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Survival and success rate of dental implants placed in autologous compressed particulate corticocancellous bone graft post-tumour ablative surgery in the mandible

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Survival and success rate of dental implants placed in autologous compressed particulate corticocancellous bone graft post-tumour ablative surgery in the mandible

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TABLE OF CONTENTS

Declaration……IV

Dedication……V

Abstract……VI

Acknowledgments……..VIII

List of figures……..IX

List of tables…….....X

List of abbreviations…….. XI

Chapter 1

1.1 Introduction and Background……1

1.2 Mandible Pathology and Treatment Modality……2

1.3 Bone Graft Healing……6

1.4 Dental Implant Success and Survival Evaluation Criterion……9

1.5 Rational for study……10

1.6 Aim of the study……10

1.7 Objective of the study……..11

Chapter 2 Research Methodology

2.1 Materials and methods……12

2.2 Study design……18

2.3 Study group……..18

2.4 Inclusion criteria……18

2.5 Exclusion criteria……..21

2.6 Data collection……21

2.7 Statistical analysis……21

2.8 Ethical considerations……22

Chapter 3 Results

3.1 Biographical and Clinical characteristics……..23

3.2 Implant site, Size, and Distribution……25

3.3 Implant Success and Survival……27

3.4 Peri-Implant Tissues Assessment……..29

3.5 Bone Loss Around Implants……29

3.6 Complications……30

Chapter 4

4.1 Discussion……32

Chapter 5

5.1 Conclusions……..40

References……42

Appendix A

Data collection Sheet……52

Appendix B

Human Research Ethics Committee Clearance Certificate letter……..54

Appendix C

Patient Consent and Information sheet……..56

Appendix D

Patient Identifier Form……...57

Declaration

I Abdulaziz Abdullah Alharbi declare that this research report is my own, unaided work. It is being submitted to the University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master in Dentistry. It has not been submitted before for any degree or examination at any other institution.

_____

(Signature of candidate & date)

Dedication

I dedicate this work to my beloved and supportive wife (Safiah) and to our awesome motivative kids (Omar & Assel)

Abstract

Background

Oro-dental rehabilitation is one of the most important concerns after ablative surgery of maxillofacial pathology. Discussion around dental implant use in vascularised bone graft (VBG) and nonvascularized bone graft (NVBG) has been evaluated thoroughly in the literature. Outcome of dental implants in NVBG has largely focussed on non-vascularised block graft, with paucity of studies that have evaluated success and survival of dental implants in particle bone and cancellous marrow (PBCM) type of bone graft.

Aim

The aim of this study was to evaluate the success and survival rate of the dental implants placed in autologous PBCM grafts.

Materials and Methods

All patients who had been reconstructed with nonvascularized PBCM graft after benign tumour ablative surgery and had dental implants inserted in the bone graft after healing were included in the study. Minimum requirement was 1 year of implants loaded with dental prosthesis continuously. Albrektsson's success criteria and International Congress of Oral Implantologists recommendation were used to evaluate the success and survival rate of the dental implants. Assessment of bone level, peri-implant tissue, implant mobility, and pain were done as part of implant evaluation criteria.

Results

A total of 16 patients were included in the study (10 females and 6 males, mean age of 31.3 years). The mean mandibular continuity defect reconstructed with reconstructed with PBCM graft was 11.3 cm. Sixty-seven (67) dental implants were implanted in the grafted bone. Of the 67 implants, 5 failed (four of them failed before loading with dental prosthesis). One of the remaining 63 implants dental implant failed after loading of prosthesis. Accumulative success and survival rate of dental implant in particulate bone graft are 80.6% and 98.6% respectively.

Conclusion

Reconstruction of mandibular continuity defects with PBCM graft offer a viable alternative to vascularized bone graft. With this technique mandibular shape, width, height, and continuity were restored. The implant success and survival rate in this study are comparable to those implanted in fibula or native bone. It is recommended that future studies be designed to compare and evaluate the performance of dental implants in vascularized and nonvascularized PBCM bone graft.

Acknowledgments

To the Head of School, Prof S. Nemutandani, thank you for giving me the opportunity to conduct my study.

To the Head of Department of Maxillo-Facial and Oral Surgery, and my Supervisor Prof. Rikhotso, thank you for your guidance, valuable advices and for precious time.

To my colleagues in Prosthodontic Dept, especially Prof. Howes, and all his registrars. Thank you very much and I wish you the best in your future career.

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List of figures

Figure 2.1: Reconstruction plate with spacer.

Figure 2.2: Autologous PBCM packed into the recipient bed following removal of spacer

Figure 2.3: Panoramic radiographic showing regenerated bone 3 months post-grafting.

Figure 2.4: Implants placement planning using CBCT.

Figure 2.5: Clinical picture showing implants placement in grafted bone.

Figure 2.6: Post implants placement panoramic radiograph.

Figure 2.7: Post implant loading x-ray.

Figure 2.8: Post implant loading, the patient in occlusion.

Figure 3.1: Implant positions distribution.

Figure 3.2: Soft tissue recurrence of ameloblastic carcinoma.

Figure 3.3: Successful implant in grafted bone despite soft tissue recurrence.

List of tables

Table 2.1: Peri-implant tissues evaluation scoring system.

Table 2.2: Success, Survival, and Failure criteria by ICOI 2008.

Table 3.1: Demographic data of participant, implants number, defect size, and reconstructive time frame.

Table 3.2: Implant site, diameter, and Length.

Table 3.3: Measurements of implant success criterion.

Table 3.4: Bone loss evaluation throughout post loading time

List of abbreviations

VBG = vascularized bone grafts

NVBG = non-vascularised autogenous bone grafts

FFF = free fibula flap

PBCM = particulate bone and cancellous marrow

BMP = Bone morphogenic protein

TGFβ = transforming growth factor beta

ICOI =International Congress of Oral Implantologists

CBCT = cone beam computed tomography

SD = standard deviation

Chapter 1

1.1 Introduction and background

As part of his study on bone healing and regeneration, Brånemark placed titanium metal cylinders into the bone marrow of the legs of rabbits. Nine months later after he completed his study, he noticed that bone had grown around and was effectively adhering to the titanium metal cylinders. This serendipitous discovery heralded the discovery of titanium screw-form implants which were subsequently used to support teeth following tooth loss experimentally in dogs. A two-stage surgical technique for placement of dental implant was used. In 1965, permission was obtained from Swedish authorities to use titanium screw dental implants to support full mandibular dental prosthesis for the first human subject by utilizing Brånemark's two-stage protocol. Brånemark et al., (1977) published a report which revealed a 90% success rate of dental implants placed in the anterior mandible using a two-stage protocol. Since then numerous studies have been conducted to evaluate the predictability of this procedure. Adell et al., (1981) published a 15 years' study that showed the use of 2768 fixtures in 410 jaws of which 191 were in the upper and 219 were in the lower edentulous jaws in 371 patients. The success rate was 89% in the maxilla and 100% in the mandible. The mean marginal bone loss was 1.5 mm in the first year and 0.1 mm annually thereafter.

1.2 Mandible Pathology and Treatment Modality

Resection of mandibular tumours causes significant facial deformities and loss of function such as mastication, speech, swallowing, and associated psychological problems. The reconstruction of resultant defects utilizing free vascularized bone grafts (VBG) or non-vascularised autogenous bone grafts (NVBG) has become a valuable solution for rehabilitation of these patients. It provides restoration of facial contour and bony support for the dental implants.

Vascularised bone grafts retain nutrient vessels and become instantly viable when anastomosed to the vessels at the recipient site. This is more favorable to poorly vascularised beds, such as irradiated areas, or in recipient beds that have excessive scarring (Shpitzer et al., 1997; Tang et al., 1998; Shpitzer et al., 1999). VBG is advantageous because of reduced resorption and its creation of an environment that allows immediate implant placement for dental reconstruction. Additionally, the same composite graft may be utilized further for soft tissue and bone reconstruction. Commonly utilised VBG donor sites are the fibula, iliac crest, radius and scapula, with the first three flaps being the most frequently used VBG to reconstruct mandibular and maxillary defects.

Vascularised free fibula flap (FFF), described by Taylor et al., (1975) is considered by many as the gold standard technique for reconstruction of segmental mandibular and maxillary bone defects (Urken et al., 1991; Wei et al., 1986; Schrag et al., 2006). FFF has become the cornerstone of reconstruction in the head and neck by restoring continuity defects to the remaining native structures and allowing

placement of dental implants to achieve stable oral rehabilitation (Sozzi et al., 2017). The advantages of FFF include the following:

a. Availability of adequate transplanted bone, quantity and quality
b. Vascular pedicle, which is ideal for anastomosis with vessels in the recipient site.
c. Harvested graft can be harvested with or without a soft tissue component
d. Bony component can be easily adapted to the shape of the maxilla or mandible (Hidalgo, 1989)

Disadvantages of VBG in reconstruction of mandibular defects include among others, long lead time of surgical harvesting and re-anastomosing of blood vessels, resulting in significant post-operative morbidity, monstrous donor site defects, and high costs (Oppenheimer et al., 2008; Chan et al., 1997; Elsalanty et al., 2009; Shpitzer et al., 1997). Moreover, VBG fail to reconstitute the ultimate shape, form and height of the mandible (Buchbinder et al., 1989). Inadequate vertical dimension of the fibula may impede prosthetic rehabilitation due to the large bony step between the graft and the native mandible (Bodard et al., 2011). A double-barrel technique may provide a solution to this problem.

Non-vascularised autogenous bone grafts (NVBG) can be harvested from intra-oral or extra-oral sites, depending on the defect size that is being reconstructed. NVBG can either be cortical, cancellous or cortico-cancellous; and can be harvested in two different forms, either particulate or block graft. Advantages of NVBG include the significant volume of bone that can be procured, reduced

surgery time, reduced donor site morbidity and minimal scarring of the recipient site. Non-vascularised particulate bone and cancellous marrow (PBCM) grafts are effective in restoring defects of any length because the distance to well-vascularised soft tissue interface (the nearest angiogenic source) determines the success, not the distance of the defect between the bony margins (Buchbinder et al., 1989). The corollary is that NVBG do not perform well in poorly vascularised beds, irradiated areas or excessively scarred tissues. Dental implant success rate in NVBG vary from 60 - 90 % (Shpitzer et al., 1997; Tang et al., 1998; Shpitzer et al., 1999).

The use of free vascularized bone grafts with dental implants placed in rehabilitated areas has largely been documented in the past two decades. Gabr et al., (2004) evaluated the success of vascularized flaps in 50 patients after mandibular pathology resection. The success rate of VBG was 95.9% in this study. However, swallowing, speech, and esthetic evaluation was around 60%. Immediate reconstruction of mandible after ameloblastoma resection with FFF and simultaneous dental implant placement showed high success rate in the study by Chana et al., (2004). Thirteen patients (who received 44 dental implants) were included in the study. None of the dental implants or the flaps failed on a follow up period of two to five years. However, length of hospital stay and restoration of function were not reported (Chana et al., 2004). Jaquiery et al., (2004) found a high success rate of inserted dental implants in free fibula flaps equal to the implants placed in native bone with similar amount of bone resorption around the implants.

On the other hand, fewer studies are available about reconstruction of mandibular defects together with implant rehabilitation with NVBG. Foster et al., (1999) conducted a study between VBG versus NVBG for mandibular reconstruction comparing rates of primary bony union and success of endosseous implants. Of the 75 patients who had mandibular reconstruction, 22 (8 patients NVBG and 14 patients VBG) received 104 implants. They concluded that the primary bony union successful rate was 69% in NVBG versus 96% in VBG. Regarding endosseous implant successful rate they reported 82% (27/33) success rate in NVBG and 99% (70/71) in VBG. This study was one of the first studies to compare vascularized with non-vascularized bone graft in mandibular reconstruction and implant success with reasonable follow up period with large number of implants. The authors concluded the following from the study:

a. VBG are preferred for cases that had radiation to the mandible.
b. VBG are preferred when bone and soft tissue reconstruction is needed.
c. VBG are preferred for the immediate implant placement situations.
d. VBG are preferred for virtually any size of defect, whilst NVBG is restricted for shorter bony defects (less than 5-6 cm).

A study by Chiapasco et al., (2008) evaluated implants in 16 patients who had resected mandibles reconstructed with NVBG (block bone grafts) from iliac or calvarial sites. These patients received 60 dental implants four to seven months post-grafting. The mean follow-up period after loading of the prostheses was 94 months. Uneventful postoperative recovery after implant insertion was reported in

15 of the 16 patients. Two implants which failed to osseo-integrate before loading of the prosthesis were removed at the time of abutment connection in one patient, whilst two other implants (albeit still osseo-integrated) presented with marked peri-implant bony resorption. The reported cumulative success and survival rates of implants at the end of the follow-up period were 93.3% and 96.7 respectively. Although the authors fail to elaborate on how sterility was maintained in the 11 patients who had simultaneous intra-oral tumour resection and immediate reconstruction with calvaria/iliac crest bone graft, the major value of this study is its demonstration that mandibular defect size did not limit the use of NVBG, contrary to other authors (Pogrel et al., 1997; Foster et al., 1999) who reported that failure rates were very high in case of defects exceeding 6 cm in length. The credence and scientific value of this study was elevated by its meticulous use of peri-apical radiographs to record peri-implant bone loss and long-term follow-up.

1.3 Bone Graft Healing

Harvested bone graft carries tremendous growth factors (especially, Bone morphogenic protein “BMP” and Transforming growth factor beta “TGFβ”) and osteogenic cellular component. These components are the driving mechanisms of bone remodeling and formation of new bone (Stevenson et al., 1996; Axhausen 1956).

Bone graft healing occurs in two phases (Axhausen, 1956). During phase one of bone healing, no measurable differences are seen between cortical and PBCM grafts, which include blood clot formation, organization and release of growth

factors. The initial regenerative process takes place within few hours of packing the graft. Osteoblasts start the deposition of osteoid and the haematopoietic stem cells begin differentiating into osteoblasts (Buchardt, 1983). After this initial regenerative stage, angiogenic rates differ between cortical and cancellous grafts. Neovascularization of PBCM is derived from surrounding soft tissue recipient bed: the cancellous graft marrow spaces in PBCM degenerate and creates channels for the new vessels ingrowth from the recipient bed (this revascularization is usually completed by one week). Neovascularization of cortical bone graft occurs by ingrowth of new vessels into pre-existing Volkmann's and Haversian channels and that may take six to eight weeks. During phase one of PBCM graft healing, the survival of transplanted osteocompetent cells results in new bone formation, which form the bases of new ossification (Axhausen 1956; Ferretti et al. 2016). This newly deposited bone, called woven bone, is highly cellular and disorganized, without meaningful structural integrity.

The second phase of bone healing is initiated by several angiogenic and transforming growth factors. The growth factors that is paramount in this phase of bone graft healing belong to the transforming growth factor beta ("TGFβ") superfamily (Ferretti et al., 2016; Urist,1965; Sampath and Reddi, 1981). Active osteoclasts secrete coupling chemokines that cause maturation and recruitment of osteoblasts and is an essential factor of the bone graft remodeling process (Boyle et al., 2003). This phase of bone remodeling is known as lamellar

compaction phase. This bone is less cellular, but more mineralized and highly organized (Burchardt, 1987).

Block cortico-cancellous grafts undergo volumetric decline greater than PBCM grafts due to the differences in cellular concentration and the velocity by which the blood vessels derived from the soft tissue bed can gain access to the graft. The distance from the closest source of angiogenic invasion rather than the distance from the bony margins is the key to successful grafting (Ferretti et al., 2016). Bone graft healing failure occurs when the biological factors of the graft (number of transplanted cells, handling and graft storage) and the host's systemic or local factors are violated. The graft factors may include the amount of viable cells transplanted with the graft, the environment's temperature, and the storage medium. Systemic illnesses, radiation therapy to recipient site, intra-oral or extra-oral access to the recipient site, and immobilization of the grafted bone are host factors that may determine success of the bone graft (Marx, 1994; Marx and Morales, 1988; Marx, 1993; Ferretti et al, 2016).

The previously accepted dogma of limiting NVBG for defects size six centimeters or less has been challenged many times in literature, and reconstruction of larger defects with PBCM have been reported with high success rates (Marx 2007; Iion et al., 2009; Ferretti et al., 2013).

Vascularised block cortical bone grafts heal via anastomosis of blood vessels of donor to recipient vessels which has less bone remodeling and fuses with neighboring bone and heals as secondary bone healing (Foster et al., 1999).

1.4 Dental Implant Success and Survival Evaluation Criterion

The criteria used to evaluate dental implant success has changed over time. Harvard National Institute (Schanitman et al., 1979) suggested the following criteria as measures for dental implant success:

- Less than 1mm mobility in any direction.
- Bone loss of less than one third vertical height of the implant.
- No symptoms of pain, infection, numbness or any maxillary or nasal sinus symptoms.
- Functional implant for 5 years.

However, a new criterion for implant success has been suggested by Albrektsson et al., (1986) including:

- Clinical immobility of dental implant.
- No evidence of peri-implant radiolucency radiographically.
- Vertical bone loss of 0.2mm or less after the first year of functioning.
- No signs or symptoms of infection, pain, or any neuropathies.

Based on this criterion, success rate of 85% at five years and 80% at ten years follow-up were published (Albrektsson et al., 2001).

The International Congress of Oral Implantologists (ICOI) formulated a 4 group implant quality of health scale to describe the clinical conditions of success, survival or failure of the implants (Table 2.2) (Misch et al., 2008). The success category described optimum conditions, the survival category described implants still functioning in the mouth but not with ideal conditions and the failure of an implant represented an implant that should be or has already been removed.

1.5 Rational for the Study.

There is paucity of studies that have evaluated the success and survival rate of dental implants placed in autologous compressed particulate corticocancellous bone grafts. Against this background, this study was undertaken to review and assess the success and survival of implants placed in autologous compressed particulate corticocancellous graft as reconstructive modality for mandibular discontinuity. It is envisaged that the result obtained from this study will be used to review and/or modify the current protocol of reconstruction of mandibular continuity defects.

1.6 Aim this Study.

The aim of this study is to evaluate the clinical outcome of dental implants placed in autologous compressed particulate corticocancellous bone grafts.

1.7 Objectives of the Study.

a. Evaluate success of dental implants.

b. Evaluate survival rate of dental implants.

c. To evaluate bone loss in osseointegrated implants in mandibles grafted With PBCM.

d. Assess complications associated with the graft and loaded implants.

Chapter 2

Research Methodology

2.1 Materials and Methods

All patients treated at the Wits Oral Health Centre since 2009 to 2017 who had mandibular defects post-tumour resection and temporary reconstruction with prebent reconstruction mandibular plate (Biomet Microfixation, Jacksonville, Florida, USA) and space maintenance placement (Fig.2.1), followed eight weeks later by definitive reconstruction by harvesting autologous bone from anterior or posterior iliac crest unilateral or bilateral (Ferretti et al., 2013). The bone was ground into particles using power bone mill (Stryker Leibinger, Michigan, U.S.A) and then transferred to twenty millimeters' plastic syringe for manual compression to evacuate the excess blood, fat and air. The patient was then placed in supine position and extra-oral approach made to access the defected mandible. The spacer that was placed during the resection time was then removed and the recipient site prepared to receive the particulate bone graft by refreshing the mandibular bone interface to ensure perfect adaptation between graft and remaining mandibular bone. The particulate bone graft was then packed in the space and in contact with reconstruction plate (Fig.2.2). The patient was then placed in intermaxillary fixation for six weeks after packing of bone graft. The graft was accepted to be successful if six months passed and the grafted bone showed normal architecture on panoramic x-ray (Fig.2.3), invisible graft/mandible interface,

and the regenerated bone capable to accept osseointegrated fixtures for oral rehabilitation four months later (Fig.2.5).

Two stages dental implant protocol was used: first stage involved placement of dental implants, which were buried for minimum of three to four months. The second phase entailed exposure and placement of healing abutments. The dental implants distribution on the reconstructed defect were planned using cone beam computed tomography (CBCT) (Fig.2.4). Implant position was changed intra-operatively only if the prepared site was found to have some fibrous tissue or if the quality of the bone was not optimum. The distribution of the implants in relation to defect size was done based on achieving occlusion to the first molar area minimally. It depended as well on the length and width of the grafted bone. A surgical guide was used to help in increasing accuracy of implant placement. Dental prostheses were fabricated by prosthodontists (Figs. 2.6, 2.7, & 2.8). Clinical examination and multiple panoramic radiographs were used to evaluate the healing and function after prosthesis loading.

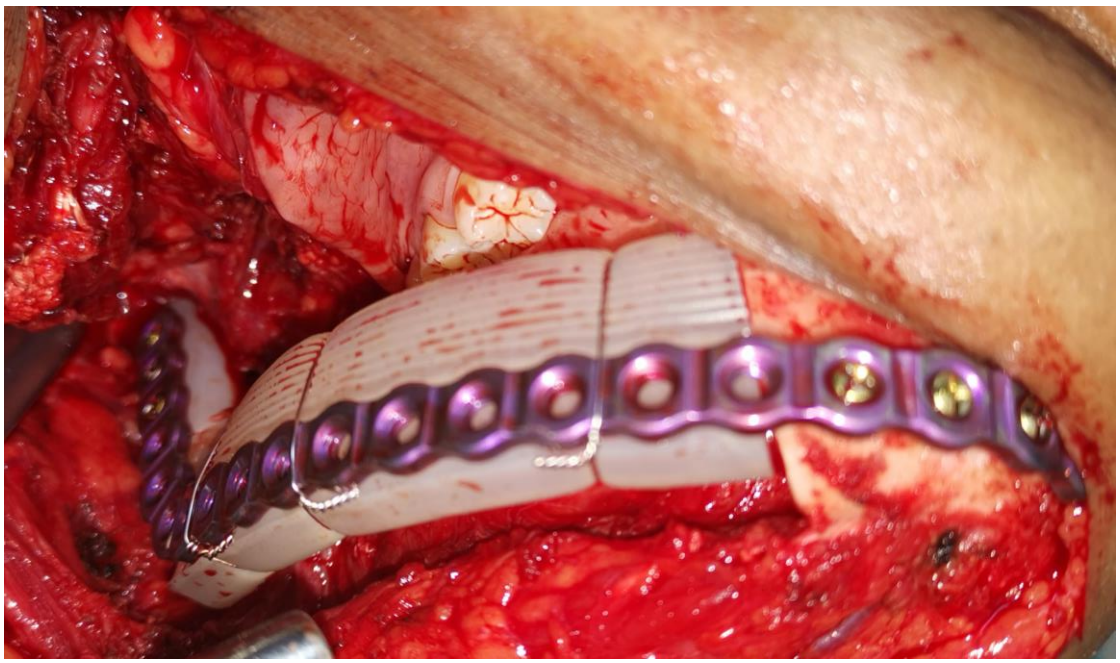


Fig 2.1: Reconstruction plate with spacer

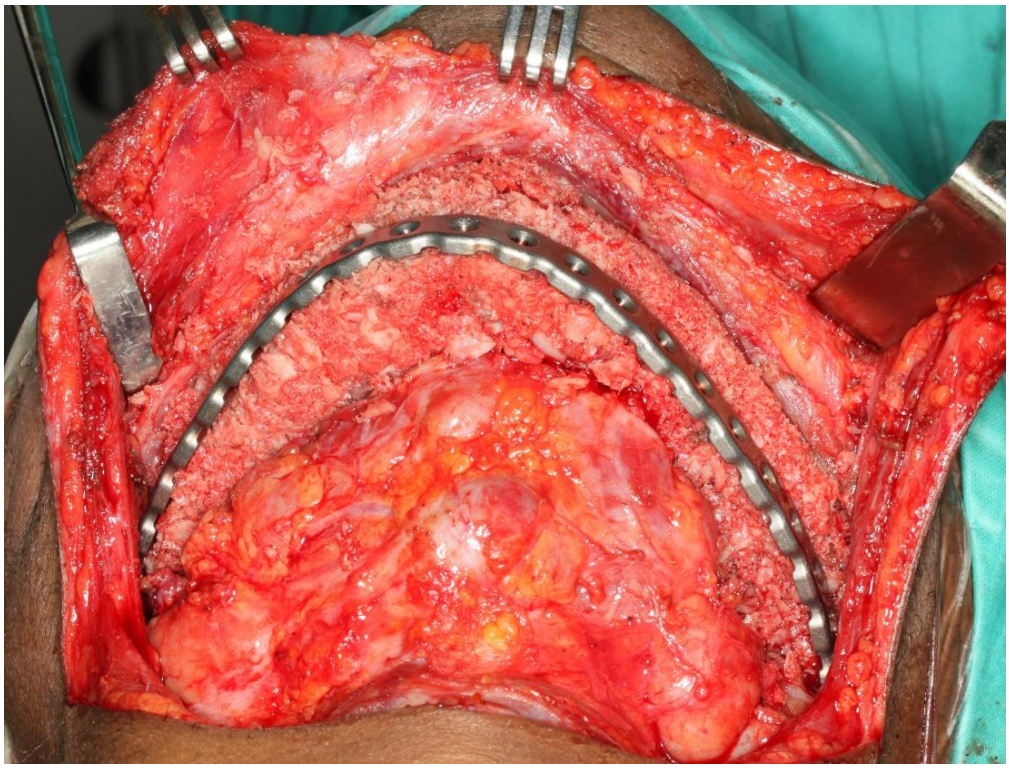


Fig 2.2: Autologous particulate corticocancellous bone graft packed into the recipient bed following removal of spacer.

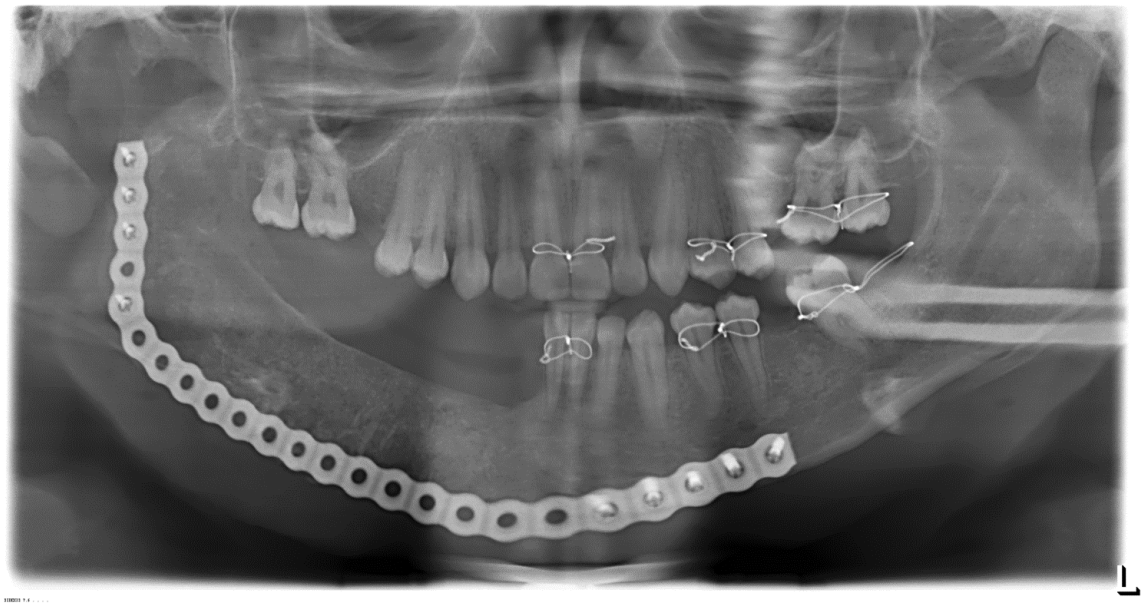


Fig 2.3: Panoramic radiographic showing regenerated bone 3 months post-grafting.

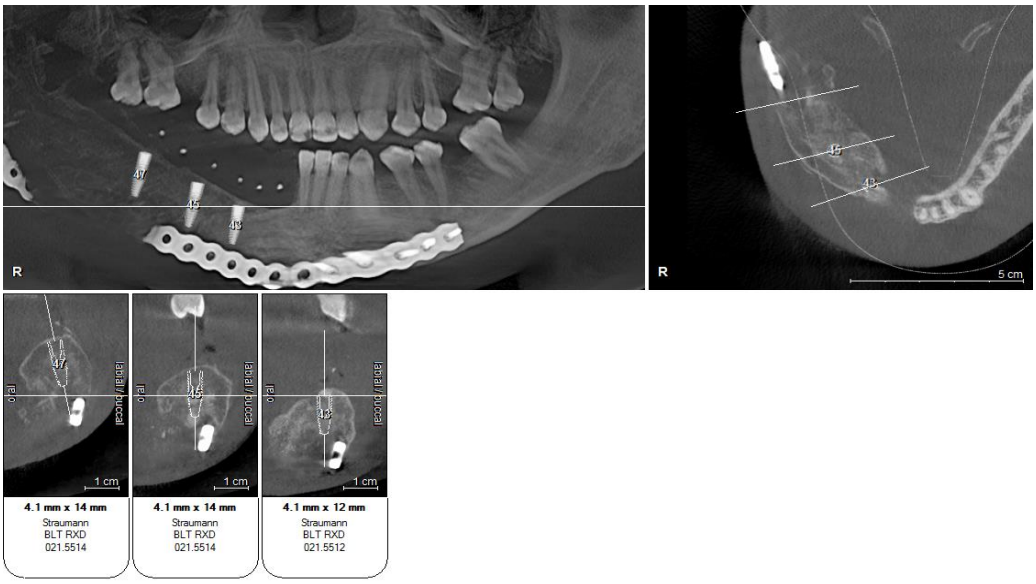


Fig 2.4: Implant position planning.

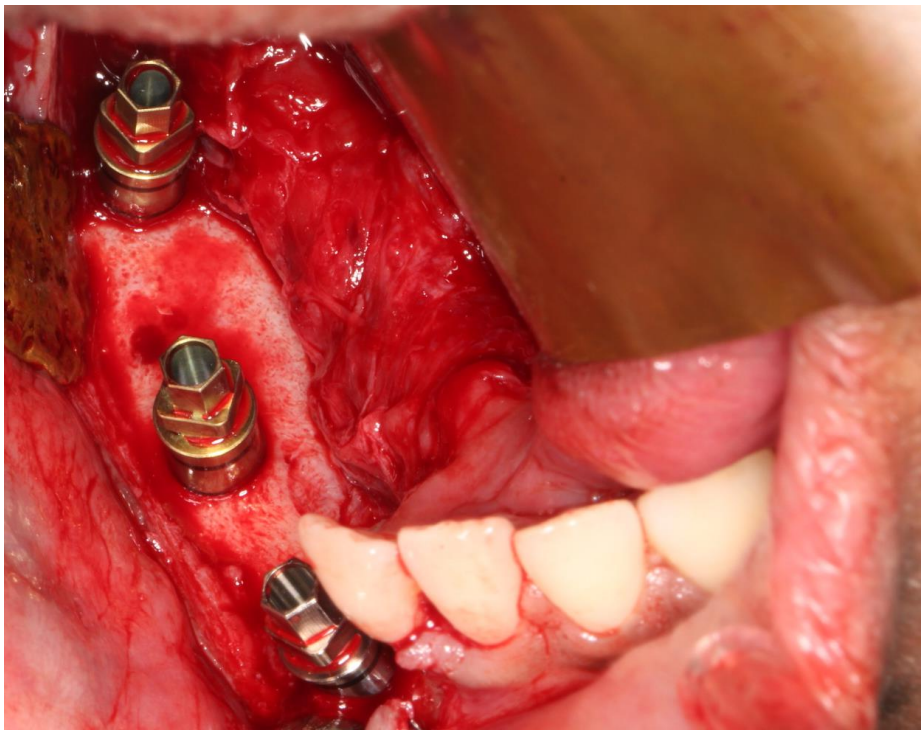


Fig 2.5: Clinical picture showing implants placement in grafted bone.

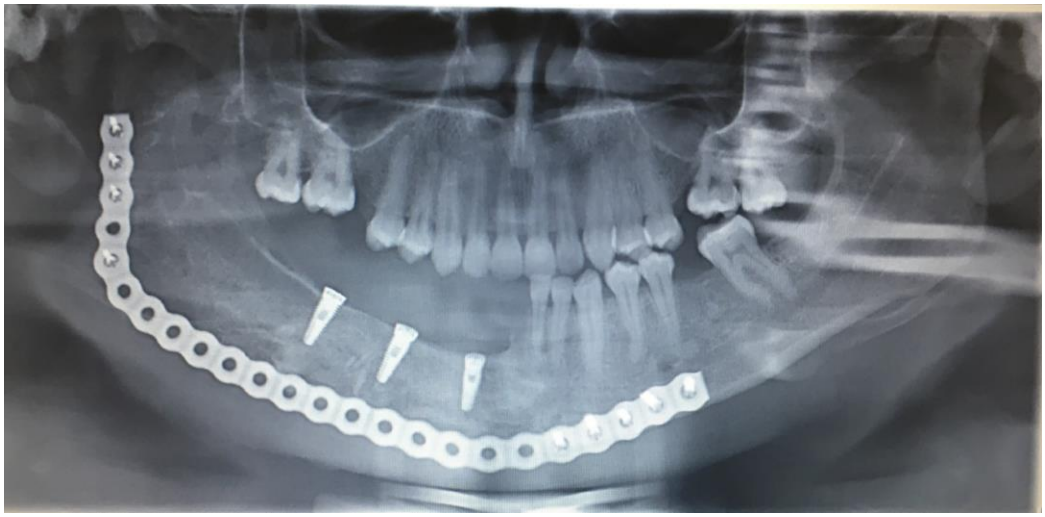


Fig 2.6: Panoramic radiograph following implant placement

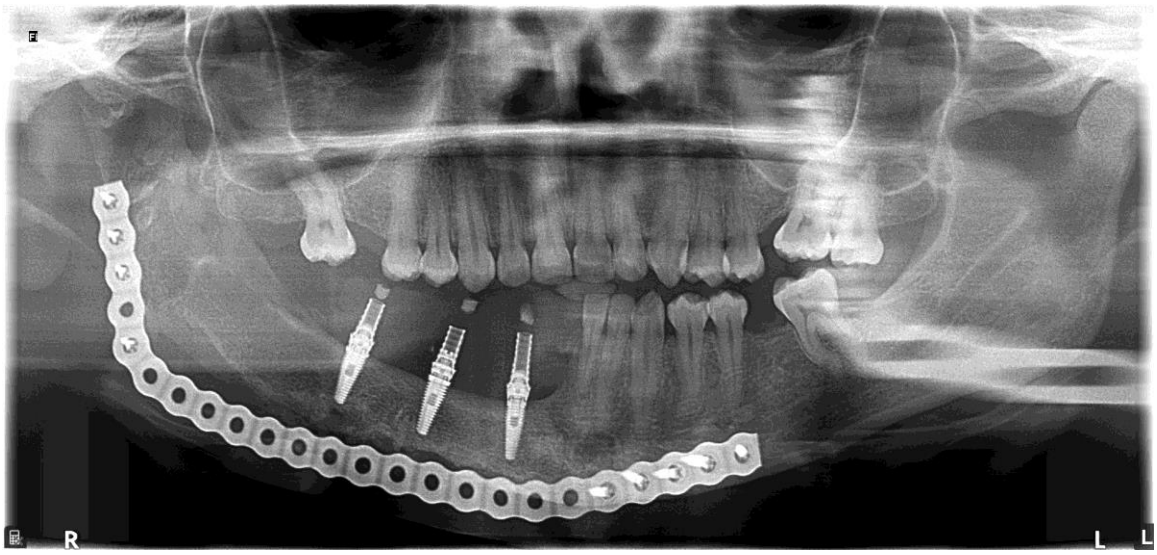


Fig. 2.7: Post implant loading x-ray.



Fig. 2.8: Post implant loading, the patient in occlusion.

2.2 Study design

This was an observational prospective study designed to evaluate implants in patients who had mandibular defects reconstructed with non-vascularized, PBCM grafts.

2.3 Study population

All patients treated for their mandibular continuity defects using PBCM graft followed by implant placement at the Department of Maxillofacial and Oral surgery and School of Oral Health Sciences at the University of the Witwatersrand were included in the study.

Convenience sampling that involved recruiting all the available patients that had been treated with the technique described above, utilized after the dental prosthesis had been loaded, was used.

2.4 Data collection

The evaluation started after implant loading (delayed loading) with prosthetic appliance. Immediate panoramic radiograph taken post implants placement and post-prosthetic appliance placement; and other panoramic x-rays taken at 6, 12 months, and annually thereafter were assessed.

The following radiographic and clinical measurements were recorded:

- Evaluation of gingival heath for any sign of inflammation and recording of bleeding on probing.

- Evaluation of periapical or panoramic x-ray for any signs of bone graft resorption at the level of the implant crestal margin.
- Implant stability measured by recording any mobility of the implant observed under the prosthetic restoration.
- Presence of pain from the implant during function

Peri-implant soft tissue evaluation was done using Mombelli et al., (1987), and Apse et al., (1991) systems for assessment of marginal mucosal conditions around oral Implants as described in (Table 2.1).

Table 2.1: peri-implant tissues evaluation scoring system.

0: No bleeding when a periodontal probe is passed along the mucosal margin adjacent to the implant with normal mucosa
1: Isolated bleeding spots visible with minimal inflammation with color change and minor edema
2: Blood forms a confluent red line on mucosal margin redness, Moderate inflammation with edema, and glazing
3: Heavy or profuse bleeding with severe inflammation with redness, edema, ulceration, and spontaneous bleeding without probing

The following success, survival, and failure criteria in (Table 2.2) published by ICOI used to measure those parameters (Misch et al., 2008).

Table 2.2: Success, Survival, and Failure criteria by ICOI 2008

Implant Quality Scale Group	Clinical Conditions
I. Success (optimum health)	a) No pain or tenderness upon function b) 0 mobility c) <2 mm radiographic bone loss from initial surgery d) No exudates history
II. Satisfactory survival	a) No pain on function b) 0 mobility c) 2–4 mm radiographic bone loss d) No exudates history
III. Compromised survival	a) May have sensitivity on function b) No mobility c) Radiographic bone loss >4 mm (less than 1/2 of implant body) d) Probing depth >7 mm e) May have exudates history
IV. Failure (clinical or absolute failure)	Any of following: a) Pain on function b) Mobility c) Radiographic bone loss >1/2 length of implant d) Uncontrolled exudate e) No longer in mouth

2.5 Inclusion criteria:

- Patient grafted using autologous PBCM grafts who received dental implants.
- Patient who had dental prosthesis loaded over these implants.
- Patient who attended follow-up for at least one year.

2.6 Exclusion criteria:

- Patients lost to follow up.
- Patients who refused to wear dental prosthesis.

2.7 Statistical analysis:

Data collected was imported into Graphpad Instat (version 5) statistical software. In general characteristic described by using frequencies and percentages for categorical variables. Continuous variable reported as mean $\pm$ standard deviation or median (interquartile range). Mean reported if the variable is normally distributed. The mean length of bone loss was calculated for each year by dividing total bone loss by the total number of participants in the study in that year.

The complications that happened after loading of the prosthesis were described using frequency and percentages.

The association between the sociodemographic and clinical characteristics and peri-implant tissue was reported as percentages.

2.8 Ethics Consideration:

Ethics approval obtained for this study from Human Research Ethics Committee (HREC) of the University of the Witwatersrand. Ethics clearance certificate issued with serial number of M171017. Informed consent obtained from the patients with regards to participate in this study, all the patients given the option of withdrawal from the study at any time with no effect on treatment delivery. Confidential coding system used to record patients' information rather than using patients' details.

Chapter 3:

Result

3.1 Biographical and Clinical characteristics

A total of 16 patients who met the inclusion criteria were recruited in the study with 10 participants being female (62.5%) and 6 being males (37.5%) (Table 3.1). The mean age of the participants was 31.3 years with standard deviation of 9.5 years. The average extent of the reconstructed defect was 11.3 cm; the longest reconstructed defect was 18 cm and shortest defect was 6.5 cm with standard deviation 3.4 cm. Condylar involvement found in 3 patients, in which they received costochondral bone graft harvested from 5^{th} or 6^{th} rib and connected to the reconstruction plate as a replacement of the interim condylar spacer. The mandibular defect was found to cross the midline in 62.5% of the case, while it confined to one side of the mandible in 37.5%.

Table 3.1: Baseline demographic data of participant, implants number, defect size, and reconstructive time frame. All values are mean & (SD) apart from gender and number of implants.

Patient number	Gender	Age	Extent of defect reconstructed (cm)	Diagnosis	Extent of defect reconstructed	No of implants	Months between implant placement & loading
1	M	30	6.5	Ameloblastoma	33 to 47	4	3,5
2	F	40	7.5	Ossifying Fibroma	36 to 45	4	6,3
3	M	32	13	Ameloblastoma	37 – 48	6	9,4
4	F	21	10.5	Ameloblastoma	34-L Ramus	2	4,1
5	F	30	9	Ameloblastoma	36-47	4	3,4
6	F	36	12	Central Giant Cell Granuloma	34 to 48	5	14,9
7	M	20	7.5	Ameloblastoma	33 to 46	4	8,6
8	M	40	8.5	Ameloblastoma	34 to R angle mandible	5	4,6
9	F	57	15	Ameloblastoma	Mandible from angle to angle	5	5,4
10	F	35	10	Ameloblastoma	33 to 48	5	3,7
11	F	29	12	Ameloblastic carcinoma	33 to L Condyle	3	3,2
12	F	31	15	Unicystic ameloblastoma	43 to R Condyle	3	9,3
13	F	31	10	Ameloblastoma	35 to L angle	4	8,2
14	F	19	9.5	Ameloblastoma	34 - L angle	4	8,2
15	M	23	17.5	Ameloblastoma	angle to angle	6	15,4
16	M	26	18	Odontogenic Myxoma	31 to R Condyle	3	8,6
Total: 16	M/F – 6/10	31.3 (9.5)	11.3 (3.4)			4 (2-6) Median (range) 67 implants	7.3 (3.8)

M= Male. F= Female. L= Left. R= Right.

3.2 Implants: number, site, size, and distribution

The total number of implants placed in the PBCM graft was 67 implants, with an average of 4 implants per patient. The mean waiting period between implant placement and loading was 7.3 months with standard deviation of 3.8 months (Table 3.1).

As shown in Table 3.2, wider diameters and longer implants were used to support the dental prosthesis. The commonly used dental implants were between 4 and 5 mm in diameter. The length of loaded implants was more than 10 mm in 87.3% of the implants while it was less than 10 mm in 12.7%. Different implant company types were implanted in the transplanted PBCM grafts. The distribution of the implants in relation to defect size was done based on achieving occlusion to the first molar area minimally. Posterior mandible had more implants placed with 56.7% in premolar and molar area with site 44 and 46 being the most used sites. Anterior mandible had only about 43.3% of the placed implants with site 41 being the most common site (Fig.3.1).

Table 3.2: Implant site, diameter, and Length.

Patient number	Implant Diameter	Implant site	Implant Length
1	5/5/5/4	33/42/44/46	13/13/10/13
2	5/5/4/4	34/31/42/44	13/13/13/13
3	4/4/4/5/4/4	35/34/33/41/45/47	10/10/10/10/10/10
4	4.1/4.8	35/37	12/12
5	4.1/4.8/4.8/4.8/4.1	34/31/44/46/35	10/10/12/10/12
6	4.1/4.8/4.1/4.8/4.1	34/31/42/44/45	10/12/12/12/10
7	5/5/5/5/5	33/41/43/46	13/13/10/13
8	4/6/6/6/6	43/32/41/44/46	10/6/6/6/6
9	4/5/5/5/5	35/33/31/43/45	11.5/10/10/8/8
10	5/5/5/4/4	33/31/42/44/45	11/11/11/10/10
11	4/4/4	36/35/34	13/13/13
12	4/4/4	43/45/46	13/13/13
13	5/4/5/5	32/42/44/46	10/10/10/8.5
14	4/5/5/5	36/34/31/42	10/13/13/13
15	4.1/4.1/4.8/4.8/4.1/4.1	36/33/31/42/44/46	10/12/10/10/12/12
16	4/4/4	42/44/46	13/11/13

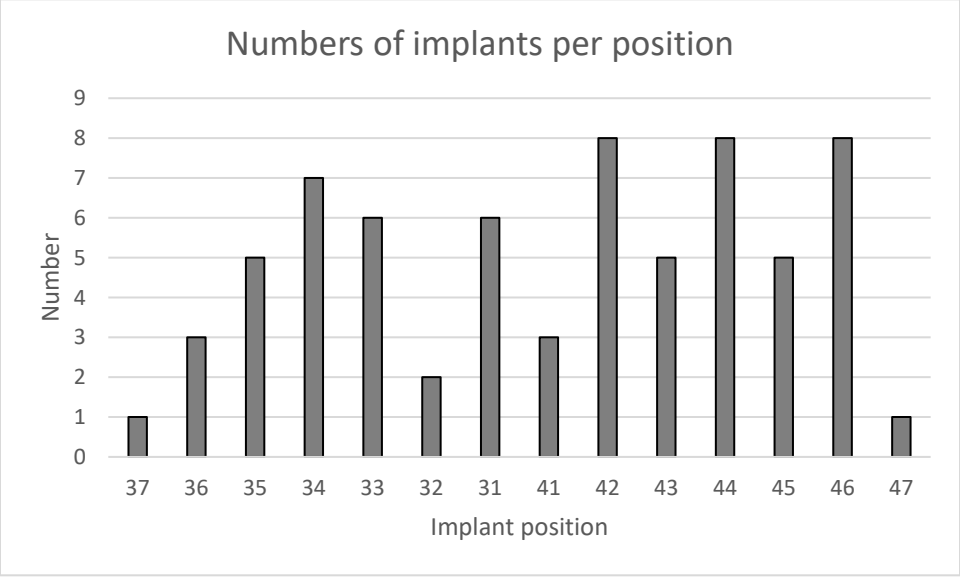


Fig 3.1: implant positions distribution.

3.3 Implant Success and Survival

Dental implant success criteria were used to evaluate the dental implant inserted in those patients. Postoperative recovery after implant placement (67 implants) was uneventful in 62 implants, resulting in a success rate of 92.5%. Five (7.5%) of the 67 dental implants failed before (4 implants) and after loading (1 implant) respectively (Table 3.3).

Four of the failed implants occurred before loading with dental prosthesis and were subsequently removed (two implants were associated with partial graft loss, and the other two implants had no primary stability on placement and were removed during exposure and impression taking stage). The fifth implant failed seven months post-loading and was subsequently removed without replacement. The survival rate of the loaded dental implants placed in PBCM graft was 98.4%.

Regarding other success criteria, none of the remaining implants had mobility or pain on percussion.

3.4 Peri-Implant Tissues Assessment.

The following clinical periodontal indices were assessed in an attempt to evaluate the outcome of implants:

a. Bleeding on probing was found to be nil in 9.7%, mild in 67.8%, and moderate in 22.5% of the peri-implant tissue (Table 3.3). Collectively, the success rate of the dental implants which met the success criteria is around 80.6% of the total loaded implants.
b. Pain.
c. Mobility.

Table 3.3: Measurements of implant success criterion.

Pt no	Bleeding 0/1/2/3	Pain	Mobility	Failed (Y/N)	Diff bone level (mm) Mean	N=≤0.2mm
1	1/1/1/1	No	No	No	0.2	3/4
2	1/1/1/1	No	No	No	0.17	4/4
3	1/2/2/2	No	No/for the remaining	Yes (2/6)	1.32	1/4
4	1/1	No	No	No	0.2	2/2
5	1/1/1/1	No	No/for the remaining	Yes (1/5)	0.25	2/4
6	1/2/2/2	No	No/for the remaining	Yes (1/5)	0.52	3/4
7	1/1/1	No	No/for the remaining	Yes (1/4)	0.16	3/3
8	1/2/2/2	No	No	No	0.52	1/5
9	1/1/1/1/1	No	No	No	0.18	5/5
10	1/0/1/1/0	No	No	No	0.18	5/5
11	1/1/1	No	No	No	0.2	3/3
12	1/1/2	No	No	No	0.23	2/3
13	2/1/1/1	No	No	No	0.12	4/4
14	0/0/0/0	No	No	No	0.2	4/4
15	1/1/2/1/2/2	No	No	No	0.05	6/6
16	2/1/1	No	No	No	0.1	3/3
T: 16	N:6, Mi:29, Mo:27	No pain	No mobility	62/67 Preloading: 4 Postloading: 1	Mean: 0.28	50/62

N= Normal. Mi= Mild. Mo= Moderate.

3.5 Bone Loss Around Implants

Evaluation of bone loss around the dental implants using digital panoramic radiograph reported in mean of 0.28 mm. Bone loss after one year was less than 0.2 mm in 80.6% (50/62) of the loaded implants (Table 3.3). The maximum bone loss found in patient number 3, 6 and 8 (all these 3 patients had a score 2 of bleeding on probing).

Table 3.4 shows bone loss level in patients as per periodic follow up visit. Bone loss for the last four categories (1-2 years up to 4-5 years) was compared using a non-parametric ANOVA, the Kruskal-Wallis test. The overall P value for the ANOVA was 0.0991, which is not significant and therefore means there were not statistically significant between these four sets of data points.

Table 3.4: Bone loss evaluation throughout post loading time.

Time elapsed	1-6m	6m – 1y	1.1-2y	2.1-3y	3,1 – 4y	4.1-5 y
Number	8	21	32	22	22	13
Mean (mm)	0,18	0,42	0,36	0,27	0,36	0,18
SD	0,08	0,69	0,53	0,18	0,51	0,06
Minimum	0,1	0	0	0,1	0	0,1
25	0,1	0,2	0,1	0,2	0,1	0,1
Median	0,2	0,2	0,2	0,2	0,2	0,2
75	0,2	0,33	0,2	0,28	0,39	0,2
Maximum	0,3	3	2	0,8	2	0,3

M= Month. Y= Year. SD= Standard Deviation.

3.6 Complications

The following complications were noted in this study:

a. Lack of osseointegration: Two implants were removed before loading due to lack of osseointegration. Both these implants had peri-implant radiolucency.

b. Loss of reconstruction plate and bone graft: One patient had exposed reconstruction plate (6 months after implants insertion) and subsequent implant and graft loss. The reconstruction plate was replaced.

c. Tumour recurrence (ameloblastic carcinoma) (Fig.3.2): This was a soft tissue recurrence with no involvement of the bone. As such, the implants were not affected. (Fig.3.3). Patient was planned for resection of soft tissue recurrent lesion.



Fig. 3.2: Soft tissue recurrence of ameloblastic carcinoma.

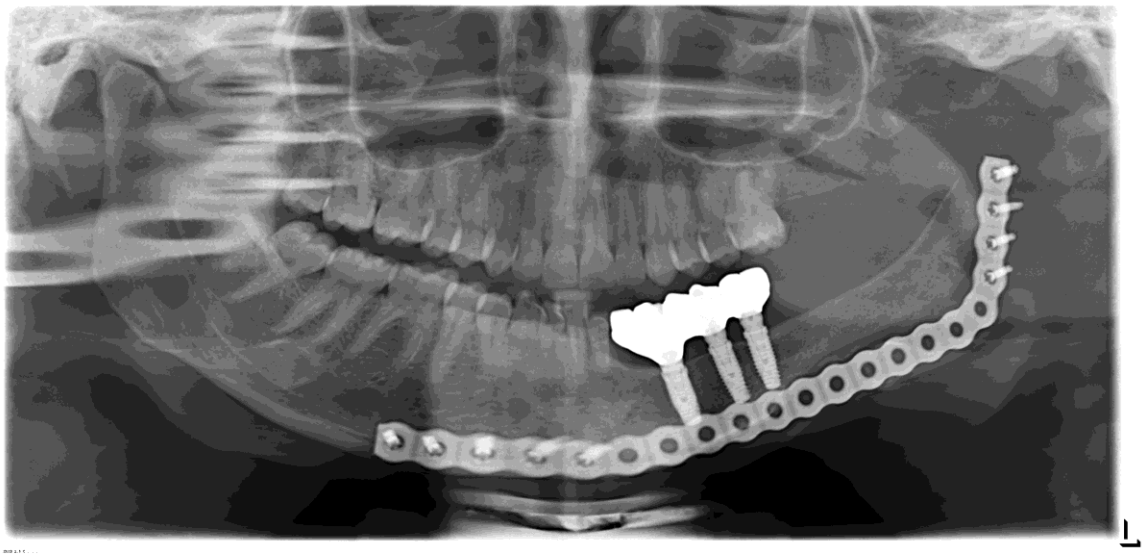


Fig. 3.3: Successful implant in grafted bone despite soft tissue recurrence.

Chapter 4:

Discussion

Mandibular defects following ablation of tumours often result in significant facial deformities, impairment of oral functions (such as speech, mastication and deglutition) and associated psychological problems. Available reconstructive options to rehabilitate these patients include vascularized bone flaps (free vascularized flaps) and non-vascularized bone grafts. In our setting, VBGs are generally reserved for poorly vascularized beds (such as irradiated tissues) and in recipient beds requiring both hard and soft tissue reconstruction, as is often the case in malignant tumour resection cases.

According to Carlson and Marx (1996), the goals of mandibular reconstruction includes amongst others the following:

a. Restoration of mandibular continuity
b. Restoration of alveolar bone height
c. Restoration of osseous bulk
d. Maintenance of osseous content
e. Restoration of acceptable facial form
f. Acceptability of implants
g. Recoverable non-debilitating donor site surgery

Reconstruction of mandibular continuity with NVBG or VBG is imperative for restoration of facial contour and mandibular function, but is mostly insufficient for completely restoring mastication, speech and swallowing parameters. The latter can be achieved only by recreating an appropriate dental occlusion (Chiapasco et al., 2000). A successful bone graft is therefore one that is able to accommodate a number of restorative dental techniques, dental implants in particular.

This study aimed to evaluate clinical outcome of dental implants placed in non-vascularized bone graft post- ablative surgery of benign tumours in the mandible.

A total number of 16 patients were recalled for evaluation of dental implants which were placed and loaded for at least one year. The majority of patients had mandibular ameloblastomas resected and were female with an average age of 31.3 years.

The bone graft technique utilized in this study involved reconstruction of the mandibular continuity defects with PBCM graft that harvested from posterior and anterior iliac crest. In the present study the mean mandibular defect size was 11.3 cm, with a range of 6.5 cm to 18 cm (Table 3.1). Post-operative recovery after the bone graft was uneventful in 15 of the 16 grafted patients (with a success rate of 93.7%) and graft consolidation and primary union occurred. This finding suggests that defect size does not limit the use of PBCM non-vascularized grafts. A similar conclusion was reached by Chiapasco et al., (2008). Chiapasco et al., (2000) initially suggested use of NVBG for continuity defects not more than 9 cm in length.

This finding however contradicts the widely-held and persistent dogma that failure rates of non-vascularized bone grafts in defects exceeding 6 cm are very high (up to 75% for grafts over 12 cm). This belief has its origin from studies conducted by Chen et al., (1994); Pogrel et al., (1997) and Foster et al., (1999). They reported that the use of NVBG be restricted to short bone defects (less than 5-6 cm). These studies however referred predominantly to cortico-cancellous block bone grafts, and incorrectly contended that all non-vascularized grafts heal in a similar fashion (Ferretti et al., 2016). This belief often overshadows well-established advantages of PBCM graft that include less operative time, no need for specialized training skills and armamentarium, decreased hospital stay, greater available bone volume and improved contours for aesthetics and implant or prosthetic functionalization (Carlson and Marx, 1996). Whilst there is unanimity on the use of VBG in poorly vascularized tissues and malignant conditions, our study confirms the findings of other investigators that the defect size is not a restriction for use of NVBGs in benign conditions of the jaws (Ferretti et al., 2016; Chiapasco et al., 2008), provided that there is adequate soft tissues enveloping the graft. Marechek et al., (2019, In press) also found in their study that NVBGs are a feasible, safe and efficient treatment option for patients with segmental mandibular defects over 6 cm in length with no radiation history to the area. They concluded by stating that the pervasive belief that there is a correlation of success of NVBGs based on a 6 cm cut-off mark should be questioned with further investigation.

The cumulative success and survival rates of implants in this study (92.5% and 98.4% respectively) confirm that non-vascularized compressed PBCM allows not only restoration of mandibular continuity and adequate facial contour, but also creation of a solid foundation for implant-supported prosthetic rehabilitation by restoration of alveolar bone height. This reproducible and predictable outcome by PBCM harvested mainly from posterior iliac crest is achieved with minimal morbidity. Decreased morbidity is complemented by the achievement of graft morphology that more closely duplicates mandibular contour and morphology than a free flap could. The pliable nature of the PBCM graft and its ease of implantation into a recipient bed molded by a spacer allows duplication of the mandibular arch shape (Ferretti et al., 2016).

Implant survival and success rates in the present study is comparable to that reported by Chiapasco et al., (2000, 2008). In the latter study, Chiapasco et al., (2008) primarily and secondarily reconstructed mandibular defects with autogenous non-vascularized iliac crest and calvarial grafts. 16 of these patients received implants and had survival and success rates of 96.7% and 93.3% respectively after a mean follow-up of 94 months. Their patients were however reconstructed with cortico-cancellous bone blocks.

The earlier study by Chiapasco et al., (2000) evaluated the behavior of implants in NVBG or VBG (before and after insertion of dental implants) after tumour resection in the mandible. Group I (10 patients) were treated with NVBG (corticocancellous blocks) from fibula or anterior iliac crest and Group II (8 patients) were treated with

iliac or fibula VBG. After a period of 4 to 8 months, 72 endo-osseous dental implants were inserted in the two groups of patients. The implants were then loaded with implant-borne prosthesis 4-6 months after osseointegration. After the assessment of bone resorption in the two groups before and after implant insertion and after loading of the implants up to a period of 24 months, they concluded the following:

a. Prior to implant placement, significant difference in bone resorption ($p<0.001$) between NVBG/group I (mean 3,53 mm) and VBG/group II (mean 0.9 mm)
b. After implant placement and loading, there was no significant difference in bone resorption between the two groups (mean 1,16 mm in NVBG and 1.02 mm in VBG 24 months after loading the dental prosthesis

The overall failure rate was 4.9% in group I and 3.2% in group II (yielding success rates of 95% and 97% for groups I and II respectively). This study confirmed that there is less bone remodeling in VBG after reconstruction and before implant insertion and loading because an immediately vital tissue was transferred and bone resorption and substitution is very minimum (Riediger 1988; Buchbinder et al., 1989; Urken et al., 1991). The study also suggests that the placement of implants and their subsequent loading minimize bone resorption in NVBG. The mean bone loss in the present study 1-2 years post-loading (0.36 mm) of the implants was insignificant compared to that in the 4-5 years post-loading category (0.18 mm), confirming that the placement of dental implants and the utilization of implant-supported prosthesis appear to significantly decrease bone resorption as reported by Hotz (1996) and Pogrel et al., (1997). This seems to suggest that

loaded endo-osseous implants can significantly reduce bone resorption. Peri-implant bone loss in the present study is comparable to that reported in the literature: Gbara et al., (2007) stated that crestal bone loss was <1 mm in 62 implants, 1-2 mm in 35 and > 2mm in 20 dental implants. Attia et al., (2018) assessed bone loss around 118 dental implants and found that of these 93 had ≤1 mm of bone resorption, 11 exhibited 1-2 mm and 14 showed ≥ 3 mm.

Foster et al., (1999) conducted a comparative study (between NVBG and Fibula osteocutaneous free flap) on bone healing and the success of osseointegration of dental implants in patients with mandibular defects. Of the 75 patients who received mandibular reconstruction procedure, only 22 patents had a total of 104 dental implants inserted into: NVBG (8 patients, 33 implants) and VBG (14 patients, 71 implants). The overall implant success was 82% (27/33) in NVBG and 99% (70/71) in VBG respectively. They concluded that despite the fact that patients treated with VBG were older, had larger defects and were treated primarily for malignant diseases (and therefore had a higher rate of radiation to the recipient site); the bony union in these patients was found to be higher and the success rate of inserted dental implant was significantly greater ($p<0.0001$) than for patients treated with NVBG. This study had an uneven, non-randomized distribution of patients (and implants) between the two groups, at a ratio of 35%:65%. The exclusion of patients with malignancies and history of irradiation from NVBG group could have yielded a different outcome.

Nelson et al., (2006) evaluated success of endosseous implant placed in non-vascularized bone graft block harvested from fibula to atrophic mandible. Implant success was defined according to Buser et al., (2002):

a. Lack of subjective complaints, such as foreign body sensation, pain and/or altered sensation that is persistent.
b. Lack of peri-implant disease and/or suppuration.
c. Lack of implant mobility.
d. Lack of radiolucency around the functioning implant.

Resorptive changes in the grafted bone were evaluated with panoramic radiographs. Overall success rate of the implants in the grafted bone was of 97%, which is close to our observation in the present study. They also reported maximum bone loss of 7.21% during the first year, but thereafter no significant bone loss was seen. However, they had a smaller sample size and number of endosseous implants (10 and 40 respectively) in their study and their patients (unlike ours) had no segmental defects (i.e. no loss of continuity of the mandible). A recent study by Attia et al., (2018) retrospectively evaluated survival of 134 dental implants inserted in 34 patients who went through ablative tumour surgery and mandibular reconstruction using microvascular FFF. The criteria for dental implants success used were those of Albrektsson et al., (1986). The panoramic radiograph used to measure bone resorption was taken immediately after implants placement (which was done 5-6 months post-grafting), and was compared with a panoramic x-ray taken a minimum of one-year post insertion. The one year and

11-year cumulative survival rates were 93% and 78% respectively. Interestingly, even though the mandibular and maxillary defects were grafted with vascularized fibula grafts, implants were only inserted after a period of 5-6 months of tumour-free surveillance, a sensible and similar protocol as ours. Implants placement, even when it involves free vascularized grafts, at the time of reconstruction is very difficult and rarely satisfies the expectations of the restorative dentist (Roumanas et al., 1997; Riediger 1988). A staged protocol as applied in our study seems more preferable and offer satisfactory outcomes. We suggest an ideal waiting time of about 4-6 months between reconstruction with PBCM and implant placement. This waiting period offers the possibility to verify the take and consolidation of grafts and allows for sufficient revascularization of the bone grafts. It also allows the prosthodontist to correctly plan the dental rehabilitation, and to prepare the surgical stents which can give to the surgeon all the indications for optimum position of implants (Chiapasco et al., 2000). A much longer waiting period (beyond 12 months) is however not advocated in cases of reconstruction with non-vascularized bone grafts, as it may predispose the bone graft to excessive resorption.

A similar study by Sozzi et al., (2017) concluded (after a 98% implant survival rate), that implant survival is high and implant-supported dental prostheses are a reliable rehabilitation option in patients whose jaws are reconstructed with vascularized fibula-free flaps. The difference in survival rates between fibula free flaps is usually due to the sensitivity of the technique.

Chapter 5

CONCLUSION

This study sought to evaluate clinical outcome of dental implants placed in non-vascularized bone graft following ablation of benign tumours in the mandible. The most common pathology was an ameloblastoma. The mean mandibular defect size was 11.3 cm, with a range of 6.5 cm to 18 cm. Patients were grafted with PBCM harvested from posterior iliac crest. Complete graft loss was reported (6 months after implants insertion) in one of the sixteen patients

Despite the small sample size and the shorter follow-up period, results from this study showed that PBCM is a viable and predictable technique for rehabilitation of patients with implants and implant-supported prosthesis. As long as there is adequate soft tissue enveloping the graft, defect size is not a restriction for use of PBCM in benign conditions of the jaws. Also, PBCM allows for restoration of not only mandibular continuity and arch form but also creation of a solid foundation for implant supported prosthetic rehabilitation by restoring the alveolar bone height. The use of a spacer helped to maintain mandibular width, height, and shape to receive long and wide dental implants in the correct position.

The cumulative success and survival rates of implants in the present study was 92.5% and 98.4% respectively, which is not only comparable with implants in reconstructed mandibles with vascularized bone grafts but also with implants in

native jaw bones (Chiapasco et al., 1997, 2000, 2008; Pogrel et al., 1997; Albrektsson et al., 1986, 1988).

The mean bone loss 1-2 years post-loading of implants (0.36 mm) was insignificant compared to that in the 4-5 years post-loading category (0.18 mm). This suggests that insertion of implants and their subsequent loading significantly reduces bone resorption.

A similar study with a larger sample size and longer follow-up will help validate the findings of this study. It is recommended that future studies be designed to compare and evaluate the performance of dental implants, evaluate morbidity, hospital stay and patient satisfaction in vascularized and nonvascularized PBCM bone graft.

Notwithstanding its limitation, this study has demonstrated a viable technique for reconstruction and rehabilitation of segmental mandibular defects with compressed particulate bone and cancellous marrow grafts and dental implants.

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ANNEXURE A

Data collection sheet

Patient code: _____

Age: _____

Gender: _____

Race: _____

Number of implants: _____

Resection site					
Resection length					
Implant diameter					
Implant site					
Implant length					

Peri-implant tissue evaluation:

Bleeding on Probing Score 0 to 3. 0: No bleeding when a periodontal probe is passed along the mucosal margin adjacent to the implant. 1: Isolated bleeding spots visible. 2: Blood forms a confluent red line on mucosal margin. 3: Heavy or profuse bleeding.					

Implant evaluation

Percussion test					
Implant mobility					
Failed Implant					

Radiographic evaluation:

Difference in bone level on Panorex x-ray from the post loading x-ray: / /20

Date of the next x-ray: / /20					
Date of the next x-ray: / /20					
Date of the next x-ray: / /20					
Date of the next x-ray: / /20					

ANNEXURE B

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG	HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

Office of the Deputy Vice-Chancellor (Research & Post Graduate Affairs)

TO: Dr A A Alharbi
School of Oral Health Sciences
Department of Maxillo-facial and Oral Surgery
Medical School

E-mail: dr.aljabry@hotmail.com

CC: Supervisor: Dr R Rikhotso <Risimathi.Rikhotso@wits.ac.za>

FROM: Iain Burns
Human Research Ethics Committee (Medical)
Tel: 011 717 1252

E-mail: Iain.Burns@wits.ac.za

DATE: 23/01/2018

REF: *R14/49*

PROTOCOL NO: **M171017** *(This is your ethics application study reference number. Please quote this reference number in all correspondence relating to this study)*

PROJECT TITLE: *Survival and success rate of dental implants placed in autologous compressed particulate corticicancellous bone graft post-tumour ablative surgery in the mandible*

Please find attached the Clearance Certificate for the above project. I hope it goes well and that an article in a recognized publication comes out of it. This will reflect well on your professional standing and contribute to the Government funding of the University.

MSWorks2000/Iain0007/Clearscan.wps

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Dr A A Alharbi

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M171017

NAME: (Principal Investigator)	Dr A A Alharbi
DEPARTMENT:	School of Oral Health Sciences Department of Maxillo-facial and Oral Surgery Medical School
PROJECT TITLE:	Survival and success rate of dental implants placed in autologous compressed particulate corticicancellous bone graft post-tumour ablative surgery in the mandible
DATE CONSIDERED:	27/10/2017
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr R Rikhotso
APPROVED BY:	Professor CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	23/01/2018

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on 3rd floor, Phillip V Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.
I/We fully understand the conditions under which I am/we are authorised to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to resubmit to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. in this case, the study was initially reviewed in **October** and will therefore be due in the month of **October** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature _____ Date _____

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

ANNEXURE C

PARTICIPANT CONSENT SHEET

Survival and success rate of dental implants placed in autologous compressed particulate corticocancellous bone graft post tumour ablative surgery in the mandible

1. I have been given a Participant Information Sheet which explains the nature and processes involved in this study
2. I was given time to read it, or had it read to me, in the language I best understand
3. I was given time to ask any questions I wanted to and found any answers given to me to be satisfactory
4. I believe I fully understand why the study is being conducted and what the intended outcomes will be
5. I understand that there will be no immediate benefit to me, should I agree to participate, nor will I receive any payment; conversely, participation will not cost me anything
6. I have been given a range of contact details, repeated below, should I require further information at a later stage, or have any cause for concern over any aspect of the treatment I receive
7. I understand that, even if I initially consent to take part in the study, I may subsequently withdraw at any time and would not be required to give reasons; if that happened, any data collected about me for the purposes of the study would immediately be destroyed

Contact details

Dr. AA Alharbi, Principal Investigator, telephone no. 060 826 2077, or by e-mail at dr.aljabry@hotmail.com,

Dr E Rikhotso, Supervisor, on telephone no. 083 469 5839, or by e-mail at Risimati.Rikhotso@wits.ac.za

Professor CB Penny, Chairperson of the Human Research Ethics Committee (Medical) at the University of Witwatersrand, on telephone no. 011 717 2301, or by e-mail at Clement.Penny@wits.ac.za.
Ms. Z Ndlovu or Mr Rhulani Mkansi, Committee Secretariat, telephone nos.: 011 717 2700 or 1234, or by e-mail at: Zanele.Ndlovu@wits.ac.za or Rhulani.Mkansi@wits.ac.za

On the basis of the foregoing information, I, _____ (please print name) freely consent to participate in the study.
Signature or identifying mark: _____ Date: _____

ANNEXURE D

PATIENT IDENTIFIER FORM

Patient Identifying code: …….

Patient Name: …….

File number……