roughened surfaces indicated a borderline statistically significant difference for the occurrence of peri-implantitis between implants with turned and roughened surfaces. More implants

with rough surfaces were affected by peri-implantitis (risk ratio (RR) 0.80; 95% CI 0.67 to 0.96). Implants with turned surfaces had a 20% reduction in risk of being affected by peri-implantitis (Esposito *et al.*, 2005).

The continual advancements in surface microscopic features for implants have transformed dental implantology. With the advent of newer surface modifications, implant treatment time has been drastically reduced, allowing for more predictable survival rates in shorted treatment protocols, such as immediate placement and loading. These improvements also have exciting implications in reducing the compromising effects of systemic disease, smoking and reduced bone density.

### **2.2.3 Implant dimensions**

#### **Length**

Despite the high success rates of endosseous oral implants, restrictions have been advocated to their placement in areas of reduced alveolar bone height due to anatomical limitations posed by the inferior alveolar nerve and the maxillary sinus. These restrictions can be overcome with the use of short implants (<10 mm), for which the advantages are numerous. Their use can preclude the need for extensive bone grafting and sinus augmentation prior to implant placement, thereby reducing treatment time, expense and patient morbidity (Misch, 2005; Morand & Irinakis, 2007). The implant angulation may be improved, since the basal bone beyond the original alveolar ridge for longer implants is not always in the long axis of the missing tooth, and finally, the potential for overheating the bone is less, since irrigation has a direct access in a shorter osteotomy site (Misch, 2005; Misch *et al.*, 2006).

Considering the possible advantages of short implants, it is highly relevant to examine if implant length has an effect on implant failure rates and complications. Renouard and Nisand (2006) reviewed literature from 1990-2005 to examine the association between implant length and failure rates. A relatively high number of published studies indicated an increased failure rate with short implants ( $\leq 10$  mm) (Bahat, 1993; Bahat, 2000; Grunder *et al.*, 1999; Jemt & Lekholm, 1995; Naert *et al.*, 2002; Weng *et al.*, 2003; Winkler *et al.*, 2000; Wyatt & Zarb, 1998). Similarly, Misch *et al.* (2006) reviewed the literature from 1991-2003 examining short implants and found the average success rate reported in the literature was 85.3% for 2837 implants. It was noted that the higher failure rates reported in older studies were often performed with routine surgical procedures independent of the bone quality, with machined-surfaced implants, and in restricted anatomic sites with poor bone density (Renouard & Nisand, 2006). Misch *et al.* (2006) postulated that earlier complications with short implants may have been attributed to greater crown heights (unfavourable crown root ratio), excessive bite forces in the posterior regions, and again, less bone density.

More recent publications, which utilize adapted surgical preparations for different bone densities and new implant designs with textured surfaces that increase surface area, have demonstrated that the survival rates for short implants are comparable to their longer counterparts (Blanes *et al.*, 2007; Brocard *et al.*, 2000; Feldman *et al.*, 2004; Fugazzotto, 2008; Lemmerman & Lemmerman, 2005; Malo *et al.*, 2007b; Misch *et al.*, 2006; Morand & Irinakis, 2007; Renouard & Nisand, 2006; Romeo *et al.*, 2004; Romeo *et al.*, 2010). Renouard and Nisand noted that articles dedicated to short implants published from 2003 to 2005 have reported survival rates ranging from 94.6–99.4%. In

his own retrospective report, Misch *et al.* (2006) evaluated 745 short implants placed in the posterior mandible and maxilla in partially edentulous patients between 1998 and 2004. One implant per tooth was used in independent posterior restorations and multiple implants were always splinted. The survival rate was 99.6% for implants that had a two-stage surgical approach and 98.3% for those with a one-stage approach indicating that implant length was not a factor in survival over the six year observation period. Splinted implants with no cantilever load, mutually protected or canine-guided occlusion, and implant design that optimizes bone-implant contact were suggested as factors for success with short implants (Misch *et al.*, 2006). Increasing the implant number and splinting increases functional surface area and transmits less stress to each of the bone-implant interfaces in the splint (Misch *et al.*, 2006). In another retrospective study, 408 short machined and oxidized implants were placed using one-stage protocol and restored with splinted, fixed prostheses (Malo *et al.*, 2007b). Survival rates after five years were 96.2% and 97.1% for 7.0 and 8.5 mm implants, respectively. All implant losses occurred during the first six months of healing, before prosthetic loading, and all had machined surfaces; a 100% survival was found for the rough surface implants (Malo *et al.*, 2007b). Finally, a retrospective study of patients treated between 2000 and 2007, demonstrated survival rates of 98.1% to 99.7% for 2073 short implants (6 to 9 mm) in function over a 73 to 84 month period (Fugazzotto, 2008). The survival rate of implants supporting single crowns placed in the posterior mandible and maxilla ranged from 98.1% to 99.2% and for those supporting fixed partial dentures was 98.0% (Fugazzotto, 2008). This study demonstrated excellent survival rates for unsplinted single crowns in the posterior mandible and maxilla, indicating that splinting may not be a critical factor for the success

of short implants. It appears as though reports, which include more rough surface implants, found that length did not influence success; while publications involving machined surfaces did find that shorter implants fared worse.

In terms of biomechanics, osteointegrated bone-implant interfaces distribute most prosthetic load to the crestal portion of the implant body, with little stress transferred to the apical portion (Misch, 2006a). This may indicate that implant length is not a primary factor in load distribution (Misch, 2006a). Moreover, the relative stress acting on bone surrounding an implant decreases with increasing implant diameter, possibly because the wider area in the cervical portion may better dissipate the masticatory forces (Himmlova *et al.*, 2004; Petrie & Williams, 2005). To compensate for shorter length, a surgeon may consider a wide-diameter implant (Morand & Irinakis, 2007). A 5 mm wide x 6 mm long implant has the same surface areas as a 3.75 mm wide x 10 mm long implant (Morand & Irinakis, 2007). The majority of more recent studies indicate that the use of short implants in both jaws may be a viable concept with comparable survival rates to longer implants. For more predictable treatment outcomes, some studies have recommended that cantilevers should be avoided, the mesio-distal dimension of the prosthesis reduced, the cuspal inclines flattened, and implants splinted to produce more favorable load distribution (Misch, 2006b; Morand & Irinakis, 2007). A two-stage approach has also been suggested, avoiding free-end situations without a second implant for splinting, and compensating with wider diameter implants to increase success rates, particularly in areas of poorer bone quality (Morand & Irinakis, 2007).

## Width

The choice of implant diameter can depend on the volume of the residual bone, the interradicular distance, the amount of space available for the prosthetic reconstruction, the emergence profile, and the type of occlusion (Degidi *et al.*, 2008). Most recently published studies do not correlate implant diameter as significantly associated with implant failure (Degidi *et al.*, 2007; Degidi *et al.*, 2008; Friberg *et al.*, 2002; Garlini *et al.*, 2003; Lemmerman & Lemmerman, 2005; Renouard & Nisand, 2006; Romeo *et al.*, 2004). In terms of biomechanics, finite element analysis has demonstrated that implant diameter is more important in stress distribution than implant length and should be considered as a design parameter to control the risk of bone overload (Baggi *et al.*, 2008). Himmlova *et al.* (2004) showed that relative stress acting on bone surrounding an implant decreased with increasing diameter. A stress reduction of 31.5% was noted with 4.2 mm versus 3.6 mm implants, 47.9% in 5 mm implants and almost 60% with 6.5 mm implants. The relation between relative stress and implant length showed a similar trend, however, the stress reduction around implants with lengths of 8 and 17 mm was only 7.3% indicating that implant diameter was more important for improved stress distribution than implant length (Himmlova *et al.*, 2004). A similar trend was demonstrated by Petrie *et al.* (2005), where increasing implant diameter resulted in a 3.5-fold reduction in crestal strain versus only a 1.65-fold reduction with increasing length. The maximal masticatory stress is localized to the crestal portion of the implant, therefore implants with a greater diameter and resultant surface area may better dissipate the masticatory forces (Himmlova *et al.*, 2004).

Clinical strategies to improve the survival rates of implants placed in sites with reduced bone quantity and quality have included the use of large-diameter implants

(Bahat & Handelsman, 1996). In contrast to what may be expected, some studies have demonstrated decreased survival rates for wide-diameter implants as compared to their standard counterparts. A retrospective study on 299 Branemark machined implants 3.75 mm to 5 mm in diameter demonstrated survival rates of 95%, 98%, and 82% for 3.75 mm, 4 mm, and 5 mm-diameter implants, respectively. The authors suggested that the greater failure rates in 5 mm-diameter implants may have been associated with the operators learning curves, poor quantities of poor quality bone, and the fact that 45% of them were used as 'rescue' implants when primary stability could not be achieved with a standard-diameter implants (Ivanoff *et al.*, 1999). Similar findings were demonstrated by other studies, with the authors reporting that although survival rates were lower, results were encouraging because the wide platform implants were placed in unfavourable situations with poor bone quality and quantity (Mordenfeld *et al.*, 2004; Shin *et al.*, 2004). Recent studies, which have used surgical preparation adapted to the bone density, textured-surfaced implants, and modified case selection have reported survival rates for wide diameter implants which were comparable with those obtained with standard-diameter implants (Degidi *et al.*, 2007; Friberg *et al.*, 2002; Garlini *et al.*, 2003; Lemmerman & Lemmerman, 2005; Renouard & Nisand, 2006; Romeo *et al.*, 2004).

Recent studies have also indicated that narrow diameter implants (<3.75 mm) can be used as alternative treatment options in cases of reduced interradicular bone or thin alveolar crest (Degidi *et al.*, 2008). They can preclude additional bone augmentation procedures thereby allowing for a reduced treatment time, cost and patient morbidity (Degidi *et al.*, 2008). Numerous studies have reported narrow diameter implants having survival rates comparable to standard diameter implants (Degidi *et al.*, 2008; Romeo *et*

*al.*, 2006; Vigolo *et al.*, 2004; Zinsli *et al.*, 2004). Hallman *et al.* (2001) evaluated the use of reduced-diameter implants as an alternative to bone grafting for treatment of patients with severely resorbed maxillae. A total of 182 narrow (3.3 mm)-diameter TPS implants were placed with an overall survival rate of 99.4% after 1 year of loading. Similarly, Morneburg and Proschel (2008) placed 134 sandblasted implants, 2.5 mm in diameter and 9 to 15 mm in length in the edentulous mandibles with severe ridge resorption. The cumulative survival rate after 6 years was 95.5%. It is important to note, however, that smaller diameter implants have an increased risk of implant fracture because of reduced mechanical stability, and overload (Davarpanah *et al.*, 2000; Schwarz, 2000). These studies indicate that narrow-diameter implants can be considered in clinical situations where space or bone availability cannot allow for the use of standard-diameter implants. However, careful patient and site selection in terms of biomechanical conditions, bone density and occlusion is imperative (Degidi *et al.*, 2008). Further research defining their limits in regards to clinical indications and load-bearing capacity is necessary.

## **2.3 Implant placement-related risk factors**

### **2.3.1 Primary stability**

Primary implant stability, defined as ‘a sufficiently strong initial bone-implant fixation’ by Roberts (1999) is considered to play an essential role in successful osseointegration and has been reported as an important prognostic marker for the success of dental implants (Esposito *et al.*, 2009; Roberts, 1999; Sennerby & Meredith, 2008). The greater the primary stability, the smaller the micromotion present between the



surface of the implant and the surrounding bone (Trisi *et al.*, 2009). It has been demonstrated that excessive micromovement following implant placement can result in fibrous healing rather than osseointegration, and a threshold of 50–100  $\mu\text{m}$  at the interface should not be exceeded (Szmukler-Moncler *et al.*, 1998). Primary stability at implant installation is achieved by the physical congruence between the surgically created bone bed and the implant and is related to the macroscopic implant design, the surgical technique, and the bone density (Balshi *et al.*, 2005; Sennerby & Meredith, 2008).

Despite the experimental definition of these thresholds, there are no instruments currently available to dentists that are capable of clinically discriminating tolerable levels of the micromotion of an endosseous dental implant. Primary stability can be assessed intrasurgically by the measurement of insertion torque as the implant is placed in the osteotomy site. Trisi *et al.* (2009) measured the peak insertion torque in relation to different bone densities through the placement of implants in fresh bovine bone samples. He demonstrated that increasing the peak insertion torque reduced the level of implant micromotion. Furthermore, significant correlations between peak insertion torque and micromotion were found in hard and normal bone as compared with soft bone. When the insertion torque was 30 Ncm, the recorded micromotion would be at a threshold of 50  $\mu\text{m}$ . Torque values between 45-100 Ncm have been shown to produce the same degree of micromotion, well below the risk threshold (Trisi *et al.*, 2009). Conversely, in soft bone, it was demonstrated that micromotion was significantly higher and it was not possible to achieve more than 35 Ncm of peak insertion torque due to the stripping of the peri-implant bone (Trisi *et al.*, 2009). Primary stability measurements show significant

correlations with bone densities and these results support the fact that pre-surgical assessment of bone density could help in treatment planning. Modification of the surgical technique to improve initial stability by using smaller drill diameters and preparation of narrower osteotomes, in addition to the adaptation of loading protocols or design and surface characteristics of the implant, could improve the primary stability in softer bone densities (Molly, 2006). However, it is noteworthy that under-preparation of the osteotomy requires significant clinician experience to be able to assess the compression forces generated on the surrounding bone by the implant being placed. Too much compression could lead to cell death and necrosis at the site (Ueda *et al.*, 1991).

Currently the two most commonly used non-invasive instruments by which the clinical stability of an implant can be measured objectively include the Periotest (Medizintechnik, Gulden, Bensheim, Germany) and Osstell device (Integration Diagnostics, Gothenburg, Sweden). The Periotest is a computer-mechanical device that projects a rod against the implant or abutment using a magnetic pulse at a certain speed. The apparatus measures the deceleration time needed before the rod comes to a standstill. This is transformed in an arbitrary unit, which reflects the rigidity of the bone-to-implant continuum (Olive & Aparicio, 1990). A soft surface or mobile object gives higher recordings (up to +50) than a hard or rigid object (-8). A clinical evaluation of zero mobility may correspond to -8 to +9 Periotest value (PTV) and the bone density around the implants may be correlated with these numbers (Olive & Aparicio, 1990). The limitations of this device include lack of resolution, poor sensitivity and susceptibility to operator variables (Olive & Aparicio, 1990). The Osstell device comprises a small transducer attached to the implant that imposes a series of frequencies and measures the

overall resonance frequency, which is dependent on the stiffness or rigidity of the implant-bone interface. The resultant Hertz waves are converted into a numeric value, called the implant stability quotient (ISQ). The scale ranges from 1 to 100 with a higher ISQ value corresponding to a greater rigidity of the implant bone-interface (Meredith *et al.*, 1996). Measurements of implant stability by Periotest and Ostell devices during time of implantation, and at three and six weeks, are well correlated and are affected by bone density, and the degree of compact bone (Oh *et al.*, 2009). Additionally, both methods provide a correlation to the degree of osseointegration (Oh *et al.*, 2009). This was in agreement with results reported by Turkyilmaz and McGlumphy (2008), who found statistically significant correlations between bone density as assessed by CT scans, resonance frequency analysis (RFA), and insertion torque and implant survival. In spite of these results, there is still a lack of precise information on the correlation between PTV and ISQ values and the short and long-term implant outcomes, mostly with regards to implants with low primary stability (Molly, 2006).

Contrary to results reported in earlier literature, more recent studies have demonstrated that the attainment of primary implant stability may not be a prerequisite for osseointegration and implant survival (Balshi *et al.*, 2007; Roccuzzo *et al.*, 2001; Rodrigo *et al.*, 2010). The diagnostic validity of primary implant stability to predict implant outcomes was assessed for more than 4000 SLA Straumann implants (Rodrigo *et al.*, 2010). Primary stability was tested by two methods, the surgeon's clinical perception and the Ostell device. Implants were stratified into groups based on the degree of implant rotation when tightening the healing cap; group A (3899 implants) exhibited primary stability, while category B, C and D (213 implants) had no rotational stability

and progressive loss of resistance, with the final group demonstrating lateral oscillation. Implants with primary stability demonstrated a significantly higher survival (99.1%) than implant without rotational stability (97.2%). In spite of the significant effect of lack of primary stability on implant failure, the high implant survival rate (97.2%) observed for these unstable implants is remarkable. The failure rate increased according to the degree of lesser resistance to implant rotation with category B (n=158) having a 98.1% survival rate versus category C (n=51) with 94.1%. Interestingly, all four implants in the lateral oscillation group (category D) survived. Implants were also stratified in two groups according to a threshold ISQ value of 60. There was a good correlation between RFA and the proposed clinical classification of primary stability. However, there was no significant association between primary stability and implant survival; in fact, there was not a single implant with an ISQ <60 during implantation that failed (Rodrigo *et al.*, 2010). The explanation for this positive outcome may lie in the implant surface used, as suggested from the results of the study by Balshi *et al.* (2007) who attained higher implant survival rates in unstable implants with a rough surface when compared with implants with a turned surface (91.7% vs. 70%) and by Orenstein *et al.* (1998) who demonstrated a higher success rate in mobile implants coated with HA (100%) than in implants without this coating (81.5%). It is important to note that implants without rotational stability were submerged and unloaded during healing. Conversely, another study has reported that mean bone density and insertion torque was higher for successful implants ( $645 \pm 240$  HU and  $37.2 \pm 7$  Ncm) as compared to those that failed ( $267 \pm 47$  HU and  $21.8 \pm 4$  Ncm) (Turkyilmaz & McGlumphy, 2008).

In the case of immediate or early loading of dental implants, it is well documented

that a high degree of primary implant stability is one of the prerequisites for success (Esposito *et al.*, 2009). In some studies, higher torque has been thought to be associated with better implant survival and better bone density, provided it is within a range that is biologically compatible with maintenance of crestal bone vitality (Ottoni *et al.*, 2005; Turkyilmaz & McGlumphy, 2008). Ottoni *et al.* (2005) evaluated 46 implants placed with a minimum insertion torque of 20 Ncm; half of which were restored immediately. During a two-year observation period, 10/46 implants failed, and nine of which were in the immediately loaded group with a recorded insertion torque of <20 Ncm. The authors concluded that to achieve osseointegration with immediate loading, an insertion torque above 32 Ncm was necessary. Taken together, these results indicate that primary stability may not be necessary for implant survival as long as a submerged protocol is followed. However, most studies support the claim that primary stability during implantation yields more predictable and higher survival rates, regardless of the loading protocol employed, and should continue to be the goal during implant placement.

## **2.4 Anatomic site-related risk factors**

### **2.4.1 Bone density and location in the arch**

Bone quality and bone density are often used interchangeably in dental literature, however, bone quality is a collective term referring to the mechanical properties, architecture, degree of mineralization of the bone matrix, chemistry and structure of the bone mineral crystals, remodeling, and vascularity; all of which may influence implant outcome (Molly, 2006). This report will discuss bone density, which has been shown to be associated with primary implant stability and the predictability of implant treatment

outcomes (Esposito *et al.*, 2009; Turkeyilmaz & McGlumphy, 2008).

Histomorphometric evaluation has been considered as the golden standard for pre-operative measurements of jaw bone density, however it is too invasive and time consuming for clinical use (Molly, 2006). When comparing the histology of the biopsy of osteotomy sites with the subjective perception of bone density by the surgeon during the preparation and placement of oral implants, it was noted that the surgeon was able to distinguish between extremely dense bone and extremely soft bone but could not distinguish any other bone densities (Trisi & Rao, 1999).

The most popular method of bone density assessment is that developed by Lekholm and Zarb, who introduced a scale of I to IV based on both the radiographic assessment and the sensation of resistance experienced by the surgeon during preparation of implant sites (Lekholm & Zarb, 1985). Type I bone is reported to be most dense, and type IV the least dense. Truhlar *et al.* (1997) evaluated the distribution of bone quality intrasurgically during the placement of nearly 3000 implants using this classification system. It was reported that highest bone density occurred in the anterior mandible, followed by the posterior mandible, anterior maxilla, and finally in the posterior maxilla. This subjective assessment criterion has proven difficult to reliably and predictably differentiate between Type II and Type III bone densities. Alternatively, differentiating between more extreme bone qualities of Type I and IV has yielded more consistent results (Alsaadi *et al.*, 2007; Trisi & Rao, 1999). Therefore, some clinicians have chosen to categorize bone qualities according to three types: dense or hard (type I), medium (type II, III) and soft (type IV) in order to assess bone quality in a more reliable manner (Alsaadi *et al.*, 2007; Irinakakis & Wiebe, 2009).

The grading of bone quality intrasurgically refers to individual experience and has been questioned due to poor objectivity and reproducibility (Shapurian *et al.*, 2006; Turkyilmaz & McGlumphy, 2008). Attempts have been made to classify jawbone tissue prior to implant treatment on the basis of Hounsfield units (HUs), as measured by computerized tomography (CT). Based on CT imaging, the highest bone density recordings occurred in the anterior mandible ( $846 \pm 234$  HU), followed by anterior maxilla ( $591 \pm 176$  HU), the posterior mandible ( $526 \pm 107$  HU) and in the posterior maxilla ( $403 \pm 95$  HU) (Turkyilmaz & McGlumphy, 2008). These are comparable to what has been reported in other publications (Bergkvist *et al.*, 2010; Shapurian *et al.*, 2006). Bone mineral density, as assessed by CT scans prior to implant placement, was significantly correlated with bone quality classification in both arches as well as with implant stability values as measured by insertion torque and RFA (Bergkvist *et al.*, 2010). The bone density values from pre-operative CT scans may provide an objective assessment of bone quality, and since significant correlations have been noted between bone density and implant stability parameters, the information can be used by clinicians to modify surgical technique or loading protocol in order to achieve more predictable treatment outcomes.

Numerous studies have reported that implants placed in the maxilla fail more frequently than those in the mandible, particularly when the posterior maxilla is compared to the mandible (Buser *et al.*, 1997; Buser *et al.*, 1997; Hinode *et al.*, 2006; Jaffin & Berman, 1991; Lazzara *et al.*, 1996; Moy *et al.*, 2005). A number of these reports have attributed the higher failure rates to reduced bone density between the mandible and maxilla, and between anterior and posterior sites (Turkyilmaz & McGlumphy, 2008). In more recent years, implant design advances and surface

modification have led to higher success rates in all bone types, with only minor disparities, if any, in different anatomic locations (Aykent *et al.*, 2007; Ferrigno *et al.*, 2002; Kline *et al.*, 2002; Morand & Irinakis, 2007). A recent study compared survival rates of over 4000 smooth and rough surface dental implants and demonstrated that anatomic location and implant length  $\leq 10$  mm were only associated with failures in smooth-surface implants (Balshe *et al.*, 2009). The results of this report suggest that with the advent of rough surface implants, implant length and the anatomic location of implant placement no longer have a significant effect on implant survival rates.

That said, in areas with poorer bone density, it has been reported that emphasis should be given to maximizing implant surface area contact with available bone in order to increase primary stability during placement; this is especially important in cases of immediate loading. Primary stability can be improved by using a threaded implant design with surface roughness and increased length and diameter (Morand & Irinakis, 2007). Under-preparation of the osteotomy site can also bestow compression of the surrounding low-density bone during implant placement, thereby resulting in enhanced primary stability in softer bone (Irinakis & Wiebe, 2009; O'Sullivan *et al.*, 2004).

#### **2.4.2 Previous and simultaneous bone regeneration or sinus augmentation**

##### **Guided bone regeneration**

Guided bone regeneration (GBR) has been extensively studied and reviewed. This procedure enables the surgeon to augment the width of deficient alveolar ridges, cover exposed threads around implants during implantation, and allow for immediate placement of implants in osseous defects or large extraction sites (Chiapasco *et al.*, 2009). Predictable regeneration requires both a high level of technical skill and a



thorough understanding of underlying principles of wound healing. Four major biologic principles termed 'PASS' have been described as necessary for predictable bone regeneration: i) primary wound closure to ensure undisturbed wound healing ii) angiogenesis to provide necessary blood supply and undifferentiated mesenchymal cells iii) space maintenance/creation to facilitate adequate space for bone in growth and iv) stability of the wound and implant to induce blood clot formation and uneventful healing events (Wang & Boyapati, 2006). Countless publications have demonstrated that implant survival in regenerated bone is comparable to survival rates in native bone (Aghaloo & Moy, 2007; Blanco *et al.*, 2005; Brocard *et al.*, 2000; Chiapasco *et al.*, 2009; Christensen *et al.*, 2003; Esposito *et al.*, 2008; Fiorellini & Nevins, 2003; Fugazzotto, 2005; Juodzbalsys *et al.*, 2007). A discussion of the different materials used for GBR and their advantages and disadvantages is beyond the scope of this review and will not be discussed in this section.

### **Sinus augmentation**

Resorption of the alveolar process, pneumatization of the maxillary sinuses, and poor bone quality often associated with the posterior maxilla can complicate implant therapy. Numerous treatment options are available for this challenging area including placement of shorter implants, GBR and most commonly, grafting of the sinus floor using a lateral window or osteotome approach (Wallace & Froum, 2003). A maxillary sinus floor augmentation procedure was first performed by Tatum in 1974, and the first publication on the technique was authored by Boyne and James in 1980. The lateral window technique, as it is currently termed, requires a window to be prepared in the lateral wall of the sinus and the elevation of the Schneiderian membrane to create a cavity

into which bone is traditionally inserted. It is a widely used technique that allows for the placement of implants either simultaneously or following a period of healing (Esposito *et al.*, 2010; Wallace & Froum, 2003). Alternatively, Summers (1994) described a less invasive technique for sinus floor elevation with simultaneous implant placement called the osteotome sinus floor elevation. For a one-stage approach, at least 6 mm of residual bone was recommended, otherwise, a two-stage approach was utilized. Concave tipped osteotomes of increasing diameter applied using a crestal approach advanced bone beyond the level of the original sinus floor, elevating the membrane. A disadvantage of this technique is that the amount of bone that can be gained is usually less than that obtained with the lateral window technique.

Implant placement following or simultaneous with lateral window sinus augmentation has demonstrated excellent survival rates (Aghaloo & Moy, 2007; Chen *et al.*, 2007; Esposito *et al.*, 2010; Lambert *et al.*, 2010; Pjetursson *et al.*, 2008; Sorni *et al.*, 2005; Wallace & Froum, 2003). Adequate residual bone height and primary stability is recommended for predictable treatment outcomes (Lambert *et al.*, 2010). This augmentation procedure has been well documented and the long-term success/survival of implants placed compares favorably to rates reported for implants placed in ungrafted areas of the maxilla. This similar observation was noted for osteotome sinus elevation (Fermergard & Astrand, 2008; Ferrigno *et al.*, 2006; Pjetursson *et al.*, 2009; Pjetursson *et al.*, 2009; Tan *et al.*, 2008). In a systematic review evaluating 43 studies, survival of implants placed in lateral window augmented sinuses ranged from 61.7% to 100%, with an average survival of 91.8% (Wallace & Froum, 2003). Among others, Wallace and Froum demonstrated that rough surface implants had higher survival rates than

machined-surface implants in grafted sinuses (95.2% vs. 82.4%) (Del Fabbro *et al.*, 2004; Del Fabbro *et al.*, 2008; Esposito *et al.*, 2010; Pjetursson *et al.*, 2008; Wallace & Froum, 2003). Implants had higher survival rates when particulate grafts were used instead of block grafts (92.3% versus 83.3%) and grafts were more successful when resorbable membranes were placed over lateral windows as compared to those when the resorbable membrane was omitted (100% versus 92.6%) (Wallace & Froum, 2003). Contrary to what was previously thought, the use of autogenous bone in sinus grafting does not appear to improve graft and implant survival (Wallace & Froum, 2003). In a recent Cochrane systematic review, it was also suggested that bone substitutes such as BioOss could replace autogenous bone for sinus lift procedures (Esposito *et al.*, 2010).

Furthermore, a systematic review evaluating 5128 implants reported higher success with BioOss as compared with autogenous bone (95.6% vs. 92.0%) (Aghaloo & Moy, 2007). The first systematic review to evaluate the effect of different bone grafting materials on implants with rough surfaces identified that in previous reports, machined implants had been used more frequently in combination with autogenous bone, while rough surface implants had been used with bone substitutes (Pjetursson *et al.*, 2008). When the type of graft used was considered only for rough implants, all grafting materials showed similar annual failure rates (1.13% for bone substitutes, 1.1% for combination and 1.27% for autogenous) (Pjetursson *et al.*, 2008). Implant failure rates have been demonstrated to be higher in cases where machined surface implants are used, residual ridge heights are less than 3 mm, and when block grafts are used (Lambert *et al.*, 2010; Pjetursson *et al.*, 2008; Sorni *et al.*, 2005; Wallace & Froum, 2003).

More recently, studies have evaluated the survival of implants placed

simultaneously with the lateral window technique, without the use of a bone graft. Based on their findings with an experimental animal model, Lindhe *et al.* (1993) proposed that bone may regenerate *in situ* after an isolated space is created and maintained between the periosteum and the calvarial cortex of the rat. The isolated space, which was filled initially with clotted blood, was later occupied by newly formed bone. This observation is consistent with the possibility that fillers of the newly created space for sinus lifting might not be required if adequate time were allowed for regeneration of new bone. The efficacy of two techniques for lateral window sinus augmentation: placement of a rigid synthetic resorbable barrier versus particulate bovine bone (BioOss) was assessed in a split-mouth analysis in ten patients. After six months, bone height of 14.4 mm was gained for the barrier membrane versus 14.1 mm for BioOss. Histologically, more new bone formed at BioOss treated sites (36.1% versus 24.2%) (Felice *et al.*, 2009). The authors concluded that although it is sufficient to keep space with a rigid barrier, bone was histologically more mature, appeared to be clinically harder, and was simpler to use with BioOss. A retrospective review assessed the survival of 47 implants placed simultaneously with a lateral window sinus augmentation without bone graft and found a 100% survival rate after two years of loading (Chen *et al.*, 2007). Increases in lifted sinus bone height ranged from 3 mm to 9 mm with an average of 4.5 mm (Chen *et al.*, 2007). This finding was supported by a recent Cochrane systematic review, which concluded that elevating the sinus lining in presence of 1 – 5 mm of residual bone height without the addition of a bone graft may be sufficient to regenerate new bone and allow rehabilitation with implant-supported prostheses (Esposito *et al.*, 2010). Similar results were attained in a recent study comparing the survival rates of 280 implants placed using

the osteotome technique with simultaneous bone grafting and those without grafting. A cumulative survival rate of 95.7% was found with no significant difference between the two techniques. The residual bone height was  $4.7 \pm 2.1$  mm for the grafted group and  $5.6 \pm 2.5$  mm for the non-grafted group. New bone formation was visible in both groups with a gain in height of  $2.26 \pm 0.92$  mm and  $2.66 \pm 0.87$  mm at three and nine month follow ups, respectively. Residual bone height did not have a significant influence on implant survival (Lai *et al.*, 2010). Although results are preliminary, these studies challenge the utility of the conventional approach involving placement of bone graft into a sinus space created either through a lateral window or by osteotome sinus floor elevation, and may offer the advantage of reducing surgical time and financial burden for the patient.

## ***2.5 Timing of implant placement***

### **2.5.1 Immediate placement**

Dental implants placed in fresh sockets just after tooth extraction have been defined as 'immediate' implants (Esposito *et al.*, 2006). The timing of implant placement can affect the quantity of bone volume that is available to receive an implant. It has been demonstrated that a 50% reduction in the ridge width occurs in the first twelve months following extraction, two-thirds of which can occur in the first three months accompanied by a 0.1-0.3 mm loss in the vertical dimension (Schropp *et al.*, 2003). Another publication has demonstrated apicocoronal crestal bone height reduction of 0.7 to 1.5 mm over a six-month period (Lekovic *et al.*, 1998). Dimensional changes following tooth extraction can be influenced by factors such as the number and proximity of teeth to be extracted, the condition of the socket following extraction, the anatomic location of the

socket, and the type of interim prosthesis used (Chen *et al.*, 2004; Irinakis, 2006; Schropp *et al.*, 2003). The immediate placement of implants has been suggested as a way to minimize this resorption. However, recent clinical studies have indicated that bundle bone often resorbs especially facially, even when implants are placed in fresh extraction sockets leaving a reduced horizontal ridge dimension which may lead to facial recession (Araujo *et al.*, 2006; Botticelli *et al.*, 2004). In light of these results, it may be reasonable to allow for soft and hard tissue healing for a few weeks prior to implant placement to increase in the area and volume of soft tissue, without undue loss of bone volume (Esposito *et al.*, 2006). If the implants is placed immediately, positioning is important; it should be placed lingual or palatally and a soft tissue graft can be provided to compensate for buccal resorption (Quirynen *et al.*, 2007).

### **Classifications**

Several classifications have been proposed for the time of implant placement following tooth extraction, however, there is lack of uniformity in the interpretation of the terms used in literature. Hammerle *et al.* (2004) proposed a classification of the timing of implant placement based on soft and hard tissue healing parameters: i) Implant placement immediately following tooth extraction and as part of the same surgical procedure ii) Complete soft tissue coverage (typically 4–8 weeks) iii) Substantial clinical and/or radiographic bone fill of the socket (typically 12–16 weeks) iv) Healed site (typically >16 weeks) (Chen & Buser, 2009; Hammerle *et al.*, 2004). This classification seems appropriate, as it considers variations in subjects' healing capacity and is consistent with that proposed by Esposito *et al.* (2006) who defined 'immediate-delayed' implants as those placed within eight weeks after tooth extraction, and 'delayed' for any

implants placed at least two months after tooth extraction. The necessity of consistent definitions regarding implant placement that are based on the morphologic dimensional and histologic changes following tooth extraction remains.

### **Advantages and disadvantages**

In consideration of the results mentioned above, the placement of implants into fresh extraction sockets immediately after tooth removal can reduce the bone resorption that would potentially occur following extraction and may preclude the need for future bone grafting. In addition, immediate implant placement also provides the added benefits reducing the treatment time, and the number of surgical interventions (Bhola *et al.*, 2008; Hammerle *et al.*, 2004). Other suggested advantages of immediate implant placement include improved aesthetics, maintenance of the hard and soft tissues at the extraction site, and higher patient satisfaction compared with delayed implant placement protocols (Bhola *et al.*, 2008; Hammerle *et al.*, 2004; Schropp & Isidor, 2008). On the other hand, because of the nature of this treatment method, a higher risk of complications and failures may be expected. These can include unpredictable site morphology and a potentially limited amount of soft tissue (Hammerle *et al.*, 2004) and the risk of failure due to residual periosteal infection (Hammerle *et al.*, 2004; Waasdorp *et al.*, 2010; Wang *et al.*, 2006).

### **Immediate placement in infected sites**

Following removal of a tooth, residual infection at the extraction site may influence the treatment success of immediately placed implants. Earlier publications have suggested that immediate placement of an implant into an infected site is

contraindicated (Schwartz-Arad & Chaushu, 1997), as sites exhibiting pathology have been thought to compromise osseointegration (Quirynen *et al.*, 2003). A greater tendency toward implant failure was reported in sites with apical lesions, especially with machined surface implants (Alsaadi *et al.*, 2008). In contrast, other publications investigating immediate placement in sites exhibiting periapical pathology reported successful outcomes (Del Fabbro *et al.*, 2009; Lindeboom *et al.*, 2006; Novaes & Novaes, 1995; Novaes *et al.*, 2003). A RCT demonstrated no statistical differences in failure rates, mean ISQ values, gingival aesthetics, radiographic bone resorption, and periapical microbiologic characteristics between immediate and delayed implants (Lindeboom *et al.*, 2006). Another study, which included the placement of 30 implants into infected sites with simultaneous bone augmentation and ePTFE membrane demonstrated one implant failure (survival = 96.7%). Antibiotics were prescribed four days prior to the procedure and maintained for ten days (Casap *et al.*, 2007). Crespi *et al.* (2010b) compared the outcome of immediate placement of implants when used in the replacement of 30 teeth with and without chronic periapical lesions (without signs of pain, fistulas, or suppuration). At the 24-month follow up, a survival rate of 100% was reported for all implants. The mean bone loss was  $0.86 \pm 0.54$  mm and  $0.82 \pm 0.52$  mm for sites with and without periapical lesions respectively; this difference was not significant. Limited short-term data from animal and human studies suggest that placement of immediate implants into infected sites may be a viable treatment option, provided thorough debridement of the chronically infected extraction socket is performed prior to implantation and antibiotics are used (Lindeboom *et al.*, 2006; Waasdorp *et al.*, 2010). Conversely, reports indicate lower success rates for immediate implants placed in periodontally susceptible



patients (Evian *et al.*, 2004; Horwitz *et al.*, 2008; Polizzi *et al.*, 2000). Increased risk of implant failure was also correlated with periodontal infection (Evian *et al.*, 2004; Horwitz *et al.*, 2008).

### **Principles of immediate placement**

The tooth at the site of implantation should be extracted atraumatically and multi-rooted teeth should be sectioned prior to removal in order to preserve bone and reduce trauma to the surgical site (Schropp & Isidor, 2008). It has been shown that primary implant stability is crucial for successful osseointegration, and that sufficient bone apical or palatal to the socket wall must be present for stability to be achieved (Chen *et al.*, 2004; Lang *et al.*, 2007; Lioubavina-Hack *et al.*, 2006). Anatomy of the sinus in the maxilla and inferior mandibular nerve in the mandible can limit the amount of bone available apical to the extraction socket necessary for implantation and primary stability. Furthermore, the extraction of a molar will often leave a large socket, which may impede achievement of primary stability (Schropp & Isidor, 2008). In the intact socket, a critical component of the peri-implant defect is the size of the horizontal defect, which is the distance from the implant surface to the socket wall (Wilson *et al.*, 1998). For implants with a horizontal defect of <2 mm, spontaneous bone healing and osseointegration will place if the implant has a rough surface (Chen *et al.*, 2004; Paolantonio *et al.*, 2001; Wilson *et al.*, 1998; Wilson *et al.*, 2003). At sites with horizontal defects >2 mm or where one or more walls of the sockets are missing, concomitant augmentation procedures with combinations of barrier membranes and bone grafts are required (Paolantonio *et al.*, 2001; Wilson *et al.*, 2003).

### **Submerged versus transmucosal healing**

The original implant treatment protocol recommended that the implant should be covered with mucosa after placement to ensure osseointegration (Branemark *et al.*, 1977). Likewise, simultaneous bone augmentation with immediate implant placement was thought to be possible only in a submerged environment (two-stage protocol). However, investigations have demonstrated that high predictability of immediate implants with simultaneous bone augmentation can also be achieved with a one-step transmucosal healing approach (Cangini & Cornelini, 2005; Hammerle *et al.*, 1998; Lang *et al.*, 2007). A systematic review on immediate placement reported slightly lower failure rates for submerged immediate implants (3.8%) as compared to immediately placed transmucosal implants (6.2%) when evaluating prospective studies (Quirynen *et al.*, 2007).

### **Treatment outcomes**

Several studies have demonstrated that survival rates of immediate and immediate-delayed implant placement are comparable with those of implants placed in healed alveolar bone (Chen *et al.*, 2004; Chen & Buser, 2009; Esposito *et al.*, 2006; Schropp & Isidor, 2008). When evaluating immediate, early and late loading, it was found that late implants scored slightly better than immediately placed implants, and that both scored better than early placed implants (Quirynen *et al.*, 2007). It was noted that the heterogeneity between studies made valid and accurate comparisons of different insertion strategies impossible. It was also noteworthy that the three review articles still reported survival rates of greater than 95% for immediately placed implants (Chen & Buser, 2009; Quirynen *et al.*, 2007; Schropp & Isidor, 2008). Some reviews have found it difficult to draw conclusions on the effect of immediate placement on marginal bone

loss due to insufficient radiographic assessments and lack of included frequency distributions (Quirynen *et al.*, 2007; Schropp & Isidor, 2008). Other studies reported no significant differences in radiographic crestal bone levels at immediately placed implants as compared to delayed protocols (Chen *et al.*, 2004).

### **Immediate placement and esthetic outcomes**

Some publications have reported greater gingival recession on immediately placed implants that often resulted in exposure of the metal margin of the implant (Chen & Buser, 2009; Evans & Chen, 2008; Gotfredsen, 2004; Schropp *et al.*, 2004). When comparing esthetic outcome between immediate-delayed and delayed implant placement, the best results were obtained with implants placed after twelve weeks of healing as compared to four weeks (Gotfredsen, 2004). Conversely, another study reported better esthetics with implants after ten days instead of twelve weeks (Schropp *et al.*, 2004). In a Cochrane systematic review, a RCT by Schropp *et al.* (2003) compared delayed-immediate implants (ten days after extraction) to delayed implants in 46 patients. After one and a half years of loading, there were no statistically significant differences for prosthesis and implant failures. The level of the peri-implant marginal mucosa in relation to the adjacent teeth was found to be more favourable in the immediate-delayed group. Based on the limited data available, it was concluded that immediate implants and immediate-delayed implants may be associated with better outcomes in terms of aesthetics and patient satisfaction, as compared with conventionally placed implants (Esposito *et al.*, 2006). Evans and Chen (2009) evaluated the esthetic outcomes of 42 single implants and observed a significant labial marginal tissue recession of  $0.9 \pm 0.78$  mm during an average 18.9 month follow up period. A trend of greater recession in thin

versus thick tissue biotype was observed, and three times more recession was noted when the implant shoulder was placed buccal to the tangent line of the incisal edges of adjacent teeth as compared to lingual of this reference point. This was in agreement with a publication reviewing 91 studies, which demonstrated that facial recession was a common finding in immediately placed implants reporting 1 mm recession in 8-40% of sites (median 21.4%) (Chen & Buser, 2009). In fact, they noted a higher frequency of recession in immediate placement as compared to early placement with partial bone healing (Chen & Buser, 2009). Recession occurred soon after restoration of the implant. Early placement with soft tissue healing was associated with relatively low incidence of recession when implant placement was combined with GBR. Risk factors for recession included a thin biotype, facial malposition and thin or damaged facial plates (Chen & Buser, 2009). Data on long-term outcomes is limited. Bianchi and Sanfilippo (2004) reported six to nine year results on 22 single implants that were submerged with simultaneous connective tissue grafts and 20 implants without grafts serving as controls. The proportion of sites with recession greater than 1 mm was 5% in the connective tissue group as compared to 20% in the control sites. Although improvement of aesthetics has frequently been pointed out to be one advantage of immediate or early implant placement, there is a lack of studies with control groups and contradictory conclusions have been published. A new classification system was recently presented as a tool for the assessment and categorization of the maxillary anterior extraction sockets into adequate, compromised and deficient groups based upon soft and hard tissue parameters in order to help achieve predictable esthetic results (Juodzbaly *et al.*, 2008). Sockets were deemed 'adequate' according, but not limited, to the following parameters: no soft vertical

deficiency,  $KT > 2$  mm, thick biotype ( $\geq 2$  mm), availability of bone beyond the apex ( $\geq 4$  mm), facial bone thickness of  $> 2$  mm etc. If these parameters were met, then a good esthetic outcome could be anticipated for immediate implant placement. Conversely, for sites with compromised soft and hard tissue conditions, a staged implant approach with soft tissue or hard tissue grafting was recommended (Juodzbalsky *et al.*, 2008). Taken together, these reports highlight the need for careful case selection and surgical technique for immediate implants in the aesthetic zone. To achieve optimal aesthetic results, other factors such as the position and angulation of the implant, bone and / or soft tissue grafting, gingival biotype, immediate/early restorations, and flapless procedures can be considered.

## **Conclusion**

Based on a review of the current literature, it can be concluded that immediate or early placement of implants may be a viable alternative to delayed placement. Along with careful case selection, the surgical and prosthetic protocols must be closely followed. Immediate implant placement is technique-sensitive and may be more difficult to execute than conventional placement, therefore it is advocated that this treatment modality should be restricted to skilled, well-trained clinicians.

### **2.5.2 Immediate restoration/loading**

In the late 1960's, Branemark *et al.* introduced the concept of osseointegration, whereby predictable long-term implant function could be achieved by following strict protocol. This documented the placement of titanium implants in a two-stage surgical procedure with a submerged healing period of three to six months depending on the bone

quality, followed by a delayed phase of prosthetic loading on a cross-arched prostheses in the edentulous jaws (Branemark *et al.*, 1977). The recommendation was based on the notion that increased vertical or lateral forces on an implant during the healing phase may result in implant motion, aberrant healing, and fibrous tissue encapsulation rather than the bone formation required for osseointegration (Brunski, 1999; Szmukler-Moncler *et al.*, 1998). Experimental studies have demonstrated that this rationale does not hold true under controlled conditions, and they have emphasized that these time periods were set up empirically and have not been verified experimentally (Szmukler-Moncler *et al.*, 1998). Within the last two decades, the original Branemark protocol has been modified to allow for shorter healing periods and expedited treatment. This was made possible with the advent of newer, more refined surgical techniques and the improvement of biomaterials and implant surfaces aimed at obtaining more predictable osseointegration. Shortened treatment periods by means of immediate implant placement in extraction sockets and immediate loading of the implant-supported prostheses has been reported and reviewed in increasing frequency with comparably high survival rates (Attard & Zarb, 2005; Nkenke & Fenner, 2006; Sennerby & Meredith, 2008).

### **Terminology**

A review of literature reveals inconsistent definitions for different loading protocols. Consensus reports and systematic reviewers alike have attempted to define the term immediate loading from both the context of timing of the prosthesis and the amount of occlusal loading it receives, with inconsistent results. In a consensus statement regarding loading protocols for dental implants by Cochran *et al.* (2004), the following definitions were proposed:

Immediate restoration (also known as immediate provisionalization or non-functional loading (Degidi & Piattelli, 2003) pertains to the insertion of a restoration within 48 hours of implant placement, without contact to the opposing dentition. Immediate loading or functional loading (Degidi & Piattelli, 2003) has been most often defined as the placement of an implant-supported restoration in contact with the opposing dentition within 48 hours of implant placement. Early loading refers to the placement of an implant-supported restoration in occlusion with the opposing dentition at a second procedure between 48 hours to three months from the time of implant placement. Conventional loading pertains to the placement of a restoration in a second procedure three to six months after implant surgery. Finally, delayed loading occurs when an implant-supported prosthesis is placed after a period longer than the conventional healing period of three to six months. Although these definitions continue to be debated, they are consistent with numerous subsequent consensus reports and reviews (Cochran *et al.*, 2004; Cooper *et al.*, 2007; Glauser *et al.*, 2006; Henry & Liddel, 2008; Wang *et al.*, 2006). A more recent consensus report by Weber *et al.* (2009) recommends the ITI definitions for dental implant loading be modified from the 2004 report to include immediate loading as earlier than one week after placement, early loading between one week and two months following placement, and conventional loading as greater than two months following implantation (Weber *et al.*, 2009; Esposito *et al.*, 2009).

### **Advantages**

The advantages of immediate loading are numerous. In addition to providing a reduction in overall treatment time, it can provide an immediate aesthetically pleasing and functional result, a potentially superior, stable soft tissue profile, and a psychological

benefit that may result in increased patient acceptance (Avila *et al.*, 2007; Misch *et al.*, 2004a; Oh *et al.*, 2006; Wang *et al.*, 2006). Furthermore, it precludes the need for a removable prosthesis during initial bone healing, which greatly increases comfort, function, speech, stability, and does not interfere with healing of simultaneous bone grafting (Misch *et al.*, 2004a). It is indisputable that immediate loading provides a valuable treatment alternative, therefore it is justifiable to question whether a healing period is a prerequisite for obtaining osseointegration or, if under certain circumstances, this period can be shortened without jeopardizing osseointegration and long-term treatment outcomes.

Several experimental studies have shown that early or immediately loaded implants are associated with a greater percentage of BIC and more mature cortical bone than delayed-loaded controls. Histological evaluation of the mineralized bone tissue around unloaded, delayed, and immediately loaded dental implants in the *Macaca fascicularis* three months after placement revealed new bone formation and active remodeling when bone was mechanically stimulated through loading (Romanos *et al.*, 2003). A clinical study evaluating the bone-titanium interface of submerged and immediately loaded implants histologically at four and eight weeks after placement demonstrated the submerged implants had lower bone quality and BIC at four and eight weeks (54.7% and 62.3% respectively) as compared to immediate-loaded implants (BIC 65.6% and 76.2% respectively) (Degidi *et al.*, 2009). Volumetric computed tomographic (CT) analysis of the surrounding bone in immediately loaded and conventionally loaded SLA implants six months after placement showed significantly greater mineralized bone in the group with immediate loading (Barone *et al.*, 2003). Together, these publications



suggest that early occlusal loading may enhance bone remodeling and increase bone density compared with unloaded dental implants. The difference in results between earlier studies in which fibrous encapsulation was observed following immediate loading and more recent studies that indicate osseointegration and improved BIC following immediate loading protocols, may be attributed to variability in study design, loading conditions, micromotion, bone quality, and materials used (Chiapasco, 2004).

### **Primary stability and the concept of micromotion**

Implant primary stability has been identified as the single most important clinical factor influencing success of immediate loading (Chiapasco, 2004; Cochran *et al.*, 2004; Esposito *et al.*, 2009). Stability of the implant can be influenced by surgical-related factors including drilling protocol and non-traumatic surgical technique, host-related factors such as quality and quantity of bone, implant-related factors including design, surface, length and diameter, and finally, occlusion-related factors pertaining to the prosthetic design including splinting (Avila *et al.*, 2007; Cochran *et al.*, 2004; Misch *et al.*, 2004a). It has been shown that implant-bone interface is weakest and at highest risk of overload at approximately three to six weeks after surgical insertion due to bone remodeling, characterized by an increased ratio of woven to lamellar bone (Glauser *et al.*, 2003; Henry & Liddel, 2008; Misch, Wang *et al.*, 2004a). This is translated clinically in a critical period during which the primary stability decreases and the implant bone interface may become more susceptible to the effects of micromotion, increasing the risk of impairment of osseointegration (Henry & Liddel, 2008). These findings are in agreement with clinical primary stability assessments using resonance frequency analysis (RFA) taken at 30, 60 and 90 days following implantation. RFA measurements showed a

decrease in bone-implant stability in the first month after implant placement from 70.4 to 66.4, followed by increases in stability in the second and third months (68.0 and 68.8 respectively), suggesting a process of adaptive bone remodeling around the implant (Balshi *et al.*, 2005). In light of these findings, it is recommended that superstructures not be removed for at least the first two months, so there is no disturbance during healing (Balshi *et al.*, 2005; Tarnow *et al.*, 1997). In full mouth restorations, it is often recommended to avoid chewing hard foods prior to implant integration, as early failures were suspected to be attributed to micromotion during healing (Bergkvist, 2008; Jaffin *et al.*, 2004; Tarnow *et al.*, 1997). Furthermore, to achieve predictable immediate loading, insertion torque of at least 30-35 Ncm (Attard & Zarb, 2005; Drago & Lazzara, 2006; Glauser *et al.*, 2006; Ostman *et al.*, 2005; Testori *et al.*, 2008; Wang *et al.*, 2006) and ISQ values of 60 (Degidi *et al.*, 2008; Ostman *et al.*, 2005; Schincaglia *et al.*, 2007) have been recommended as a prerequisite for immediate loading.

### **Bone quality**

It has been proposed that lower bone densities may correlate with lower primary stability, greater micromotion, and increased risk of osseointegration failure in the maxilla when implants are immediately loaded (Degidi & Piattelli, 2003; Ibanez *et al.*, 2005; Nordin *et al.*, 2007). Using RFA, it was noted that during implantation that lower initial stabilities were seen in softer bone types in the posterior portions of the jaw when compared to anterior areas (Balshi *et al.*, 2005). When softer bone is encountered, a revised drilling protocol can be employed in order to achieve the higher primary stability necessary for immediate loading. This may involve avoiding tapping and countersinking to maximize cortical bone contact, engaging both cortices for bicortical

stabilization, and under-preparing the osteotomy site by using narrower drills than the standard protocol (Attard & Zarb, 2005; Cooper *et al.*, 2007; Nkenke & Fenner, 2006; Rocci *et al.*, 2003a; Wang *et al.*, 2006). Finally, implant positions with greater anterior-posterior dimensions, reduced cantilevers, and splinting of immediately loaded implants to provide better biomechanical distribution over a greater surface area, should all be considered in lower density bone types (Misch *et al.*, 2004a).

### **Implant design and dimensions**

The functional surface area of each implant support system is primarily related to the geometry and diameter of the implant (Misch *et al.*, 2004a). The greater the thread number and thread depth, the more functional surface area available, thereby providing greater likelihood for initial stabilization during immediate loading (Misch *et al.*, 2004a). As discussed earlier, most of the stresses on an implant bone interface are concentrated at the crestal bone, so the increased implant length does little to decrease the stress that occurs at the bone crest around the implant (Misch *et al.*, 2004b). However, because the immediately restored implant loads the interface before the establishment of a cellular connection, implant length is also relevant, especially in softer bone types (Misch *et al.*, 2004b). As such, the benefit of increased length may not be found at the crestal bone interface, but rather in the initial stability of the bone–implant interface. Although some studies have suggested that immediately loaded implants should be  $\geq 10$  mm long to ensure high success rates (Tarnow *et al.*, 1997; Wang *et al.*, 2006), numerous studies have demonstrated high survival rates for immediately loaded implants in all anatomical locations irrespective of implant length (Degidi & Piattelli, 2003; Ibanez *et al.*, 2005; Schincaglia *et al.*, 2007).

## **Prosthetic considerations**

In terms of immediate loading, prosthetic restoration in partially dentate patients should have non-occlusal contact without lateral contacts in partially dentate restorations (Wang *et al.*, 2006). It has been suggested that multiple implants should receive non-rigid splinting of the provisional prostheses for an increased area of load transfer, which decreases the stresses along the bone interface and increases the stability, retention, and strength of the transitional prosthesis during the initial healing phase (Jaffin *et al.*, 2004). A screw-retained, passively fitting restoration may be superior to a cement-retained option as they are less likely to loosen and are easier to remove during recalls (Jaffin *et al.*, 2004). Another study recommended the number of prosthetic units to the number of implants ratio (PU/I) should be as close as possible to 1.0, and cantilevers should be minimized (Degidi & Piattelli, 2003). Degidi and Piattelli recommend the PU/I value should not exceed 1.4 in the maxilla and 1.5 in the mandible. A high PU/I value could produce bending and flexure of the interim restoration leading to micro-movement at the implant interface and fibrous encapsulation. Finally, patients with parafunctional habits, if not excluded, should at least be informed about the greater potential risks associated with implant failure when immediate loading is considered (Avila *et al.*, 2007; Jaffin *et al.*, 2004).

## **Site-specific immediate loading**

### **i) Edentulous mandible**

In edentulous mandibles, the immediate loading of four implants with an overdenture in the interforminal area with rigid bar fixation and cross-arch stabilization is predictable, with survival rates of 90%-100% consistently reported (Attard & Zarb, 2005;

Cochran *et al.*, 2004). This situation is extremely favorable from a biomechanical point of view due to an excellent bone quality and is irrespective of implant type and surface topography (Attard & Zarb, 2005). A meta-analysis of immediately loaded dental implants by Ioannidou & Doufexi (2005) included two RCTs on immediate loading of mandibular overdentures supported by four interforaminal implants with rigid bar connections. Both studies reported no statistically significant difference in prosthesis or implant failures between the immediately and conventionally loaded implants. These results are in agreement with a review that reported survival rates of 96-100% and success rates of 88.2-100% for four implant retained overdentures (Chiapasco, 2004). Sufficient evidence also exists to support overdentures retained by two bar-splinted implants, with survival rates of 98% (Alfadda *et al.*, 2009; Stoker & Wismeijer, 2009). However, another study published a twelve-month survival rate of 81.8% for the placement of one or two dental implants with ball attachments for the support a mandibular overdentures (Kronstrom *et al.*, 2010). It was concluded that immediate loading of one implant by means of ball attachment supported mandibular overdentures should be performed with caution, as a higher than expected implant failure rate was observed.

Immediate loading of implants supporting fixed restorations in the edentulous mandible is also a predictable and well-documented procedure with survival rates ranging from 90-100% over follow up periods of one to ten years (Nkenke & Fenner, 2006). A prospective study evaluated 126 implants supporting immediate fixed restorations and found a cumulative survival rate of 99.4% and success rate of 98.4% over a one to six year period. The cumulative mean crestal bone resorption was 0.56 mm, 0.76 mm, 0.84

mm, 0.82 mm, 0.83 mm and 0.94 mm at 12, 24, 36, 48, 60, and 72 months respectively (Ibanez *et al.*, 2005). In case of fixed hybrid prostheses, publications have included a minimum of five or six implants placed both interforaminally and posteriorly in order to reduce the cantilever effect (Drago & Lazzara, 2006; Testori *et al.*, 2004). In full porcelain fixed prostheses, the number of implants necessary was determined according to the rigidity of the prosthesis and a greater number was generally employed (Degidi & Piattelli, 2003; Ibanez *et al.*, 2005). The publications reported that crestal bone loss was comparable to that in conventionally loaded implants (Ibanez *et al.*, 2005; Testori *et al.*, 2004). An alternative protocol termed “All-on-Four” includes the placement of four interforaminal implants (or more if the torque is inadequate) with tilting of the posterior implants, thereby allowing the fixed final prostheses to hold as many as twelve teeth with only a short cantilever (Malo *et al.*, 2003). A survival rate of 96.7% and bone loss of  $0.6-1.2 \pm 0.6-1.2$  mm was published for 176 immediately loaded implants using this protocol (Malo *et al.*, 2003). Using finite element studies, it has been demonstrated that tilting of the splinted implants resulted in less stress at the implant bone interface as compared to the cantilevered model (Zampelis *et al.*, 2007). A more recent study evaluated 93 immediately loaded mandibular full-arch fixed prostheses supported by two distal tilted implants and two anterior axially placed implants. Implant survival at one year was 99.73% for the mandible, and marginal bone loss averaged  $1.2 \pm 0.9$  mm. Interestingly, no difference was found in marginal bone loss between axial and tilted implants (Agliardi *et al.*, 2010). Based on these recent publications, preliminary results suggest that the immediate fixed restoration of as few as four implants, some of which are tilted may also be a viable treatment option for the rehabilitation of the edentulous mandible.

## ii) Edentulous maxilla

The reported success of immediate loading in the mandible has encouraged the application of similar treatment in the maxilla. While establishing the foundation for others to follow, Tarnow *et al.* (1997) demonstrated that a similarly high survival rate (100%) could be achieved in immediate loading of the maxilla using a full-arch fixed prosthesis. Although a high level of evidence for supporting immediate loading in the edentulous maxilla is more limited as compared to the mandible, reported success rates are highly encouraging. Insufficient data exists to support immediate loading of dental implants with overdenture prostheses in the edentulous maxilla (Cochran *et al.*, 2004; Weber *et al.*, 2009). In terms of fixed prostheses, literature demonstrates that, as a general rule, more implants are inserted in the edentulous maxilla compared with the edentulous mandible (Chiapasco, 2004; Misch *et al.*, 2004b). It is postulated that the maxilla requires more implant support because the bone is often less dense and the direction of force is outside of the arch in all excursive movements (Misch *et al.*, 2004b). Jaffin *et al.* (2004) reported twelve-month survival rates of 92.2% for immediately loaded, full-fixed prostheses in the maxilla. Each jaw included six to eight implants in each of 34 edentulous maxillae. Degidi *et al.* (2008) reported a 100% implant survival rate and mean marginal bone loss of 0.57 mm after twelve months of loading. Comparably high survival rates and favourable marginal bone loss measurements were reported by other studies (Ibanez *et al.*, 2005; van Steenberghe *et al.*, 2005). Successful immediate loading with a fixed hybrid prosthesis following placement of five to seven implants in the edentulous maxilla over 32 month follow up period has also been demonstrated with a survival rate of 98.2% and mean marginal bone loss slightly higher than that reported by previous studies (1.6 mm at 8 months after loading, an additional

0.41 mm from 8 to 20 months and 0.08 mm from 8 to 32 months) (Bergkvist *et al.*, 2009). It was suggested that the lower bone loss observed in studies by Ibanez, *et al.*, van Steenberghe, *et al.* and Degidi, *et al.* was likely attributed to the placement of the final restoration immediately after implantation, which eliminated steps necessary to make a traditional final restoration (e.g., multiple impressions and trying in of restorations) thereby diminishing the risk of damage to the peri-implant tissue and subsequent bone resorption (Degidi *et al.*, 2008). Using the “All-on-Four,” protocol, a study found a one-year survival rate of 97.6% and mean marginal bone loss of 0.9 mm for 128 immediately loaded implants supporting a fixed maxillary prostheses (Malo *et al.*, 2005). These results were supported by studies reporting survival rates of 98.8% and 98.4% respectively for four to six implants placed in axial and tilted orientations and mean marginal bone loss of 0.8-0.9 mm (Agliardi *et al.*, 2010; Testori *et al.*, 2008). By tilting the posterior implants, the cantilever can be reduced, sinus augmentation procedures can be avoided and a longer implant can be placed, thereby increasing BIC. In addition, the use of fewer implants to support the prosthesis and the application of the immediate loading protocol, can reduce the overall treatment costs (Testori *et al.*, 2008). Although long-term, evidence based studies for the maxilla are less numerous, the available reports indicate that similar success and survival rates can be achieved with immediate loading as compared to conventional protocols. However, case selection remains important and more long-term data is necessary before immediate loading of implants can be recommended as a standard procedure in the maxilla.



### iii) Partial edentulous sites – single crowns and fixed partial restorations

Numerous studies have presented results on immediate loading of fixed partial dentures in all anatomic locations. It was suggested that perhaps the highest proposed risk lies in the posterior segments, as they must withstand the greatest occlusal forces (Misch *et al.*, 2004a). In a systematic review on posterior maxillary partial edentulous loading protocols, six articles reported high survival rates (>95% for rough surface implants), but it was noted that the protocol was technique sensitive and dependent on good primary stability (Roccuzzo *et al.*, 2009). In a RCT evaluating implants in the posterior mandible and maxilla, survival rates were 98% and 97% in the immediate and early group respectively. Mean marginal bone loss for immediate and early loading was  $0.90 \pm 0.90$  mm and  $0.63 \pm 0.95$  mm, however, after adjusting for initial implant depth, the difference was no longer significant (Ganeles *et al.*, 2008). Well-designed RCTs with a large number of patients are necessary to make immediate loading protocols in posterior maxilla evidence based, but current reports indicate that under good case selection, it is possible to achieve successful immediate loading of implants in the posterior maxilla. TiUnite surface implants placed in the posterior mandible demonstrated a cumulative success rate of 95.5% after one year of prosthetic load. The corresponding cumulative success rate for machined-surface implants was 85.5% (Rocci *et al.*, 2003b). It is noteworthy that in the case of the machined-surface implants, the number of failed implants was significantly higher in smokers and in sites with lower bone density. A multicenter trial evaluated treatment outcomes following immediate restoration of NobelActive and NobelReplace tapered implants. Of those restored by single crowns and fixed dental prostheses, the majority of the implants were placed in the posterior mandible (Kielbassa *et al.*, 2009). After one year, the implant survival rates were 96.6%

for the NobelActive internal hex, 96.3% for NobelActive external hex and 97.6% for NobelReplace. The associated mean marginal bone loss was  $0.95 \pm 1.37$  mm,  $0.64 \pm 0.97$  mm,  $0.63 \pm 1.18$  mm respectively (Kielbassa *et al.*, 2009). A Cochrane systematic review identified publications evaluating immediate, early and conventional loading protocols and found no significant difference between the different loading protocols in implant survival or marginal bone loss (Esposito *et al.*, 2009). However, trends did suggest that immediately loaded implants failed more often than those conventionally loaded, but less commonly than those early loaded. It was noted that a high degree of primary implant stability was one of the prerequisites for a successful clinical outcome (Esposito *et al.*, 2009). Although the survival rates reported for immediately loaded, partial fixed prosthesis in the posterior segments are greater than 95% (for rough surface implants), a benefit-risk ratio must be assessed for each patient condition to ascertain whether immediate occlusal loading is a worthwhile alternative in this area, especially in non-splinted, single standing implants. Since a provisional restoration is often required, it may contribute to unnecessary expenses for the patient.

### **Marginal bone loss in immediately loading vs. conventional loading**

Few studies have compared marginal bone level changes in immediately loaded/restored implants to conventionally loaded implants. In a RCT, single-unit restorations in mandibular molar sites were evaluated in terms of immediate versus delayed loading. After twelve months of loading, the average bone level change was significantly less for the immediate versus delayed protocol ( $0.77 \pm 0.38$  mm and  $1.2 \pm 0.55$  mm respectively) (Schincaglia *et al.*, 2008). This was in agreement with another report that demonstrated cumulative survival rates of 98.5% with no discernible peri-implant

bone loss in 88% of surviving implants. Among 32 implants that sustained crestal bone loss, 91% and 9% exhibited 1 and 2 mm of crestal bone loss, respectively. A greater prevalence of bone loss was found in the delayed loading group than in the immediate loading group (Ormianer & Palti, 2008).

## **Conclusion**

While immediate loading is emerging as a worthwhile and attractive treatment alternative, the risk-benefit ratio must continually be assessed on an individual and site-specific basis. The most salient feature of the reviewed literature is that immediate loading of implants is a modality requiring a higher degree of experience and clinical competency. Immediate loading in the mandible has consistently documented high, long-term success rates that are comparable to that of conventional loading. Although a high level of evidence for long-term immediate loading in the maxilla is lacking as compared to the mandible, results available to date are promising. High success rates have been documented, even in the posterior maxilla, provided that careful case selection, surgical preparation, excellent primary stability, considerations in prosthetic design, and a regular recall regime is implemented.

### **2.5.3 Immediate restoration/loading of immediately placed implants**

In the last two decades, several investigators have reported on immediate placement of dental implants into extraction sockets, and more recently, immediate loading has become an emerging technique increasingly documented in literature. Advantages of placing implants in fresh extraction sockets followed by immediate loading are numerous. In addition to the reduction in treatment time and to the number of

procedures involved, it is purported to minimize the shrinkage of hard tissue and soft tissue recession (Vanden Bogaerde *et al.*, 2005). Removal of a tooth will often have a negative psychological effect on the patient and the immediate replacement of an extracted tooth within the same day, particularly if it is in the anterior region, is an extremely attractive treatment option. However, strong evidence-based reports are lacking for the evaluation of immediate loading/restoration of implants placed in fresh extraction sockets. In addition, they are based on limited sample sizes with short follow up periods and are often without control groups.

### **Treatment outcomes**

#### **i) Systematic reviews**

Few studies have made direct comparisons of immediately loaded implants placed in extraction sockets versus healed sites. Those that have, demonstrated no difference in survival rates or marginal bone loss between the two protocols (Degidi *et al.*, 2007; Knoernschild, 2010; Pieri *et al.*, 2009) or less marginal bone loss in favour of immediate restoration (De Rouck *et al.*, 2009). A systematic review evaluated 19 prospective studies on single teeth in the esthetic zone and compared immediate loading of implants placed in extraction sockets to immediate loading in healed sites, and to conventional loading in healed sites (two-thirds of patients received implants in healed edentulous sites). The survival rate was 95.5% for single-tooth implants after one year of function. A meta-analysis identified no difference in survival rates based upon timing of implant placement and loading. Survival of single-tooth implants ranged from 92.4% for conventional placement with immediate loading, to 97.5% for immediate placement with immediate loading (Knoernschild, 2010). Another meta-analysis identified 0.20 mm of

marginal bone loss for implants in function over one year (Knoernschild, 2010). These results are contrary to that reported by Quirynen *et al.* (2007), who in a systematic review evaluating immediate placement, concluded that there was a trend toward a greater incidence of implant loss when combining immediate placement and immediate loading as compared to immediate loading alone (10.4% versus 5-6.2%). Due to the lack of evidence-based studies, it was reported that conclusions could not be drawn on the effects of marginal bone loss.

#### ii) Retrospective and parallel study designs

A large retrospective analysis evaluated immediately loaded implants that were placed in extraction sockets (test group) and healed sites (control group). Only 8 of 1074 implants were lost (survival rate of 99.3%) and no differences were detected among the studied variables or in marginal bone loss measurements (Degidi *et al.*, 2007). Harder bone was related to a lower marginal bone loss and thus a better outcome. Poor bone quality and older age correlated with a slightly higher bone resorption (Degidi *et al.*, 2007). A prospective parallel study evaluated 144 implants, 59 placed after tooth extraction (test group) and 85 in healed sites (control group). Within 48 to 72 hours of implant placement, nine maxillary and 15 mandibular arches received screw-retained, fixed prostheses. One implant failure occurred in each group resulting in a cumulative success rate of 98.6%. At the one-year follow up, no statistically significant difference was found between the control and test sites with respect to marginal bone loss ( $0.47 \pm 0.18$  mm versus  $0.57 \pm 0.27$  mm) (Pieri *et al.*, 2009). The influence of the restorative protocol (immediate vs. delayed restoration) on the esthetic outcome of immediately placed single-tooth implants over a one-year period was evaluated by means

of a RCT including 49 patients. Incisor and canine replacements accounted for more than 60% of the cases. One implant was lost in the immediate group (survival 96%) and two in the delayed group (survival rate of 92%). Bone loss was <1.0 mm at twelve months; at six months, distal bone loss was significantly lower in the immediate loading group as compared to the delayed group. The mean papilla shrinkage was 2.5 – 3 times higher in the delayed group as compared to the immediate group (De Rouck *et al.*, 2009). It was proposed that greater shrinkage in the delayed group may have been attributed to the collapse of the soft tissues during the three month healing period, and to inflammation, if primary closure was not achieved. In contrast, tissues were continuously supported by the prosthesis in the immediate loading group, which may have contributed to the improved maintenance of the papillary height. This is contrary to the findings of Chen and Buser (2009), who reported that immediate restoration and loading protocols had similar outcomes with respect to soft tissue alterations. Chaushu *et al.* (2001) compared 19 immediately loaded single-tooth implants placed in fresh extraction sites to that of nine immediately loaded single-tooth implants placed in healed sites. Three implants failed in the immediate group with resultant survival rates of 82.4% and 100% for immediate and non-immediately placed implants respectively, after a follow up period of 6 – 24 months. Radiographic marginal bone loss after three to six months did not extend beyond the abutment-implant junction. The results attained by Chaushu *et al.* (2007) were consistent with that reported by Quirynen *et al.* (2007), however the sample size in the study was extremely small and the results have to be interpreted with caution.

### iii) Case series

In subsequent reports, no comparison group (control) was used to compare the

clinical outcomes of immediately placed/immediately loaded implants, however, high survival rates were continually reported. One study evaluated the long-term survival of 24 immediate single-tooth implants in the anterior maxilla and provided non-functional immediate loading. One implant failed, resulting in an implant survival rate of 95.8%; the mean marginal bone loss was  $0.9 \pm 1.1$  mm after 24 – 72 months of restoration (Mijiritsky *et al.*, 2009). Another study evaluated the effect of keratinized mucosa (KM) on immediately placed/immediately loaded implants. Implants were categorized into two groups:  $KM \geq 2$  mm and  $KM < 2$  mm. A survival rate of 100% was reported at the four-year follow up and the presence of KM was found to be significantly associated with less gingival inflammation, plaque accumulation, and gingival recession (Crespi, *et al.*, 2010a). Marginal bone loss in the two groups was  $0.85 \pm 0.23$  mm and  $0.99 \pm 0.58$  mm respectively; interestingly, lack of keratinized tissue did not have a significant effect on marginal bone loss (Crespi, *et al.*, 2010a). Two studies reported results on implant placement in the posterior segments with favourable clinical outcomes (Vanden Bogaerde *et al.*, 2005; Glauser *et al.*, 2003). Vanden Bogaerde *et al.* (2005) evaluated 50 implants placed in extraction sockets in the maxilla and posterior mandible and restored them immediately or within seven days ('early function'). None of the implants failed in the 18-month follow up period (survival rate of 100%), however, one implant showed signs of failure after six weeks. The authors reported that once the occlusal load was removed, the implant regained its stability completely and could be used successfully for prosthetic rehabilitation. The marginal bone resorption was  $0.9 \pm 1.1$  mm after 18 months of loading. Glauser *et al.* (2003) evaluated 102 implants, 23 of which were immediately placed and loaded. The majority of implants were placed in posterior sites. Neither smoking, nor

immediate or recent extraction sites had an effect on survival outcome. A cumulative success rate of 97.1% and a mean marginal bone resorption of  $1.2 \pm 0.9$  mm after one year of prosthetic loading was observed. The following two studies evaluated immediately placed with immediately restored/loaded implants in the edentulous arches, reporting similar treatment outcomes. Cannizzaro *et al.* (2007) evaluated 202 immediately loaded implants in the maxilla, 53 of which were inserted in fresh extraction sockets using a flapless technique. All restorations (21 fixed prostheses and 12 overdentures) were functionally loaded the same day of the surgery and followed for one year after loading. Only two failures occurred resulting in a survival rate of 99%; no information regarding bone loss was included. Immediately loaded implants with bar-retained overdentures in edentulous maxillae demonstrated high overall implant survival and success rates (97.1% and 95.2% respectively) and a mean marginal bone loss of  $0.78 \pm 0.79$  mm after one year of function (Pieri *et al.*, 2009).

## **Conclusion**

Studies published to date on immediate implant placement with immediate restoration/loading have reported high survival and success rates comparable to rates achieved with conventional implant placement and loading. Excellent treatment results have been demonstrated in single implant restorations, fixed partial dentures and complete arch prostheses. However, limitations in the level of evidence, study designs, sample sizes, and follow up periods indicate that the results must be interpreted with caution. Although, it was not reiterated in this section, the previously mentioned principles of immediate placement and loading protocols were strictly adhered to in these publications. Primary stability, as measured during placement by insertion torque and



RFA, was considered a prerequisite to immediate placement with immediate loading. It is important to note that the treatment outcomes achieved with this challenging protocol may be misleading, as most publications were written by exceptionally experienced, highly skilled practitioners working under tightly controlled clinical conditions on a relatively small, statistically inconclusive number of implants and patients. Therefore, similarly high survival rates and marginal bone loss measurements may not be achieved by the average clinician.

### 3. OBJECTIVE

The objective of this retrospective chart review was to evaluate the clinical outcome of the novel NobelActive internal hex implant in terms of survival rate and marginal bone loss after an average of one year of function. Patient, site, and implant design-related factors that may impact these two outcome variables were also investigated. The implants were placed by experienced practitioners in two private clinics and by senior Graduate Periodontics residents at the University of British Columbia.

The following *hypotheses* were tested:

- I. Implant survival and marginal bone loss of the novel NobelActive implant system is comparable to that of current validated implant systems, regardless of timing of implant placement or loading
- II. Patient, site, or implant-related factors do not significantly impact implant survivals
- III. A history of smoking negatively affects marginal bone levels
- IV. Denser bone quality and higher insertion torque positively affect marginal bone levels

## 4. MATERIALS AND METHODS

A retrospective chart review of patients treated by two experienced periodontists in two private clinics (Vancouver and Calgary) and by four senior Graduate Periodontics residents at the University of British Columbia between December 4, 2007 and April 28, 2009 was performed. Human ethics approval was attained from the Clinical Research Ethics Board, University of British Columbia Office of Research Services. NobelActive internal connection implants (Nobel Biocare) were evaluated over a period of 4 to 27 months following loading, with an average post-loading period of 12.9 months. The implants were placed in partially dentate and edentulous sites of the maxilla and mandible, in either native bone or in sites augmented previously or simultaneously with implant placement. Bone augmentation procedures included previous or simultaneous guided bone regeneration (socket preservation, lateral ridge augmentation) and previous or simultaneous sinus augmentation (lateral window or osteotome technique). Implants were placed immediately in fresh extraction sockets or in native bone and were restored with immediate or delayed loading protocols (Cochran *et al.*, 2004). The inclusion criterion is outlined in Table 1 below. Exclusion criteria included an incomplete follow up period and unrestored implants.

Table 1. Inclusion Criteria

<ul style="list-style-type: none"><li>• Patients who had one or more NobelActive implant(s) placed at two private practices and at the UBC graduate periodontics program</li></ul>
<ul style="list-style-type: none"><li>• Availability of post-loading radiographic and clinical follow up assessments</li></ul>
<ul style="list-style-type: none"><li>• Radiographs depicting implants in their entirety with clearly discernable threads during placement and follow up appointments</li></ul>

The primary outcome variable was implant failure. An implant was considered to

be a failure if it exfoliated or had to be removed from the oral cavity due to the following reasons: implant mobility, peri-implant radiolucency, irresolvable clinical symptoms experienced by the patient, mechanical problems that would preclude the prosthodontic restoration and the removal of stable implants due to progressive marginal bone loss or infection.

The secondary outcome variable was marginal bone loss as measured on conventional and digital radiographs at baseline and follow up appointments. The assessment of radiographic bone level changes around implants may be a useful diagnostic tool for the early detection of disease, thereby allowing for timely treatment. Periapical radiographs were used, except in three cases (seven implants), where only orthopantomograms were available for baseline registrations. Intraoral radiographs were taken at implant placement and during follow up appointments with a long-cone parallel technique using a paralleling device (Dentsply Rinn, Rinn Cooperation, USA).

Conventional radiographs were photographed with a digital camera on a light desk and all digital images were measured using Image J 1.42q software (National Institutes of Health, Maryland, USA). Digital radiographs taken at UBC were measured in the Romexis 2.2.7R software system (Planmeca; Helsinki, Finland). The coronal margin of the implant collar and the most coronal aspect of the bone-to-implant contact were used as reference points for the linear measurements of marginal bone loss (Appendix C). Measurements of the mesial and distal crestal bone levels adjacent to each implant were performed. In order to compensate for angulation and magnification distortion in the radiographs, the known implant lengths (10, 11.5, 13, 15 mm) were used for the calibration of the measurements (Appendix E, F, G) (Guncu *et al.*, 2008; Sennerby

& Meredith, 2008). The amount of true bone resorption, the difference between the initial bone level, and the bone level at follow-up examinations were calculated. For those implants placed intentionally in a supracrestal position, the height of the implant collar above the alveolar crest during placement was subtracted from follow up radiographs. The mesial, distal, average and worst marginal bone loss values were recorded for each implant. In order to reduce measurement error and bias in the radiographic assessment of the marginal bone loss, one ‘blinded’ examiner who was not involved in the treatment of patients, evaluated all radiographs. Twenty-five periapical radiographs were measured twice, once at baseline, and again after four months to assess intra-examiner reliability.

Criteria for success according to Albrektsson *et al.* (1986) and Albrektsson & Zarb (1993) included absence of implant mobility, pain, infection, neuropathy, paresthesia and peri-implant radiolucency. With the advent of rough surface implants, 1 mm of bone loss was reported as acceptable during the first year after placement and 0.1 mm annually thereafter (Albrektsson & Zarb, 1993). The use of success as an outcome variable was not possible in this study due to the limited follow up data available and due to the fact that implants cemented into multiunit and splinted constructions could not be individually tested for mobility. Furthermore, post-operative complications were assessed using only the chart notes, as patients were not re-examined for this report. Due to the aforementioned limitations and the inherent challenges typical of a retrospective design, it was inappropriate to make conclusions regarding implant “success” in this study.

Patient demographic and clinical data was collected throughout the study and

entered into a computer database (Microsoft Excel 2008; Microsoft Corporation, Redmond, WA). Implant related information relevant to osseointegration such as the presence of signs or symptoms of mobility, infection, pain, neuropathy and radiographic signs of peri-implant radiolucency were evaluated at follow up appointments. Variables that may present as possible risk factors for implant failure were identified as follows: patient-related factors (age, gender, medical and smoking status), anatomic site-related factors (bone quantity, implant location, previous or simultaneous bone regeneration), implant properties (length, width), primary stability (insertion torque), timing variables (one versus two-stage protocol; implant placement and loading), prosthodontic considerations (type of prosthesis) and the use of peri-operative antibiotics. The same data was also collected for replacement implants placed in sites of previous implant failures.

Patients were classified as current, former or never smokers based on information in the medical history questionnaire. The quality of bone was documented during placement and was based on the experience of the clinicians and residents. It has been demonstrated that it is difficult to differentiate between type II and type III bone, but relatively straightforward to determine if the implants were placed in dense type I bone or soft type IV bone (Alsaadi *et al.*, 2007; Trisi & Rao, 1999). As such, for the purposes of this study, the bone density categories were divided into soft, medium and dense. The insertion torque was measured and documented for all cases using the NobelActive hand wrench instrument from the NobelActive surgery kit (Appendix D). This manual torque wrench has the ability to measure insertion torque up to 70 Ncm (markings of 35 Ncm and 70 Ncm present). ‘Immediate placement’ referred to placement following tooth

extraction and ‘immediate loading’ was performed within 48 hours of implant placement. Prosthetic rehabilitations included single unit crowns, splinted crowns, fixed partial dentures and fixed complete-arch prostheses.

Statistical analysis was completed using the PASW statistics program (PASW, Chicago, IL, version 18.0). Descriptive statistics were used for all evaluated parameters, and baseline patient and implant characteristics were summarized in terms of frequencies and percentages for categorical variables. Survival rates were calculated and bivariate analyses were used to identify risk factors associated with implant survival. All predictor variables were analyzed at the implant level. Since the mean mesial and distal marginal bone loss measurements were highly correlated (Pearson correlation coefficient = 0.643,  $p = 0.000$ ), the average of the mesial and distal bone loss measurements was used for the bivariate analyses to identify risk factors associated with marginal bone resorption. Risk factors with  $p$ -values  $< 0.05$  or predictors considered important based on previous implant studies, were included in logistic regression analysis and in a stepwise linear multiple regression analysis. The outcome variables for these analyses were implant failure and marginal bone loss. The  $P$ -value of 0.05 was considered to be statistically significant. The Pearson chi-square test was used to compare two categories to identify possible significant differences ( $p < 0.05$ ). Results from the Fisher’s Exact test were recorded when a category had fewer than five cases. Multivariate logistic regression analyses were performed to evaluate the relationships between the risk factors identified and the occurrence of implant failure and marginal bone loss. Multicollinearity and the tolerance values of the predictors were evaluated. Tolerance is an estimate of the collinearity of predictors, or how closely two predictors are related to one another

(Altman, 1991). A tolerance value of 1.0 means that the effect of the tested predictor is completely unrelated to the other independent predictors. A tolerance value approaching 0.0 indicates colinearity, meaning the predictor shares its effects with other predictors (Altman, 1991).



## 5. RESULTS

A total of 87 patient charts from the three centres were available for analysis. Radiographs were in digital format at two centres (UBC clinic and Vancouver private practice) and in analog format at the Calgary private practice. Of the available charts, 23 had incomplete records and were excluded from the study. The majority of these records were lacking post-operative radiographs of the restored implants, often because patients would not present for follow up appointments (n=21). In two cases, implants remained unrestored because the decision was made to place additional implants in the same arch prior to final restoration; these cases were excluded because the outcome measures were only assessed for restored implants (n=2) (Table 2). Two charts included eight implants that were not restored due to failures of adjacent implants within the same jaw. These charts were included for statistical analysis of the primary outcome variable of implant survival, but not for secondary outcome assessment of marginal bone loss since these implants remained unrestored throughout the study period. This report included 64 charts with a total of 124 NobelActive implants available for analysis of the primary outcome variable and 116 available for the marginal bone loss measurements.

Table 2. Reasons for exclusion of charts

	<b>Number of charts</b>
Missing follow up radiograph of restored implant	21
Implants remain unrestored due to placement of additional implants prior to final restoration	2
<b>Total</b>	23

### ***5.1 Implant follow up period after loading***

A total of 124 NobelActive implants placed between December, 2007 and April, 2009 for 64 patients were evaluated in this report. The average follow up period ( $\pm$ SD) from the placement of the implant restoration was 12.87 ( $\pm$ 4.83) months with a range of 4 to 27 months.

### ***5.2 Distribution of implants***

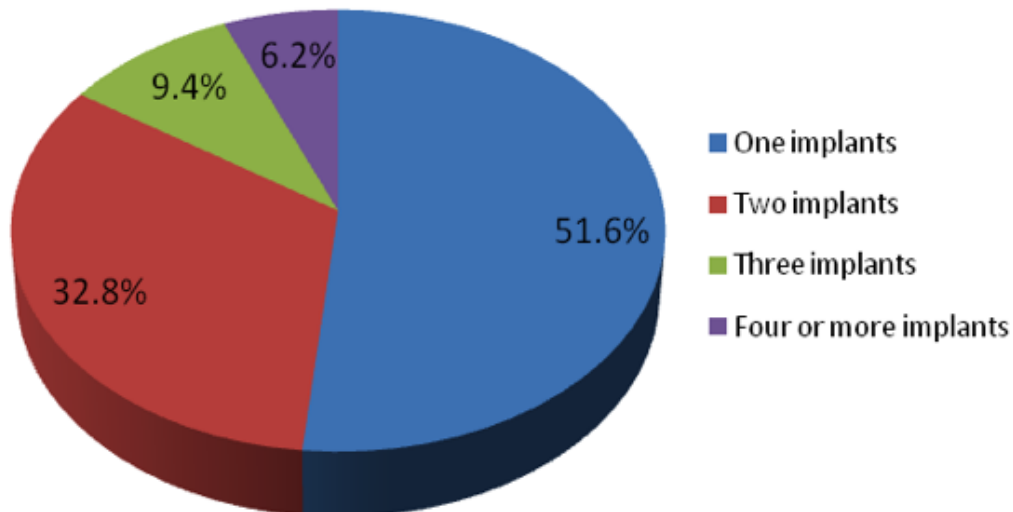


Figure 1. Percentage of patients with one or more implants placed at the three centres

The majority of patients (51.6%) received one implant, while 32.8% received two implants, 9.4% received three implants and 6.2% received four or more implants.

### 5.3 Outcome variables

#### 5.3.1 Primary outcome variable - implant survival

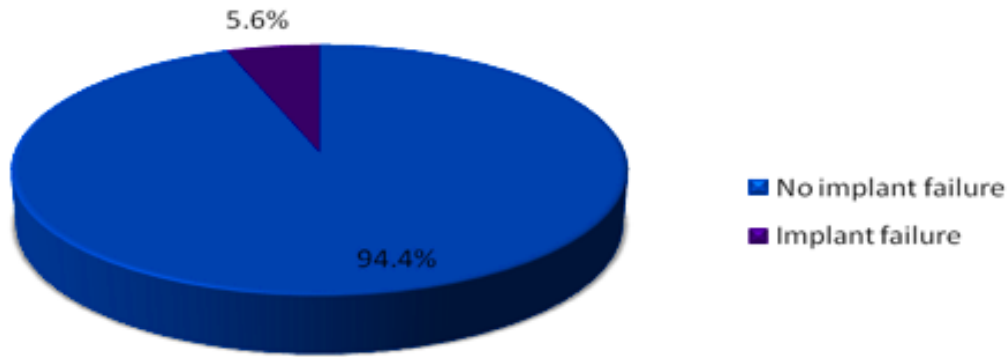


Figure 2. Implant failures and resultant implant survival rate

Of the 124 implants placed, seven failed and were removed, resulting in a survival rate of 94.4%. 10.9% of patients experienced an implant failure (7/64) and no patient experienced two implant failures.

Table 3. Description of failures

	Site	Bone Density	Torque	Smoking Status	Diabetes	Placement	Loading	GBR*/Sinus augmentation	Time from implantation until removal
1	36	Soft	70 Ncm	Non-smoker	Non-diabetic	C	C	Simultaneous GBR (LRA*)	5 months
2	25	Soft	20 Ncm	Former smoker	Non-diabetic	C	C	Simultaneous GBR (O*)	3 months
3	35	Medium	50 Ncm	Non-smoker	Diabetic	C	C	Previous GBR (SP*)	1 month
4	44	Dense	50 Ncm	Smoker	Non-diabetic	I	I	None	11 months
5	22	Medium	40 Ncm	Non-smoker	Non-diabetic	I	C	None	5 months
6	24	Dense	70 Ncm	Former smoker	Non-diabetic	I	C	None	3 months
7	34	Dense	70 Ncm	Smoker	Non-diabetic	C	C	None	19 months

\* C – conventional implant placement in native bone / conventional loading after a healing phase

\* I – immediate placement into fresh extraction socket / immediate restoration or loading

\* GBR – guided bone regeneration

\* O – osteotome sinus augmentation

\* LRA – lateral ridge augmentation

\* SP – socket preservation

Implants failed an average of 6.71 months following implant placement, with a minimum of 1 month and maximum of 19 months. Six of the seven failures occurred prior to implant restoration and one failure occurred eleven months after immediate loading.

### 5.3.2 Secondary outcome variable - marginal bone loss

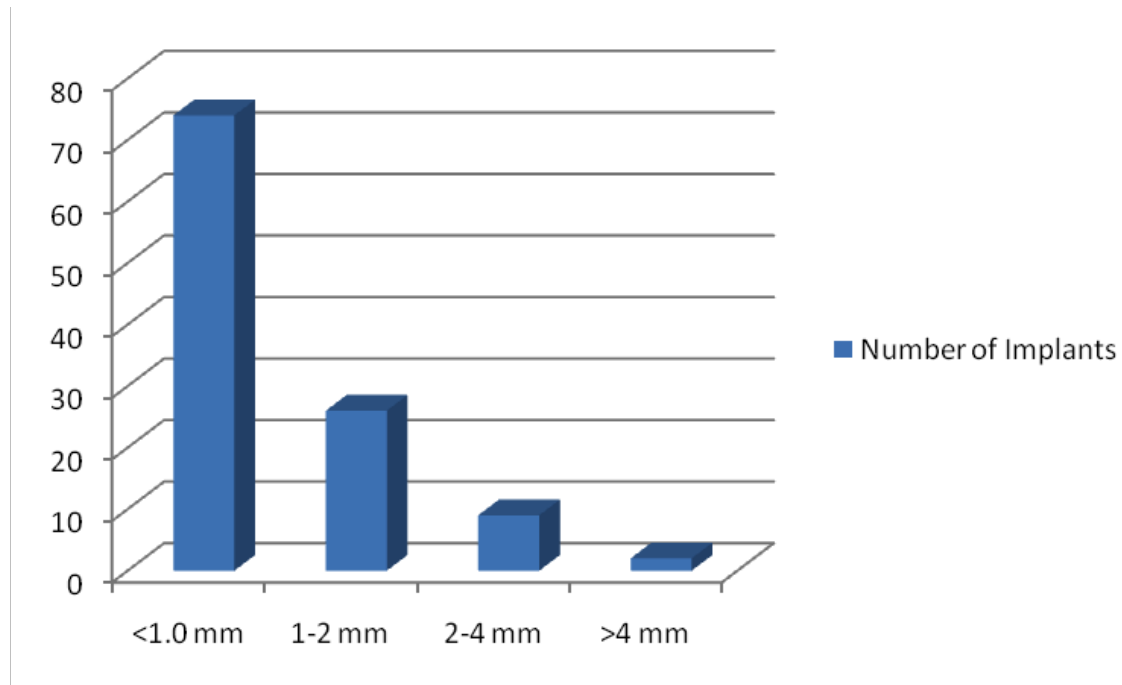


Figure 3. The number of implants and mean marginal bone loss grouped

Data for marginal bone loss measurements was available for 111 restored implants with a mean follow up period of 12.9 months. 66.7% of the implants placed during the study period had marginal bone loss of  $\leq 1.0$  mm, 23.4% had 1-2 mm, 8.1% had 2-4 mm and 1.8 % had > 4mm.

### Marginal bone loss

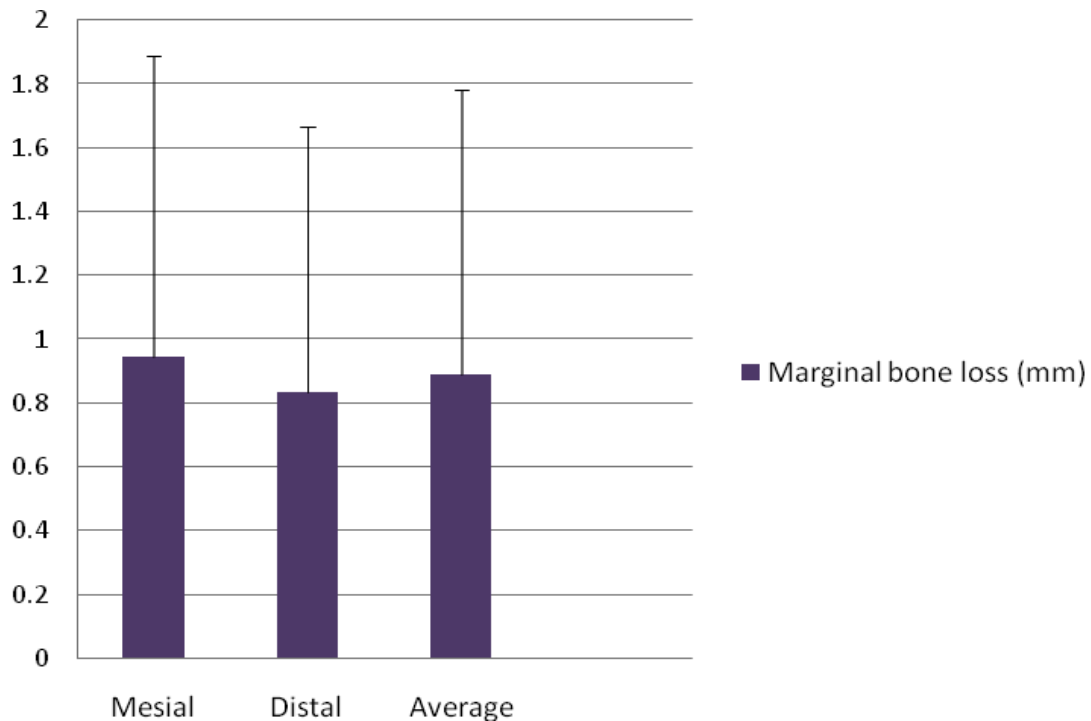


Figure 4. Mean marginal bone loss for the mesial, distal and average of the mesial and distal measurements

The mean mesial marginal bone loss ( $\pm$ SD) was 0.94 ( $\pm$ 1.05) mm with a minimum of 0 mm and maximum of 5.63 mm. The mean distal marginal bone loss ( $\pm$ SD) was 0.83 ( $\pm$ 1.00) mm with a minimum of 0 mm and maximum of 5.32 mm. Since the mean mesial and distal marginal bone loss measurements were highly correlated (Pearson correlation coefficient = 0.643,  $p=0.000$ ), the average mean marginal bone loss ( $0.89\pm0.95$  mm) was used for subsequent statistical analysis (min. 0 mm, max. 5.48 mm). A separate category of the mean ‘largest or worst’ bone loss ( $1.15\pm1.08$  mm; min. 0, max. 5.48), which depicted the worst mesial or distal measurement for each implant was included, however, this value was not used for subsequent analyses as it can over-estimate the marginal bone resorption that occurred.

## 5.4 Patient-related factors

### 5.4.1 Age

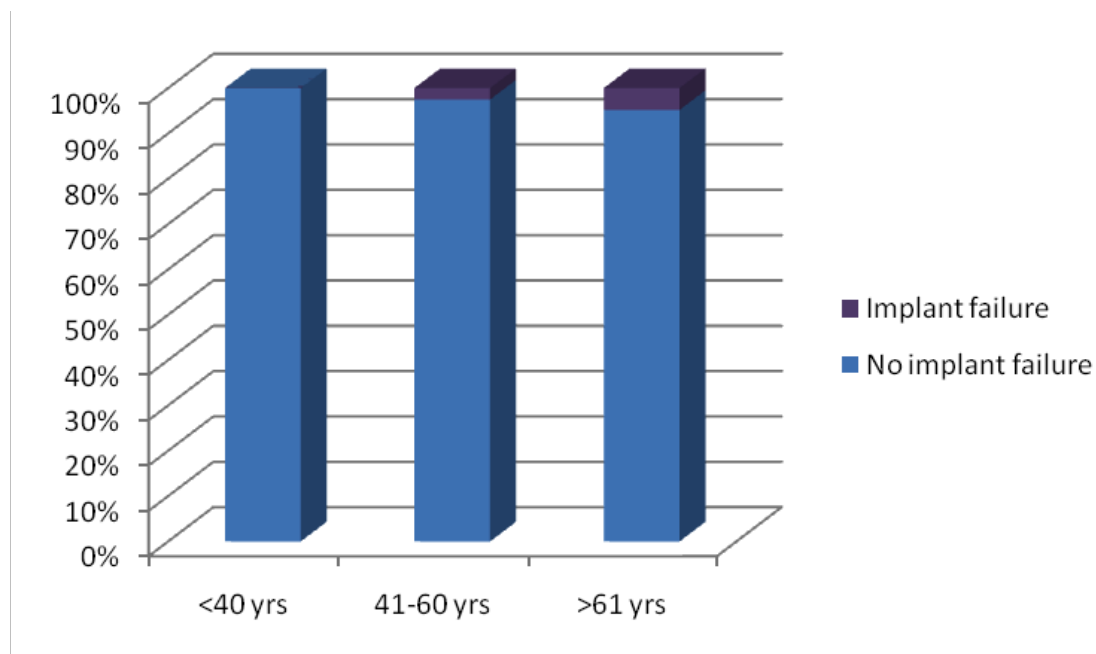


Figure 5. Implant survival and failure in each group

Patients in the study ranged in age from 20 to 81 years, with a mean age of 56.31 ( $\pm 16.20$ ) years during implant placement. Patients were categorized into three age groups: less than 40 years, 40-60 years and greater than 60 years of age. 21 patients (16.9%) comprised the age group of <40 years, 41 patients (33.1%) were in the middle age group and 62 patients (50%) were in the >60 years of age group. Three implants failed in the 40-60 year age group (survival = 97.5%), and four implants failed in the >60 year age group (survival 95.1%). Statistical analysis was performed on the raw data prior to categorization; groupings were done for visual purposes only. There was no statistically significant association between age and in implant survival rate ( $p=0.593$ ).

## Age and marginal bone loss

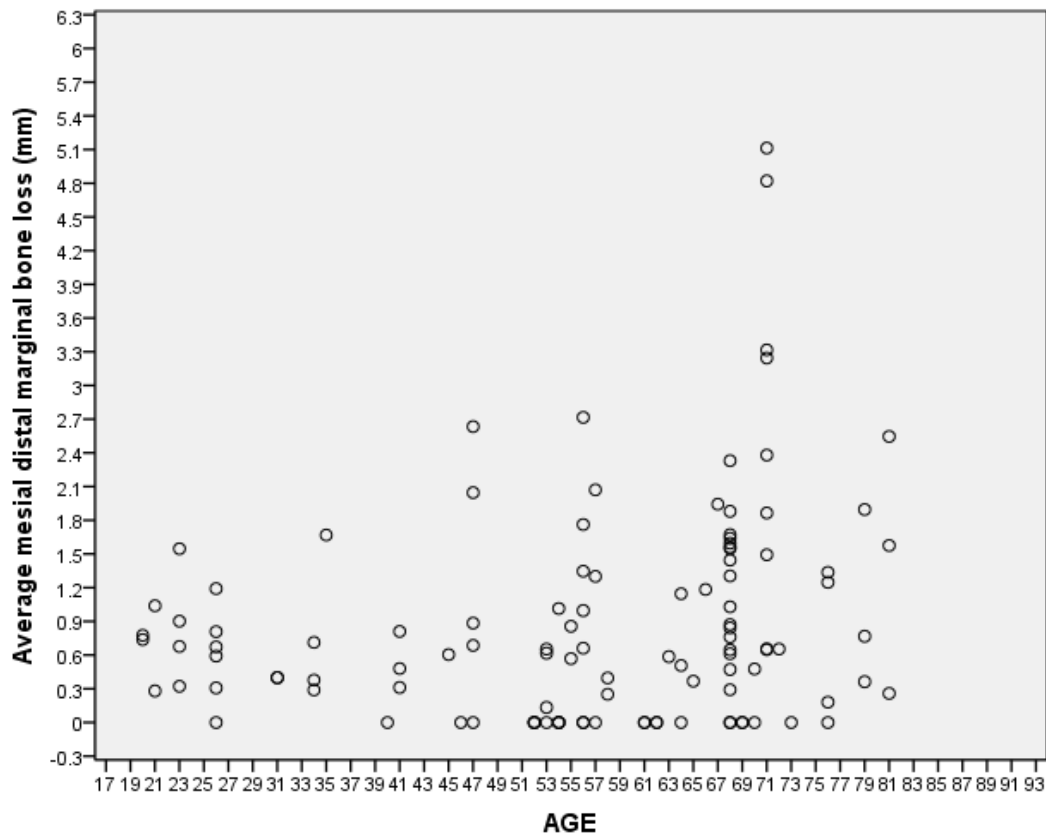


Figure 6. Distribution of age and marginal bone loss

The mean marginal bone loss was  $0.65 \pm 0.44$  mm in the less than 40 year age group,  $0.68 \pm 0.77$  mm in the 40-60 year group and  $1.11 \pm 0.95$  mm in the greater than 60 year age group. There was no statistically significant association between age and marginal bone loss ( $p=1.000$ ).

### **5.4.2 Gender**

There was an even distribution of males and females in the study population (61 and 63 cases, respectively). Two of the failures occurred in males (survival = 96.7%) and five in females (survival = 92.1%). There was no statistically significant effect between gender and implant survival ( $p=0.440$ ) or marginal bone loss ( $p=0.493$ ).

### **5.4.3 Diabetes**

Six of the 124 implants (4.8%) were placed in two diabetic patients. One of the implant failures occurred in a diabetic patient, while six failures occurred in non-diabetics. There was no statistically significant effect of diabetes on implant failure ( $p=0.300$ ).

The mean marginal bone loss in the diabetic patients ( $\pm$ SD) was 2.79 ( $\pm$ 2.32) mm as compared to 0.80 ( $\pm$ 0.75) mm in non-diabetics. Using bivariate statistical analysis, diabetes did not have a significant effect on marginal bone level changes ( $p=0.128$ ).



#### 5.4.4 Smoking

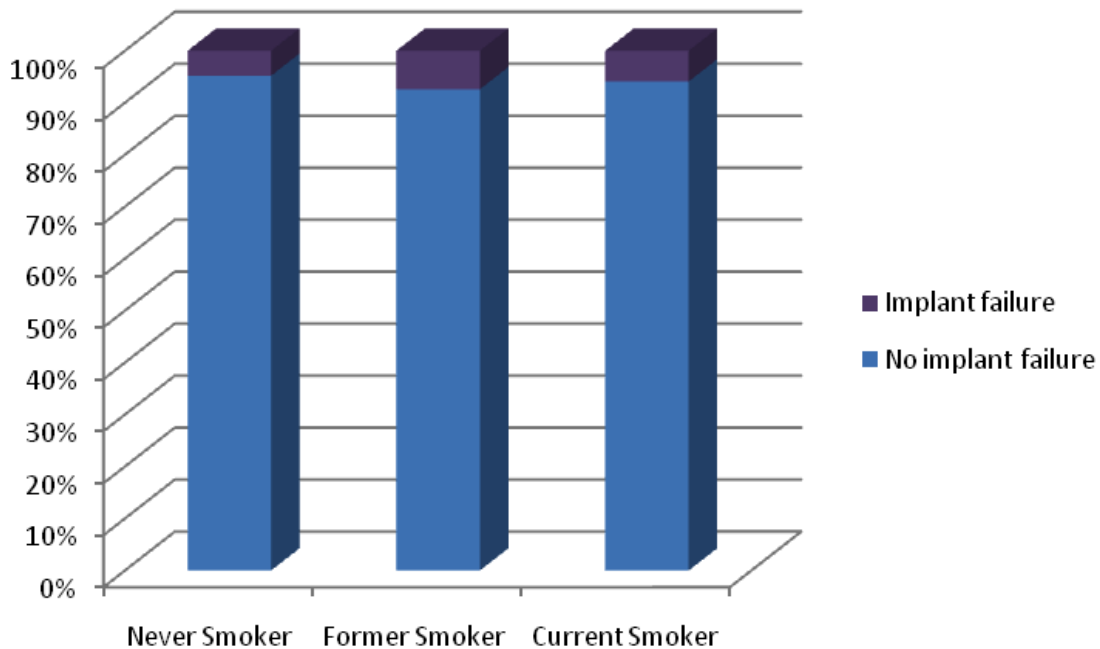


Figure 7. Implant survival and failure in never, former and current smokers

50.8% of patients had never smoked, 21.8% were ‘former’ smokers and 27.4% of patients were ‘current’ smokers at the time of implant placement. The implant survival rate was 95.2% in ‘never’ smokers (n=60/63), 92.6%, in ‘former’ smokers (n=25/27) and 94.1% in ‘current’ smokers (n=32/34). There was no statistically significant difference in implant survival between the smoking groups (p=0.881).

### Smoking status and marginal bone loss

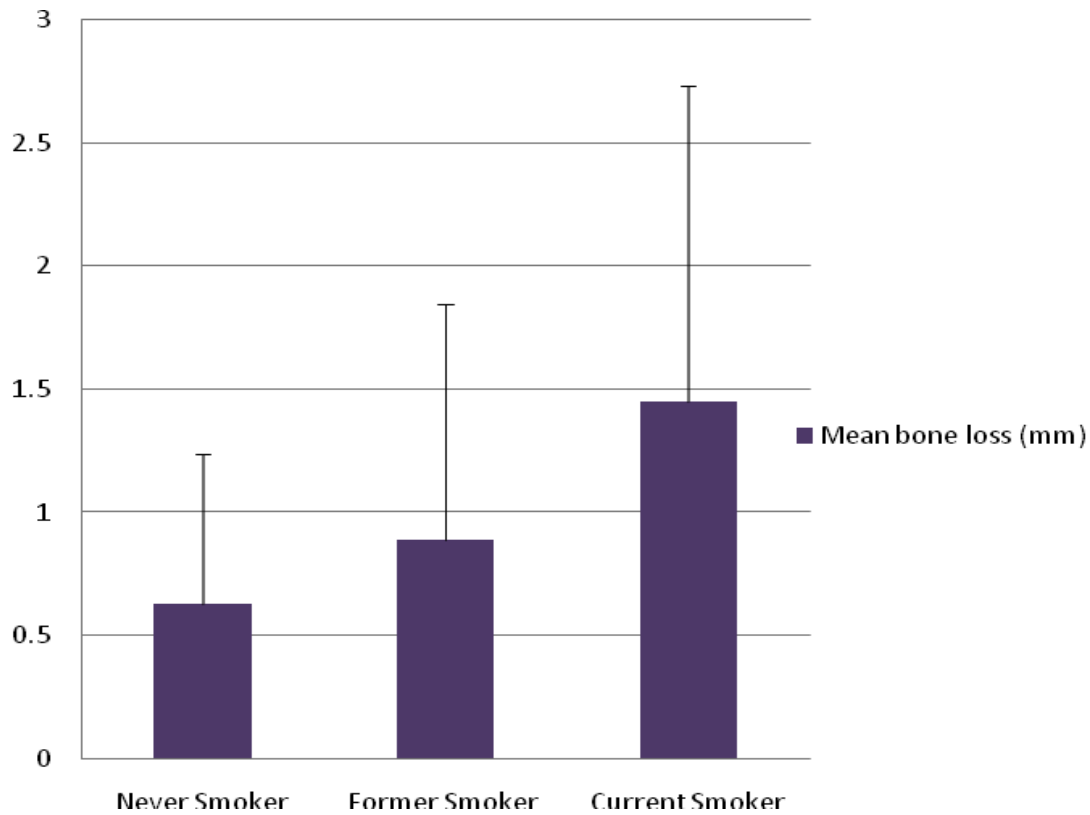


Figure 8. Mean marginal bone loss in never, former and current smokers

The mean marginal bone loss ( $\pm$ SD) was 0.63 ( $\pm$ 0.61) mm in ‘never’ smokers, 0.89 ( $\pm$ 0.96) mm in ‘former smokers’ and 1.45 ( $\pm$ 1.28) mm in current smokers. In terms of marginal bone loss, a significant difference was observed between ‘current’ and ‘never’ smokers ( $p=0.001$ ) (95% CI: -1.32; -0.32). In smokers, the mean number of pack-years (number of packs smoked per year) was  $10.6 \pm 15.4$  years. The number of pack-years was significantly associated with marginal bone loss ( $p=0.000$ ).

## 5.5 Implant-related factors

### 5.5.1 Implant dimensions - length

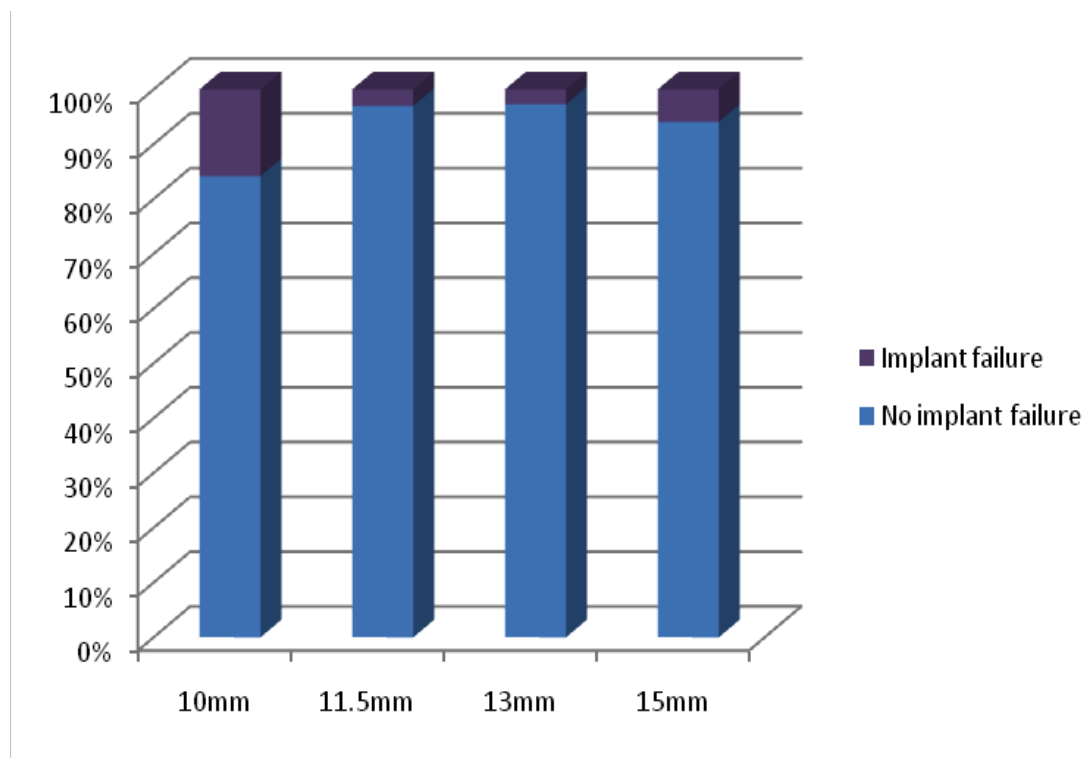


Figure 9. Implant survival and failure as related to implant length

15.3% of the evaluated implants were 10 mm, 27.4% were 11.5 mm, 29.8% were 13 mm and 27.4% were 15 mm. Survival rates were 84.2% (3/16 failed) in 10 mm implants, 97% (1/34 failed) in the 11.5 mm group, 97.3% (1/36 failed) in the 13 mm group and 94.1% (2/34 failed) in the 15 mm group. Implant length did not have a significant effect on implant survival ( $p=0.192$ ).

### Length and marginal bone loss

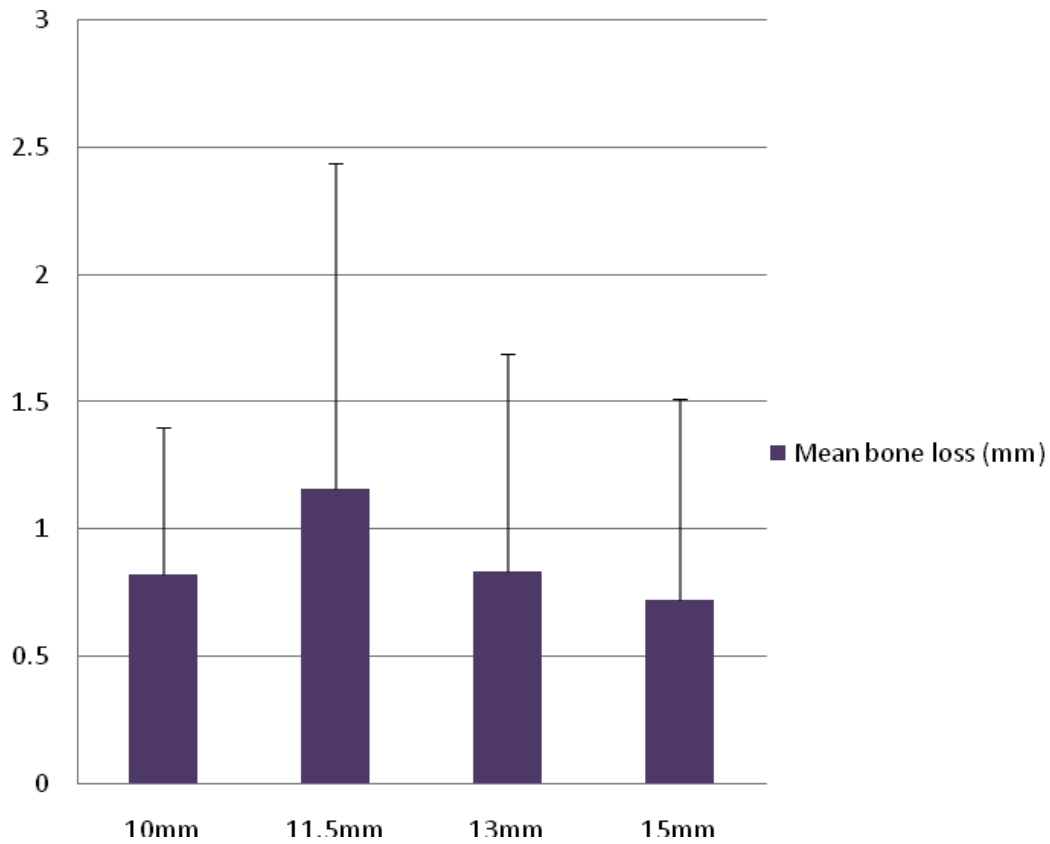


Figure 10. Mean marginal bone loss as related to implant length

Mean marginal bone loss ( $\pm$ SD) was 0.82 ( $\pm$ 0.58) mm for 10 mm implants, 1.16 ( $\pm$ 1.28) mm for 11.5 mm implants, 0.83 ( $\pm$ 0.86) mm for 13 mm implants and 0.72 ( $\pm$ 0.80) mm for 15 mm implants. Implant length did not have a significant effect on the marginal bone loss ( $p=0.304$ ).

### 5.5.2 Implant dimensions - width

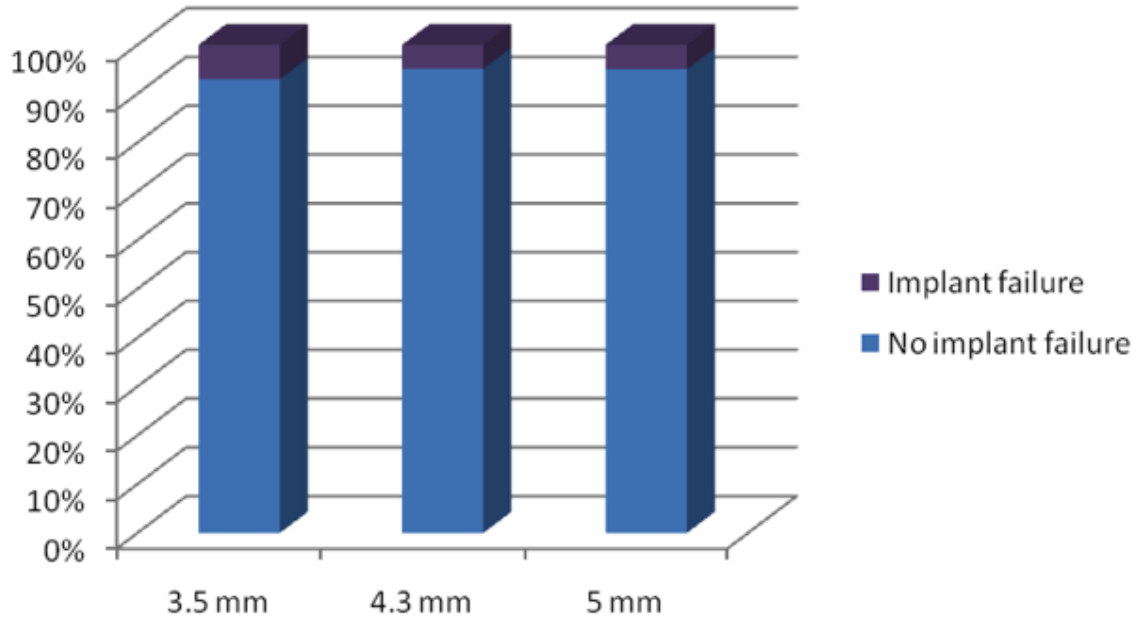


Figure 11. Implant survival and failure as related to implant width

With respect to implant diameter, 34.7% of the implants placed were 3.5 mm (n=43), 49.2% were 4.3 mm (n=61) and 16.1% were 5 mm (n=20). Three failures occurred in the 3.5 mm diameter implants (survival=93%), three in the 4.3 mm group (survival=95.1%) and one in the 5.0 mm group (survival=95%). Implant diameter did not have a significant effect on implant survival ( $p=0.896$ ).

### Implant width and mean marginal bone loss

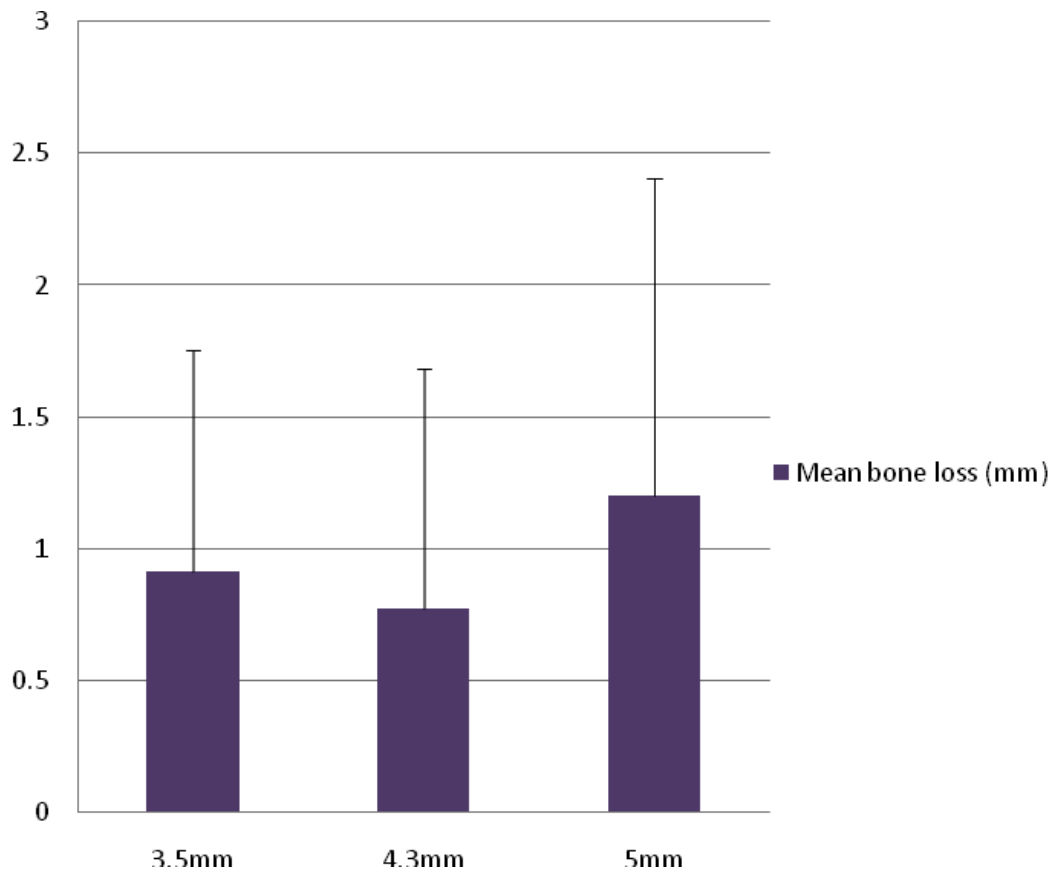


Figure 12. Mean marginal bone loss as related to implant width

The mean marginal bone loss ( $\pm$ SD) was 0.91 ( $\pm$ 0.84) mm for implants 3.5 mm in diameter, 0.77 ( $\pm$ 0.91) mm for 4.3 mm diameter implants and 1.20 ( $\pm$ 1.21) mm for 5 mm diameter implants. Implant diameter did not have a significant effect on the marginal bone loss ( $p=0.235$ ).

### 5.6 Primary stability as measured by insertion torque

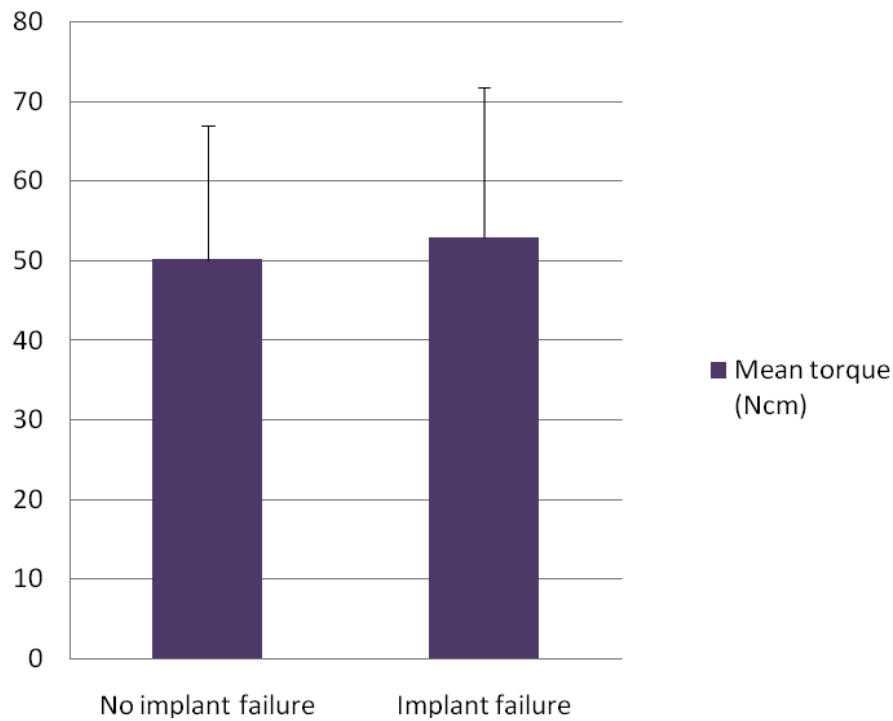


Figure 13. Effect of insertion torque on implant survival and failure

Implant insertion torque ranged from 10-70 Ncm, with a mean insertion torque ( $\pm$  SD) of 50.4 ( $\pm$ 16.9) Ncm. The mean insertion torque ( $\pm$  SD) for implants that survived was 50.09 ( $\pm$ 16.87) Ncm as compared to 52.86 ( $\pm$ 18.90) Ncm for failed implants.

Insertion torque did not have a significant effect on implant survival ( $p=0.717$ ).

### Insertion torque and mean marginal bone loss

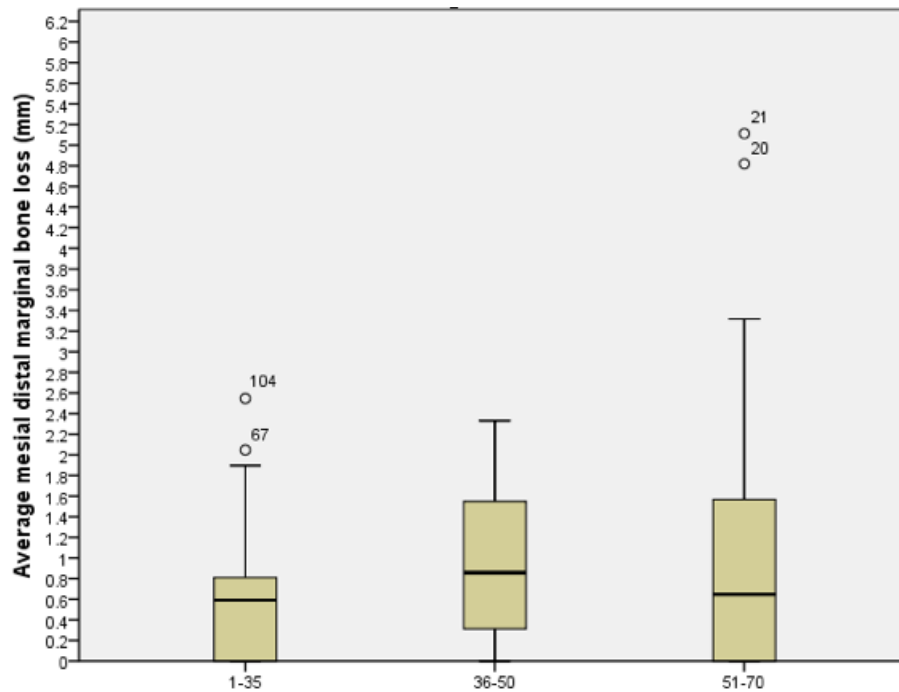


Figure 14. Effect of insertion torque (Ncm) on marginal bone loss (mm) (data was grouped for visual purposes only)

Statistical analysis was performed on the raw, ungrouped data and it was demonstrated that insertion torque had a statistically significant impact on marginal bone loss ( $p=0.011$ ). Insertion torque values were categorized into three groups:  $\leq 35$  Ncm, 36-50 Ncm and  $\geq 50$  Ncm with corresponding mean marginal bone loss ( $\pm$ SD) values of 0.62 ( $\pm 0.65$ ) mm, 0.93 ( $\pm 0.66$ ) mm and 1.05 ( $\pm 1.26$ ) mm respectively. No statistically significant impact of torque on marginal bone loss was observed when the categorization of  $\leq 35$ , 36-50, and  $> 50$  Ncm was employed ( $p=0.152$ ), however, a tendency towards greater bone loss with increasing torque categories was observed. A further categorization of insertion torque into groups of  $\leq 50$  Ncm and  $> 50$  Ncm revealed mean marginal bone loss ( $\pm$ SD) measurements of 0.78 ( $\pm 0.66$ ) mm and 1.05 ( $\pm 1.26$ ) mm respectively, again, a statistically non-significant difference ( $p=0.268$ ).



Insertion torque was highly correlated with bone density ( $p=0.000$ ). The mean torque was  $58.9 \pm 13.8$  Ncm in dense bone,  $45.8 \pm 12.5$  Ncm in medium bone and  $47.9 \pm 20.3$  Ncm in soft bone. More specifically, an analysis with multiple comparisons revealed a significant difference in torque values between dense and medium bone ( $p=0.000$ ) and dense and soft bone ( $p=0.029$ ).

Moreover, a significantly higher mean insertion torque was consistently achieved in the mandible ( $53.9 \pm 13.8$  Ncm) as compared to the maxilla ( $46.1 \pm 17.2$  Ncm) ( $p=0.001$ ). According to anatomic location, the insertion torque achieved was as follows:  $53.7 \pm 15.6$  Ncm in the anterior mandible,  $53.6 \pm 12.0$  Ncm in the posterior mandible,  $51.2 \pm 17.7$  Ncm in the posterior maxilla and finally  $41.2 \pm 15.0$  Ncm in the anterior maxilla. There was a significant difference between insertion torque in the posterior mandible and the anterior maxilla ( $p=0.027$ ), between the anterior mandible and the posterior maxilla ( $p=0.036$ ) and between the anterior maxilla and the posterior maxilla ( $p=0.034$ ).

## 5.7 Anatomic site-related factors

### 5.7.1 Bone density

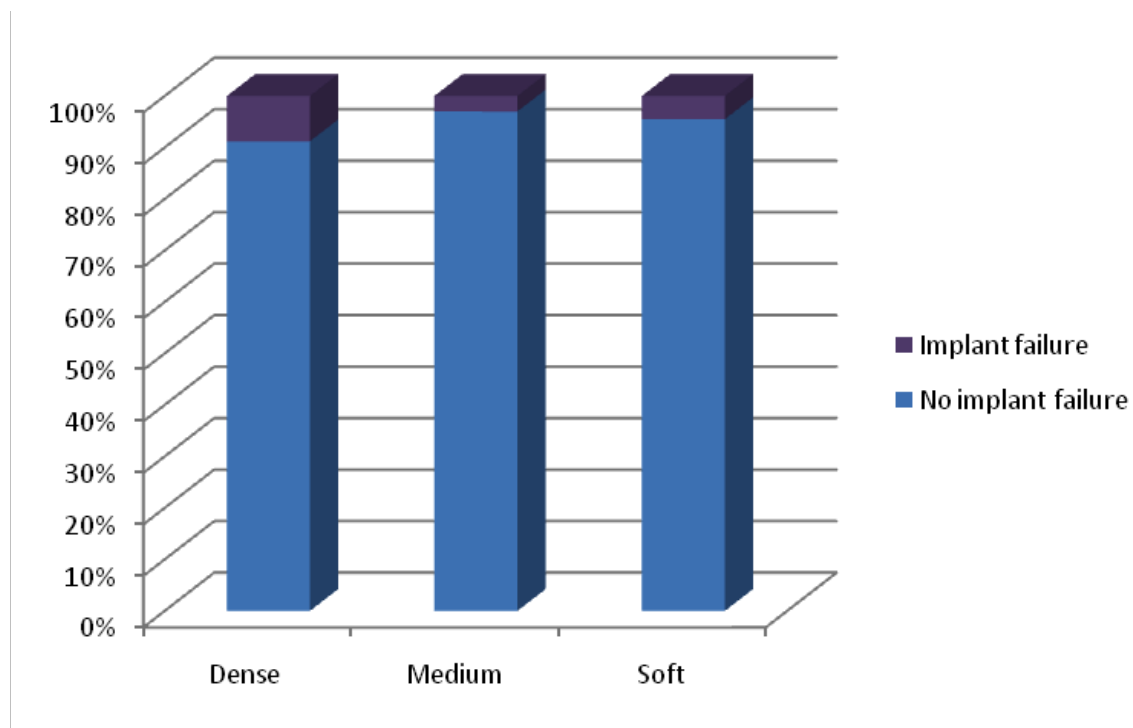


Figure 15. Implant survival and failure as related to bone density

Bone density was categorized according to dense, medium and soft according to the surgeon's perception of resistance during implant placement. 27.4% of sites were assessed as dense, 54.0% as medium and 18.5% as soft bone. Survival rates were 91.2% in dense bone (3/34 failed), 97% in medium bone (2/67 failed) and 95.5% in soft bone (2/23 failed). Bone quality did not have a statistically significant effect on implant failure ( $p=0.380$ ).

### Bone density and marginal bone loss

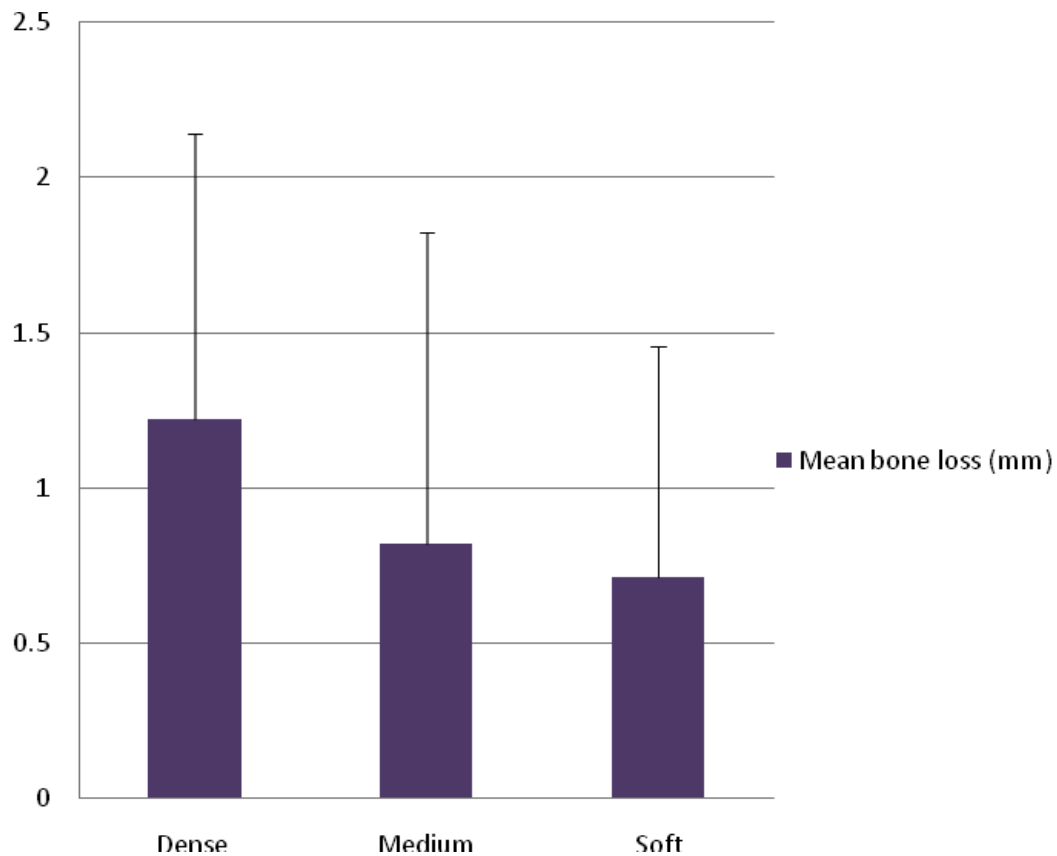


Figure 16. Mean marginal bone loss as related to bone density

Mean marginal bone loss ( $\pm$ SD) was 1.22 ( $\pm$ 0.92) mm for dense bone, 0.8 ( $\pm$ 1.00) mm for medium bone and 0.71 ( $\pm$ 0.75) mm for soft bone. There was no significant effect of bone density on mean marginal bone loss ( $p=0.123$ ). However, a trend is observed towards increasing bone loss with increasing bone density.

### 5.7.2 Anatomic location

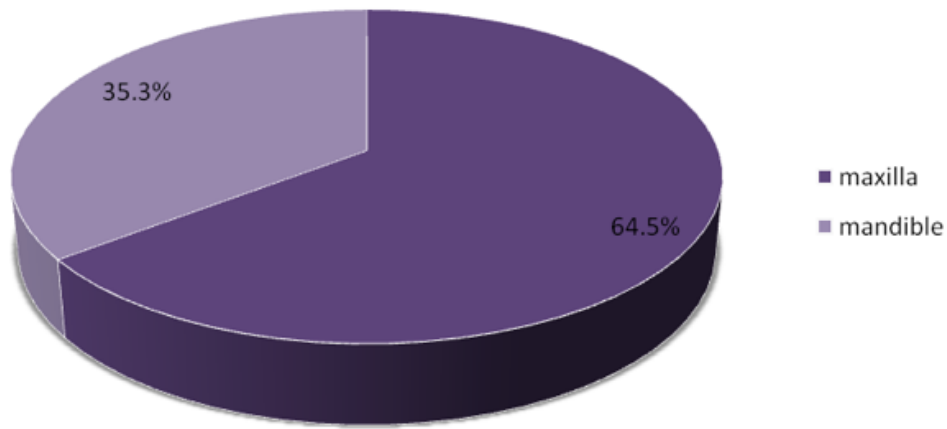


Figure 17. Distribution of implants as related to the location in the arch

The majority of implants were placed in the maxilla (n=80) as compared to the mandible (n=44). Survival rate in the maxilla was 94.6% as compared to 92.3% in the mandible, this difference was not statistically significant ( $p=0.244$ ).

### Anatomic location and mean marginal bone loss

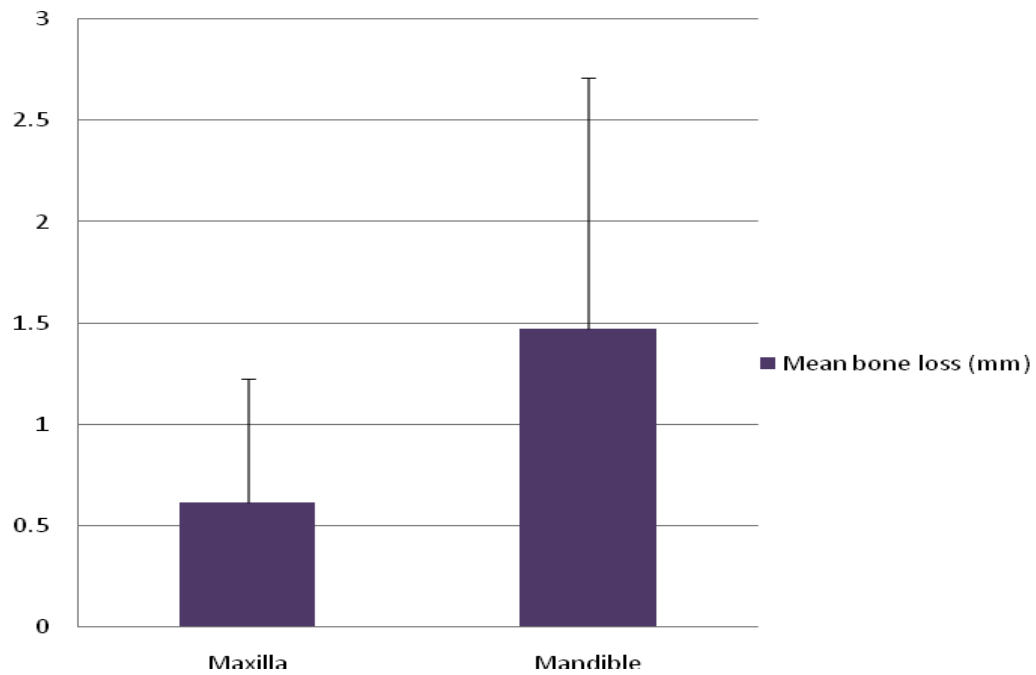


Figure 18. Mean marginal bone loss as related to the location in the maxillary and mandibular arch

Mean marginal bone loss ( $\pm$ SD) was 0.61 ( $\pm$ 0.61) mm in the maxilla and 1.47 ( $\pm$ 1.24) mm in the mandible. Implants placed in the mandible had significantly greater marginal bone loss than those placed in the maxilla ( $p=0.000$ ).

### Anatomic location and mean marginal bone loss by quadrant

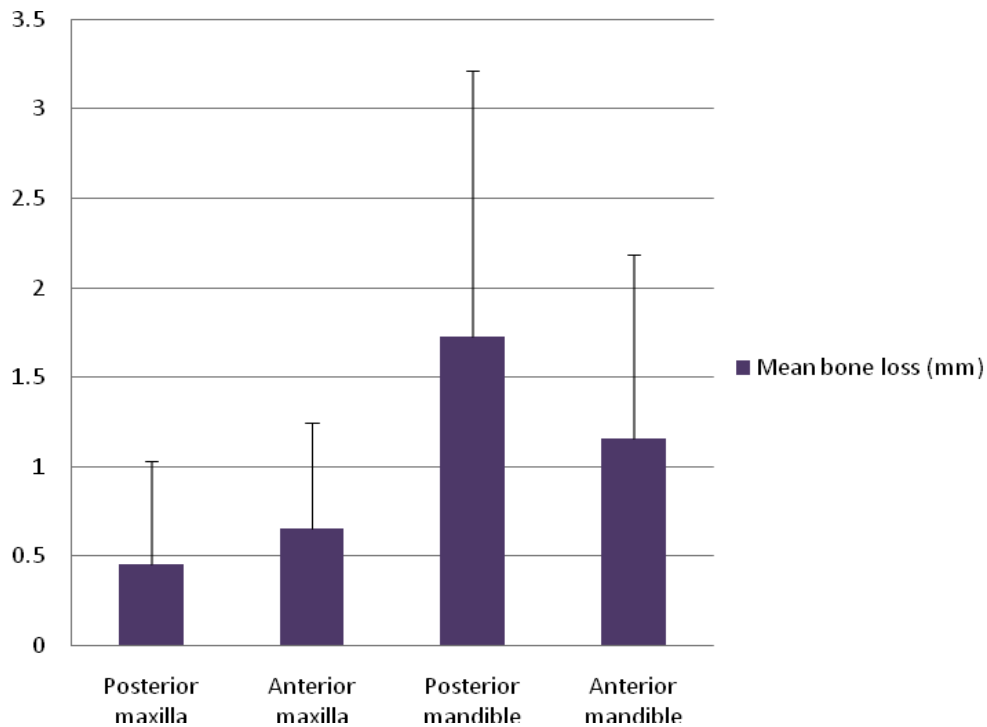


Figure 19. Mean marginal bone loss as related to the location in the arch by sextant

Anatomic sites were further subdivided into sextants. The mean marginal bone loss ( $\pm$ SD) was 0.45 ( $\pm$ 0.58) mm in the posterior maxilla, 0.65 ( $\pm$ 0.59) mm in the anterior maxilla, 1.16 ( $\pm$ 1.03) mm in the anterior mandible, and 1.73 ( $\pm$ 1.48) mm in the posterior mandible. The mean marginal bone loss in the posterior mandible was significantly greater than the marginal bone loss in the anterior maxilla ( $p=0.000$ ) (95% CI: 0.37; 1.78) and the posterior maxilla ( $p=0.000$ ) (95% CI: 0.62; 1.94). The mean marginal bone loss in the posterior maxilla was significantly less than the marginal bone loss in the anterior mandible ( $p=0.050$ ) (95% CI: -1.42; 0.0) and the posterior mandible ( $p=0.000$ ) (95% CI: -1.94; -0.62). Moreover, the mean marginal bone loss in the anterior mandible was significantly greater than that in the posterior maxilla ( $p=0.05$ ) (95% CI: 0.00; 1.42).

### 5.7.3 Previous guided bone regeneration or sinus augmentation

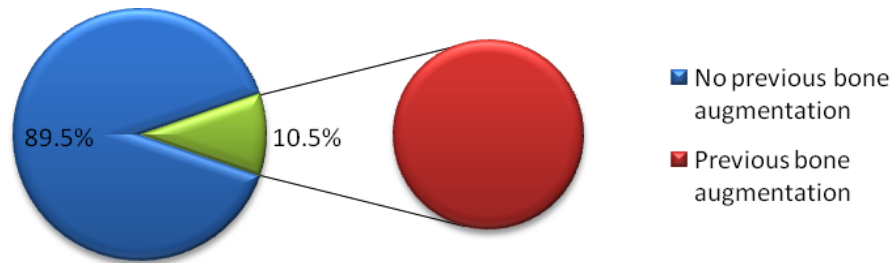


Figure 20. Percentage of sites treated with previous bone augmentation

Guided bone regeneration (GBR) or sinus augmentation was performed prior to implant placement in 13 of the 124 cases (10.5%).

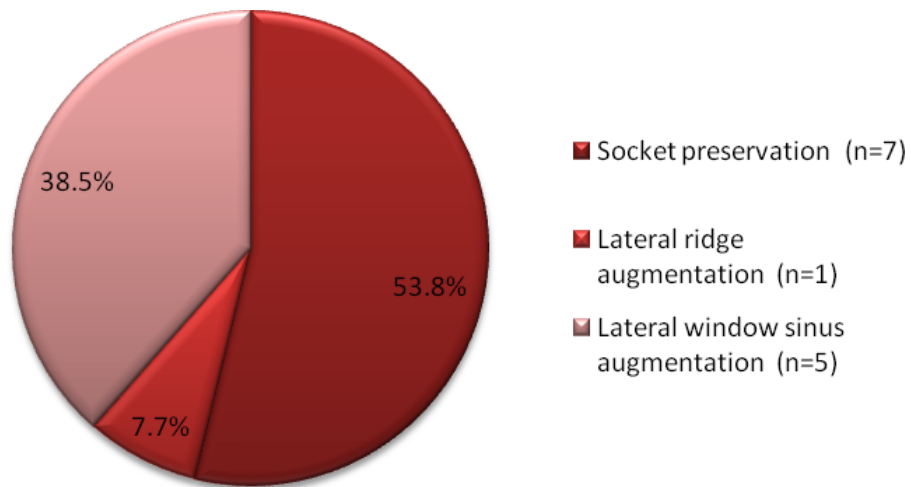


Figure 21. Types of bone augmentation procedures performed prior to implantation

Of the grafted cases, seven sites received socket preservation (53.8%), one lateral ridge augmentation (7.7%) and five lateral window sinus augmentations (38.5%). From

the 13 bone grafted cases included, there was only one reported failure (survival = 92.3%) as compared to six failures in the non-grafted group (survival = 89.5%). The effect of bone augmentation prior to implant placement on implant survival was not significant ( $p=0.549$ ), nor was the type of augmentation performed ( $p=0.717$ ).



## Previous guided bone regeneration or sinus augmentation and marginal bone loss

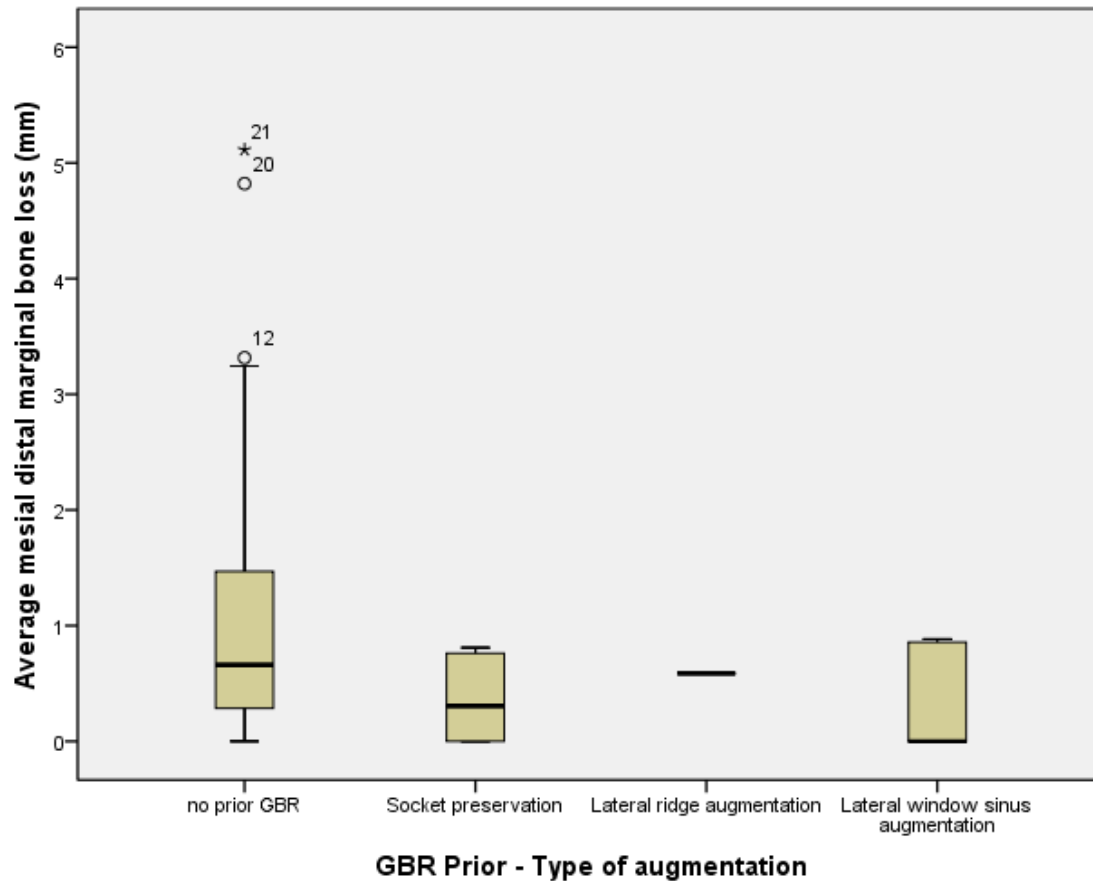


Figure 22. Effect of previous bone augmentation on marginal bone loss according to the type of graft procedure performed

The mean marginal bone loss for cases without prior bone augmentation (n=111) was  $0.95 \pm 0.98$  mm as compared to  $0.38 \pm 4.0$  mm for cases with prior bone augmentation (n=13). There was less mean marginal bone loss in the socket preservation group (7/13 implants) and in the sinus augmentation group (5/13 implants) as compared to the non-grafted group. Overall, there was a significantly greater mean marginal bone loss for cases without prior bone augmentation ( $p=0.048$ ).

#### 5.7.4 Simultaneous guided bone regeneration or sinus augmentation

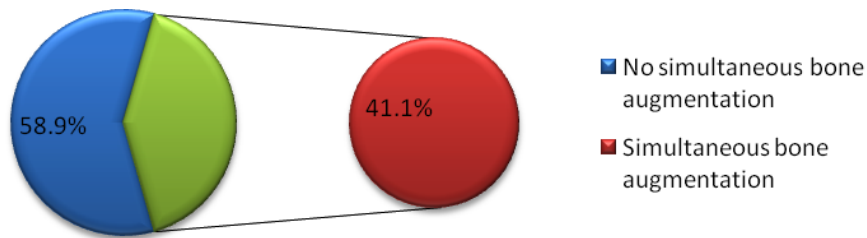


Figure 23. Percentage of sites treated with simultaneous bone augmentation

Simultaneous guided bone regeneration or sinus augmentation was performed in 51 of the 124 implants (41.1%).

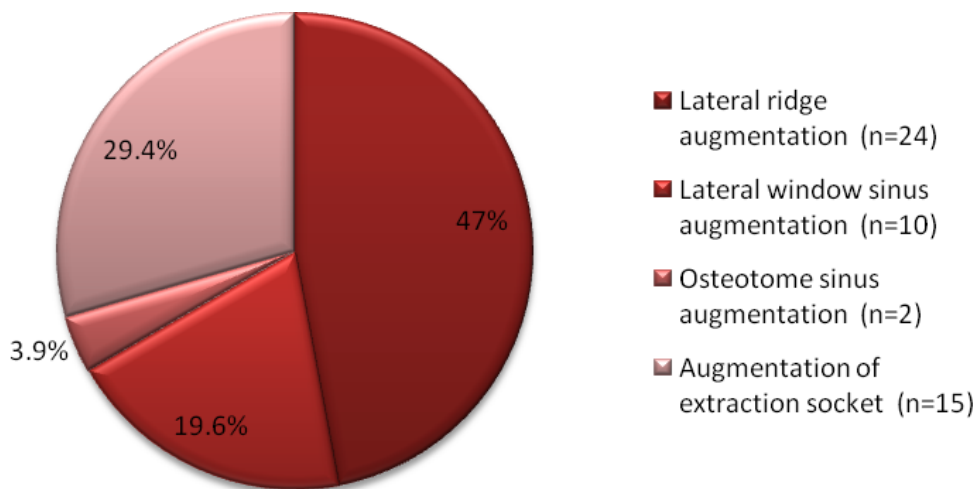


Figure 24. Types of bone augmentation cases performed simultaneously with implant placement

More specifically, 24 of the simultaneous grafting procedures included lateral

ridge augmentation (47.0%), ten were lateral window sinus augmentation (19.6%), two were osteotome indirect sinus augmentations (3.9%) and 15 were augmentations of extraction sockets during immediate implant placement (29.4%). Of the 51 simultaneously bone grafted cases, there were only two reported failures (survival = 96.1%), one occurred in the lateral ridge augmentation group (1/24) and one in the osteotome group (1/2). The effect of the type of simultaneous sinus augmentation on implant failures was not significant ( $p=0.487$ ), nor was the type of augmentation preformed ( $p=0.058$ ).

## Simultaneous guided bone regeneration or sinus augmentation and marginal bone loss

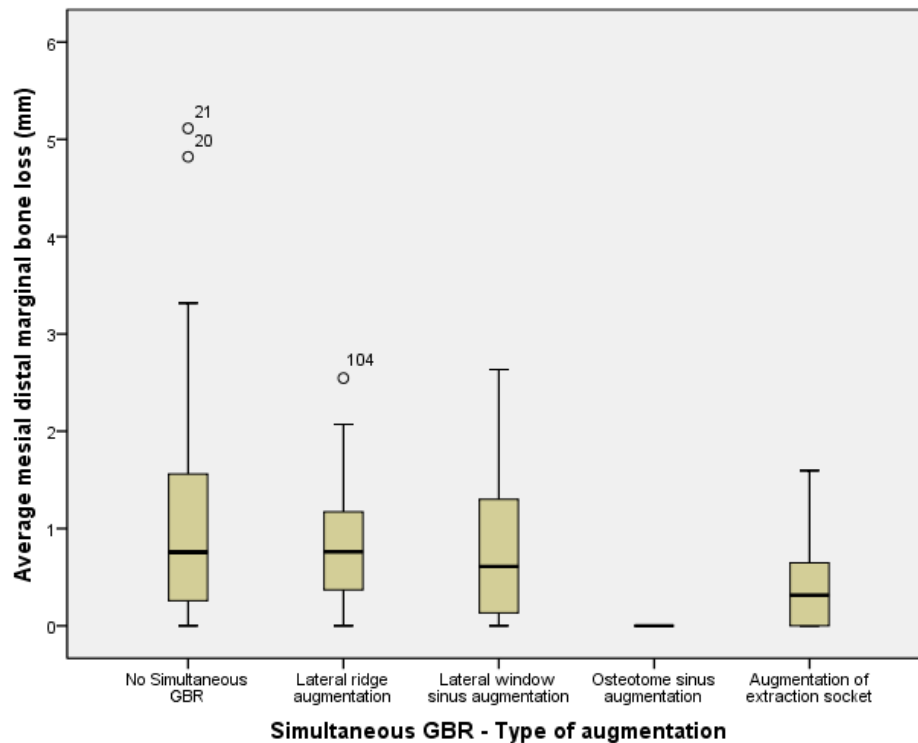


Figure 25. Effect of simultaneous bone augmentation on marginal bone loss according to the type of graft procedure performed

The mean marginal bone loss was  $1.03 \pm 1.09$  mm for cases without simultaneous bone augmentation and  $0.70 \pm 0.694$  mm for cases with simultaneous bone augmentation. This difference was not statistically significant ( $p=0.052$ ), however, there was a tendency towards less mean marginal bone loss for cases with simultaneous bone augmentation. The least marginal bone loss occurred around immediate implants that received bone grafting to fill in the gap between the extraction socket ( $n=15$ ), however caution must be exercised with the interpretation due to the limited sample size. There was no statistically significant effect of the type of simultaneous bone augmentation on marginal bone loss ( $p=0.203$ ).

## ***5.8 Timing of implant placement and restoration/loading***

The effect of a one-stage (healing abutment placed during implant surgery) and two-stage protocol (implant is submerged during healing phase) on implant survival and crestal bone loss was assessed. Moreover, the effect of immediate placement and/or immediate loading as compared to conventional placement and loading on implant survival and marginal bone loss was evaluated.

### **5.8.1 Staging protocol**

A one-stage implant protocol was employed for 68.5% of implants and a two-stage protocol for 31.5% of the implants. Four failures occurred in the one stage protocol (survival = 95.3%) and three using the two-stage protocol (survival = 92.3%). The staging protocol did not have a statistically significant effect on implant survival ( $p=0.677$ ).

The mean marginal bone loss ( $\pm$ SD) was 0.95 ( $\pm$ 1.05) mm for the one-stage implant protocol and 0.73 ( $\pm$ 0.65) mm for the two-stage protocol. This difference was not statistically significant ( $p=0.181$ ).

### Timing of implant placement and restoration/loading

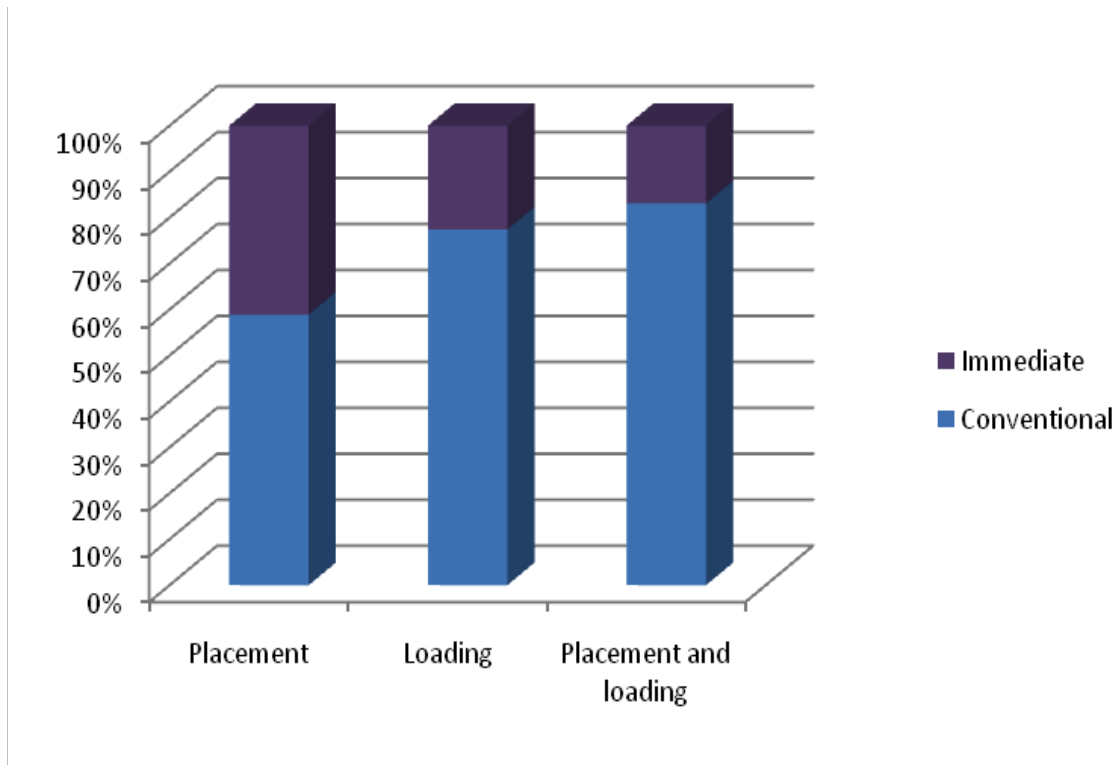


Figure 26. Proportion of cases involving implant placement and loading protocols

41.1% of the evaluated implants were immediately placed (n=51), 22.6% were immediately loaded (n=28), while 17.7% were both placed immediately into fresh extraction sockets and immediately loaded (n=22)

### 5.8.2 Immediate placement vs. conventional placement in native bone

Of the implants evaluated, 58.9% were placed in native bone and 41.1% were placed immediately into fresh extraction sockets. Four of the implant failures occurred in conventionally placed implants and three occurred in immediately placed implants into extraction sockets (survival was 94.5% and 94.1% respectively). There was no statistically significant effect of timing of implant placement on implant failure ( $p=1.000$ ).

#### Immediate placement and marginal bone loss

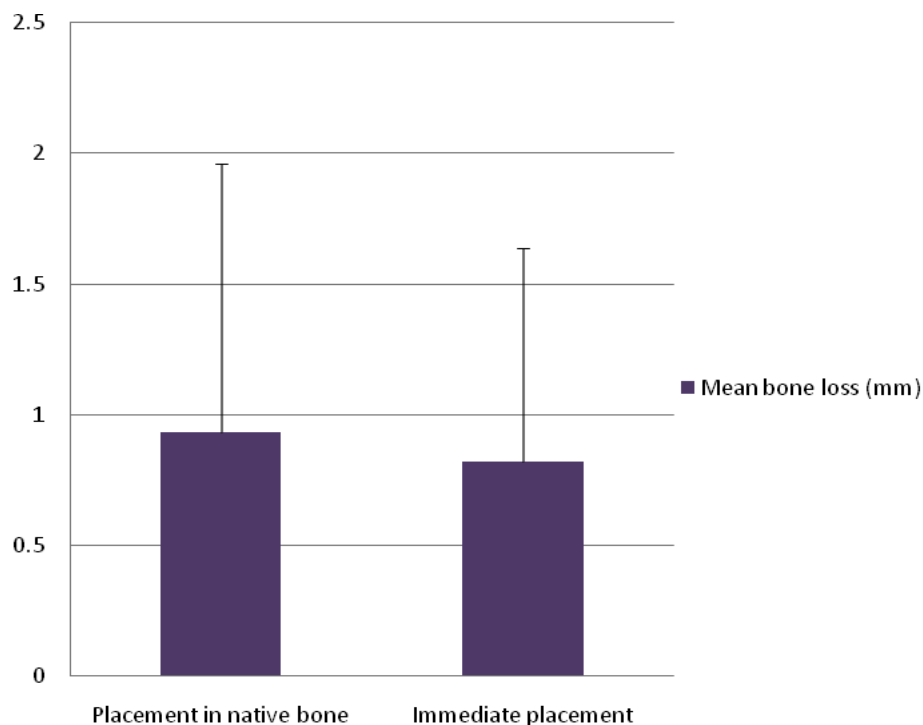


Figure 27. Effect of immediate placement on marginal bone loss

The mean marginal bone loss ( $\pm$ SD) for implants placed in native bone was 0.93 ( $\pm$ 1.03) mm as compared to 0.82 ( $\pm$ 0.82) mm for those placed immediately. There was no significant difference in marginal bone loss in implants placed in native bone as compared to those placed immediately into fresh extraction sockets ( $p=0.535$ ).

### 5.8.3 Immediate restoration/loading vs. conventional loading

Immediate restoration or loading was provided within 48 hours for 28 of the 124 implants (22.6%) as compared to conventional loading protocols (77.4%). Six implants failed in the conventionally loaded group (survival = 93.8%) and one implant failed in the immediately restored group (survival = 96.4%). Immediate restoration or loading did not have a statistically significant effect on implant failures ( $p=1.000$ ).

#### Immediate restoration/loading and marginal bone loss

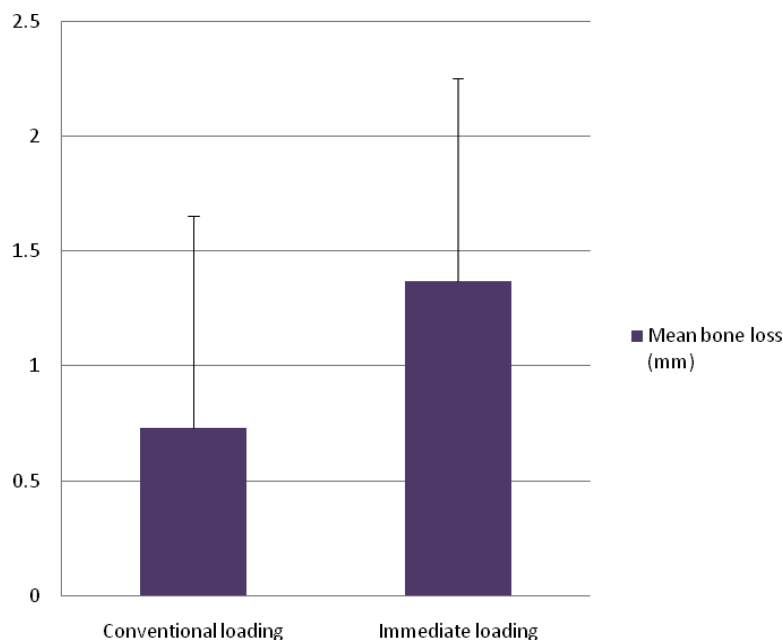


Figure 28. Effect of immediate loading on marginal bone loss

The mean marginal bone loss ( $\pm$ SD) was 0.73 ( $\pm$ 0.92) mm for implants that were loaded according to a conventional or delayed loading protocol and 1.37 ( $\pm$ 0.88) mm for immediately loaded implants. Implants that were loaded immediately had significantly greater mean marginal bone loss as compared to those loaded using a conventional or delayed protocol ( $p=0.002$ ) (95% CI: -1.034; -0.239).



#### 5.8.4 Immediate placement with immediate restoration/loading

22 implants (17.7% of the total sample) were placed immediately in extraction sockets and were immediately restored or loaded within 48 hours. One implant failure occurred in the group with immediate placement and immediate restoration/loading (survival 95.2%) as compared to six failures that occurred in the remainder of the study population (94.2%). There was no significant effect of simultaneous immediate placement and immediate restoration/loading on implant failures ( $p=0.635$ ).

#### Immediate placement with immediate restoration/loading and marginal bone loss

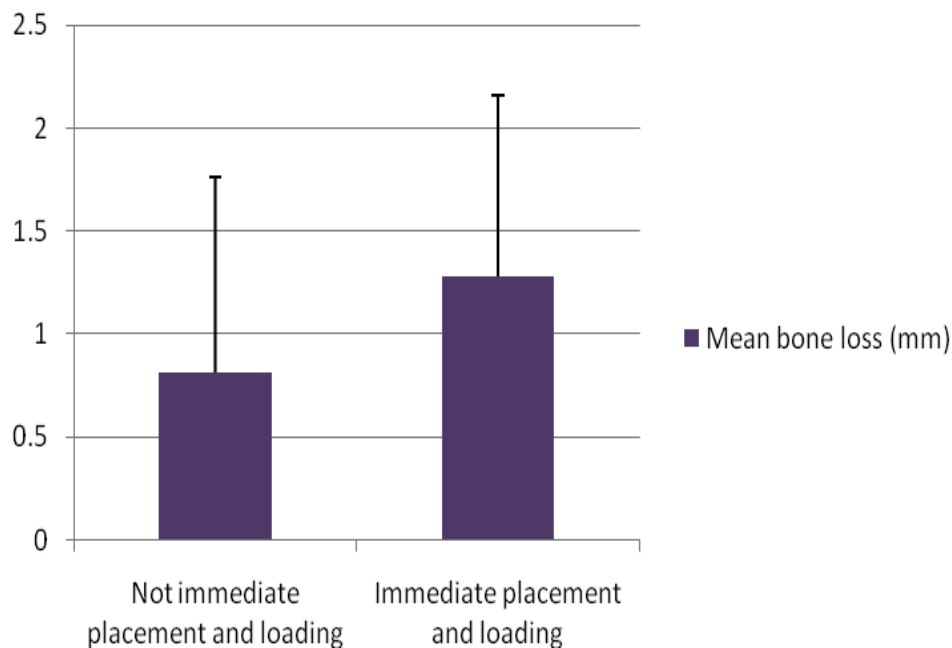


Figure 29. Effect of immediate implant placement and immediate restoration/loading on marginal bone loss

The mean marginal bone loss ( $\pm$ SD) was 1.28 ( $\pm$ 0.21) mm for implants that were placed immediately in fresh extraction sockets and immediately restored or loaded. The mean marginal bone loss for implants not placed and loaded immediately (remainder of

the implant cases), was 0.81 ( $\pm 0.95$ ) mm. Implants that were immediately placed and loaded had significantly greater mean marginal bone loss as compared to those not immediately placed and immediately restored or loaded ( $p=0.040$ ).

### 5.9 Distribution of implant supported restorations

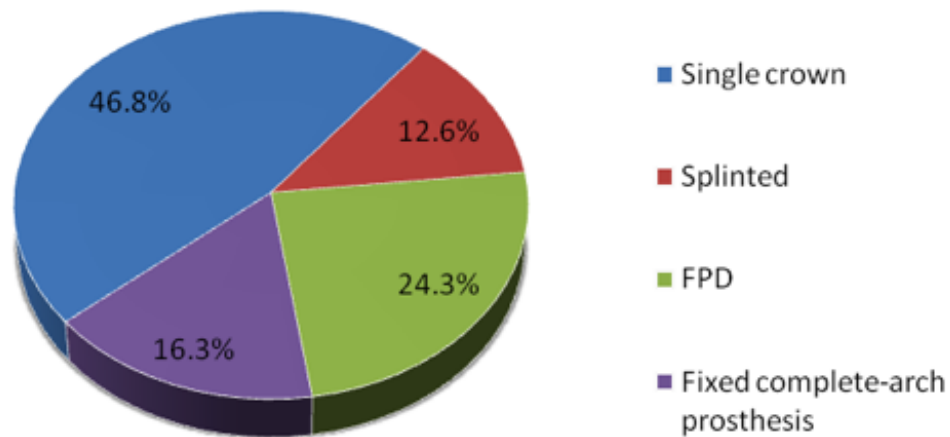


Figure 30. Types of implant supported restorations expressed as percentages

Of the restorations placed for the 111 implants remaining, 52 were single crowns (46.8%), 14 were splinted (12.6%), 25 supported fixed partial dentures (24.3%), and 18 supported fixed complete-arch prostheses (16.3%). Six of the seven failures occurred prior to restoration of the implant. One of the failed implants was immediately loaded and incorporated into five implant supported fixed mandibular prosthesis. The implant was removed after eleven months of placement and another implant was placed distal to the site during the same surgical appointment.

### Marginal bone loss and implant supported restorations

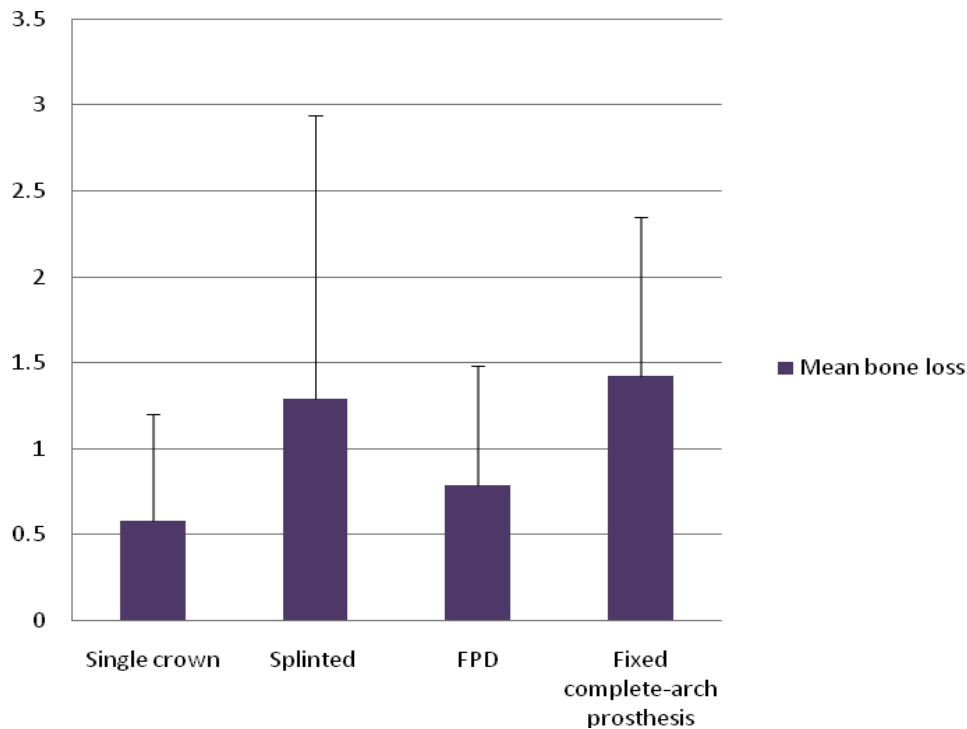


Figure 31. Marginal bone loss in the various implant supported restorations

Fixed complete arch prostheses had the most significant amount of bone loss ( $1.42 \pm 0.93$  mm) followed by splinted crowns ( $1.29 \pm 1.65$  mm), fixed partial dentures ( $0.79 \pm 0.69$  mm) and finally single crowns ( $0.58 \pm 0.62$  mm). There was a significant difference between single crowns and splinted crowns ( $p=0.034$ ) between single crowns and fixed complete-arch prostheses ( $p=0.004$ ).

### 5.10 Post-operative antibiotics

Post-operative antibiotics were prescribed for 70.2% of implants as compared to no antibiotics for 29.8% of implants. Four failures occurred in the antibiotic group (survival = 95.4%) and three in the group without antibiotics (survival = 91.9%). The use of antibiotic therapy did not have a statistically significant effect on implant survival ( $p=0.425$ ).

#### Post-operative antibiotics and marginal bone loss

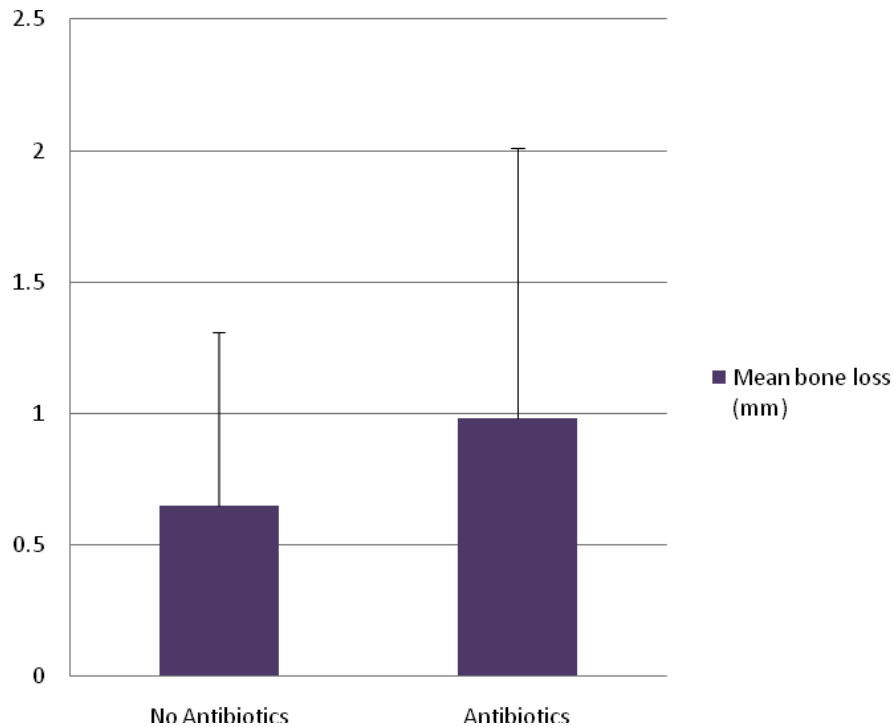


Figure 32. Effect of post-operative antibiotics on marginal bone loss

Mean marginal bone loss was  $0.98 \pm 1.03$  mm for the antibiotic treatment group and  $0.65 \pm 0.66$  mm for the group not treated with antibiotics. This difference was not statistically significant ( $p=0.097$ ).

### 5.11 Level of training of the surgeon

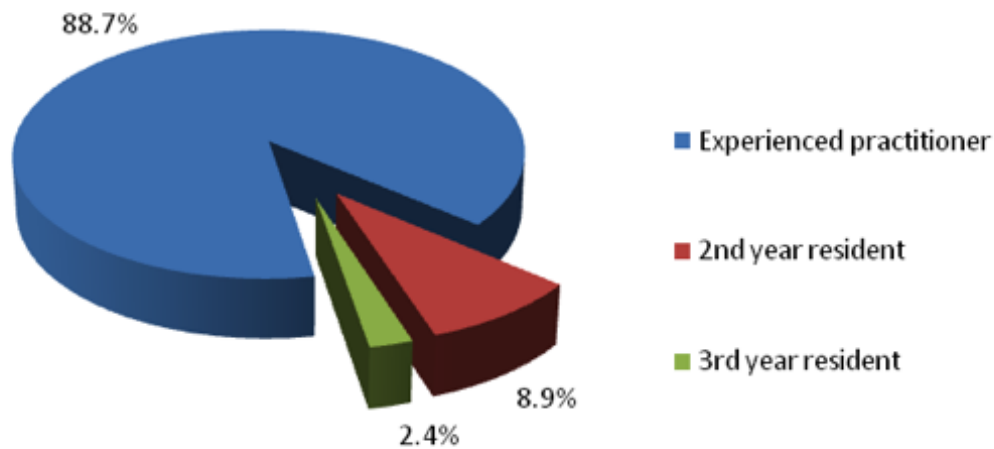


Figure 33. Percentage of implants placed by surgeons that were experienced periodontists and senior Graduate Periodontics residents

The majority of the implants (88.7%) were placed by experienced practitioners, while the remainder (11.3%), were placed by Graduate Periodontics residents (8.9% by second and 2.4% by third year residents). 100% of the failures occurred in cases performed by the experienced practitioners. The level of training of the practitioner did not have a statistically significant effect on implant failure rate ( $p=0.624$ ), or mean marginal bone loss ( $p=0.913$ ).

### ***5.12 Additional findings***

Infection was observed in six of the 124 implants placed (4.8%), four of which failed and were removed. In a patient who experienced an implant failure, purulence and significant marginal bone loss (2.92 to 4.92 mm) was noted in two other implants in the arch. These implants were treated for peri-implantitis with open flap debridement, systemic antibiotic therapy and chlorhexidine rinse. The patient is currently being monitored; instead of restoration with a complete-arch fixed prosthesis, the patient will receive a mandibular overdenture. There was no case of paraesthesia reported. Mobility was noted in two of the seven failures (1.6%) and peri-implant radiolucencies were present in radiographs of four of the seven failures (3.2%).

### ***5.13 Replacement of failed implants***

Of the documented failures in this review, three implants were not replaced, one failed implant was replaced by a Nobel Active Implant, two were replaced with a different implant system and one implant was placed distal to the failed site. Therefore, three of the seven failed implants were replaced in the same site but due to the time limitation of this study, limited post-operative data is available on these implants.

### **5.14 Regression analyses**

Regression analysis is a technique for modeling and analyzing several variables, when the focus is on the relationship between a dependent variable (implant failure and marginal bone loss) and one or more independent variables (patient-, site-, implant-related risk factors). More specifically, it demonstrates how the dependent variable changes when any one of the independent variables is varied, while the other independent variables are held fixed. Logistic regression analysis was completed with implant failure as the dependent outcome variable. Stepwise multiple linear regression analysis was performed with the marginal bone loss following loading (average of mesial and distal measurements) as the dependent outcome variable.

The predictor variables included in the stepwise linear multiple regression analysis were as follows: diabetes (diabetic, non-diabetic), smoking status (never, former and current smokers), jaw (maxilla vs. mandible), location in the arch (posterior maxilla, anterior maxilla, posterior mandible, anterior mandible), bone quality (soft, medium, dense), GBR (prior or simultaneous with implant placement), insertion torque, immediate placement, immediate loading, and post-operative antibiotics.

Based on the tolerance values, the assumption for the independence of predictors was fulfilled (all tolerance values  $> 0.500$ ). The overall model for marginal bone loss was highly statistically significant ( $p=0.000$ ). The Adjusted R square of 0.432 demonstrated that 43.2% of the variation of the outcome (marginal bone loss) was explained by a set of independent variables.

Beta values (standardized regression coefficients) were used to compare the effect of the predictor variables. A coefficient of zero indicates no effect and a coefficient of



one indicates a maximum effect. The predictor variables demonstrating the largest statistically significant effects are listed Table 4. These included diabetes (with greater bone loss in diabetic patients), implant placement as related to the jaws (with greater bone loss around mandibular implants), immediate placement (with greater bone loss in the non-immediate group), immediate loading (with greater bone loss in immediately loaded cases), and smoking status (with greatest bone loss in current smokers).

Table 4. Variables achieving statistical significance in the multiple linear regression analysis

Predictors	Beta Values	Significance (P values)
Diabetes	0.331	0.000
Jaws	0.274	0.030
Immediate placement	0.266	0.003
Immediate loading	0.206	0.011
Smoking status	0.186	0.045

Logistic regression analysis was performed to evaluate the effect of the different predictors on the failure outcome variable. The predictor variables included: diabetes, smoking status, jaw, bone quality, insertion torque, immediate placement, immediate loading, post-operative antibiotics, GBR prior to and simultaneously with implant placement. Odds ratio (OR) was used to assess the risk of implant failure if a certain predictor variable is present. The OR is a relative measure of risk and demonstrates how much more likely it is that someone exposed to a risk factor will develop the outcome as compared to someone who is not exposed to it. The closer the OR is to one, the smaller the difference in effect between the risk factor and the outcome (Altman, 1991). Consistent with the results attained in the bivariate analysis, the logistic regression analysis demonstrated that the independent variables examined did not show a significant effect on implant failure. Odds ratio (OR) was used to assess the risk of

implant failure if a certain predictor variable is present. The OR was 3.01 for the location of implant placement in the maxilla or mandible (favouring the maxilla); 2.70 for the presence of bone augmentation prior to implant placement (favouring bone augmentation) and 2.23 for the presence of the diabetes (favouring absence of diabetes).

### ***5.15 Intra-examiner reliability***

Intra-examiner correlation coefficient was used to assess intra-examiner reliability in a sample of 25 randomly selected double recordings of marginal bone loss. The two recordings were highly correlated with Pearson correlation coefficient of 0.981 ( $p=0.000$ ) and 0.994 ( $p=0.000$ ) at the mesial and distal measurements, respectively.

## 6.0 DISCUSSION AND CONCLUSIONS

The ability to anticipate outcomes is an essential part of risk management in an implant practice. Recognizing conditions that place the patient at a higher risk of failure will allow the surgeon to make informed decisions and refine the treatment plan to optimize the outcomes. In general, the low failure rates documented reflect the predictability of dental implants, and this observation is consistent with the clinical outcomes attained for NobelActive implants evaluated in this report. As mentioned earlier, analysis was performed on the implant rather than the patient level. This has the risk of showing a more favourable result in comparison with patient/subject-based analysis because the prevalence calculated from implant-based data becomes diluted from the large number of implants included in the subject sample (Fransson *et al.*, 2005). When a patient has two or more implants used for statistical analysis, each implant is not independent, which would have an effect on the survival confidence interval when performing survival analysis. This was not as much of a concern in this study since the observed failure rate was low and no patient experienced more than one failure.

A large proportion of the charts were excluded from the study (26.4%) due to incomplete radiographic records or because the inclusion criteria were not met. Some patients would choose not return to the periodontal practice for a final check up after their implants were restored; instead, they attended follow up appointments at their general dentist office (n=21). Such patients could not be included due to the unavailability of a radiograph representing the restored implant(s).

Limitations of this report include lack of standardized calibration between

surgeons and lack of standardized radiographs with radiographic stents. Radiographs were taken with a long-cone parallel technique using a paralleling device (Dentsply Rinn, Rinn Cooperation, USA) by multiple practitioners with different radiographic equipment. Furthermore, baseline registrations for three cases (seven implants) used orthopantomograms instead of periapical radiographs. These were included because the implants were placed flush with the alveolar crest. As a result, baseline levels could be taken as '0' and follow up periapical radiographic marginal bone loss measurements could be easily compared to baseline levels. Since the quality of the radiographs differed regarding projection of the beam and angulation, accuracy of the marginal bone loss measurements may have been affected. Sewerin (1990) analyzed errors in radiographic assessment of marginal bone height around osseointegrated Branemark implants in an experimental model. He demonstrated that very small deviations of the x-ray beam from the perpendicular with respect to the long axis of the implant would compromise the accuracy of the bone height measurements. In order to compensate for angulation and magnification distortion in the radiographs, the known implant lengths were used for the calibration of the measurements. In attempt to limit measurement error and bias in the radiographic assessment of the marginal bone loss, one 'blinded' examiner, who was not involved in the treatment of patients, evaluated all radiographs. Intra-examiner reliability of the selected double recordings was highly correlated demonstrating that measurements were performed in a consistent, reliable manner.

## **6.1 Implant follow up after loading**

The average follow up period from the placement of the implant restoration was 12.87 ( $\pm 4.83$ ) months with a range of 4 - 27 months for 64 patients who received 124 NobelActive implants. This short-term, average follow up period of twelve months is consistent with what has been reported by other short-term evaluations (Guncu *et al.*, 2008; Kielbassa *et al.*, 2009; Kronstrom *et al.*, 2010; Malo *et al.*, 2005; Ostman *et al.*, 2005; Pieri *et al.*, 2009; Sennerby *et al.*, 2008). However, restored implants with less than twelve month follow up marginal bone loss measurements were accepted in the study in order to increase the sample size for this new implant system. The practice of including a large range in the follow up period has been noted in previous publications (Agliardi *et al.*, 2010; Casap *et al.*, 2007; Chaushu *et al.*, 2001; Degidi & Piattelli, 2003; Sennerby *et al.*, 2008; Stoker & Wismeijer, 2009). The sample size compares favorably to other publications that have reported data on novel implant systems or novel surgical or restorative techniques (Achilli *et al.*, 2007; Casap *et al.*, 2007; Chaushu *et al.*, 2001; Crespi *et al.*, 2010a; Guncu *et al.*, 2008; Pieri *et al.*, 2009; Sennerby *et al.*, 2008).

## **6.2 Outcome variables**

### **6.2.1 Primary outcome – implant survival**

An implant survival rate of 94.4% was observed over an average follow up period of 12.9 months. At the patient level, 89.1% of patients experienced no implant failures. Of the 10.9% of patients who experienced failures, no patient experienced two failures. These survival rates are comparable to that described in literature (Brocard *et al.*, 2000; Buser *et al.*, 1997; Chen & Buser, 2009; DeLuca *et al.*, 2006; Garcia-Bellosta *et al.*, 2010;

Levin *et al.*, 2006; Quirynen *et al.*, 2007; Schropp & Isidor, 2008; Schwartz-Arad *et al.*, 2002). The seven failures occurred in the first nine months of the study period.

### **6.2.2 Secondary outcome – marginal bone loss**

The average marginal bone loss reported in this study is within the acceptable threshold recommended by Albrektsson and Zarb for rough surface implants (Albrektsson & Zarb, 1993). It is also comparable to marginal bone loss measurements reported by short-term reports (Crespi *et al.*, 2010a; Degidi *et al.*, 2007; Ganeles *et al.*, 2008; Kielbassa *et al.*, 2009; Pieri *et al.*, 2009; Testori *et al.*, 2004; Testori *et al.*, 2008; van Steenberghe *et al.*, 2005; Vanden Bogaerde *et al.*, 2005).

The concern with using mean marginal bone level assessments is that the averaging process may dilute severe marginal bone loss, affecting only a few implants. In addition, once an implant has failed, its values are removed from the calculations, thereby improving the bone level measurements. These limitations of the mean marginal bone level measurements may delay an early detection of a statistically significant difference. This problem was addressed by dichotomizing the average marginal bone loss measurements into groups (<1.0 mm, 1-2 mm, 2-4 mm and >4 mm) to identify the patients who had at least one implant affected by more significant bone loss. According to this stratification, 66.7% of the implants placed had marginal bone loss of  $\leq 1.0$  mm (n=74), 23.4% had 1-2 mm (n=26), 8.1% had 2-4 mm (n=9) and 1.8 % had >4 mm (n=2). The two implants with >4 mm bone loss occurred in one patient who had diabetes and was a heavy smoker.

## **6.3 Patient-related factors**

### **6.3.1 Age**

This report did not show statistically significant association between age and implant survival rate or marginal bone loss. As noted in this study, numerous reports have demonstrated that after adjustment for other factors, age does not have a significant impact on implant survival (Blanes *et al.*, 2007; Bornstein *et al.*, 2008; DeLuca *et al.*, 2006; Garcia-Bellosta *et al.*, 2010; Lemmerman & Lemmerman, 2005; Levin *et al.*, 2006; Moy *et al.*, 2005).

### **6.3.2 Gender**

A statistically significant effect was not observed between gender and implant survival or marginal bone loss. This is consistent with what has been reported by innumerable large-scale publications with long observation periods (Blanes *et al.*, 2007; Bornstein *et al.*, 2008; DeLuca & Zarb, 2006; Garcia-Bellosta *et al.*, 2010; Lemmerman & Lemmerman, 2005; Levin *et al.*, 2006; Moy *et al.*, 2005).

### **6.3.3 Diabetes**

The patient population included two patients with diabetes (six implants, 4.8%), one with asthma (0.8%), one with hypothyroidism (0.8%), and 15 with controlled hypertension (44 implants, 35.5%). One of the seven implant failures occurred in a diabetic patient, while six failures occurred in non-diabetics, this difference was not significant. A greater mean marginal bone loss was observed in the diabetic patients ( $2.79 \pm 2.32$  mm) as compared to non-diabetics ( $0.80 \pm 0.75$  mm). Although there was no significance in the bivariate statistical analysis, there was a statistically significant effect

of diabetes on marginal bone loss when other variables were controlled in the regression analysis. Since the study population only included two patients with diabetes, the results attained may be attributed to natural variation due to the limited sample size.

Nonetheless, this observation is consistent with that reported by Ferriera *et al.* (2006) who noted a greater risk of peri-implant complications in diabetic patients. Moreover, it was demonstrated that poor metabolic control in diabetic subjects did not present a statistically significant association with peri-implant mucositis; however, they did present a higher risk of developing peri-implantitis (Ferreira *et al.*, 2006). Unfortunately, the level of diabetic control could not be objectively assessed in this retrospective chart review since glycosylated hemoglobin (HbA1c) levels were not recorded.

#### **6.3.4 Smoking**

A large number of publications have reported a significant impact of smoking on implant failures (Bain & Moy, 1993; DeLuca *et al.*, 2006; Hinode *et al.*, 2006; Klokkevold & Han, 2007; Moy *et al.*, 2005; Strietzel *et al.*, 2007). Three of the aforementioned systematic reviews have revealed that the majority of studies evaluated included implants with turned or moderately rough surfaces. More recently, numerous reports have demonstrated no significant differences between smokers and nonsmokers in terms of implant failures (Alsaadi *et al.*, 2008; Bain *et al.*, 2002; Blanes *et al.*, 2007; Brocard *et al.*, 2000; Grunder *et al.*, 1999; Lambert *et al.*, 2000; Lemmerman & Lemmerman, 2005; Machtei *et al.*, 2008; Peleg *et al.*, 2006; Schwartz-Arad *et al.*, 2002; Sverzut *et al.*, 2008). The improvement is attributed to the surface-modifications on the dental implants, which render them less susceptible to the effects of smoking (Balshe *et*



*al.*, 2008; Feldman *et al.*, 2004). It has been demonstrated that greater failures occurred in smokers versus non-smokers only when smooth-surface implants were used (Balshe *et al.*, 2008). The current report evaluating NobelActive implants did not demonstrate a significant effect of smoking on implant survival, an observation that is consistent with more recent reports evaluating rough surface implants.

In terms of marginal bone loss, a significant difference was observed between ‘current’ and ‘never’ smokers. This result is congruous with the undisputed association observed between smoking and increased implant complications. Greater peri-implant marginal bone loss in smokers has been documented in countless studies (Cochran *et al.*, 2009; Heitz-Mayfield & Huynh-Ba, 2009; Kan *et al.*, 2002; Levin & Schwartz-Arad, 2005; Nitzan *et al.*, 2005; Strietzel *et al.*, 2007). The current report also demonstrated a significant association between the number of pack years and marginal bone loss. This is in agreement with previous reports, which have demonstrated that the quantity and duration of cigarette smoking has been associated with significantly higher incidence of implant complications and failure rates (Bain & Moy, 1993; DeLuca *et al.*, 2006; Levin & Schwartz-Arad, 2005; Mundt *et al.*, 2006).

## **6.4 Implant-related factors**

### **6.4.1 Length**

Implant length did not significantly impact implant survival or marginal bone loss. This finding is consistent with numerous reports, which have demonstrated that short implants have similar implant survival rates as their longer counterparts (Blanes *et al.*, 2007; Fugazzotto, 2008; Malo *et al.*, 2007b; Misch *et al.*, 2006; Morand & Irinakis, 2007;

Renouard & Nisand, 2006).

#### **6.4.2 Width**

Implant width also did not significantly effect implant survival or marginal bone loss. This is in agreement with numerous reports that have found no association between implant diameter and survival rate (Degidi *et al.*, 2007; Degidi *et al.*, 2008; Friberg *et al.*, 2002; Garlini *et al.*, 2003; Lemmerman & Lemmerman, 2005; Morand & Irinakis, 2007; Renouard & Nisand, 2006; Romeo *et al.*, 2004). Considering the fact that length and width do not appear to have a significant effect on implant survival, the dimension of an implant should be dictated primarily by the surrounding anatomic structures, the available bone, the type of bone and the prosthetic space (Morand & Irinakis, 2007).

#### **6.5 Primary stability as measured by insertion torque**

Insertion torque did not have a significant impact on implant survival, however, its effect on marginal bone loss was statistically significant in the bivariate analysis. Insertion torque, as categorized into groups of  $\leq 35$  Ncm, 36-50 Ncm and  $\geq 50$  Ncm was associated with increasing mean marginal bone loss measurements of  $0.62 \pm 0.65$  mm,  $0.93 \pm 0.66$  mm and  $1.05 \pm 1.26$  mm respectively. The torque at time of implant placement serves as an indication of initial stability, which is accepted as an important prognostic marker for osseointegration and implant success (Esposito *et al.*, 2009; Sennerby & Meredith, 2008). Primary stability was attained for all implants placed during the study period, with consistently high torque values achieved (mean  $50.4 \pm 16.9$  Ncm).

The higher insertion torque achievable with NobelActive implants is related to its design features and drilling protocol. Instead of creating an osteotomy site that is comparable to the size of the implant, as in the case of traditional straight-walled or tapered implants systems, the osteotomy site of NobelActive implants are slightly under-prepared, depending on the bone density of the implantation site. During insertion of the implant into the osteotomy, the surrounding bone is compressed laterally conferring a higher insertion torque in a more reliable manner. This method is similar to that proposed by Summers using osteotomes instead of using the drills (Summers, 1994). The consistently higher torque values achievable with this implant system make it an optimal candidate for use in immediate placement and immediate loading protocols, and in lower density bone. It is noteworthy that the surgeons, especially in the initial stages, aimed to achieve torques under or near 70 Ncm, since according to the manufacturer, the NobelActive implants were designed for a greater insertion torque without risk of damaging the internal hex prosthetic connection or inducing pressure necrosis (Irinakis & Wiebe, 2009).

The results of the study indicate that greater insertion torque results in increased marginal bone loss. There is no significant difference between the torque categories of  $\leq 50$  Ncm and  $> 50$  Ncm with respect to the marginal bone loss observed, however, mean bone resorption was  $< 1$  mm in the  $\leq 50$  Ncm group ( $0.78 \pm 0.66$  mm) as compared to  $> 1$  mm in the  $> 50$  Ncm group ( $1.05 \pm 1.26$  mm). In an experimental model using cadavers, Ueda *et al.* (1991) has reported that the maximum insertion torque exerted without breaking the threads in bone surrounding the fixture was 50 Ncm in unicortical bone. It was recommended that final tightening should be performed below 50 Ncm since over-

tightening the fixture can cause continuous compression to the surrounding bone and especially to the bone threads around the fixture. Too much compression was thought to lead to bone resorption because of the disruption of microcirculation, which can lead to necrosis of osteocytes. In light of these findings, it may be reasonable to suggest that insertion torque should not exceed 50 Ncm. This level of torque would still provide the surgeon with excellent primary stability that is necessary for more complex procedures such as immediate implant placement and immediate loading, even in reduced quality bone, without causing an increased risk of marginal bone resorption.

## **6.6 Anatomic site-related factors**

### **6.6.1 Bone density and anatomic location**

Bone quality did not have a statistically significant effect on implant failure or marginal bone loss, however, there was a clear tendency towards greater mean marginal bone loss with increasing bone density. It has been demonstrated that highest bone density occurs in the anterior mandible, followed by the posterior mandible, anterior maxilla, and finally in the posterior maxilla (Misch, 2006a; Truhlar *et al.*, 1997). The difference in success rates as it relates to jaw and implant position is often attributed to bone quality (Turkyilmaz & McGlumphy, 2008).

In terms of anatomical location, there was no statistically significant difference in implant survival rate between the maxilla and the mandible. However, mean marginal bone loss was significantly greater in the mandible as compared to the maxilla. When anatomic sites were further subdivided into sextants, the mean marginal bone loss was greatest in the posterior mandible, then the anterior mandible, the anterior maxilla, and

finally the posterior maxilla. The bone quality assessments of marginal bone loss correlated well with the bone loss measured in the different anatomic locations. The greatest bone loss occurred in the mandible (which is associated with higher density bone) and the lowest bone loss occurred in the posterior maxilla (which is most commonly associated with soft bone). These findings are contrary to earlier reports in literature that have demonstrated lower success rates in the maxilla as compared to the mandible, particularly in the posterior maxilla (Becker *et al.*, 1999; Buser *et al.*, 1997; Hinode *et al.*, 2006; Jaffin & Berman, 1991; Lazzara *et al.*, 1996; Moy *et al.*, 2005).

In this study, there was no significant difference in survival rates in the maxilla and the mandible, or in different bone densities. This is consistent with more recent reports that have published high success rates in all bone types; a finding that seems to be attributed to advances in implant design and surface modifications (Aykent *et al.*, 2007; Brocard *et al.*, 2000; Ferrigno *et al.*, 2002; Kline *et al.*, 2002; Lemmerman & Lemmerman, 2005; Morand & Irinakis, 2007; Schwartz-Arad *et al.*, 2005).

It is possible that the greater marginal bone loss detected in the mandible as compared to the maxilla may be related to the higher torque values attained with the NobelActive system. Insertion torque was highly correlated with bone density and anatomic location. Within reason, there is a possibility that the effect of greater insertion torque on higher density bone found in the mandible may have caused over-compression of the bone during placement leading to crestal resorption. It has been postulated that excessive torque placed on an implant may result in high levels of strain transmitted to the adjacent bone (Bashutski *et al.*, 2009). The crestal region of an implant, which is often composed of dense cortical bone with a less vascularity, experiences the most strain

upon insertion, thereby making it more susceptible to bone necrosis when excessive pressure is applied during implant placement (Bashutski *et al.*, 2009). Moreover, early crestal bone loss resulting in implant failure may be related to excessive forces, which would place additional stress on the crestal bone during implant placement (Misch, 1999). Reversing the implant by one-quarter turn after insertion may minimize stress on the adjacent bone, especially when tapered implants are used (Bashutski *et al.*, 2009). In addition, pre-tapping is essential when placing implants into dense bone, and it may prevent the need to use high torque values to place the implant (Bashutski *et al.*, 2009).

In the multiple regression analysis, torque was no longer a significant predictor of marginal bone loss, while anatomic location continued to show a significant effect. Needless to say, further research is necessary to elucidate this finding as it can have significant implications in the treatment outcomes of this implant system.

#### **6.6.2 Previous and simultaneous guided bone regeneration or sinus augmentation**

Bone augmentation, either prior to or simultaneously with implant placement, did not have a significant effect on implant survival. In addition, the type of augmentation performed was not found to significantly impact implant survival. This finding is consistent with studies that have reported similar success rates of implants in socket preserved sites (Fugazzotto, 2005; Kohal *et al.*, 1998) and in sites with guided bone regeneration as compared to native bone (Aghaloo & Moy, 2007; Blanco *et al.*, 2005; Brocard *et al.*, 2000; Chiapasco *et al.*, 2009; Christensen *et al.*, 2003; Esposito *et al.*, 2006; Fiorellini & Nevins, 2003; Fugazzotto, 2005; Juodzbalsys *et al.*, 2007). Moreover, numerous studies have shown that sinus augmentations, either previous or simultaneous

with implant placement, have survival and success rates similar to implants placed in the posterior maxilla without sinus augmentation (Aghaloo & Moy, 2007; Esposito *et al.*, 2006; Sorni *et al.*, 2005; Wallace & Froum, 2003). This similar observation was noted for osteotome sinus lifts (Fermergard & Astrand, 2008; Ferrigno *et al.*, 2006; Pjetursson *et al.*, 2009; Tan *et al.*, 2008).

The mean marginal bone loss was greater for cases without prior bone augmentation compared to those with augmentation and this difference was statistically significant. It is possible that cases with GBR provided bone with more adequate ridge dimensions so that optimal implant placement could be performed in terms of adequate thickness of bone surrounding the socket, minimal thread exposure, and favourable angulation could be performed. It is more likely, however, that the difference noted was due to the presence of a small sample size. As a result, the effect observed was likely due to natural variation as compared to a true effect.

There was a tendency towards less mean marginal bone loss for cases with simultaneous bone augmentation, however no statistically significant effect was observed with respect to the type of simultaneous bone augmentation. Again, due to the small sample size, it is likely that the tendency observed is attributed to natural variation as compared to a true effect.

## ***6.7 Timing of implant placement***

### **6.7.1 One-stage versus two-stage protocols**

Implant placement protocol in terms of one- or two-stage procedures did not influence implant survival or marginal bone loss. This finding is consistent with that

reported in literature (Cangini & Cornelini, 2005; Esposito *et al.*, 2009; Hammerle *et al.*, 1998; Lang *et al.*, 2007; Lemmerman & Lemmerman, 2005). In this study, there was some bias in case selection since cases involving more complex bone grafting procedures and edentulous arches with removable prosthesis were done as two-stage (submerged) surgeries. This is consistent with a recent Cochrane review, which concluded that a two-stage submerged approach may be indicated when an implant has not obtained an optimal primary stability, when barriers are used for guided tissue regeneration or when it is expected that removable temporary prostheses could transmit excessive forces on the penetrating abutments, especially in fully edentulous patients (Esposito *et al.*, 2009).

#### **6.7.2 Immediate placement**

There was no statistically significant effect of timing of implant placement on implant failure. The mean marginal bone loss was slightly greater in implants placed in native bone as compared to those placed in immediate sites, but this difference was not significant in terms of the bivariate analysis. This finding is in agreement with several studies that have demonstrated that success rates of immediate and immediate-delayed implant placement are comparable with those placed in native bone (Chen *et al.*, 2004; Chen & Buser, 2009; Esposito *et al.*, 2006; Schropp & Isidor, 2008). It is noteworthy, that some studies have not been able to comment on the effect of immediate placement on marginal bone loss (Quirynen *et al.*, 2007), whereas others have reported no significant differences between at the two protocols (Chen *et al.*, 2004).



### 6.7.3 Immediate restoration/loading

Immediate restoration or loading did not have a statistically significant effect on implant failures. These observations are supported by studies reporting similar survival rates between immediate restoration and immediate loading in the edentulous mandible (Agliardi *et al.*, 2010; Alfadda *et al.*, 2009; Attard & Zarb, 2005; Cochran *et al.*, 2004; Ibanez *et al.*, 2005; Ioannidou & Doufexi, 2005; Nkenke & Fenner, 2006; Stoker & Wismeijer, 2009; Testori *et al.*, 2004), the edentulous maxilla (Bergkvist *et al.*, 2009; Chiapasco, 2004; Degidi *et al.*, 2008; Ibanez *et al.*, 2005; Tarnow *et al.*, 1997; van Steenberghe *et al.*, 2005) in maxillary and mandibular partial edentulous sites (Achilli *et al.*, 2007; Esposito *et al.*, 2009; Ganeles *et al.*, 2008; Rocci *et al.*, 2003b; Roccuzzo *et al.*, 2009).

The mean marginal bone loss for implants that were loaded according to a conventional or delayed loading protocol were significantly less than those that were immediately loaded implants. Immediate loading of implants is a more technically challenging procedure. That said, the numerous publications have reported marginal bone loss  $\leq 1.0$  mm in the first year of function, which is consistent with the recommendations made by Albrektsson and Zarb (1993) for rough surface implants in the conventional loading protocol (Degidi *et al.*, 2008; Ganeles *et al.*, 2008; Ibanez *et al.*, 2005; Kielbassa *et al.*, 2009; Testori *et al.*, 2004; Testori *et al.*, 2008; van Steenberghe *et al.*, 2005)). Other studies that have made direct comparisons between the two protocols have found less bone loss in the immediately loaded as compared to the delayed loaded group (Schincaglia *et al.*, 2008 and Ormianer & Palti, 2008).

Conversely, some studies have reported marginal bone level changes  $>1.0$ mm in the first year of loading (Agliardi *et al.*, 2010; Bergkvist *et al.*, 2009; Glauser *et al.*,

2003). These results are more consistent with the observations in this report, which were measured as  $1.37 \pm 0.88$  mm of bone loss associated with the immediate loading group. These results however, must be interpreted with caution because the sample size was only 28 implants placed in five patients; 24 of which were placed in three patients. After further analyzing the data, it was noted that two of the patients who received 18 of the 28 implants had severe periodontal disease prior to implant therapy. In addition, statistical analysis was only performed at the implant-level, not the patient-level, therefore, clustering of implants within patients was not taken into account.

#### **6.7.4 Immediate placement with immediate restoration/loading**

In this report, there was no significant effect of simultaneous immediate placement and immediate loading on implant survival. Few studies have made direct comparisons between immediately loaded implants placed in extraction sockets versus healed sites, however, those that have demonstrated no difference in survival rates between the two protocols (Degidi *et al.*, 2007; Knoernschild, 2010; Pieri *et al.*, 2009). These results are contrary to that reported by Quirynen *et al.* (2007), who in a systematic review evaluating immediate placement, concluded that there was a trend toward a greater incidence of implant loss when combining immediate placement and immediate loading as compared to immediate loading alone.

A significantly greater marginal bone loss was observed in the immediately placed, immediately loaded group as compared to the remainder of the cases in this report. This is contrary to publications that have demonstrated marginal bone loss levels of <1.0 mm to be unaffected by this treatment protocol (Crespi *et al.*, 2010a; Degidi *et*

*al.*, 2007; Knoernschild, 2010; Mijiritsky *et al.*, 2009; Pieri *et al.*, 2009; Pieri *et al.*, 2009; Vanden Bogaerde *et al.*, 2005). In fact, one study demonstrated less marginal bone loss in favour of immediate placement and restoration. The authors suggested the soft tissues were continuously supported by a prosthesis in the immediate loading group, a factor that may have contributed to the improved maintenance of the papillary height (De Rouck *et al.*, 2009). Again, the results attained with respect to immediate placement and immediate loading must be interpreted with caution because the sample size was only 22 implants placed in five patients; 18 of which were placed in three patients. As mentioned earlier, statistics were only performed at the implant-level, not the patient-level, therefore, clustering of implants within patients were not taken into account.

### **6.8 Distribution of implant supported restorations**

There was no significant association between the type of restoration and implant survival rate, however a significant association was seen in marginal bone loss between single crowns and fixed complete-arch prostheses, and single crowns and splinted crowns. The greatest marginal bone loss was observed in fixed complete-arch prostheses, followed by splinted crowns, fixed partial dentures, and finally single crowns. This is in contrast to numerous studies that have demonstrated fixed complete-arch prostheses showing comparable marginal bone loss with measurements of <1.0 mm following at least a year of function (Agliardi *et al.*, 2010; Bergkvist *et al.*, 2009; Ibanez *et al.*, 2005; Malo *et al.*, 2005; Malo *et al.*, 2007a; Testori *et al.*, 2008). It should also be mentioned that the majority of implants supporting the fixed complete-arch prostheses were placed immediately into fresh extraction sockets and immediately loaded. These marginal bone

loss values are consistent with those observed in the immediate loading and immediate placement with immediate loading groups. These variables are likely not independent from one another, indicating that the marginal bone loss results attained for the immediate loading groups and the fixed complete arch prosthesis may be confounded.

### **6.9 Post-operative antibiotics**

The use of antibiotic therapy did not have a statistically significant effect on implant survival or marginal bone loss. Patients who did not receive antibiotics most commonly had one or two implants placed without simultaneous grafting procedures. The impact of antibiotic therapy on implant survival is equivocal. A Cochrane review assessing the effects of antibiotics on implant treatment concluded that 2 g of amoxicillin given orally, 1 hour pre-operatively, significantly reduce failures of dental implants placed in ordinary conditions. However, they were not able to comment on whether postoperative antibiotics are beneficial, and which is the most effective antibiotic (Esposito *et al.*, 2008).

### **6.10 Level of training of the surgeon**

The level of training of the practitioner did not have a statistically significant effect on implant failure rate or mean marginal bone loss. All failures occurred in the experienced practitioner group, however, it is noteworthy that the limited cases performed by the residents were less complex, often involving only one or two implants and requiring limited, if any additional bone augmentation. It has been demonstrated in

some studies that clinician experience does effect implant survival rates (DeLuca *et al.*, 2006; Lambert *et al.*, 1997). Nonetheless, conclusions regarding the effect of clinician training on implant survival cannot be elucidated based on this report due to the limited sample size of the resident group.

### **6.11 Regression analyses**

Both the bivariate analysis and stepwise linear multiple regression analysis revealed that smoking, anatomic location and immediate restoration/loading had a statistically significant effect on marginal bone loss. Using bivariate analyses, a significant effect of diabetes and immediate placement was not observed, however a clear effect was demonstrated after controlling for other variables in the regression analysis. Finally, the effect of insertion torque and previous bone augmentation was no longer a significant predictor of marginal bone loss in the regression model once other predictor variables were controlled for. In terms of previous bone augmentation, it is possible that the significance detected in the bivariate model was due to natural variation and not to a real effect considering the small sample size. Furthermore, the effect of increasing insertion torque on greater marginal bone loss was no longer significant after controlling for other variables. The association between torque and marginal bone loss needs to be validated by future research.

The observed negative effect of diabetes on marginal bone loss is consistent with observations noted in literature, which has demonstrated a greater risk of peri-implant complications in diabetic patients (Ferreira *et al.*, 2006). The significant effect of smoking on marginal bone loss observed in this report is also well documented in

literature (Cochran *et al.*, 2009; Heitz-Mayfield & Huynh-Ba, 2009; Kan *et al.*, 2002; Levin & Schwartz-Arad, 2005; Nitzan *et al.*, 2005; Strietzel *et al.*, 2007). A greater marginal bone loss was observed in the mandible as compared to the maxilla in this report. This is contrary to the low failure rates and marginal bone loss data published for mandibular implants (Becker *et al.*, 1999; Buser *et al.*, 1997; Glauser *et al.*, 2003; Hinode *et al.*, 2006; Jaffin & Berman, 1991; Lazzara *et al.*, 1996; Moy *et al.*, 2005; Stach & Kohles, 2003). As discussed earlier, the greater marginal bone loss observed in the higher density mandibular bone may be related to the higher torque values achieved in the mandibular arch (although torque was no longer a significant factor after controlling for other variables). A larger sample size is necessary (there were only 44 mandibular implants as compared to 80 maxillary implants) in order to further evaluate this effect.

The multivariate analysis revealed that significantly greater bone loss occurred in implants placed in native bone as compared to those placed immediately into extraction sockets, albeit the difference is likely not clinically significant. These findings are inconsistent with that reported by Chen *et al.* (2004), who demonstrated no difference in marginal bone loss for implants placed immediately and in native bone. In terms of immediate loading, numerous publications have reported marginal bone loss <1.0 mm in the first year of function, which is consistent with the recommendations made by Albrektsson and Zarb (1993) for rough surface implants in the conventional loading protocol (Agliardi *et al.*, 2010; Degidi *et al.*, 2008; Ganeles *et al.*, 2008; Ibanez *et al.*, 2005; Kielbassa *et al.*, 2009; Testori *et al.*, 2004; Testori *et al.*, 2008; van Steenberghe *et al.*, 2005). Conversely, some studies have reported marginal bone level changes >1.0 mm in the first year of loading (Agliardi *et al.*, 2010; Bergkvist *et al.*, 2009; Glauser *et*

*al.*, 2003). These results are more consistent with what was observed in this report. However, as mentioned earlier, our sample size for implants that were immediately loaded was relatively small, therefore further research with greater sample sizes is necessary in this regard before any definitive conclusions can be made.

### **6.12 Limitations**

Many of the shortcomings of this type of retrospective chart review have been discussed in previous sections of this paper. Since the implant failures are generally small, a limitation of this study is the small patient population and short-term follow up; both factors make the detection of significant differences or correlations between contributing factors and failure rates difficult, even if a true difference exists. Other limitations include a lack of comparison group, lack of randomization and blinding, lack of standardization of radiographs and the completion of statistical analysis on the implant rather than the patient level. Moreover, the retrospective nature of the study relies on the accuracy of chart records. Finally, it must also be noted that there was a “learning curve” for the new implant system and that the implants were often placed in more difficult sites due to their proposed properties.

### **6.13 Conclusions**

Based on the results of this multicentre study, the following conclusions have been deduced:

- NobelActive implants demonstrated a survival rate of 94.4% during an average follow up period of 12.9 months, which compares favourably with rates reported in literature for other marketed implant systems
- 10.9% of patients experienced one implant failure (seven of 64 patients)
- In terms of implant survival, none of the risk factors evaluated had a significant effect on the failure rate. However, due to the high survival rates of implants, even if an association exists, the small sample size does not allow for trends in the data to reach statistical significance
- The average mean marginal bone loss of the mesial and distal measurements was  $0.89 \pm 0.95$  mm; these measurements are consistent with those reported in literature for a one year follow up period
- In the bivariate analysis, marginal bone loss was significantly effected by: smoking (in favour of non-smokers), insertion torque (in favour of lower insertion torques), anatomic location (in favour of the maxilla over the mandible), previous bone augmentation (in favour of bone augmented sites) and immediate loading (in favour of non-immediate loading)
- Significant correlations were observed between insertion torque and bone quality, and insertion torque and anatomic location
- In the regression analyses, the predictors that had the largest impact on marginal bone loss were: diabetes (in favour of non-diabetics), smoking (in favour of non-smokers), anatomic location (in favour of the maxilla), immediate placement (in favour of immediate placement) and immediate loading (in favour of non-immediate loading)
- The effect of insertion torque and previous bone augmentation on marginal bone loss was no longer significant after controlling for confounding variables in the regression analysis



#### **6.14 Future directions**

Although preliminary clinical outcomes for the NobelActive implant system are favourable as compared to other clinically validated implant systems, the findings of the present study further elucidate the need for longitudinal investigations including a larger sample size to examine the effect of predictor variables such as diabetes, smoking, insertion torque, anatomic location, immediate loading and immediate placement, on implant survival rates and marginal bone loss. Furthermore, the possible association between insertion torque and implant placement in the higher bone density often found in the mandible, should be examined as it may have implications on the modification of the manufacturer's protocol for the NobelActive implant system.

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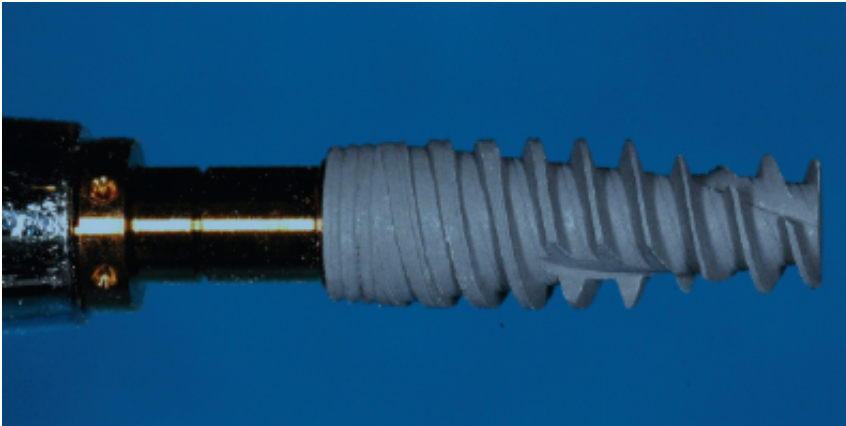
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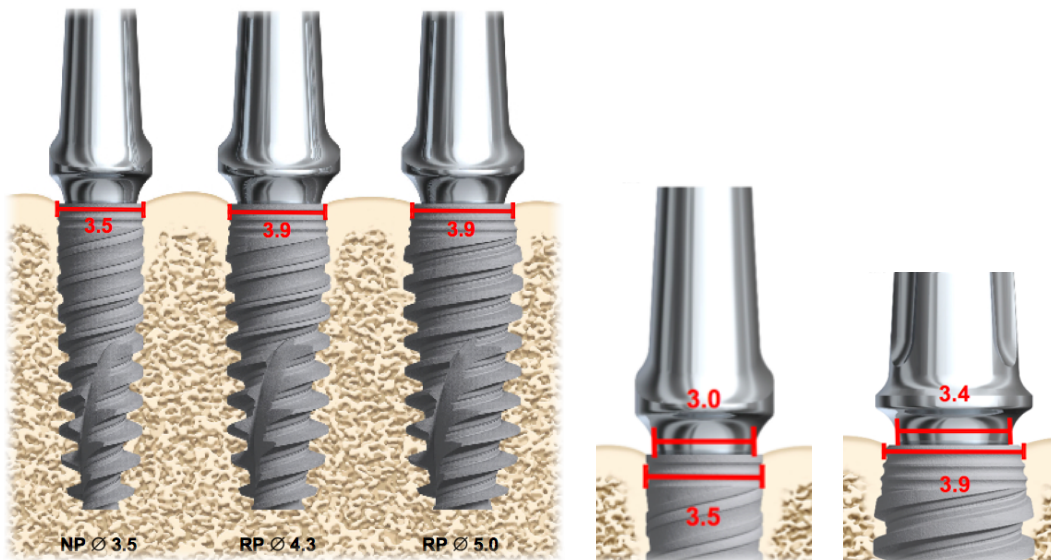
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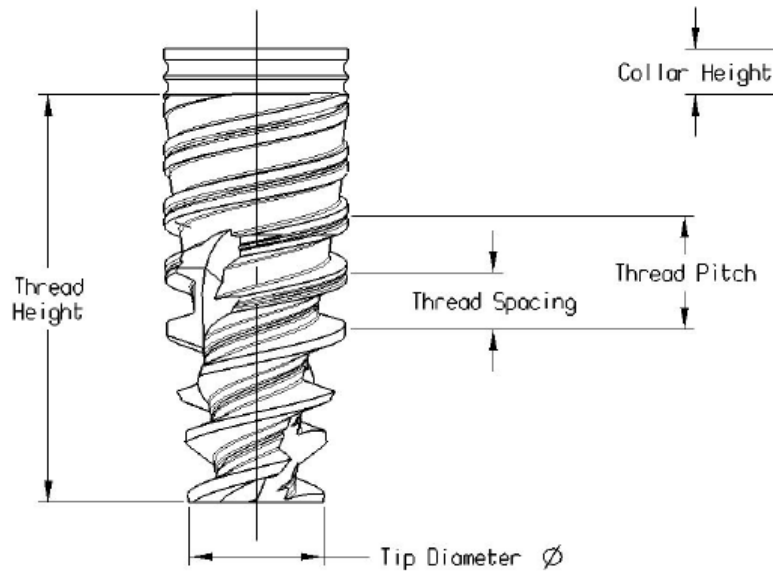
## APPENDICES



Appendix A. Design features of the NobelActive implant

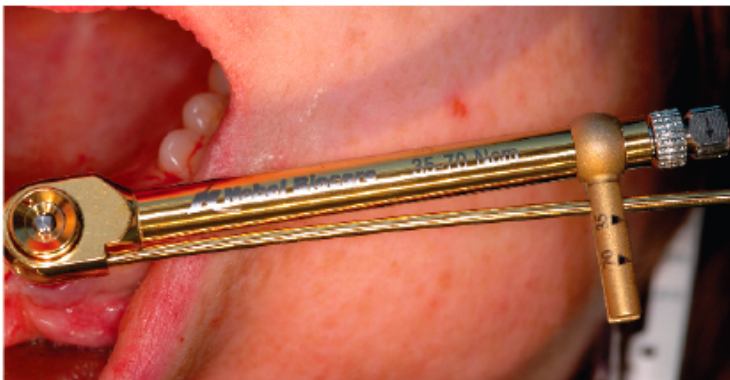


Appendix B. Platform shifting design

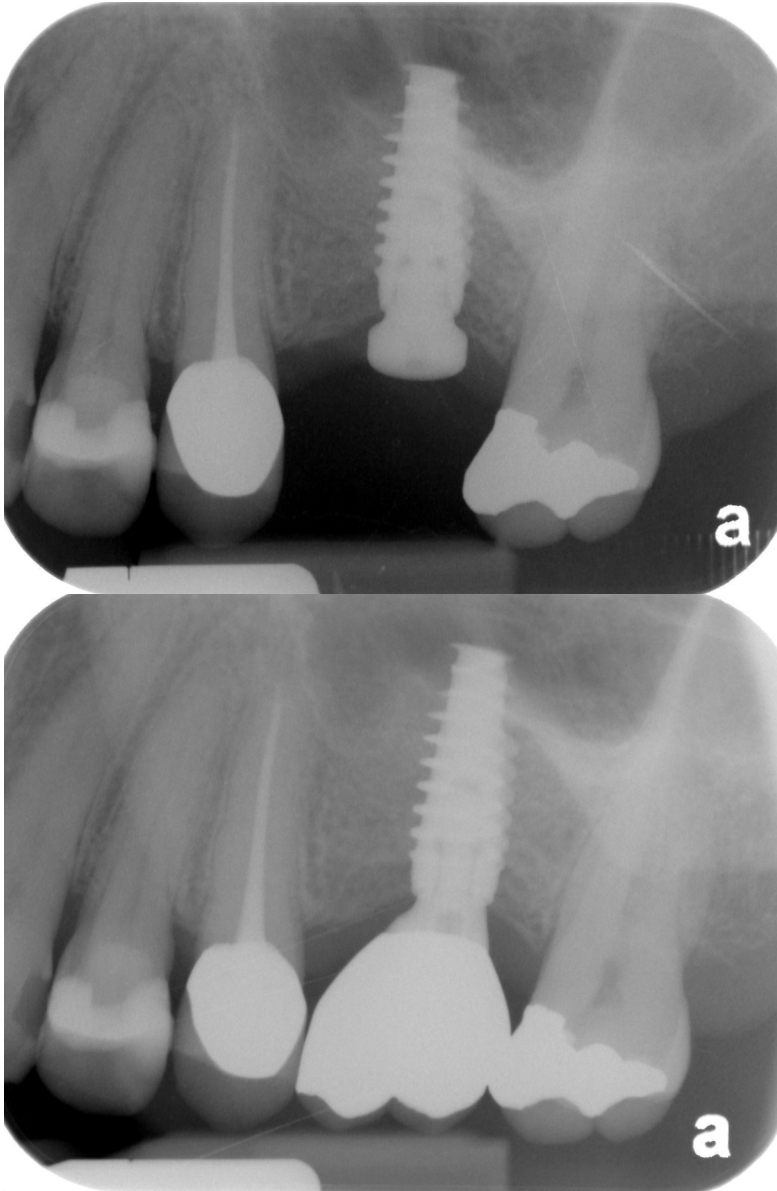


Platform		Tip Diameter	Major Diameter	Collar Height	Thread Height	Double Lead Thread	
						Thread Spacing	Thread Pitch
NP	3.5x10mm	2.6	3.5	0.9	8.54	1.2	2.4
	3.5x11.5mm	2.6	3.5	0.9	10.04	1.2	2.4
	3.5x13mm	2.6	3.5	0.9	11.54	1.2	2.4
	3.5x15mm	2.6	3.5	0.9	13.54	1.2	2.4
RP	4.3x10mm	3.2	4.3	1.3	8.13	1.2	2.4
	4.3x11.5mm	3.2	4.3	1.3	9.63	1.2	2.4
	4.3x13mm	3.2	4.3	1.3	11.13	1.2	2.4
	4.3x15mm	3.2	4.3	1.3	13.13	1.2	2.4
RP	5.0x10mm	3.6	4.9	1.3	8.2	1.2	2.4
	5.0x11.5mm	3.6	4.9	1.3	9.6	1.2	2.4
	5.0x13mm	3.6	4.9	1.3	11.1	1.2	2.4
	5.0x15mm	3.6	4.9	1.3	13.1	1.2	2.4

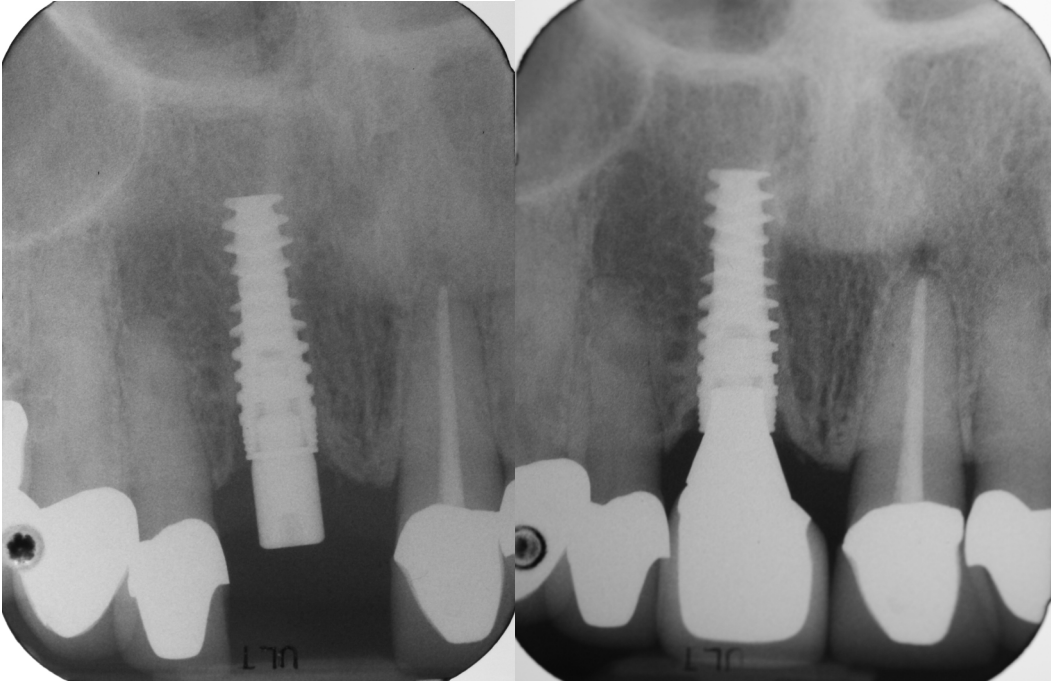
## Appendix C. NobelActive implant specifications



## Appendix D. NobelActive torque wrench

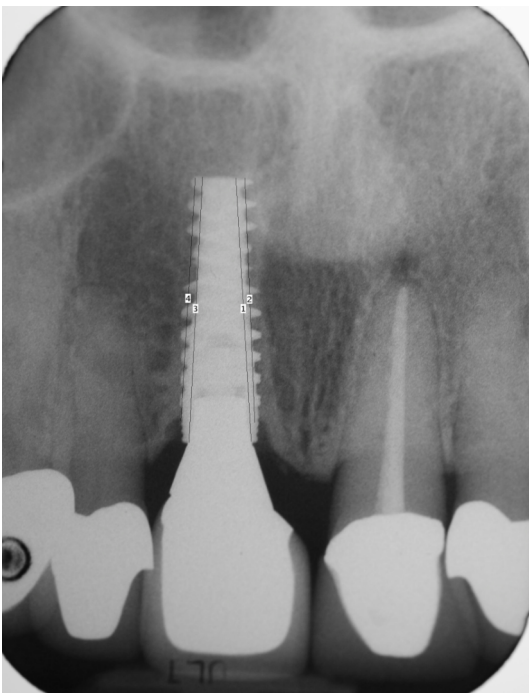


**Appendix E. Radiographs depicting no marginal bone loss**  
Radiographs taken during implant placement and at follow up appointment.



#### **Appendix F. Radiographs depicting marginal bone loss**

Radiographs taken during implant placement and at follow up appointment. Marginal bone loss is observed on the mesial and distal aspects of the implant.



#### **Appendix G. Example of measurements taken using Image J 1.42q software**





The University of British Columbia  
Office of Research Services  
Clinical Research Ethics Board – Room 210, 828 West 10th Avenue, Vancouver, BC  
V5Z 1L8

## ETHICS CERTIFICATE OF EXPEDITED APPROVAL

<b>PRINCIPAL INVESTIGATOR:</b> Anastasios (Tassos) Ilnaklis	<b>INSTITUTION / DEPARTMENT:</b> UBC/Dentistry/Oral Biological & Medical Sciences	<b>UBC CREB NUMBER:</b> H10-00464				
<b>INSTITUTION(S) WHERE RESEARCH WILL BE CARRIED OUT:</b>						
<table border="1"> <thead> <tr> <th>Institution</th> <th>Site</th> </tr> </thead> <tbody> <tr> <td>UBC</td> <td>Vancouver (excludes UBC Hospital)</td> </tr> </tbody> </table>			Institution	Site	UBC	Vancouver (excludes UBC Hospital)
Institution	Site					
UBC	Vancouver (excludes UBC Hospital)					
Other locations where the research will be conducted: Vancouver Implant Perio Centre: Suite 205 777W Broadway, Vancouver BC V5Z4J7 South Calgary Periodontal Group: Private practice - 201 747 Lake Bonavista Dr. SE, Calgary AB T2J 0N2						
<b>CO-INVESTIGATOR(S):</b> Edward E. Putnins Anastasios (Tassos) Ilnaklis Hannu B. Larjava						
<b>SPONSORING AGENCIES:</b> N/A						
<b>PROJECT TITLE:</b> Implant and guided bone regeneration treatment outcomes at the UBC graduate periodontics program and its affiliated clinics: retrospective analyses.						

THE CURRENT UBC CREB APPROVAL FOR THIS STUDY EXPIRES: May 4, 2011

The UBC Clinical Research Ethics Board Chair or Associate Chair, has reviewed the above described research project, including associated documentation noted below, and finds the research project acceptable on ethical grounds for research involving human subjects and hereby grants approval.

<b>DOCUMENTS INCLUDED IN THIS APPROVAL:</b>			<b>APPROVAL DATE:</b>
<u>Document Name</u>	<u>Version</u>	<u>Date</u>	May 4, 2010
<u>Protocol:</u>			
Implant and Bone Graft Study Proposal	1	February 11, 2010	
<u>Consent Forms:</u>			
UBC consent for dental care		February 11, 2010	

**CERTIFICATION:**  
In respect of clinical trials:  
1. The membership of this Research Ethics Board complies with the membership requirements for Research Ethics Boards defined in Division 5 of the Food and Drug Regulations.  
2. The Research Ethics Board carries out its functions in a manner consistent with Good Clinical Practices.  
3. This Research Ethics Board has reviewed and approved the clinical trial protocol and informed consent form for the trial which is to be conducted by the qualified investigator named above at the specified clinical trial site. This approval and the views of this Research Ethics Board have been documented in writing.

The documentation included for the above-named project has been reviewed by the UBC CREB, and the research study, as presented in the documentation, was found to be acceptable on ethical grounds for research involving human subjects and was approved by the UBC CREB.

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Approval of the Clinical Research Ethics Board by one of:  Dr. Peter Loewen, Chair Dr. James McCormack, Associate Chair
--

### Appendix H. Ethics certificate of approval