DENTAL IMPLANT OUTCOMES IN PATIENTS WITH OSTEOPOROSIS:
A MATCHED COHORT STUDY

By

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A thesis submitted in conformity with the requirements for the degree of Master of Science (Prosthodontics)

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Abstract

This study evaluated differences in dental implant outcomes in patients with osteoporosis and their matched controls. Twenty-four patients, who received dental implants at the University of Toronto, were 60+ yrs and had osteoporosis at the time of implant placement, and their controls matched for age, sex and implant related features were examined clinically and radiographically. Clinical and demographic variables recorded at implant placement and follow-up examination, were analyzed. Implant survival rates of 95.1% and 100%, and success rates of 91.4% and 100% were noted in the osteoporosis and control samples respectively. All failures in the osteoporosis sample occurred in the maxilla of a single subject, raising suspicion that these were related to individual problems specific to this subject. Due to the paucity of adverse outcomes and with all the implant failures having occurred in one subject, no relationship of adverse outcomes with clinical and demographic variables could be analyzed.
Acknowledgments:

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I humbly dedicate this manuscript to my family.
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List of Abbreviations

BMD: Bone Mineral Density
BOP: Bleeding on probing
BRONJ: Bisphosphonate related osteonecrosis of jaws
c is-FDP: complete implant supported fixed dental prosthesis
CRF: Case Report Form
DEXA: Dual Energy X-Ray Absorptiometry
DRI: Dietary Reference Intake
ERT: Estrogen Replacement Therapy
FNB: Food and Nutrition Board
FRAX: Fracture Risk Assessment Tool
IFO: International Osteoporosis Foundation
is-OD: implant supported overdenture
NIH: National Institutes of Health
ONJ: Osteonecrosis of jaws
p is-FDP: partial implant supported fixed dental prosthesis
PTH: Parathyroid hormone
SERM: Selective Estrogen Receptor Modulator
WHO: World Health Organization
1 Introduction

Dental implants have been used as a viable option for replacement of missing natural teeth for the last four decades since their introduction in clinical dentistry (Brånemark et al, 1977; 1985). Dental implants help to maintain bone, function, esthetics and phonetics, thus improving oral health–related quality of life (Heydecke et al, 2003). The demand for dental implants is continuously increasing, parallel to improvements in life expectancy since aging is accompanied by increased tooth-loss (Meskin and Brown, 1988; Caplan and Weintraub, 1993). The over 65 year old age group is expected to increase to become more than one-fifth of the living population and is the fastest growing segment of Canadian society (Statistics Canada-Seniors and Aging Health Canada). Concomitantly, there is a general increase of chronic illness, various forms of cancer, and other diseases, including skeletal and metabolic disorders such as osteoporosis and diabetes respectively (Statistics Canada). Osteoporosis is recognized as a common skeletal disorder characterized by low bone mass and microarchitectural deterioration leading to higher fragility and consequently to an increased fracture risk (WHO, 1984). Approximately 75 million people in Europe, USA and Japan are estimated to be affected by osteoporosis (International Osteoporosis Foundation [IOF], 2009).

Osteoporosis results in markedly increased bone turnover and is especially prevalent among post-menopausal females. Estimates are one out of every four women and one out of every eight men above the ages of fifty years. Moreover 70% of fractures in persons over the age of forty-five years are attributed to osteoporosis. (Seniors and Aging, Public Health Canada). It is estimated that 33% women and 20% men in the age group above 50 yrs will experience one or more osteoporotic fractures (IOF, 2009).
The patient cohort at greatest risk of developing osteoporosis is also to the most common patient group that have a need for dental implant therapies. Patients with osteoporosis are also frequently taking medications to control their disease, which may themselves have an effect on the outcomes of dental implant therapies (Jeffcoat, 2006; Grant et al, 2008). Relatively few clinical studies report outcomes of endosseous implant treatments in patients with osteoporosis. Several of these studies have multiple methodological problems and some do not differentiate between the effects of the actual osteoporosis therapy, the duration of the disease and dental clinical variables such as the arch of implant location, site, number of implants and relationship with the dentate/implant status of the opposing arch (Slagter et al, 2008, Tsolaki et al, 2009). Further clinical data are needed to assist clinicians and patients to determine optimal treatment choices for patients with osteoporosis.
2.1 **Dental implants and osseointegration**

Implants were introduced to dentistry by Brånemark in 1965 (Brånemark et al, 1977; Brånemark et al, 1985). In one of the early definitions of osseointegration, Albrektsson et al in 1981 defined osseointegration as “direct functional and structural connection between living bone and the surface of a load bearing implant” (Albrektsson and Brånemark, 1981). Osseointegration has also been described as a time dependent healing process whereby clinically asymptomatic, rigid fixation of alloplastic material is achieved and maintained in bone during functional loading (Zarb and Albrektsson, 1991).

A surgically created bony defect that receives an implant made from a bio-inert material such as titanium undergoes three typical stages of wound healing. The first phase is an inflammatory phase, during which local plasma proteins are first adsorbed on the implant surface and a clotting cascade is initiated causing the release of various cytokines from local cellular elements, which regulate adhesion molecule production, increase vascularisation rate, enhance collagen synthesis, regulate bone metabolism and activate osteoclasts (Fritz et al, 2002). This is followed by an acute inflammatory response with neutrophil migration and aggregation 3-4 days after surgery, followed by macrophages becoming the main phagocytic cells present in the wound 5-6 days after surgery. A second proliferative phase is characterized by new vascularisation, differentiation, proliferation, activation of cells and formation of an immature connective tissue matrix. During this phase, undifferentiated mesenchymal cells differentiate into fibroblasts, osteoblasts and chondroblasts, of which osteoblasts are responsible for the major part of bone repair (Davies et al, 2009). Coupled osteoclast-osteoblast action results in the repair of cortical necrotic border by creeping substitution. Blood vessels enter the necrotic border zone, osteoclasts resorb it and osteoblasts lay new bone around the blood vessels. The healing wound
becomes more organized with the passage of time and the fibrocartilaginous callus is transformed into a bone callus. Finally, in the maturation phase, remodelling of the immature bone matrix occurs, and coupled resorption and deposition of bone by the osteoclasts and osteoblasts continues for many years (Davies, 2003).

Data from experimental research indicate that both contact osteogenesis, which include direct bone formation on the implant surface and distant osteogenesis, which is the formation of new bone on the surface of already existing bone around the implant may occur (Davis, 1998). Moreover, the peri-implant bone healing can be categorized into three distinct phases: (1) osteoconduction, which relies on the migration of differentiating osteogenic cells to the implant surface through a connective tissue scaffold; (2) formation of de novo bone that results in a mineralized interfacial matrix being laid on the implant surface and (3) bone remodelling, which also creates bone implant interface comprising de novo bone at discrete sites (Davies, 1998).

2.2 Outcomes and factors affecting outcomes of dental implants

The success rates of dental implants in edentulous patients and partially dentate patients (also including single tooth replacements) are very impressive, ranging up to 98% after 10 years (Academy of Osseointegration, 2007). To be considered successful, an osseointegrated oral implant should meet certain criteria related to function, tissue physiology and patient satisfaction (Esposito et al, 1998). Implant survival refers to the oral implant being still in function, but not necessarily meeting all the success criteria (Albrektsson and Zarb, 1993). In contrast, implant failure is defined as the first instance at which the performance of the implant measured in a quantitative aspect falls below a specified acceptable limit (Mombelli and Lang, 1994). Systemic conditions such as diabetes mellitus, osteoporosis, cardiovascular disease, Sjögren’s syndrome may affect oral tissue by increasing their susceptibility to other diseases or by interfering with
healing (Bornstein et al, 2009). Additional effects may be caused by the medications often used by patients with systemic conditions that can affect the tissues supporting the implants (Bornstein et al, 2009). There are relatively few absolute contraindications to rehabilitation with dental implants, which include recent myocardial infarction and cerebrovascular accident, valvular prosthesis surgery, immune-suppression, bleeding issues, active treatment of malignancy, drug abuse, psychiatric illness, and intravenous bisphosphonate treatment (Hwang and Wang, 2006). Some relative contraindications and conditions that may unfavourably impact dental implant outcomes discussed in the literature include, e.g., adolescence, aging, osteoporosis, smoking, diabetes, positive interleukin-1 genotype, human immunodeficiency virus infection, cardiovascular disease and hypothyroidism (van Steenberghe et al, 2003; Hwang and Wang, 2007; Alsaadi et al, 2007). Especially osteoporosis has been subjected to some controversy about importance and effects on dental therapy outcomes (Habsha and Zarb, 2002; Tenenbaum et al, 2002).

Data from a limited number of clinical studies are supplemented by a larger body of data from in vitro experiments and animal studies. To discuss these findings in a bigger context, a short review of the bone anatomy and metabolism is presented, followed by a brief resume of the pathophysiology of osteoporosis. Particular issues related to the diagnosis and treatment of osteoporosis that is of relevance to dental implant therapy is also described, albeit it is recognized that the narrative of these two complex topics is reasonably superficial.

2.3 **Bone: gross structure, formation, modeling and turnover**

Bone is a dynamic mineralized connective tissue consisting of 33% organic content and 67% inorganic content (Nanci et al, 2003). Its functions include support, protection, locomotion as well as acting as a reservoir of minerals. All bones comprise of a dense outer compact bone
and a central medullary cavity which contains trabecular bone. The compact: trabecular ratio in human bones is 80:20 (Nanci et al, 2003). Mature bones consist of microscopic lamellae, with three distinct types of layers recognized as circumferential lamellae, concentric lamellae and interstitial lamellae. Concentric lamellae make up the bulk of compact bone and form its basic metabolic unit, the osteon (Nanci et al, 2003) [Fig. 1].

The process by which bones establish their overall size and shape is called bone modeling which starts from embryonic bone development and continues till the preadult period of human growth. During bone modeling, bone forms on the outer periosteal surface while there is destruction occurring simultaneously within the endosteal surface. During growth, bones increase in length and thickness as bone formation rates exceed bone resorption rates.

Although bone is one of the hardest tissues of the human body, it is very plastic and in a constant state of flux. It is continuously being resorbed and deposited in response to the functional and nutritional demands with increased functional needs leading to new bone formation.
formation and decreased function leading to decrease in volume of bone (Wolff’s Law, 1892). Replacement of old bone with new bone is called bone remodelling or turnover, in growing children, bone turnover can be 10 times greater than in adults (Rauchenzauner et al, 2007). During adulthood, bone turnover rates decrease, but in healthy states, remain steady with the amount of bone resorption being balanced by the amount of bone formation. Trabecular bone of the vertebral column has been shown to remodel at a rate of 20% to 30% per year as compared to most cortical bone, which has an annual turnover rate of 2% to 10% (Parfitt, 1983).

Osteoclasts (bone dissolving cells) and osteoblasts (bone forming cells) are the cellular elements whose activities determine the balanced state between bone resorption and bone deposition. During skeletal development and throughout life, cells from the osteoblast lineage synthesize and secrete molecules that in turn initiate and control osteoclast differentiation (Ducy et al, 2000). Bone formation is slower than bone resorption, which is why during increased bone remodelling there is net loss of bone.

Bone is built up throughout life (and mainly during adolescence) to reach the peak bone mass at around 30 yrs (Bonjour, 1994) and then there is subsequent bone loss due to effects of aging, mechanical fatigue, and superadded medical conditions. Bone loss increases with age, and by age 80 yrs, many women have lost approximately 30% of their peak bone mass (Looker et al, 1998). Histological studies have shown that the amount of intracortical porosities increase in human cortical bones, which is due to an increase in the number and diameter of haversian systems. The inner cortex is more affected than the outer cortex (Martin et al, 1980). Trabecular bone is lost faster than cortical bone because trabecular bone turnover rate is greater than cortical bone turnover rate due to the much greater number of bone cells and greater surface area of trabecular bone. Trabecular bone thins over time, eventually is perforated and gets disconnected.
from its surrounding tissue. The trabeculae weaken and ultimately are less resistant to fracture. Microcracks also accumulate exponentially in cortical bone after the age of 40 yrs causing a decrease in cortical osteocyte lacunar density (Vashishth et al, 2000). An imbalance between bone resorption and new bone formation leads to small deficits of bone at the end of every bone remodelling cycle. The remodelling process becomes less effective at repairing damaged bone with age, which may be due to osteocyte death. While bone becomes less dense with age, it becomes more mineralized, which makes it more stiff and less tough (Grynpas, 1993). Increased bone turnover induced by menopause reduces bone mass and bone strength and the increased porosity also affects its toughness to resist fracture (Grynpas, 2002). It has been shown that aging increases the stromal/osteoblastic cell expression of biomolecular signalling factors which increase the recruitment and stimulation of greater osteoclasts as the pre-osteoclast pool also increases (Cao et al, 2005). On the other hand, the number of osteoblasts markedly decreases (Erben et al, 2000).

2.4   **Bone metabolism**

Androgens build and maintain muscle mass, leading to a favorable biomechanical response and build up of bone. Estrogen conserves calcium by suppressing bone remodelling (Frost, 1973). After menopause, remodelling is enhanced, leading to greater loss of calcium since every remodelling cycle is associated with loss of calcium from the bone (Heaney, 1990), increasing the chances of developing osteoporosis. For this reason, ERT has been recommended for many years for calcium preservation and to prevent osteoporosis in post menopausal women (Consensus conference report on osteoporosis, 1984). However, the use of hormonal replacement therapy remains debated regarding its potential association with greater risk for ovarian and breast cancer (Minelli et al, 2004; Coombs et al, 2005; Zhou et al, 2008). The current daily
intake recommendations for calcium as provided in the Dietary Reference Intakes (DRIs) developed by the Food and Nutrition Board (FNB) at the Institute of Medicine of the National Academies (USA) describe adequate daily intakes to be between 1000 mg and 1300 mg (NIH, 2009), with the higher recommended value advised for pregnant and lactating women and individuals over 50 yrs in age. The richest dietary sources of calcium are dairy products, which can be rapidly absorbed by the body.

2.5 Osteoporosis: Definition, types and pathophysiology

The National Institutes of Health Consensus Panel on Osteoporosis Prevention, diagnosis and Therapy (2009) defined osteoporosis as a skeletal disorder characterized by compromised bone strength predisposing a person to an increased risk of fracture. Osteoporosis has been described as a multifactorial age related metabolic bone disease characterized by low bone mineral density, the deterioration of the microarchitecture of cancellous bone, and changes in the material properties of bone, leading to enhanced bone fragility and to a consequent increase in the risk of fractures (Wasnich, 1996). Osteoporosis is categorized as either primary or secondary. Primary osteoporosis usually occurs due to bone loss that occurs with aging, while secondary osteoporosis is a result of medications such as glucocorticoids or diseases such as malabsorption that severely affect skeletal health. Primary osteoporosis is further divided into two types: type I osteoporosis, also called post menopausal osteoporosis which is characterized by loss of trabecular bone due to increased turnover related with lack of estrogen at menopause; and type II osteoporosis, also called senile osteoporosis, which affects both elderly women and men and is characterized by loss of trabecular and cortical bone due to long term remodelling deficiency (Grynpas, 2002; Friedman, 2006). (Fig. 2)
The activity of osteoclasts, relative to bone-forming osteoblasts, dictates the development of osteoporosis, wherein skeletal mass has decreased to the point of structural instability, causing an increased susceptibility to fracture (Teitelbaum, 2000). Microdamage accumulation and failure of its proper repair cause osteoporotic bone to fracture more readily than non osteoporotic bone (Burr et al, 1997).

2.6 **Diagnosis and prevalence of osteoporosis**

Osteoporosis is in clinical practice diagnosed by taking into account the patient’s history, physical examination and any necessary diagnostic tests (for example measurement of BMD). The disease remains often undiagnosed until the affected person has suffered a fracture (Edwards and Migliorati, 2008). Bone strength, which is intimately related with fracture risk, is dependent on many qualities of bone, of which BMD accounts for 75% of bone strength (Edwards and Migliorati, 2008). BMD is expressed as weight of mineral per area or volume (i.e., g/mm$^2$ or g/mm$^3$). Dual Energy X-Ray Absorptiometry (DEXA) [Fig. 3] is considered the gold standard method of determining BMD (Carey et al, 2007).
Fig. 3: Examples of representative DEXA scans of the hip and lumbar spine regions. (Images courtesy of Dr N Khandelwal, used with permission)

T-scores are used to express BMD and is calculated by comparing the patient’s BMD to the mean peak BMD of a normal, young adult population of the same gender with the reference being white, non race adjusted women. One criteria for the diagnosis of osteoporosis established by the World Health Organization (WHO) included having a BMD T-score being more than 2.5 standard deviations below the mean for young healthy adults in the total hip, femoral neck or lumbar spine anatomical regions. A BMD between 1.0 and 2.5 standard deviations below the young adult mean is classified as osteopenia (ie T-score of -1.0 to -2.5) while BMD T-scores above or equal to -1.0 are considered normal (Kanis, 1994).

The WHO definition on its own has several drawbacks. It is recognized that it by itself is not the optimal diagnostic parameter for clinical practice. In a very large longitudinal study based on 149524 women in the US, it was seen that >50% osteoporotic fractures occurred in women with BMD T-scores between -1.0 and -2.5 (Siris et al, 2004). The absolute fracture risk can vary substantially in any of the WHO categories because the fracture risk can be modified due to other factors such as age and sex (Kanis et al, 2001).
In order to increase the efficiency of assessment of fracture risk WHO developed more recently the Fracture Risk Assessment tool (FRAX™) (Kanis et al, 2008). Risk factors were identified from meta-analyses of 9 prospective population based cohort studies from Europe, North America, Asia and Australia (Kanis et al, 2008). It is based on individual patient models that integrate the risks associated with clinical risk factors as well as BMD at the femoral neck. The FRAX(R) algorithms estimate the 10-year probability of fracture based on readily accessible calculation methods made available online. The risk factors for osteoporotic fractures included in FRAX(R) are age (50-90 yrs), sex, weight, height, low femoral neck BMD, prior fragility fracture, parental history of hip fracture, current tobacco smoking, use of glucocorticoids, rheumatoid arthritis, excessive alcohol intake and other causes of secondary osteoporosis (FRAX(R) website, September 2010). Currently, the WHO advice is that the history and clinical examination of patients undergoing diagnostic assessment for osteoporosis related fractures should include the clinical risk factors for osteoporosis and fractures as well as consideration of secondary causes of bone loss such as hyperthyroidism and type I diabetes (Kanis, 2008).

Diagnostic evaluation of osteoporosis according to the Osteoporosis Canada guidelines (2010) includes assessment of age, sex, fracture history, glucocorticoid intake and using the lowest bone mineral density T-score to determine the person’s 10 years absolute fracture risk. For women over 60 years, the 10 year fracture risk for women based on the lowest of the BMD T-scores recorded at the lumbar spine, total hip, femoral neck or trochanter was seen to be low (< 10%) when BMD T-score was >-1.4, moderate (10%-20%) when it was between -1.4 and -3.0 and high (>20%) when <-3.0 (Siminoski et al, 2005).

Biochemical markers of bone turnover measured in the blood serum or urine are indicators of osteoclastic bone resorption and osteoblast functioning, but have not been shown to
be able to diagnose osteoporosis and have varying abilities to predict fracture risks when studied on patients in clinical trials (Schousboe et al, 2007; Delmas et al, 2009). These markers also have varying value in predicting individual patient responses but may show an individual patient’s response to treatment earlier than BMD changes (within a couple of months), because BMD changes may become evident only in 1 to 3 yrs (Markus et al, 1999; Miller et al, 1999).

The combination of undiagnosed patients as well as false negative diagnoses confounds the question of prevalence of osteoporosis in the population. Nevertheless, estimates of approximately 11.4 million affected people in North America and 1.4 million people in Canada have been suggested (IOF, 2009). In Canada, 1 in every 4 women over 50 years and 1 in every 8 men over 50 years are diagnosed with osteoporosis (Hanley and Josse, 1996). Edwards and colleagues prognosticated that by 2010, roughly 12 million people over 50 years were expected to have osteoporosis and 40 million people over 50 years were expected to have osteopenia, and these figures were expected to increase to 14 million and 47 million people, respectively, by 2020 (Edwards, 2008).

2.7 Treatment of osteoporosis

Current treatment approaches in Osteoporosis include lifestyle approaches, including balanced diet (calcium, vitamin D) for bone development and maintenance including weight bearing exercises, smoking prevention and pharmacological interventions. Various systemic pharmacological treatment modalities, which aim to increase bone mass include Estrogen replacement therapy, bisphosphonates, selective estrogen receptor modulators, calcitonin and parathyroid hormone (Friedman, 2006; Canadian Consensus Conference on Osteoporosis, 2006). Estrogen Replacement therapy has been shown to conserve bone and protect from osteoporotic fractures after menopause (Rosen and Kessenich, 1997). However, long term use of estrogen has
been shown to be associated with an increased risk of coronary heart disease, breast cancer and
stroke (Writing Group for the Women’s Health Initiative Investigators, 2002; Anderson et al,
2004). Raloxifene currently is the only SERM approved in Canada for treatment of osteoporosis.

Bisphophonates are the drugs which form the mainstay of pharmacotherapeutic options
for patients with osteoporosis. Bisphophonates are analogues of pyrophosphates that contain a
phosphate-carbon-phosphate (PC-P) backbone structure giving these drugs great affinity for
calcium and calcified structures such as bone. Their three-dimensional structure is capable of
chelating divalent cations such as Ca^{++}, and they target bone surfaces that are undergoing
remodelling (Licata, 2005; Friedman, 2006). Bisphophonates cause osteoclast apoptosis and
inhibit osteoclast function, which decreases bone resorption (McClung, 2003; Licata, 2005).
Adverse effects of bisphosphonates include renal toxicity, acute phase reaction, GI toxicity and
more recently reported, bisphosphonate related osteonecrosis of jaws (BRONJ).

Etidronate is a first generation bisphosphonate containing minimally modified side chains
(marketed as Didrocal® as a 400 mg tablet taken daily for 14 days every 3 months with calcium
taken between cycles). Alendronate, a second generation amino-bisphosphonate, is the most
frequently prescribed bisphosphonate (marketed as Fosamax®) as an oral tablet in daily doses of
5 mg, or 35 mg weekly, or 10 mg daily or 70 mg weekly. Alendronate is also prescribed as a
single weekly dose of 70 mg along with 5600 IU of vitamin D (marketed as Fosavance®).
Risedronate, a third generation bisphosphonate which contains a nitrogen atom with a
heterocyclic ring (marketed as Actonel®), is prescribed in doses of 5 mg/day or 35 mg/week or
75 mg on two consecutive days once a month or 150 mg once a month. It has been claimed that
highly potent bisphophonates when administered intravenously carries a risk of developing
bisphosphonate related osteonecrosis of jaws (BRONJ) (Benhamou, 2007). Although
intravenous bisphosphonates are considered to be a major risk factor for BRONJ, a recent review indicates that there is not enough data yet to establish a link between the intake of oral bisphosphonates and BRONJ (Bornstein et al, 2009).

Calcitonin and parathyroid hormone (PTH) also used systemically in the treatment of osteoporosis (Canadian Consensus Conference on Osteoporosis, 2006). Calcitonin is an inhibitor of bone resorption by inhibiting osteoclastic activity (Civitelli et al, 1988). In clinical usage, however, the reduction in remodelling with calcitonin is much less than with other antiresorptive agents. PTH or its analogues, given by subcutaneous injection once daily, directly stimulate osteoblastic bone formation, and show increased trabecular bone density in women with postmenopausal osteoporosis (Dempster et al, 2001). However, a continuous endogenous production or exogenous administration of PTH as is the case in primary or secondary hyperparathyroidism can lead to deleterious consequences to the skeleton, particularly for cortical bone. Intermittent administration of PTH results in an increase in the number and activity of osteoblasts leading to an increase in bone mass and improvement in skeletal architecture at both trabecular and cortical bone (Neuprez and Reginster, 2008).

2.8 Osteoporosis and possible implications in oral implant therapy

Patients with osteoporosis display a range of skeletal changes that may impact on the possibility of placing dental implants without the need for bone augmentation. Reported findings are a greater alveolar ridge resorption than average (Jeffcoat and Chestnut 3rd, 1993); altered trabecular pattern in the anterior maxilla and posterior mandible (White and Rudolph, 1999); erosions of the inferior border of the mandible as compared to unaffected individuals (Klemetti et al, 1994; Taguchi et al, 1996) and increased resorption and thinning of the mandibular inferior cortical margin (Bollen et al, 2000). As a characteristic feature of the disease, subjects with
osteooporosis show a decrease in the number and thickness of trabecular plates. There are anecdotal reports that in patients with osteoporosis the incidence of maxillofacial fractures during the placement of endosseous implants is increased (Mason et al, 1990).

It has been suggested that bone changes evident on panoramic radiographs can be correlated with general osteoporosis (Devlin and Horner 2008) and even that both intraoral and panoramic radiographs are reliable indicators of bone loss in osteoporosis, and useful as diagnostic tools for axial skeleton osteoporosis (Taguchi et al, 2008). The general opinion though is more guarded as more research is needed to determine whether a correlation exists between bone changes in the mandible and bone mass elsewhere (Elsubeihi and Heersche, 2002).

Osseointegration of an implant is a wound healing process, which depends upon host bone quality and quantity, its healing capacity and various other systemic conditions. Osseointegration is based on intimate bone–implant contact achieved during healing. Thus, any condition affecting bone quality or quantity, or microarchitectural changes in bone structure, including reduction in cancellous bone volume and bone to implant contact (which results in reduced bone tissue available around the implant) could theoretically have a negative impact on the survival and function of an endosseous implant (Qi et al, 2004).

In context to implant placement, a clinical classification system for the alveolar bone quality and quantity was developed by Lekholm and Zarb in 1985. The bone quality was classified on a scale from 1 to 4 depending on ratio of trabecular:compact bone. Type 1 bone is when homogeneous compact bone is present at the entire jaw, type 2 when a thick layer of compact bone surrounds a core of dense trabecular bone, type 3 when a thin layer of compact bone surrounds a core of dense trabecular bone and type 4 when a thin layer of compact bone surrounds a core of low density trabecular bone (Lekholm and Zarb, 1985). Various longitudinal
Implant studies have reported increased failure rates of implants placed in jaws with type 4 bone (Jaffin and Berman, 1991; Friberg et al, 1991), which concomitantly is the typical bone quality seen in osteoporosis patients (van Steenberghe et al, 2003). In a large retrospective cohort of 2004 patients having 6946 implants analyses with multivariate statistics identified osteoporosis as a significant variable associated with early dental implant failure (Alsaadi et al, 2007). On the other hand, a histological study that evaluated bone-implant contact of retrieved failed implants found no differences whether the implant came from patients with or without osteoporosis (Shibli et al, 2008). It has also been proposed that dental implant placement may help to preserve alveolar bone in patients with osteoporosis due to more favorable mechanical loading and stimulation of the bone (Beikler and Fleming, 2003).
Systematic searches in online bibliometric databases for longitudinal clinical studies that have reported dental implant therapy outcomes amongst patients with osteoporosis resulted in identifying two systematic reviews (Slagter et al, 2008, Tsolaki et al, 2009) and five longitudinal clinical reporting on a total of 92 patients with osteoporosis (Table I).

**Table 1: Human Clinical Studies on Osteoporosis and Dental Implants**

<table>
<thead>
<tr>
<th>Author (study design)</th>
<th>Sample size</th>
<th>Follow up period</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Becker et al 2000 (Retrospective case-control)</td>
<td>49 cases (5 osteoporosis) 49 control (7 osteoporosis)</td>
<td>3.9 yrs</td>
<td>No association between DEXA values or diagnosis of osteoporosis and implant loss</td>
</tr>
<tr>
<td>Friberg et al 2001 (Retrospective cohort)</td>
<td>13 osteoporosis</td>
<td>3.4 yrs</td>
<td>Implant successful in osteoporosis provided adapted bone technique used and increased healing time allowed</td>
</tr>
<tr>
<td>von Wowern and Gottfredsen 2001 (Retrospective cohort)</td>
<td>7 osteoporosis 11 control</td>
<td>5 yrs</td>
<td>Mandibular osteoporosis at time of implant placement is a risk factor for peri implant bone loss</td>
</tr>
<tr>
<td>Amorim et al 2007 (Retrospective case-control)</td>
<td>19 osteoporosis 20 control</td>
<td>9 mos</td>
<td>No difference in implant survival in two groups</td>
</tr>
<tr>
<td>Holahan et al 2008 (Retrospective cohort)</td>
<td>94 non osteoporosis 57 osteopenia 41 osteoporosis</td>
<td>5.4 yrs</td>
<td>Equal implant survival with dental implants in all groups</td>
</tr>
</tbody>
</table>
2.9 Clinical studies on dental implant therapy in patients with osteoporosis

Slagter et al (2008) proposed on basis of the four clinical studies (Becker, 2000; von Wowern and Gotfredsen, 2001; Amorim et al, 2006; Holahan et al, 2008) that dental implant therapy may not be a contraindication in osteoporotic patients. Tsolaki et al (2009) identified six prospective and six retrospective human studies in addition to 16 animal studies. Also these investigators concluded that osteoporosis may not be a contraindication for dental implant placement provided the surgical technique was adjusted and longer healing time was provided. The investigators identified frequent drawbacks in the studies such as small sample sizes (commonly less than 20 patients) and short follow up periods.

Becker et al (2000) conducted a case-control study to evaluate an association between osteoporosis status and dental implant failure. A total of 49 cases (aged 44-82 yrs) who had received 184 dental implants and who had experienced dental implant loss were compared with 49 controls (aged 43-85 yrs) who had received 180 implants and had not experienced dental implant loss. In the cases with implant failures, there were 5 who had osteoporosis, while in the controls, who had no implant failures, there were 7 who had osteoporosis. The average follow up period was 3.9 yrs. The peripheral DEXA values were measured for all the patients at the proximal and distal ulna. The mean DEXA scores did not differ significantly between the groups. The resulting T-scores showed that there were 7 patients with osteoporosis in the control group and 5 in the case group. They found no significant association between the T-scores and implant loss. However, implant failure was 3.7 times more likely in sites where the bone quality was recorded as type 3 or type 4. They did not mention the healing time allowed for osseointegration before the implants were loaded and did not discuss whether bone augmentation had or not been
done for any cases. They also did not mention details on the frequency and dosage of the drugs the patients were using to control osteoporosis (Becker et al, 2000).

Friberg et al (2001) reported from a retrospective analysis of 13 patients (11 women and 2 men) with osteoporosis. Five were completely edentulous and 6 were edentulous in the maxilla, and 3 were partially edentulous. Dental implant placement was done using adapted bone site preparation technique and an increased mean healing period of 8.5 months in the maxilla and 4.5 months in the mandible (compared to conventional healing time of 6 months in the maxilla and 4 months in the mandible). The average follow up was 3 yrs, 4 months (range 6 months- 11 yrs). Marginal bone height (by taking a mean value of mesial and distal of the implants) was evaluated with intraoral radiographs and it was seen that at 1 the year follow-up bone loss was measured at 0.6 ± 0.6mm. A 97% success rate was observed after increased healing time and bone compaction. They concluded that implant placement in patients with osteoporosis may be successful over many years following adapted bone technique for primary stability and increased healing time for secondary stability. They did not specify whether there was a history of smoking and no details on concurrent use of medications were provided (Friberg et al, 2001).

von Wowern and Gotfredsen (2001) analyzed a sample of 22 long term (> 5 yrs) edentulous healthy individuals (mean age 65 yrs) which were divided in an osteoporosis group (n=7) and non osteoporosis group (n= 11) on the basis of Bone Mineral Content as measured in the anterior mandible with a dual photon bone scanner with the aim to evaluate bone height changes around dental implants in osteoporosis patients. Intraoral radiographs were undertaken periodically with a standardized technique to measure bone levels and showed a significantly greater marginal bone loss in the osteoporosis sample. They concluded that mandibular osteoporosis at the time of implant placement may be a risk factor for bone loss around dental
implants. However they noted a decreased loss of bone mineral content following treatment with dental implants (von Wowern and Gotfredsen, 2001).

In a retrospective case-control study by Amorim et al (2007), which aimed to evaluate osseointegration in patients with osteoporosis, the data from 19 osteoporosis patients diagnosed on the basis DEXA values at lumbar spine and femoral neck and 20 controls were compared diagnosed on the basis DEXA values at lumbar spine and femoral neck Patients with glucocorticoid treatment and bisphoshonate treatment were excluded as were patients with chronic disease, current smokers, chronic alcohol use, and other immunosuppressive drugs. They did not find any statistically significant difference in survival of the 39 implants placed in the osteoporosis patients and 43 implants in the controls, at 9 months of follow up. However, it needs to be kept in mind that their sample consisted of 19 patients with osteoporosis and the follow-up period was only 9 months, which is a very small duration of follow-up to address the question comprehensively (Amorim et al, 2007).

Holahan et al (2008) reported a retrospective longitudinal 5yr follow up study in which the question whether osteoporosis affects treatment outcome of dental implants in terms of their survival was explored. A retrospective chart review of female patients 50 yrs and older was carried out to identify patients with osteoporosis and osteopenia. Arch location of the implant, smoking status at time of dental implant placement and implant failure were noted. Implant failures were defined as dental implants that had to be removed for non infection related causes. They identified 57 patients with osteopenia (197 dental implants), 41 with osteoporosis (143 dental implants) and 94 non osteoporosis patients (306 implants). They found a ten year survival rate of 92.5% in general and no significant difference among the groups and they did not find any association of failure with arch location. They however found that implants were 2.6 times
more likely to fail in smokers than non smokers. They concluded that patients with a diagnosis of osteoporosis or osteopenia were not more likely to develop implant failure in comparison with non osteoporosis patients. However, they did not elaborate on regarding osteoporosis medications and their exclusion criteria were not specified (Holahan et al, 2008).
3. **Purpose and statement of the problem**

3.1 **Purpose**

From the review of the pertinent literature on this subject, it is clear that more clinical studies are required to accurately determine if dental implant outcomes are affected in patients with osteoporosis. Previous reports are few and do not clarify this issue since several aspects of the osteoporosis experience spectrum such as the effect of therapy and duration of disease have been ignored. Also, the implant location and total number of implants and dentate/implant status of the opposing arch needs to be considered in greater detail.

Dental implants have been placed in patients at the Faculty of Dentistry, University of Toronto prosthodontics clinic for the last thirty years. Dao et al (1993) reported therapy outcomes of subgroups treated in our clinics based on gender and age. The assumption was that since osteoporosis is more prevalent in women 50 yrs of age and older, the frequency of implant failure would be expected to be higher in this subgroup. No gender differences were found in the failure rates in the patients, as well as for women who were 50 yrs or older. The authors concluded that subjects at risk for osteoporosis were not significantly at greater risk for implant failure (Dao et al, 1993). It is acknowledged, that only surrogate outcomes for osteoporosis were used in this study. Thus, no direct outcomes following implant therapy of patients with osteoporosis in the prosthodontics clinic patient pool have been reported which may indicate whether osteoporosis is a risk factor for unfavorable outcomes. Today, there is a tendency to see an increased prevalence of patients with osteoporosis in the referred patient pool to the clinic (Jokstad, personal communication).
3.2 **Statement of the problem**

There is a need to document dental implant therapy outcomes in patients with osteoporosis and to assess possible adverse outcomes in relationship with demographic and clinical variables. Do elderly patients with osteoporosis have less optimal treatment outcomes following implant therapy than those without the condition? There a need to document possible adverse biological outcomes in such patients and to assess their possible relationship with demographic and clinical variables. A better understanding of these relationships will assist clinicians in making more accurate judgments about risk, prognosis, treatment selection, and outcome (Fig 4).

![Fig. 4: Left: Implants placed in 2007 to support an overdenture in a 73 yr old patient with osteoporosis. Right: Implants after 2 yrs of loading with an implant supported overdenture, showing good stability, clinical performance and healthy peri-implant mucosa.](image)
4.1 **Aims and Objectives**

The primary aim of the study was to study dental implant outcomes in 60+ years old patients with osteoporosis at the time of implant placement, compared with outcomes in a matched control group.

A secondary aim was to assess any adverse dental implant outcomes in 60+ years old patients having osteoporosis and their possible relationship with demographic and clinical variables.

4.2 **Hypothesis**

The null hypothesis for the primary aim was that there is no difference in dental implant outcomes in 60+ years old patients with osteoporosis at the time of implant placement compared to those without osteoporosis at the time of implant placement.
5  **Materials and Methods**

This clinical study evaluated dental implant outcomes in 60 years or older patients with a diagnosis of osteoporosis established by a physician at the time of receiving one or more implants in the graduate prosthodontic clinic at the Faculty of Dentistry, University of Toronto. The study protocol, case report forms (CRFs) and patient information material was approved by the University of Toronto Research Ethics Board (# 24266, appendix 5b) prior to commencing the study.

5.1  **Study Sample**

Inclusion criteria were: individuals who had dental implants placed in the graduate prosthodontics clinic at the Faculty of Dentistry, University of Toronto; were 60+yrs old at the time of implant placement; and had a physician established diagnosis of osteoporosis at the time of implant placement. The patient relations database (The Implant Tracker®, West Hartford, CT) of the discipline of prosthodontics, Faculty of Dentistry, University of Toronto was searched to identify the potential patients that met the inclusion criteria for the study sample. A total of 532 patients were identified. Of these, the clinic patient paper charts of 228 patients were still active. These charts were hand searched and reviewed with regard to details from the medical history questionnaire form at the time of implant placement. Completing the medical form is a part of the standard procedures followed in the clinics of the Faculty of Dentistry, University of Toronto and is completed by all patients when they first present for treatment at the Faculty of Dentistry, and is updated on subsequent visits. Their clinical records and medical history alerts on the faculty of dentistry clinical patient database software (Axium®, Exan Enterprise Inc, Las Vegas, NV) were also reviewed to identify those that had a medically established diagnosis of
osteoporosis at the time of implant placement. The complementing lists of patients that could potentially be included in the study sample consisted of 39 patients. An invitation letter (Appendix 3), describing the study and inviting them for a recall examination with the incentive offer of intraoral examination and assessment and scaling (as required), was sent to these patients. Of the 39 patients who were sent the invitation letter, 24 (4 Male, 20 Female) agreed to participate in the study. Various reasons resulted in the non-participation of 15 potential participants who otherwise fulfilled the inclusion criteria. These included old age and debilitating disease, death, declining to participate due to personal reasons (which were not probed by the investigator) and inability to establish contact.

5.2 Control Sample

For each study sample participant, a matched control patient without a diagnosis of osteoporosis at the time of implant placement was identified using the same database as used for identifying the study sample. The control patient was matched for sex, similarity of implant (location, number and extent of surgical procedure), type of suprastructure on the implants, status of the opposing arch (edentulous, partially dentate or completely dentate) and age in an attempt to generate the two groups comparable. The paper charts as well as Axium® notes were hand searched and reviewed to confirm that the medical history details did not indicate that the control patients had osteoporosis.

The same invitation letter sent to the study sample patients was also sent to the identified control sample patients. Two of the originally selected control patients declined to participate due to their age and general health or that of their immediate family. Therefore two alternative control sample patients were identified and sent invitation letters resulting in the participation of 24 control sample patients.
Both patients with osteoporosis and their matched control patients without osteoporosis were asked to bring to the investigator their most recent bone density measurements (DEXA: Dual energy x-ray absorptiometry) and those recorded closest to the time of dental implant placement from their physicians’ offices. The rationale was that an unknown number of elderly patients could have become diagnosed with osteoporosis after implant placement, and this needed to be accounted for, when the two groups were compared as regards outcomes of implant treatments. When the patients did not bring the DEXA results to the follow-up examination, their DEXA values recorded closest to the time of dental implant placement and the date of follow up were requested from their physicians’ offices, as per the consent given in their medical questionnaire form.

5.3 **Exclusion Criteria**

Exclusion criteria included the presence of severely debilitating disease, psychiatric conditions (such as psychosis, alcoholism, drug abuse, neuroses) and craniofacial anomalies, as recorded in their clinic charts. However, no study sample patient needed to be excluded due to any of these criteria.

5.4 **Examination**

When the study and control sample subjects arrived for the follow up examination after accepting the invitation to participate in the study, each of them signed the consent form and updated/filled a medical questionnaire form. The clinical data for any study and control sample subject were recorded after the patient had signed informed consent. Each subject and implant was assigned a study number. Data were extracted from the their patient clinic chart, the Implant Tracker® and the Axium® notes and entered into baseline CRFs (Appendix 1: Baseline data). At the follow-up examination, no fixed prostheses were removed in order to gather research data.
The implants were examined clinically to record pertinent details as described in the follow-up CRF (Appendix 2: Follow up visit). The implant(s) for each patient were provided scaling as necessary before periapical radiographs were taken. Bone levels and radiolucency around the implants was recorded as detailed in section 5.5.2. All recorded data were transferred to an electronic format created using Microsoft Access® software (Microsoft Corp. Seattle, WA).

In summary, the baseline patient data recorded included:

i) Age, sex and T-score at the lumbar spine, femoral neck and hip.

ii) Past and present history of smoking, alcohol use.

iii) General health status and medical history including details of any systemic disease, diagnosis of cancer, history of current and past medications (not including medications for osteoporosis, which were recorded separately, see iv), use of any chemotherapeutic drugs, corticosteroid therapy.

iv) History of drug therapy for osteoporosis:

   type of drug (ERT, bisphosphonate, calcitonin, supplementary osteoporosis therapy including Vitamin D, Calcium), route of administration, dose and frequency

v) Number and location of implants

vi) Any additional bone augmentation performed

vii) Time of Stage I surgery, Stage II surgery, and implant loading

5.5 **Outcome measures**

Dental implant outcomes is a broad term and several authors have described and classified outcomes as they relate to longevity and survival, physiological, psychosocial and
economic impacts (Guckes et al, 1996, Anderson, 1998) and the patient-specific burden associated with the missing tooth condition (Carr, 1998). For the purposes of this study, the variables described below were defined as outcomes, which were compared in the two groups.

5.5.1 Clinical examination

Applicable clinical criteria proposed by Albrektsson et al (1986) were recorded, which included mobility (yes/no), pain (yes/no), infection around the implant(s) (yes/no) or presence of, neuropathy and paraesthesia (yes/no). In addition, signs of inflammation and bleeding on probing of the peri-implant mucosa were recorded. Any complication noted in the patient paper charts or in the digital patient management system were recorded.

5.5.2 Radiographic examination and bone level measurements

Periapical radiographs located in the clinic charts taken at the time of implant placement (i.e. baseline radiographs that had been taken when the implants were placed or the date closest to the stage-1 surgery) and those taken at the follow-up examination were compared to assess differences in the bone levels from baseline to follow-up examinations. Measurements were made on the mesial and distal sides of the implants and averaged. All radiographs were digitalized and measurements were made using ImageJ public domain software made available by NIH (Fig. 5). The vertical distance in mm from the implant shoulder to the most apical initial point of implant bone interface was measured on the mesial and distal sides of each implant. If the implant shoulder was not clear, then a clear point visible on both baseline and follow up radiographs was used instead. Since radiographic images could have suffered from for foreshortening and elongation, the images were scaled using the ImageJ software according to the known inter-thread distance of the implant, applied to the image at the level of the implant threads closest to the bone levels since this was the region of interest for recording bone levels.
Bone level measurements using the periapical radiographs method described above were undertaken by two examiners. Inter-examiner reliability of this measurement method was tested by using intraclass correlation coefficient (ICC) analysis (Rosner, 2006) and the method error was calculated by using Dahlberg’s formula (Dahlberg, 1940). ICC values $> 0.75$ are considered representative of excellent reliability (Rosner, 2006). Excellent reliability of the method was found (the ICC of the bone loss measurements on the mesial was 0.919 with a very low Dahlberg’s error of 0.04 mm and on the distal was 0.938 with Dahlberg’s error of 0.03 mm).

In addition, where periapical radiographs were not available at baseline (such as when only panoramic radiographs had been done at the time of implant placement), the bone level at the time of implant placement was measured relative to the length of the implant from the panoramic radiographs and compared with that recorded from the periapical radiographs taken at the time of the follow-up examination. These measurements could be done for 23 case-control patient pairs. Radiographic bone level assessments could not be done for one case-control patient pair (1 implant each) because of poor radiograph quality for the patient with osteoporosis.
randomly selected implant from each patient was chosen to evaluate the change in bone height from baseline. There was perfect agreement of the two examiners in the categorization of bone loss as greater or less than 30% of the total implant length.

In addition, any radiolucency around the dental implant seen on the periapical radiograph was noted.

5.6 Analysis of data

Descriptive analysis of the demographic data was conducted at both baseline and follow-up examinations. Independent variables recorded in the study sample and control sample at baseline and follow-up examinations were compared using paired t-tests. Quantitative differences in bone loss around implants in the study sample and the control sample was estimated by selecting one random implant for each osteoporosis/control sample patient pair. From these measurements, paired t-test comparisons were made for bone loss measurements of 16 osteoporosis vs control patient pairs.

With consideration of clinical relevance of extent of bone loss a cut-off level was set at less or greater than 30% of the implant length. From the 23 case-control patient pairs, the distribution of patients and implants dichotomized into 2 groups based on whether the bone loss was greater or less than 30% of the total implant length was analyzed using the Fischer-exact test.

Adverse biological outcomes such as mobility, pain, infection around the implant, neuropathy and paresthesia and radiolucency around implant were rarely seen. The only event that to some extent was observed in a higher number of patients at the follow-up examination was bleeding on probing. From the 24 case-control patient pairs, the distribution of patients and implants, dichotomized into 2 groups based on whether they had bleeding on probing or not, was
analyzed using the Fischer-exact test. All statistical tests were conducted using SPSS software (ver. 17.0), and p values of <0.05 were considered to be statistically significant.
6 Results

6.1 Study sample demographics and characteristics

The study sample included 24 patients (4M, 20F), all of whom were more than 60 years old and had a physician established diagnosis of osteoporosis at the time they received dental implants (Table 2). The mean age of the study sample was 71.62 ± 7.66 yrs at the time of surgery. Their mean DEXA T-scores were -1.99 at the lumbar spine, -2.16 at the femoral neck and -1.73 at the hip. At the time of follow up, the mean age was 75.77 ± 7.79 yrs, while their mean T-scores were were -1.90 at the lumbar spine, -1.91 at the femoral neck and -1.61 at the hip.

6.2 Control sample demographics and characteristics

The control sample included 24 patients (4M, 20F), all of whom were more than 60 years old and did not have osteoporosis at the time of implant placement. They were age and sex matched to the study sample as well as for, similarity of implant treatment (i.e. location, number and extent of surgical procedure), type of suprastructure on the implants, status of their natural dentition, and the condition of the opposing arch (Table 2). At the time of implant surgery their mean age was 65.66 ± 8.90 yrs and their mean T-score values were -1.07 at the lumbar spine, -0.69 at the femoral neck and -0.53 at the hip. At the follow up examination, their age was 73.15 ± 6.70 yrs and their T-scores as available were -0.55 ± 1.66 at the lumbar spine, -0.71 ± 1.35 at the femoral neck and –0.35 ± 1.52 at the hip.
Table 2: Subject and implant characteristics of study and control samples

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Osteoporosis Sample</th>
<th>Control Sample</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic and health characteristics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male:Female</td>
<td>4:20 (total=24)</td>
<td>4:20 (total=24)</td>
</tr>
<tr>
<td>Age at implant placement</td>
<td>71.62±7.66 yrs</td>
<td>65.66±8.90 yrs</td>
</tr>
<tr>
<td>Age at follow-up examination</td>
<td>75.77±7.79 yrs</td>
<td>73.15±6.70 yrs</td>
</tr>
<tr>
<td>T-score (femoral neck) at implant insertion</td>
<td>-2.16</td>
<td>-0.69</td>
</tr>
<tr>
<td>T-score (femoral neck) at follow-up</td>
<td>-1.91</td>
<td>-0.79</td>
</tr>
<tr>
<td><strong>Smoking history</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Implant placement</td>
<td></td>
<td></td>
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<tr>
<td>Active smokers</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Former smokers</td>
<td>4</td>
<td>13</td>
</tr>
<tr>
<td>Never smoked</td>
<td>16</td>
<td>10</td>
</tr>
<tr>
<td>Follow-up examination</td>
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<td></td>
</tr>
<tr>
<td>Active smokers</td>
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<td>0</td>
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<tr>
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</tr>
<tr>
<td>Never smoked</td>
<td>16</td>
<td>10</td>
</tr>
<tr>
<td><strong>Implant related characteristics</strong></td>
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</tr>
<tr>
<td>Number of implants</td>
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<td>66</td>
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<tr>
<td><strong>Implant location</strong></td>
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<tr>
<td>Anterior maxilla</td>
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<tr>
<td>Posterior maxilla</td>
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<td>6</td>
</tr>
<tr>
<td>Anterior mandible</td>
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<td>34</td>
</tr>
<tr>
<td>Posterior mandible</td>
<td>13</td>
<td>12</td>
</tr>
<tr>
<td>Bone quality recorded at implant placement</td>
<td>20 subjects</td>
<td>16 subjects</td>
</tr>
<tr>
<td>Type I</td>
<td>3 (15%)</td>
<td>3 (18.75%)</td>
</tr>
<tr>
<td>Type II</td>
<td>9 (45%)</td>
<td>8 (50%)</td>
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<tr>
<td>Type III</td>
<td>8 (40%)</td>
<td>5 (31.25%)</td>
</tr>
<tr>
<td>Type IV</td>
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<td>0</td>
</tr>
<tr>
<td>Bone grafting done at implant placement</td>
<td>4</td>
<td>3</td>
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<tr>
<td>Healing period before loading</td>
<td>6.39±3.38 mos</td>
<td>10.78±12.87 mos</td>
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<tr>
<td>Duration of suprastructure function till follow-up</td>
<td>44.30±44.66 mos</td>
<td>69.57±86.97 mos</td>
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<td>Follow-up duration (from implant placement)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up &lt;3yrs (no. of subjects)</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>Follow-up 3-5yrs (no. of subjects)</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Follow-up &gt;5rs (no. of subjects)</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td><strong>Status of opposing arch</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Edentulous</td>
<td>10</td>
<td>13</td>
</tr>
<tr>
<td>Partially edentulous</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>Fully dentate</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td><strong>Implant suprastructure</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c is-FDP</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>p is-FDP</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>is-CD</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>single crown</td>
<td>8</td>
<td>8</td>
</tr>
</tbody>
</table>
6.3 **Implants**

6.3.1 **Numbers, locations and dimensions**

A total of 127 implants were placed in study and control sample subjects. The study sample had 61 implants, of which 10 had been placed in the maxillary anterior region, 9 in the maxillary posterior region, 29 in the mandibular anterior region and 13 in the mandibular posterior region (Table 2). The frequency distribution of the dimensions of the implants used is shown below in Fig. 6.

![Fig. 6: Implant dimensions in the osteoporosis sample](image_url)

A total of 66 implants had been placed in the control sample subjects, of which 14 had been placed in the maxillary anterior region, 6 in the maxillary posterior region, 34 in the mandibular anterior region and 12 were placed in the mandibular posterior region. Frequencies of implant dimensions in the control sample are shown in Fig. 7.
6.3.2 Implant suprastructure types, status of opposing arch dentition

In the osteoporosis sample the suprastructure types supported by the implants included complete implant supported fixed dental prosthesis (c is-FDP) \( [n=5] \), partial FDP/splinted crown \( [n=2] \), implant supported overdenture (is-OD) \( [n=8] \), single crown \( [n=8] \) and one patient had not received the definitive prosthesis on the implant yet. In the matched control sample, the suprastructures included c is-FDP \( [n=5] \), partial FDP/splinted crown \( [n=2] \), is-OD \( [n=9] \), single crown \( [n=8] \). The distribution of these suprastructure types in both samples is shown in Fig. 8. As is evident from this figure, the suprastructures types in the two groups were closely matched.

![Fig. 7: Implant dimensions in the control sample](image)
In regard to the status of the dentition in the opposing arch, in the osteoporosis sample, the opposing arch was edentulous in 10 patients, partially dentate in 7 and 7 had a full complement of teeth. In the control group, the opposing arch was edentulous in 13 patients, partially dentate in 4 and 7 had a full complement of teeth (Fig. 9). This figure also shows that the two groups were closely matched for the status of the opposing arch dentition.

Fig. 8: Types of Suprastructures

Fig. 9: Status of opposing arch dentition
6.4 Bone quality and bone grafting at implant placement

The bone quality entered in the clinic notes by the surgeons at the time of implant placement was in the osteoporosis sample 3 Type I, Type II in 9, Type III in 8 and Type IV in none. It had not been entered for 4 subjects. In the control sample, the bone quality was Type I in 3 patients, Type II in 8, Type III in 5 and Type IV in none, and had not been entered in the clinical notes of 8 subjects. There were no marked differences in the bone quality types in the two groups (Fig. 10).

Bone grafting had been done in 4 patients in the osteoporosis sample and in 3 patients in the control sample.

6.5 Smoking status at baseline and at follow-up examination

At the time of implant placement, 8 subjects (33%) in the osteoporosis sample had reported as having a positive history of smoking (4 were active smokers and 4 were former smokers, while 16 stated that they had never smoked) whereas in the control sample, 14 subjects
(58%) had a positive history of smoking (1 was an active smoker and 13 were former smokers, while 10 described that they had never smoked).

At the follow-up examination, 8 subjects (33%) in the osteoporosis sample had reported as having a positive history of smoking (2 were active smokers and 6 were former smokers, while 16 stated that they had never smoked) whereas in the control sample, 14 subjects (58%) reported that they were former smokers, while 10 described that they had never smoked (Fig. 12). When compared to baseline data, two subjects in the osteoporosis sample who had been active smokers at baseline, reported having quit smoking and were classified as former smokers at follow-up whereas in the control sample, one patient who was an active smoker at baseline reported that he had quit smoking and was categorized as a former smoker at follow-up.
At the time of implant placement, none of the subjects in the osteoporosis or control samples had a blood dyscrasia and none were on any kind of corticosteroid therapy (Fig 13). Two patients in the osteoporosis group were diabetic while 1 patient in the control sample had diabetes at the time implants were placed. In the osteoporosis sample, 9 subjects had hypertension while 8 were hypertensive in the control sample. Three subjects in both the
osteoporosis and control samples had cancer. One subject in the control group had a history of using chemotherapeutic drugs. Cardiac disorders were reported by 6 subjects in the osteoporosis sample and 5 subjects in the control sample while gastrointestinal disorders were reported by 5 subjects in the osteoporosis sample and none in the control sample, which was significant. Other comorbidities including arthritis, high cholesterol, asthma, depression, glaucoma, hypothyroidism, history of joint replacements etc were individually present as isolated occurrences with very small frequencies.

At the time of the follow-up examination, none of the subjects in the osteoporosis or control samples had a blood dyscrasia, as also recorded at baseline. Four subjects in the osteoporosis group were diabetic while 1 subject in the control sample had diabetes at the follow-up examination. In the osteoporosis sample, 11 subjects had hypertension while 9 were hypertensive in the control group. Four subjects in the osteoporosis sample and 3 subjects in the control sample had cancer at the follow-up examination. Only 1 subject in the control sample had a history of using chemotherapeutic drugs. One subject in the osteoporosis sample was on corticosteroid therapy at the time of follow-up examination. Cardiac disorders were reported by 7 subjects in the osteoporosis sample and 5 patients in the control sample while gastrointestinal disorders were reported by 7 subjects in the osteoporosis sample and 1 in the control sample. Similar to what was seen at the baseline examination, other comorbidities including arthritis, high cholesterol, asthma, depression, glaucoma, hypothyroidism, history of joint replacements etc were individually present as isolated occurrences with very small frequencies. Frequencies of medical conditions existing in the osteoporosis and control samples at the follow-up examination are shown in Fig.14.
6.7 **Medications for osteoporosis and osteopenia at baseline**

6.7.1 **Bisphosphonates**

6.7.1.1 **Types**

Bisphosphonate usage was isolated from other drugs as being one of the medications asked about in the CRF. This is because of its effects on bone in general (Licata, 2005; Friedman, 2006; McClung, 2003) and also it’s putative relationship with so-called bisphosphonate-related osteonecrosis of the jaw (Marx, 2003; Marx et al 2005, Bamias et al 2005). According to the data in the CRF, 22 subjects in the osteoporosis sample were taking bisphosphonates while 2 were not taking any bisphosphonates at the time of implant placement. Of these 22 subjects, 7 were taking Actonel®, 6 were taking Didrocal®, 1 had taken Didrocal® previously for three years and was then switched to Fosamax® at the time of implant placement, 7 were taking Fosamax® and 1 had been previously taking Fosavance® for 5 years but had been...
taking Actonel® for 4 years, which was the current medication at the time of implant placement. The frequency distribution of bisphosphonate drugs is presented in Fig. 15 below.

![Bisphosphonate Drugs](image.png)

Fig. 15: Bisphosphonate drugs used at baseline in the osteoporosis sample

None of the subjects in the control sample were on bisphosphonate therapy at the time implants were placed.

6.7.1 Route, dosage and frequency

All 22 subjects in the osteoporosis sample who were taking bisphosphonates at the time of implants placement were taking the drug orally, while none were taking any of the bisphosphonates parenterally. The dosage of the bisphosphonate drugs varied from 5mg to 400 mg in once daily or once weekly frequencies.

6.7.2 Other medications and therapies

None of the subjects in the osteoporosis or control samples were on estrogen replacement therapy (ERT) or calcitonin at baseline. Vitamin D was being taken by 20 subjects in the
osteoporosis sample and 4 in the control sample, while calcium supplements were being taken by 18 subjects in the osteoporosis sample and 4 in the control sample.

A summary of the comparison of subjects on medications for osteoporosis and osteopenia in the osteoporosis and control samples at baseline is presented in Table 3.

**Table 3: Medications received at baseline for treating osteoporosis and osteopenia**

<table>
<thead>
<tr>
<th>Medication for osteoporosis and osteopenia</th>
<th>Valid comparisons</th>
<th>Osteoporosis Sample N (%)</th>
<th>Control Sample N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of drugs for osteoporosis</td>
<td>24</td>
<td>22 (92%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Bisphosphonates</td>
<td>24</td>
<td>22 (92%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Oral route</td>
<td>24</td>
<td>22 (92%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Parenteral route</td>
<td>24</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Yrs of medication §</td>
<td>24</td>
<td>3.17 (+ 2.94)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Vit D</td>
<td>24</td>
<td>20 (83%)</td>
<td>4 (17%)</td>
</tr>
<tr>
<td>Calcium</td>
<td>24</td>
<td>18 (75%)</td>
<td>4 (17%)</td>
</tr>
<tr>
<td>ERT</td>
<td>24</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Calcitonin</td>
<td>24</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

§= continuous data

6.8 Medications for osteoporosis and osteopenia at follow-up examination

6.8.1 Bisphosphonates

Of the various medications for osteoporosis and osteopenia that were enquired in the CRF, 22 subjects in the osteoporosis sample were taking oral bisphosphonates while the 2 subjects who were not taking bisphosphonates at baseline were still not taking any bisphosphonates at the time of follow-up. Of these 22 patients, 7 were taking Actonel®, 6 were taking Didrocal®, 1 had taken Didrocal® previously for six years and was on Fosamax® at the time of recall, 7 were taking Fosamax® and 1 had been previously taking Fosavance® for 3 years and had been taking Fosamax® for 3 months, which was their current medication at the
time of follow-up. The frequency distribution of the oral bisphosphonate drugs the patients were taking is presented in Fig. 16 below.

At the follow-up examination 3 of the 24 subjects in the control sample were taking bisphosphonate therapy.

All 22 subjects in the osteoporosis sample who were taking bisphosphonates at the time of follow up were taking the drug orally, none by a parenteral route. The dosage of the bisphosphonate drugs varied from 5 to 400 mg in once daily, once weekly and once monthly schedules.

In the control group there were 3 subjects taking Bisphosphonates at the follow-up examination. All were taking the same drug, Actonel® orally, none by a parenteral route and the dosage was 35 mg once a week.

6.8.2 Other medications and therapies

None of the subjects in the osteoporosis or control samples were taking Estrogen Replacement Therapy (ERT) or Calcitonin at follow-up.
At follow-up, Vitamin D was being taken by 21 subjects in the osteoporosis sample and 8 in the control sample, while Calcium supplements were being taken by 19 subjects in the osteoporosis sample and 8 in the control sample.

A summary of the comparative data on medications for osteoporosis and osteopenia in the osteoporosis and control samples is presented as proportions of subjects using them (except years of medication from baseline to follow-up, which is represented as a continuous measure) in the respective samples in Table 4.

Table 4: Medications received at follow-up for treating osteoporosis and osteopenia

<table>
<thead>
<tr>
<th>Medication for osteoporosis and osteopenia</th>
<th>Valid comparisons</th>
<th>Osteoporosis Sample N (%)</th>
<th>Control Sample N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of drugs for osteoporosis</td>
<td>24</td>
<td>22 (92%)</td>
<td>3 (13%)</td>
</tr>
<tr>
<td>Bisphosphonates</td>
<td>24</td>
<td>22 (92%)</td>
<td>3 (13%)</td>
</tr>
<tr>
<td>Oral route</td>
<td>24</td>
<td>22 (92%)</td>
<td>3 (13%)</td>
</tr>
<tr>
<td>Parenteral route</td>
<td>24</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Yrs of medication§</td>
<td>24</td>
<td>6.79 (± 3.33)</td>
<td>0.08 (± 0.41)</td>
</tr>
<tr>
<td>Vit D</td>
<td>24</td>
<td>21 (88%)</td>
<td>8 (33%)</td>
</tr>
<tr>
<td>Calcium</td>
<td>24</td>
<td>19 (79%)</td>
<td>8 (33%)</td>
</tr>
<tr>
<td>ERT</td>
<td>24</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Calcitonin</td>
<td>24</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

§= continuous data

6.9 Healing periods before loading of implants and duration suprastructure function

On average, the duration of healing in the osteoporosis sample was 6.39 ± 3.38 months in comparison with 10.78 ± 12.87 months in the controls, although this difference was not statistically significant (p=0.130). One patient in the osteoporosis sample and 3 patients in the control sample had immediate loading of their implants. The average duration the suprastructures supported by the implants had been in function at the follow-up appointment was 44.30± 44.66
months in the osteoporosis sample while that in the control sample was 69.57 ± 86.97 months (p=0.101).

6.10 Outcome variables at the follow-up examination

6.10.1 Mobility and implant loss

In the osteoporosis sample, out of the 61 implants placed, mobility was noted in 2 implants that had been placed in the maxilla of 1 patient. Also, 3 maxillary implants had been lost in the same subject. No mobility of any of the implants was noted in the 66 implants that had been placed in the control sample at the follow-up examination and none had been lost. From these data, survival rates of 95.1% and 100% were noted in the osteoporosis and control samples respectively.

6.10.2 Pain, infection around the implant, neuropathy and paraesthesia

None of these adverse features were noted in either the osteoporosis or control samples. No complications or instance of osteonecrosis had been recorded from baseline till follow-up in either of these two groups.

6.10.3 Bleeding on probing

Bleeding on probing was detected in 9 implants of 6 subjects in both, the osteoporosis and control samples at the follow-up examination. The distribution of patients with one or more implant sites exhibiting bleeding on probing at follow-up and results of the Fischer exact test are shown in Table 5, while the distribution of implants exhibiting bleeding on probing at follow-up are shown in Table 6. No significant differences were demonstrated.
Table 5: Bleeding on probing detected in patients at the follow-up examination

<table>
<thead>
<tr>
<th>Bleeding on probing</th>
<th>Osteoporosis sample</th>
<th>Control sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Absent</td>
<td>19</td>
<td>19</td>
</tr>
</tbody>
</table>

Fischer-exact test=0.26

Table 6: Bleeding on probing detected in implants at the follow-up examination

<table>
<thead>
<tr>
<th>Bleeding on probing</th>
<th>Osteoporosis sample</th>
<th>Control sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Absent</td>
<td>52</td>
<td>52</td>
</tr>
</tbody>
</table>

Fischer-exact test=0.20

6.10.4 Radiolucency around implant

No peri-implant radiolucency was noted in the radiographs at base line or follow-up in either of the osteoporosis or control samples.

6.10.5 Alveolar bone loss around the implant

Based on the quantitative measurements recorded from the periapical radiographs using ImageJ, the mean bone loss from implant placement to the follow-up examination was 0.35 ± 0.93 mm in the osteoporosis sample, while that in the control sample was 0.32 ± 0.63mm. These measurements were almost identical and the minimal difference was not statistically significant (paired t-test; p=0.92).

The distribution of subjects with one or more implants having greater than 30% bone loss and the results of the Fischer-exact test are shown in Table 7. The differences were not statistically significant. The distribution of implants having greater than 30% bone loss, showed that 5 implants in the osteoporosis sample had >30% bone loss, compared to none in the control sample (Table 8) and the Fischer-exact test showed that this difference was significant (p=0.03).
However, all these 5 implants belonged to one subject. From these data, implant success rates of 91.4% and 100% were noted in the osteoporosis and control samples respectively.

**Table 7: Distribution of patients with one or more implants having bone loss**

<table>
<thead>
<tr>
<th>Bone loss</th>
<th>Osteoporosis sample</th>
<th>Control sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30%</td>
<td>22</td>
<td>23</td>
</tr>
<tr>
<td>&gt;30%</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Fischer-exact test=0.5

Note: Comparison of one case-control patient pair was not possible due to poor quality of the radiographs

**Table 8: Distribution of implants having bone loss**

<table>
<thead>
<tr>
<th>Bone loss</th>
<th>Osteoporosis sample</th>
<th>Control sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30%</td>
<td>53</td>
<td>58</td>
</tr>
<tr>
<td>&gt;30%</td>
<td>5</td>
<td>0</td>
</tr>
</tbody>
</table>

Fischer-exact test=0.03

Notes: 1) All 5 implants with >30% bone loss are from the same subject
   2) Radiographic measurements of one case-control implant pair was not possible due to poor quality of the radiographs

6.10.6 Relationship of demographic and clinical variables with adverse outcomes

All the significantly different adverse outcomes (bone loss, mobility and implant loss) in the osteoporosis and control samples were seen in a single subject in the osteoporosis sample. This precluded conducting multivariate statistics to ascertain a relationship between the demographic and clinical variables with these adverse outcomes.
7 Discussion

In current times, the average life expectancy in North America is 74.2 years in men and 81.1 years in women, which is significantly greater than just 20 years ago (US Data). An estimated 40.2 million North Americans are above 65 years old today and this number is projected to increase in the coming times. Osteoporosis occurs in a large number of ageing women and men. Although post-menopausal women are affected most frequently (1:4) the disease occurs in a significant number of older men as well (1:8) (Health Canada, Seniors and Aging-Osteoporosis, 2009). Paleopathological studies have shown that osteoporosis occurred in past populations as well, but the prevalence of osteoporotic fractures has increased in modern times (Agarwal and Grynpas, 1996). With an estimated 11.4 million aging individuals in North America being affected by osteoporosis, the reported financial burden of this disease in the US population is more than 18 billion dollars per year (U.S. Department of Health and Human Services, 2004; Tosteson and Hammond, 2002). Thus, the value of clinical research aimed at a disease that occurs so commonly among the aging population can never be overstated.

The study sample of subjects with osteoporosis described in this study consisted of seniors, all above 60 years, predominantly women (83.3%), who had been diagnosed with osteoporosis by their physician before they received dental implants (baseline). On average, they had been receiving treatment for osteoporosis for 3.17 ± 2.94 years before the date they received the dental implant surgery. In addition to the physician established diagnosis of osteoporosis DEXA values that were available indicated that at baseline in almost every subject with osteoporosis, a high T-score value was noted in at least one of the tested joints. The DEXA values of the osteoporosis sample were at least 1 standard deviation worse than those in the control sample at baseline. From baseline to follow-up examination, the DEXA values were
predominantly stable or improved for the osteoporosis sample. This favorable effect could have been partly the result of regular continued treatment with bisphosphonates, (which is clear from their medical record showing that the medications were adjusted by their physicians for type, dose and frequency according to their individual requirements). These explain the stable or reduced T-scores in the subjects who had been taking these medications and show that the disease was under good medical control during the period from baseline to follow-up.

Alveolar bone quality, in regard to implant placement, has been classified on a scale of 1 to 4, and noted as 1 when homogeneous compact bone is present at the entire jaw, 2 when a thick layer of compact bone surrounds a core of dense trabecular bone, 3 when a thin layer of compact bone surrounds a core of dense trabecular bone of favorable strength and 4 when a thin layer of compact bone surrounds a core of low density trabecular bone of unfavorable strength (Lekholm and Zarb, 1985). Type 1 and Type 4 bone qualities have both been shown to be generally associated with higher early dental implant failure rates (Friberg et al, 1991). Differences in success rates related to the jaw (maxillary or mandibular) and position (anterior or posterior) of the implant in the jaws are often the effect of regional bone quality in different regions of the jaws (Turkyilmaz and McGlumphy, 2008). Generally, the mandible is more dense than the maxilla (Morand and Irinakis, 2007; Turkyilmaz and McGlumphy, 2008). In a retrospective case-control study that investigated factors associated with multiple implant failures in edentulous maxillae restored with implant supported fixed or removable prostheses, it was found that the lack of adequate bone quality and quantity at the local implant site was a important factor to consider to prevent cluster phenomenon of implant failure in the maxilla (Ekfeldt et al, 2001). In the present study, at the time of dental implant placement, 15% of the osteoporosis sample and 18.75% of the control sample had a bone quality of 1 and none had a bone quality of
4 in either of the sample. Eighty-five% of the osteoporosis sample and 81.25% of the control sample had a bone quality of 2 or 3, which are generally considered to be relatively more favorable for dental implant placement and longevity (Turkyilmaz and McGlumphy, 2008). No patient of the osteoporosis sample having a bone quality of 4 at the time of implant placement surgery indicates that their alveolar bone quality had not been severely affected by the disease or the disease was controlled with medication. However, it should also be remembered that bone quality assessment is made clinically during the surgical placement, and due to the subjectivity associated with different surgeons’ perceptions, it has been noted that it is difficult to distinguish bone type very reliably (Lemmerman and Lemmerman, 2005), which is why bone quality 3 and 4 are sometimes collapsed together by researchers for analysis (Becker et al, 2000).

The only failures that were noted were all from the maxilla and from one subject, whose bone quality was noted as 3 when the implants were placed. In the present study, due to the paucity in number of implant failures, no association between bone quality and implant failures could be investigated.

Many reports have commented on the effect of age at the time of implant placement on implant survival (Dao et al, 1993; Lemmerman and Lemmerman, 2005; DeLuca et al, 2006; Grant et al, 2008). Some authors have reported that advanced age does not have an impact on implant survival (Dao et al, 1993; Lemmerman and Lemmerman, 2005), while others (e.g., Moy et al, 2005) have found that advanced age doubles the risk of dental implant failure. In the present study, the mean age of patients in the osteoporosis group was 71.62 yrs at implant insertion, compared with 65.66 yrs in the control group. The mean ages of the two groups were similar at follow-up (75.77 yrs in the osteoporosis group and 73.15 yrs in the control group) since this was one of the criteria for selecting the matched controls. The average functional
duration of both suprastructure and implants measured at follow-up were also not significantly different. Other than one subject in the osteoporosis group who had lost 3 implants from the time of placement till the follow-up examination, no other subject in either the osteoporosis group or the control group had suffered implant loss. Thus, in this study, there does not appear to be an adverse effect on implant survival due to advanced age, which corroborates the finding of Dao et al (1993) and Lemmerman and Lemmerman (2005).

Smoking has been described as a risk factor for osteoporosis (Tenenbaum et al, 2002) as well as for dental implant failures (Habsha and Zarb, 2002). The harmful effects of nicotine include direct cutaneous vasoconstriction, increased levels of fibrinogen, increased blood viscosity and increased carboxyhemoglobin in blood, compromised polymorphonuclear leucocyte function as well as increased platelet adhesion (Habsha and Zarb, 2002). Other deleterious effects of nicotine include effects on cellular protein synthesis, impaired gingival fibroblast adherence, impaired maintenance, integrity and remodelling of oral connective tissues, and interference with wound healing (Habsha and Zarb, 2002).

Smoking has an effect on bone density as well, causing a decrease in bone density and an impairment of osteoblast function. Aryl hydrocarbons, which are one of the by products of cigarette smoking inhibit bone formation. Due to the long half life of aryl hydrocarbons in fat and other body tissues, the exposure to these compounds persist even if the person has stopped smoking (Tenenbaum et al, 2002). In this study, 58% of the patients in the control group had a positive history of smoking (including both active smokers and former smokers) in comparison with 33% in the osteoporosis group. The number of patients who were active smokers at the time of implant placement was 4 in the osteoporosis sample and 1 in the control sample, which decreased to 2 and none respectively at the time of follow-up examination.
Of the various factors related to osteoporosis, the osteoporosis sample was, as expected, using medications (bisphosphonate drugs, Vitamin D and calcium supplements) to inhibit bone resorption and preserve bone. The use of Vitamin D and calcium supplements was seen rarely in the control sample at baseline (and none were on bisphosphonates) and much less frequently at follow-up examination. In the present report, details of the various medications for treating osteoporosis, their dosage, frequency and duration of use have been documented. Their known mechanisms of action have been discussed in the review of the literature. In most other studies on osteoporosis and dental implant outcomes, the drug details have either not been described (Becker et al, 2000; Friberg et al, 2001; von Wowern and Gotfredsen, 2001) or patients who were on glucocorticoids and bisphosphonates were excluded from the study (Amorim et al, 2007).

Of the 61 dental implants placed in the osteoporosis sample 3 had already failed (all in one patient) at the time of the follow-up examination leading to a survival rate of 95.1%, while all the 66 implants in the matched control sample without osteoporosis had survived till follow-up examination, leading to a survival rate of 100%. Of the 58 standing implants in the osteoporosis sample, 2 were mobile (both in the same patient who had lost the 3 implants) compared with none in the control sample, and both these mobile implants had more than 3mm of bone loss. None of the other adverse outcomes (pain, neuropathy, paraesthesia, infection around implant, radiolucency around implant) according to the criteria of Albrektsson and Zarb (1986) were seen in any patient from either of the samples. No instance of osteonecrosis was noted in any of the patients (osteoporosis or control sample) following implant placement although 22 of the 24 patients in the osteoporosis sample were taking oral bisphosphonates at the time of implant placement. Based on the bone loss suffered from baseline to follow-up
examination, an overall success rate of 91.4% was seen in the osteoporosis sample compared with 100% in the control sample. The survival rate that was noted in the osteoporosis sample compares favourably with survival rates generally reported in the implant literature from around the world. (Adell et al, 1990; Buser et al, 1997; Grunder et al, 1999; Lekholm et al, 1999; Brocard et al, 2000; Ferrigno et al, 2002; Romeo et al, 2002; Moy et al, 2005; DeLuca et al, 2006; Levin et al, 2006; Schwartz-Arad et al, 2008).

However, it must be emphasized that all the failures (including implants that had been lost or were mobile), were seen to have occurred in the maxilla of one subject, who was a partially edentulous Asian woman who received her implants at the age of 61 yrs, had bone quality of 3 at the time of implant placement and had baseline T-scores of -2.0 at the lumbar spine, and -0.8 at the femoral neck. No bone grafting had been done for her at the time of placement of 6 maxillary implants. At the follow-up examination, she was 65.8 yrs old, and had T-scores of -1.5 at the lumbar spine and -0.6 at the femoral neck. She had never smoked and was not diabetic at either baseline or follow-up examinations, and also did not have any cardiac, gastrointestinal disorder or systemic disease other than osteoporosis, and was under regular follow-up by her physician for her general health. She was taking Fosamax®, 70 mg once a week for 3 months at baseline and Actonel®, 35mg once a week at follow-up, which she had changed over to 1 year ago after having taken Fosamax® for 4 years. A careful examination of her baseline radiographs (Fig. 22) revealed that the bone height around the implants even at placement was quite low. She had lost 3 implants 2 yrs, 4.3 yrs and 4.6 yrs after placement respectively and 2 were mobile at the time of follow-up examination. They were subsequently removed 2 weeks later. From the foregoing, it is apparent that systemic osteoporosis probably did not influence these failures as much as did the local individual and surgical procedural
factors in terms of bone quality and quantity specific to this patient at the time of implant placement (as seen in the baseline periapical radiographs, Fig.17; clinical examination, Fig.18).

Fig. 17: Baseline (top) and follow-up (bottom) radiographs of the only patient in the osteoporosis sample that showed failures. The implant at site 15 was successful while those at sites 21 and 25 were mobile.

Fig. 18: Remaining implants of the only patient in the osteoporosis sample that showed failures as seen on clinical examination at the time of follow up examination 4.9 yrs after placement.

implant pairs representing the 16 osteoporosis-control patient pairs for whom radiographic bone level measurements were done on periapical radiographs were $0.35 \pm 0.93$mm in the osteoporosis sample and $0.32 \pm 0.63$mm in the control sample. This difference was not statistically significant. These quantitative measurements of bone loss noted in the osteoporosis
sample are comparable with those reported by von Wowern and Gotfredsen (2001) who noted bone loss of $0.47 \pm 0.22$mm (SEM) in their sample with osteoporosis at the 5 yr follow up.

Fig 19: Baseline (left) and follow-up (right) radiographs of an implant from a patient in the osteoporosis sample with favourably maintained bone levels.

Bleeding from the gingival sulcus when it is probed gently is one of the earliest symptoms of gingival inflammation (Carranza and Rapley, 2003). In the context of dental implants, bleeding on probing measures peri-implant marginal gingival tissue reaction and its state of health (Lekholm and Zarb, 1986). Peri-implant mucositis describes the presence of inflammation in the mucosa at an implant site with no signs of loss of supporting bone, while peri-implantitis is characterized by loss of supporting bone in addition to inflammation in the mucosa (Lindhe and Meyle 2008; Zitzmann and Berglundh, 2008). It has been observed that no bleeding on probing was seen in healthy implant locations while bleeding on probing was seen in 67% implant locations that had peri implant mucositis and 91% locations that had peri implantitis (Lang et al, 1994).

In this study, peri-implant bleeding on probing was seen around 9 implants in 6 subjects in each of the samples. Four of the 8 male subjects (50%) amongst all the male patients in the
osteoporosis and control samples had bleeding on probing at the follow-up examination in comparison with 8 of the 40 female patients (20%), thus showing a greater prevalence of BOP in male patients.

Corticosteroid treatment was being received by only one osteoporosis sample patient and only at follow-up, while chemotherapeutic drugs were being taken by one control sample patient at baseline and follow-up. Such minimum frequencies of these independent variables prevented analyzing any significant association they may have potentially had with outcomes.
Strengths and limitations of this study

The strengths of this study are:

1) A matched cohort design with matching for sex, similarity of implant (location, number and extent of surgical procedure), type of superstructure on the implants, dentition status of the opposing arch, age at follow-up examination as far as possible. To the best of my knowledge, no other investigation with focus on osteoporosis and dental implant outcomes have had such close matching done (see Table I).

2) A well administered, controlled university implant program with a detailed clinical database made selecting patients with closely matched variables possible. All clinical procedures had been undertaken in a controlled university graduate program setting where clinical protocols are enforced rigorously.

3) In addition to baseline T-scores, the T-scores of the osteoporosis and control samples at follow-up examination were also obtained which made it possible to follow the bone mineral density status of the axial skeleton in the participants from baseline to follow-up.

4) Details of the type, dosage and frequency of osteoporosis medications and those of supplementary therapies were recorded at baseline and follow-up examination.

The limitations of this study are:

1) This study was limited to dental implant outcomes of patients with osteoporosis and their matched controls treated in one institution.

2) The number of patients with osteoporosis that could have been recruited was 39, of which 24 agreed to participate. Thus, the final osteoporosis sample was relatively modest in comparison with some studies (see Table I). The modest sample size could also be attributed to false negatives in the population.
3) Adverse outcomes were very few to allow identification of predictors of implant failure, bone loss or mobility. For example, there were no recorded instances of paresthesia, pain or peri-implant infection at the follow-up examination for any of the implants in the osteoporosis or control samples.

4) The baseline periapical radiographs of many patients in the control sample and some in the osteoporosis sample were either not available or were of insufficient quality to allow measurements. Radiographs at follow-up examination of some of the patients in both samples were affected by severe foreshortening due to the difficult access in presence of their fixed prostheses, which precluded making measurements and led to sample attrition for the radiographic measurement of bone level component. Thus, paired t-test comparisons of bone level measurements could be made for only 16 of the 24 osteoporosis sample-control patient pairs.

5) Nearly all patients in both the osteoporosis and control samples for whom DEXA values were available showed an improvement in their scores during this follow-up period. Thus, the findings of this investigation are based on patients with osteoporosis which was under good medical control and cannot be used to predict outcomes of patients with osteoporosis where the disease activity is not under control.

6) The institution where this study was conducted serves a multiethnic and multicultural population, and racial or ethnic factors were not isolated or included in the data, which should be kept in mind when applying the results of this investigation, since it is known that the severity of the disease is different in different ethnic populations.
9 **Recommendations for future studies and clinical practice**

Keeping the strengths and limitations of the current study in perspective, it can be recommended that future studies should:

1) Be planned as prospective investigations.

2) Use standardized protocols regarding acquisition of periapical radiographs using a positioning jig.

3) Use similar study designs with close matching, a larger number of patients and longer follow-up periods.

4) Be coordinated in multiple international centres with mutually agreed clinical protocols so that a larger data pool of patients, with different ethnicities can contribute to answering this question more comprehensively.

Based on the findings from this investigation, it can be recommended that clinicians can place dental implants in their patients who have osteoporosis when the medical control of the disease is adequate, with the expectation that the outcomes are not likely to be different from those who do not have the disease. The existence of a medically established diagnosis of osteoporosis, or the medications currently used to treat it, does not lead to significantly different outcomes from those seen in individuals who do not have the condition. However, the sample was modest, and this should be considered when applying the results of this study to clinical practice.
10 Summary and conclusions

10.1 Summary

This study aimed at investigating whether dental implant outcomes in patients having osteoporosis at the time of implant placement were different from those in a matched control group. It also aimed to identify any adverse dental implant outcomes in patients having osteoporosis and explore their possible relationship with demographic and clinical variables. A retrospective matched cohort study was conducted and the null hypothesis framed for the primary aim was that there is no difference in dental implant outcomes in patients having osteoporosis at the time of implant placement compared to those not having osteoporosis at the time of implant placement. After obtaining ethical approval from the University of Toronto Research Ethics Board, using the clinical database of patients treated with dental implants in the graduate prosthodontic clinic at the Faculty of Dentistry, University of Toronto, 39 patients were identified who were at least 60 years of age at the time of implant placement and had been diagnosed by a physician with having osteoporosis. Upon invitation, 24 accepted to participate in this study. For each osteoporosis patient, a control patient matched for sex, similarity of implant (location, number and extent of surgical procedure), type of suprastructure on the implants, dentitional status of the opposing arch, age at follow-up examination was selected, so that both groups were as comparable as possible. Case Report Forms completed at baseline (time of implant placement, from existing records) and at follow-up (at the time of examination) recorded various demographic, health and treatment history, and clinical variables. Adverse dental implant outcomes (mobility, pain, infection around the implant, neuropathy and paraesthesia, inflammation/bleeding on probing of the periimplant mucosa) and any complications were noted from the clinical examination. Periapical radiographs acquired at baseline and at follow-up were
used to measure bone-level differences between these times in both samples, and to note any peri-implant radiolucency.

Paired t-tests were used to test for significant differences in various demographic and clinical variables between the two samples at baseline and follow-up and the outcome variables at follow-up. Three implants had been lost and two were mobile at the time of follow-up examination in the osteoporosis sample (all in one patient), and none in the control sample. Overall survival rates of 95.1% and 100%, and success rates of 91.4% and 100% were noted in the osteoporosis and control samples respectively. The number of implants that had greater than 30% bone loss at the time of follow-up were significantly higher in the osteoporosis sample, but all these were from one subject. Average bone loss measurements from baseline to follow-up were small and not significantly different between the samples. Furthermore, all the implant failures (losses and mobile implants) occurred in the maxilla of a single osteoporosis subject who had no other systemic condition than osteoporosis, nor a history of smoking. Other outcome variables were not significantly different and no complications were noted.

10.2 Conclusions

The null hypothesis: “there is no difference in dental implant outcomes in patients having osteoporosis at the time of implant placement compared to those not having osteoporosis at the time of implant placement” was accepted. Significant differences in the outcome variables between the two samples were not demonstrated from the analysis of the data. All the implant failures in the osteoporosis sample occurred in the maxilla of a single subject, raising suspicion that these were related to individual problems specific to this subject. Due to the paucity of adverse outcomes and with all the implant failures having occurred in one subject, no relationship of adverse outcomes with clinical and demographic variables could be analyzed.
11 Bibliography


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12  Appendices

12.1  Appendix 1: Case Report Form: Baseline Variables

Study participant number:

Age:

Sex:  M  F

Smoking status:  Active  Former smoker  Never smoked

Systemic disease:

- Osteoporosis
- Diabetes
- Hypertension
- Cancer
- Blood dyscrasias
- Cardiac disorders
- GI disorders
- Others

Use of chemotherapeutic drugs at time of implant placement:

- Using  Not using

Corticosteroid therapy at time of implant placement:

- Using  Not using
Use of drugs for osteoporosis at time of implant placement:

- Not using
- ERT
- Bisphosphonate
- Calcitonin
- Supplementary treatment- Vitamin D
- Supplementary treatment- Calcium

Route of administration of drug:

- Intravenous
- Oral

Dosage of drug therapy at implant placement

Frequency of drug therapy at time of implant placement

Duration of drug therapy at time of implant placement

Bone quality at Stage I surgery:

- Bone Quality 1
- Bone Quality 2
- Bone Quality 3
- Bone Quality 4

Implant location (FDI notation):
Edentulism type in opposing arch:

- Totally edentulous maxillary
- Totally edentulous mandibular
- Partially edentulous maxillary
- Partially edentulous mandible

Additional bone augmentative procedure at time of implant placement:

- No augmentation
- Bone augmentation done

Length and diameter of implants:

Bone levels at implant placement:

- Mesial
- Distal
12.2  **Appendix 2: Case Report Form: Follow-up Examination**

Study participant number:

Smoking status:  Active  Former smoker  Never smoked

Systemic disease:

- Osteoporosis
- Diabetes
- Hypertension
- Cancer
- Blood dyscrasias
- Cardiac disorders
- GI disorders
- Others

Use of chemotherapeutic drugs at follow up:

- Using
- Not using

Corticosteroid therapy at follow up:

- Using
- Not using

Use of drugs for osteoporosis at follow up:
Not using ERT

Bisphosphonate

Calcitonin

Supplementary treatment - Vitamin D

Supplementary treatment - Calcium

Route of administration of drug:

Intravenous Oral

Dosage of drug therapy at follow up:

Frequency of drug therapy at follow up:

Duration of drug therapy at follow up:

Implant location (FDI notation):

Edentulism type in opposing arch:

Totally edentulous maxillary

Totally edentulous mandibular

Partially edentulous maxillary

Partially edentulous mandible

Time of Stage II surgery from implant placement:

Time of implant loading from implant placement:
Inflammation/bleeding on probing of peri-implant mucosa:

| Present | Absent |

Mobility of implant

Pain around implant

Infection around implant

Neuropathy

Paresthesia

Type of prosthesis:

- Complete IS-FDP
- Partial IS-FDP
- IS-OD

Bone levels:

| Mesial | Distal |

Periapical radiolucency around implant on periapical radiograph
Dear

You are invited to participate in a clinical research study being conducted at the Faculty of Dentistry, University of Toronto. The study aim is to investigate whether the success of dental implant treatment in patients with a known history of osteoporosis is different from those without osteoporosis.

This letter has been sent to our past patients within two groups. One group of patients had osteoporosis at the time of implant placement. The second group are past patients whose age, gender and treatment received closely match that received by one of our patients with osteoporosis. Thus, this study is therefore termed a case-control study.
If you agree to participate in this study, this will provide you an opportunity to have your implants and mouth assessed for free. A free cleaning of the implants if needed will be provided. We wish to examine the condition of your implants and oral status and may document this with clinical photographs of the implants and radiographs as required.

We would also like to request you to get your most recent bone scan values from your physician which will help us to establish your diagnosis.

Your participating in this study will provide information that will be useful for treating future patients with osteoporosis. You will always retain the right to withdraw your consent to participate in the study at any time and if you choose to do so your decision in any way whatsoever will not impact your ongoing or future treatment at the Faculty of Dentistry.

If you agree to participate in this study, please contact me at the telephone number or e mail provided below or the patient manager of the Implant Prosthodontic Unit (IPU) at the Faculty of Dentistry, Ms Heather Hyslop.

If I do not hear from you in four weeks, I will send this letter again as a reminder.

Thank you in advance for your participation in the study.
The study is being conducted by Dr Sagun Suri as a part of her Masters project at the Faculty of Dentistry, University of Toronto under the supervision of Dr A Jokstad, Professor and Head of Discipline of Prosthodontics.

Feel free to contact me for any questions or concerns by telephone at 416-979-4900 ext 3917 or via e-mail: sagun.suri@dentistry.utoronto.ca or the patient manager of the Implant Prosthodontic Unit, Ms Heather Hyslop by telephone at 416-979-4900 ext 4423 or my supervisor, Dr Jokstad by telephone at 416 979 4900 ext 4427 at the Discipline of Prosthodontics, Faculty of Dentistry, University of Toronto, 124 Edward Street, Toronto M5G 1G6.
12.4 Appendix 4: Consent Form

FACULTY OF DENTISTRY, UNIVERSITY OF TORONTO
124 Edward Street, Toronto, Ontario M5G 1G6
CANADA

CONSENT FORM

Title of the Project:
Dental implant outcomes in patients with osteoporosis:
A retrospective case-control study

Investigator:
Dr Sagun Suri
Discipline of Prosthodontics, Faculty of Dentistry, University of Toronto.

Supervisor:
Dr Asbjorn Jokstad, Professor and Head
Discipline of Prosthodontics, Faculty of Dentistry, University of Toronto.

Introduction
You are asked to participate in the study titled above. The study will be conducted by Dr Sagun Suri as a part of her Masters’ project at the Faculty of Dentistry, University of Toronto under the supervision of Dr Asbjorn Jokstad, Professor and Head, Discipline of Prosthodontics, Faculty of Dentistry, University of Toronto. The following information has been provided to you in order to make an informed decision to participate in the study.
Purpose of the Study

The purpose of the study is to investigate whether the success of dental implant treatment in patients with a known history of osteoporosis is different from those without osteoporosis.

We wish to examine the condition of your implants and oral status and will take radiographs to determine the bone levels around the implants.

Your participating in this study will provide information that will be useful for treating future patients with osteoporosis. You will always retain the right to withdraw your consent to participate in the study at any time and if you choose to do so your decision in any way whatsoever will not impact your ongoing or future treatment at the Faculty of Dentistry.

Confidentiality

All the information that will be collect from you or from your treatment record will be kept strictly confidential. No information about you will be released to anyone without your written permission, unless required by law. You will be assigned a study subject number and all electronic data records will be maintained by subject number and not by name to preserve your confidentiality. Forms used in the study will be stored in a locked cabinet at the Faculty of Dentistry, University of Toronto. Only the investigators and the statistician will have access to the forms and electronic data. Records of the study will be retained in a secure area for a minimum of five (5) years following the completion of the study, and will be destroyed thereafter.

Results of this study may be presented at scientific conferences, and/or published in scientific journals, without including any names or specific individual information.

Risks

There are no known risks from participating in this study.

Benefits and compensation

If you agree to participate in this study, this will provide you an opportunity to have your implants and mouth assessed for free. A free cleaning of the implants if needed will be provided.
Right to withdraw from the Study

Your participation in this study is voluntary. If you do not want to participate in the study, or if you decide you want to stop before the end of the study, you are free to do so. The decision you make will have no effect on your current or future care at the Faculty of Dentistry, University of Toronto.

Questions about the Study

If you have any questions about this study, please contact Dr Sagun Suri, Discipline of Prosthodontics by telephone at: 416-979-4900 ext. 3917, or via e-mail: sagun.suri@dentistry.utoronto.ca; or her supervisor, Dr Asbjorn Jokstad, by telephone: 416-979-4900 ext.4423 or via e-mail: asbjorn.jokstad@dentistry.utoronto.ca.

If you have questions about your rights as a research participant, please contact the Office of Research Ethics by telephone 416-946-3273 or via e-mail: ethics.review@utoronto.ca.

I have read, or have been explained to me, the information about this study. I have had the opportunity to ask questions and have had them answered to me. I know that I can refuse to join the study, or quit the study at any time, without affecting the way I am treated at the Faculty of Dentistry, University of Toronto.

I have signed my name below that I have agreed to participate in the above study and agreed to disseminate information about the above mentioned factors from my treatment record with the understanding that my confidentiality will be maintained and my identity will not be disclosed. I have received a copy of this consent form.

____________________      ______  ______________           ____________________
Your Name                  Signature                      Date
12.5 Appendix 5a: Approval of Scientific Merit: School of Graduate Studies, University of Toronto

Faculty of Dentistry
University of Toronto

David Locker
B.D.S.; Ph.D.
Associate Dean of Graduate/Postgraduate Studies

02 July 2009

Jenny Peto
Ethics Review Coordinator
Health Sciences Research Ethics Boards Ethics Review Unit
University of Toronto
Simcoe Hall, Room 10A
27 King’s College Circle
Toronto ON M5S 1A1

Dear Ms. Peto:

This is to inform you that the following study being undertaken by a graduate student has been approved for scientific merit:

- Student Investigator: Dr. Sagar Suri
- Supervisor: Dr. A. Jokstad
- Title: “Dental Implant outcomes in patients with osteoporosis: A retrospective case control study”

Sincerely,

David Locker
Associate Dean Graduate/Postgraduate Studies

124 Edward Street Toronto Ontario M5G 1Q6 (416) 979-4508 Ext. 4490 FAX (416) 979-4644
12.5 Appendix 5b: University of Toronto Research Ethics Board Approval

University of Toronto
Office of the Vice-President, Research
Office of Research Ethics

PROTOCOL REFERENCE #24266

July 20, 2009

Dr. Aseem Jeste
Dentistry-Discipline of Prosthodontics
Faculty of Dentistry
124 Edward Street
Toronto, ON M5G 1L6

Dr. Sagun Suri
Dentistry-Discipline of Prosthodontics
Faculty of Dentistry
124 Edward Street
Toronto, ON M5G 1L6

Dear Dr. Jeste and Dr. Suri:

Re: Your research protocol entitled “Dental Implant Outcomes in Patients with Osteoporosis: A Retrospective Case Control Study”

ETHICS APPROVAL

Original Approval Date: July 20, 2009
Expiry Date: July 19, 2010
Continuing Review Level: 1

We are writing to advise you that a member of the Health Sciences Research Ethics Board has granted approval to the above-named research study, for a period of one year, under the RBB expedited review process. Ongoing projects must be reviewed prior to the expiry date.

The following consent documents (received July 8, 2009) have been approved for use in this study:
Invitation letter to patient for participation
Consent form

Any changes to the approved protocol or consent materials must be reviewed and approved through the amendment process prior to its implementation. Any adverse or unanticipated events should be reported to the Office of Research Ethics as soon as possible.

Please ensure that you submit an Annual Renewal Form or a Study Completion Report at least 30 days prior to the expiry date of your study.

If your research has funding attached, please contact the relevant Research Funding Officer in Research Services to ensure that your funds are released.

Best wishes for the successful completion of your project.

Yours sincerely,

Daniel Gyawu
Research Ethics Coordinator

McMaster Building, 12 Queen's Park Cres, W, 3rd Floor Toronto, ON M5S 1C5
TEL 416-948-5552 FAX 416-948-5763 EMAIL ethics.review@utoronto.ca
12.5 Appendix 5c: University of Toronto Research Ethics Board Approval Renewal

PROTOCOL REFERENCE #24266

Dr. Askjens Joksstad
Dentistry, Discipline of Prosthodontics
Faculty of Dentistry
124 Edward Street
Toronto, ON M5G 1G6

Dr. Segun Suri
Dentistry, Discipline of Prosthodontics
Faculty of Dentistry
124 Edward Street
Toronto, ON M5G 1G6

June 23, 2010

Dear Dr. Joksstad and Dr. Suri:

Re: Your research protocol entitled, "Dental Implant Outcomes in Patients with Osteoporosis: A Retrospective Case Control Study" by Dr. A. Joksstad (supervisor), Dr. S. Suri (Master’s student)

ETHICS APPROVAL

Original Approval Date: July 26, 2009
Expiry Date: July 19, 2011
Continuing Review Level: 1
Renewal: 1 of 4

We are writing to advise you that you have been granted annual renewal of ethics approval to the above-referenced research study through the REB’s delegated process. Please note that all protocols involving ongoing data collection or interaction with human participants are subject to re-evaluation after 5 years. Ongoing projects must be renewed prior to the expiry date.

Please ensure that you submit an Annual Renewal Form or a Study Completion Report 15 to 30 days prior to the expiry date of your study. Note that annual renewals for studies cannot be accepted more than 30 days prior to the date of expiry, as per federal and international policies.

Any changes to the approved protocol or consent materials must be reviewed and approved through the amendment process prior to its implementation. Any adverse or unanticipated events should be reported to the Office of Research Ethics as soon as possible. If your research has funding attached, please contact the relevant Research Funding Officer in Research Services to ensure that your funds are released.

Best wishes for the successful completion of your project.

Yours sincerely,

Marianne Richardson

Marianne Richardson
Research Ethics Coordinator
Appendix 6: Tricouncil Policy Statement Certificate of Completion

Certificate of Completion

This is to certify that

Dr Sagun Suri

has completed the Interagency Advisory Panel on Research Ethics' Introductory Tutorial for the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS)

Issued On: June-26-2009