

A RETROSPECTIVE ANALYSIS OF MANDIBULAR GRAFTING USING VASCULARISED FREE FIBULA FLAPS AT THE CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC HOSPITAL

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A research report submitted to the Faculty of Health Sciences,
University of the Witwatersrand, Johannesburg, in fulfilment of
the requirements for the degree of Master of Dentistry (MFOS)

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DECLARATION

I, Priyesh Gunvant Hira, declare that this research report is my own, unaided work. It is being submitted for the degree of Master of Dentistry (MFOS) at the University of Witwatersrand, Johannesburg. It has not been submitted or incorporated before in another research report, dissertation or thesis for another degree or examination at this or any other University. The experimental work was performed in the Department of Maxillofacial and Oral Surgery, School of Oral Health Sciences, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg. I also affirm that all reference material(s) contained herein have been duly acknowledged.

P G Hira

17th day of October 2019

Johannesburg

South Africa

DEDICATION

This research report is dedicated to my parents, Gunvant and Kanta, and my brothers, Yatin and Bhavik for their unwavering support and encouragement. It is also dedicated to my fiancé, Harshita for her dependable support, understanding and patience.

Above all, I wish to humbly dedicate this work to the Almighty God, whose bountiful and unmerited favour saw me through this research project and the degree program.

PRESENTATIONS

1. Hira PG, Singh S, Kourie JF, Rikhotso RE. A retrospective analysis of mandibular grafting using fibulas at the Charlotte Maxeke Johannesburg Academic Hospital. **South African Society of Maxillofacial and Oral Surgeons Annual Congress, Durban, South Africa, 10 August 2018**
2. Hira PG, Singh S, Kourie JF, Rikhotso RE. A retrospective analysis of mandibular grafting using vascularised free fibula flaps at the Charlotte Maxeke Johannesburg Academic Hospital. **24th International Conference of Oral and Maxillofacial Surgery, Rio de Janeiro, Brazil, 22 May 2019**

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ABSTRACT

Introduction: Segmental mandibular defects following significant maxillofacial trauma and ablative tumour surgery often present reconstructive challenges from the resultant mandibular bone and soft tissue defects. The volume of bone and soft tissues lost often necessitates composite microvascular flap reconstruction to be able to optimally rehabilitate these patients. Vascularised free fibula flaps have the concomitant benefit of providing adequate bone and soft tissue coverage.

Aims and objectives: The aims are to retrospectively evaluate the reconstructive outcomes of vascularised mandibular free fibula flaps and to identify factors associated with favourable and unfavourable outcomes.

Methods and materials: Patients with vascularised free fibula flaps to the mandible were included in the study. Data collected was divided into various categories, namely, demographic details, defect aetiology, the number of segments in the fibula, adjunctive radiation therapy, the subsequent immediate or delayed placement of dental implants and associated complications.

Results: Twenty patients (8 males and 12 females) were included in this study. The most common aetiology of mandibular defects was neoplasia. The overall complication rate was 40% and ranged from graft loss due to anastomosis failure to dehiscence and minor sepsis. No significant association was found between gender, aetiology of defect, radiation therapy and reconstructive outcome. Nine patients subsequently received dental implants.

Conclusion: There was a 90% fibula graft success rate. A larger sample size and a longer follow-up in a multidisciplinary team is needed to assist in the development of a better treatment and follow-up protocol in patients treated with vascularised free fibula flap.

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ABBREVIATIONS

QoL:	Quality of life
VFFF:	Vascularised free fibula flap
DBFFF:	Double-barrel vascularised free fibula flap
CAS:	Computer-assisted surgery
BIFFF:	Bone impacted vascularised free fibula flap
ART:	Alberta Reconstructive Technique
CAD / CAM:	Computer-aided design and computer-aided manufacturing
DCIA:	Deep circumflex iliac artery flap
TMJ:	Temporomandibular joint
ECG:	Electrocardiogram
DSA:	Digital Subtraction Angiography
CTA:	Computed Tomographic Angiography
MRA:	Magnetic Resonance Angiography
CDS:	Colour Duplex Sonography
2D:	Two-dimensional
3D:	Three-dimensional
VSP:	Virtual surgical planning
RPM:	Rapid prototype modelling
CT:	Computed Tomographic
DICOM:	Digital Imaging and Communication in Medicine
SADC:	South African Development Community
CMJAH:	Charlotte Maxeke Johannesburg Academic Hospital
HREC:	Human Research Ethics Committee
C.E.O.:	Chief Executive Officer
H.O.D.:	Head of Department
MRONJ:	Medication related osteonecrosis of the jaws
ICU:	Intensive Care Unit
SCC:	Squamous cell carcinoma

CHAPTER 1

1. Introduction

Trauma, tumour ablative surgery, bony necrosis after radiation, medication with antiresorptive properties and other types of pathology often results in patients having large mandibular bone and soft tissue defects requiring reconstruction. Such defects can be functionally and aesthetically debilitating, impairing speech, mastication and swallowing; thus impacting on the patient's social interaction and quality of life (QoL). The reconstruction of such defects is often challenging and the goal thereof is to restore function and aesthetics. The donor sites commonly used to restore such defects include the fibula, scapula, thoracic rib, metatarsus, radius and iliac crest. These potential donor sites may provide both non-vascularised and vascularised bone.

A non-vascularised bone graft may be cortical, cancellous or corticocancellous. A factor distinguishing non-vascularised bone grafts from vascularised bone grafts is that non-vascularised grafts do not maintain their blood supply from their donor sites and require a stable soft-tissue bed from which they draw their blood supply and heal by creeping substitution (Wells, 1996). In non-vascularised bone grafting cases the volume of bone required to restore such defects is often insufficient (Ishii et al, 2003) and the outcome is unpredictable. In addition to this, trauma and extensive pathology often result in loss of soft tissue, such as skin, oral mucosa, subcutaneous tissue and muscle; rendering a composite microvascular flap reconstruction a necessity to restore the oral mucosa and skin of the face and the respective supporting tissue. Examples of non-vascularised bone grafts include onlay block grafts, interpositional grafts and particulate corticocancellous grafts from thoracic rib, metatarsus, radius and the anterior or posterior iliac crest.

With vascularised bone grafts an intact blood supply is maintained to the bone both during and after transplantation by blood vessels from the donor site (Wells, 1996), as in the case of temporalis osteomuscular flap. These regional flaps, however, are limited by the arch of rotation of their pedicles. With

vascularised free flaps the arch of rotation of the pedicle is no longer a limitation as the vessels at the donor site are divided, followed by the bone being transported to a recipient site and the bone being revascularised by anastomosis of the vessels in the recipient site to the artery and vein of the grafted tissue (TheFreeDictionary.com, 2019), as in the case of a vascularised free fibula flap, deep circumflex iliac artery flap, scapular osteocutaneous flap or radial forearm osteocutaneous flap.

The first free vascularised bone flap used to reconstruct a mandible defect, a rib, was performed by Mckee in 1971 (Yilmaz et al, 2008). The most commonly used free vascularised bone flaps for head and neck reconstruction are radial forearm, scapula, iliac bone using the deep circumflex iliac artery flap and vascularised free fibula flaps (Yilmaz et al, 2008). The properties, donor site morbidity, blood supply, volume and quality of available bone, the ability to be osteotomized, the length of the vascular pedicle and the ability to provide a soft tissue component by each of these potential donor sites differs.

The vascularised free fibula flap (VFFF) was first described by Taylor et al, (1975) in 1975 but only adapted to the maxillofacial region by Hidalgo in 1989 (Yim et al, 1994) and is considered by many as the gold standard for head and neck reconstruction (Ferri et al, 1997; Bodard et al, 2015). It has the benefit of providing both bone and soft tissue during reconstruction (Thankappan et al, 2008; Behnia et al, 2013; Rude et al, 2014) of these large defects and thus, re-establishing continuity of the mandible. The overall success rate of VFFF is reported to be between 90% and 100% (Colletti et al, 2014). Wijbenga et al, (2016) in their systematic review of the literature found an implant survival rate in a vascularised free fibula graft of 95% while Paraque et al, (2011) found an implant survival rate of 96.1% to 98.6% using Albrektsson's success criteria.

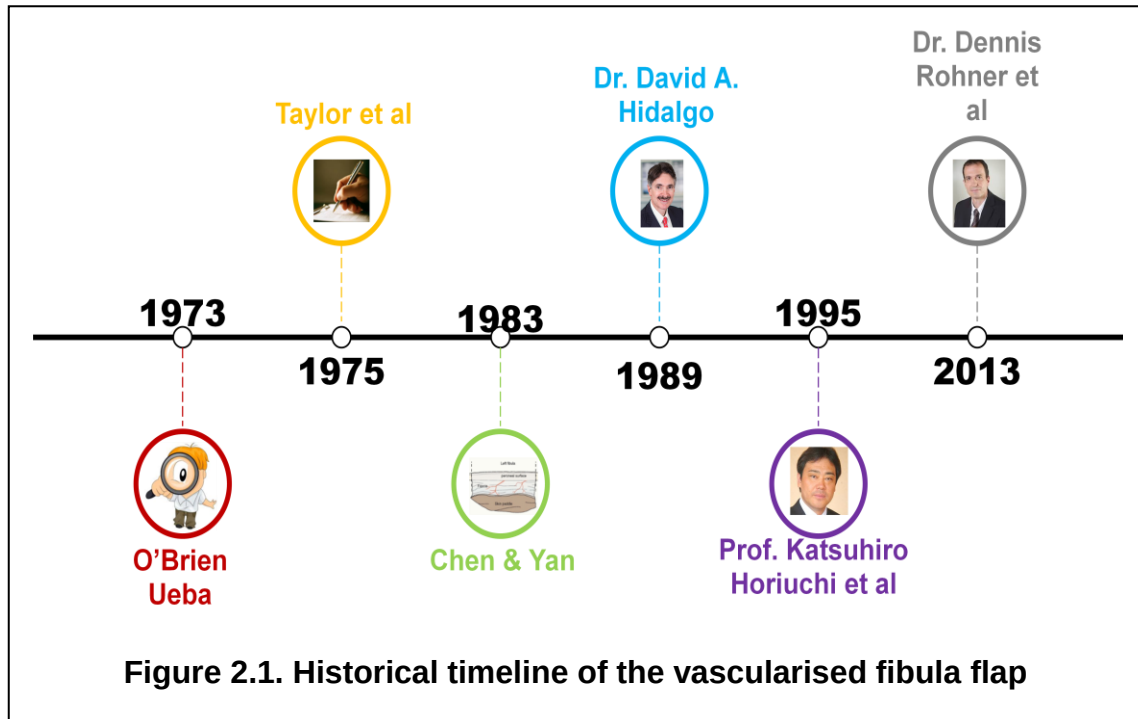
Vascularised grafts have a more predictable outcome than non-vascularised grafts especially when the defect size is extensive. However, not every patient is a candidate for vascularised grafts due to associated comorbidities, age and the morbidity and mortality associated with the procedure. Reconstruction of mandibular defects not only restores the facial aesthetics and function of an

individual but also allows the immediate or delayed placement of dental implants which subsequently allows oral rehabilitation as part of the comprehensive management of a patient.

CHAPTER 2

2. Literature Review

2.1. Historical background of the vascularised free fibula flap



The use of the fibula for a microsurgical transfer dates back to 1973 when it was first developed simultaneously by both O'Brien, in Australia, and Ueba, in Japan (Sieg et al, 1999; Catalá-Lehnen et al, 2012) and is currently used for a multitude of reconstructive procedures. In 1975 the technique was first reported and published by Taylor et al, (1975) from Melbourne. Taylor et al, (1975) used the graft to bridge a large defect of the contralateral tibia post trauma in two patients (Xu et al, 2017; Di Giuli et al, 2018; Fichter et al, 2018) as an osseous flap for the reconstruction of tibial defects (Su et al, 2014). The osteocutaneous vascularised free fibula flap for reconstruction was first reported by Chen and Yan in 1983 (Sieg et al, 1999; Punpale et al, 2006; Su et al, 2014). The use of the osteocutaneous flap enhanced the flap's ability to reconstruct composite defects (Su et al, 2014).

Hidalgo adapted the vascularised free fibula flap for use in the reconstruction of post-resection segmental mandibular defects in head and neck surgery in 1989 and numerous technical advances have been made to this technique (Cheng et al, 2018; Di Giuli et al, 2018; Fichter et al, 2018). Zlotolow et al, (1992) were the first to place osseointegrated dental implants into a vascularised free fibula flap in 1992 (Paranque et al, 2011; Hoffman et al, 2012).

In the maxillofacial region, modifications of this technique were developed and described by Horiuchi et al in 1995 (Shen et al, 2013; He et al, 2011; Chen et al, 2018). The technique is known as the double-barrel fibula free flap (DBFFF) and was developed to improve the lip support (Lee et al, 2004) as well as to double the volume of bone in the vertical plane, thus assisting with increasing the volume of bone available for the placement of dental implants as part of the comprehensive reconstruction of the patient and, thus, reducing the vertical distance to the occlusal plane in the region of the symphysis (Ferrari et al, 2013; Garcia Blanco et al, 2013; Fang et al, 2015). Chen et al agree that the support of the soft tissue of the lower third of the face was better with this technique due to the combined support of the dental rehabilitation and the bony height, however, they reported no change in the implant success rate, peri-implant bone resorption or integration of dental implants compared to a single barrel fibula flap (Chen et al, 2018). Drawbacks of the DBFFF are that it is too large for alveolar bone reconstruction and the addition in theatre time required to contour and upper strut of the double-barrel (Lee et al, 2004).

The double barrel vascularised fibula technique is recommended when the mandibular defect reaches a maximum of 15 cm (Prevost et al, 2018). It is, however, difficult to reconstruct large mandibular defects, such a hemimandibular defect, using the double barrelling technique as the fibula is usually not long enough. To overcome this pitfall Munoz Guerra et al, (2001) suggested the partial double barrel vascularised free fibula flap where the symphyseal region of the mandible is reconstructed with a DBFFF and the body region of the mandible is reconstructed with

a single fibula strut (Munoz Guerra et al, 2001; Gonzalez-Garcia et al, 2008; Shen et al, 2012; He et al, 2011).

A concern with the double barrel vascularised free fibula flap, though, is that this technique increases the operative time as well as increases the risk of vascular complications such as torsion or compression of the pedicle (Carbiner et al, 2012; Fang et al, 2015; Prevost et al, 2018). To overcome this complication, Prevost et al, (2018) suggested the positioning of vascularised free fibula flap at the alveolar level with the placement of a computer-assisted surgery (CAS) designed customized three-dimensional porous titanium implant inferiorly to prevent a discrepancy in the lower mandibular contour (Prevost et al, 2018; Shen et al, 2013). This custom implant then also ensures osteosynthesis (Prevost et al, 2018).

Other modifications of Hidalgo's technique to improve the lip support and increase the volume of bone available in the vertical plane include positioning a single-barrel fibula flap at the midpoint of the mandible rather than at the inferior border of the mandible (Lee et al, 2004), vertical distraction osteogenesis of the fibula (Su et al, 2014; Fang et al, 2015; Chen et al, 2018), the combination a vascularised fibula segment basally with a non-vascularised fibula segment superiorly (Lee et al, 2004) and the sandwich technique performed 4 months after the initial vascularised free fibula flap (Garcia Blanco et al, 2013). Further modifications to improve the stability of implants placed in a vascularised free fibula flap include the bone impacted fibula free flap (BIFFF) (Dziegielewski et al, 2014).

Placing the single-barrel fibula flap at the midpoint of the mandible reduces the vertical discrepancy but could affect the patient's facial contour (Lee et al, 2004; Kurkcu et al, 2008). Vertical distraction osteogenesis, however, increases the duration of treatment (Shen et al, 2012; Shen et al, 2013). Alignment of the fibula with the alveolar crest and vertical distraction osteogenesis decrease the vertical distance from the fibula to the occlusal plane, improves the functional rehabilitation of

patients with dental implants and address the postoperative aesthetic concerns of the patient (Shen et al, 2012).

With the technique proposed by Lee et al (2004), the inferior basal portion of the mandible is reconstructed with a conventional vascularised free fibula flap and the superior alveolar portion is reconstructed with the residual non-vascularised fibula segment (Lee et al, 2004). Advantages of this technique include that no additional donor site is required as the residual fibula is used, it is easy to contour the residual fibula segment, it improves the lower lip support and improves the implant-prosthetic mechanics by reducing the distance from the occlusal plane to the fibula (Lee et al, 2004). Disadvantages of this technique include the intervening soft tissue between the two segments and the increased susceptibility to infection due to wound dehiscence (Lee et al, 2004).

With the sandwich technique a successful vascularised free fibula flap is osteotomized four months after the initial grafting procedure and an interpositional graft of spongy iliac crest bone is placed between the two slices of the fibula flap. The upper part of the fibula was fixated in position with an osteosynthesis plates and screws places buccally. It is proposed that this increases the height of bone available for dental implant placement. (Garcia Blanco et al, 2013)

BIFFF consists of compacting milled autologous bone into the marrow space of the vascularised free fibula flap to increase the density of the fibula, primary implant stability and may improve long term implant survival rates (Dziegielewski et al, 2014; Barber et al, 2016).

A further modification of Hidalgo's technique was proposed by Rohner et al, (2013). In the technique proposed by Rohner et al, (2013) drilling and cutting guides were used to place dental implants in the fibula at the donor site according to a three-dimensional virtual plan and once the dental implants have integrated a custom osteotomy guide is used to harvest the fibula and create the required osteotomies which is then grafted to the mandibular defect using the prosthesis as a fixation device.

Drawbacks of this technique are that the patient requires two surgical procedures and the patient would go without reconstruction during the period of dental implant osseointegration (Qaisi et al, 2016). The Institute for Reconstructive Science in Medicine modified Rohner et al's technique and called it the Alberta Reconstructive Technique (ART). ART is similar to Rohner et al's technique but does not wait for osseointegration of dental implants in the leg but, rather, the fibula is osteotomized during the same procedure and osseointegration of dental implants in the fibula occurs at the recipient site (Chuka et al, 2017).

Levine et al coined the term "jaw in a day" in 2013. This is an occlusion-driven approach in which the position of the dental implants in the vascularised free fibula flap is digitally planned during the virtual surgical planning. Using Computer-aided design and computer-aided manufacturing (CAD / CAM) technology a prosthesis is constructed preoperatively. Intraoperatively dental implants are placed in the fibula at the donor site and the fibula is then osteotomized. Using an occlusal splint, the fibula-and-prosthesis complex is positioned in relation to the remaining segments of the mandible and the opposing dentition. A maxillofacial prosthodontist then checks the occlusion during surgery. Advantages of this technique include early restoration of form and function, a decrease in the number of procedures and general anaesthetics and excellent access to the fibula at the time of harvest. However, this technique is still relatively new and, despite early results being favourable, the impact on the vascularised free fibula flap survival rate and implant success rate is not known. In addition, should the flap fail there would be a significant loss in terms of the cost of the dental implants and prosthesis. (Qaisi et al, 2016)

Sometimes multiple flaps may be necessary to reconstruct multiple defects in the region. In such situations a modification of the technique of Hidalgo can be used known as the chimeric fibula flap (Kannan et al, 2013; Roan et al, 2013). This technique provides bone, muscle and multiple skin paddles all attached to a single vascular source, thus providing an outer lining, inner lining, volume filling and skeletal support

for a complex oromandibular defect. Its ability to provide three-dimensional multifunctional reconstruction is an advantage of the chimeric fibula flap. Disadvantages of this technique, however, include increased dissection and increased possibility of damage to the flap and due to the varying weights of the different component tissues there is a tendency for the different leaf components of the chimeric fibula flap to undergo torsion and cause intraluminal thrombosis, a concept known as the “puppeteer” effect. (Kannan et al, 2013)

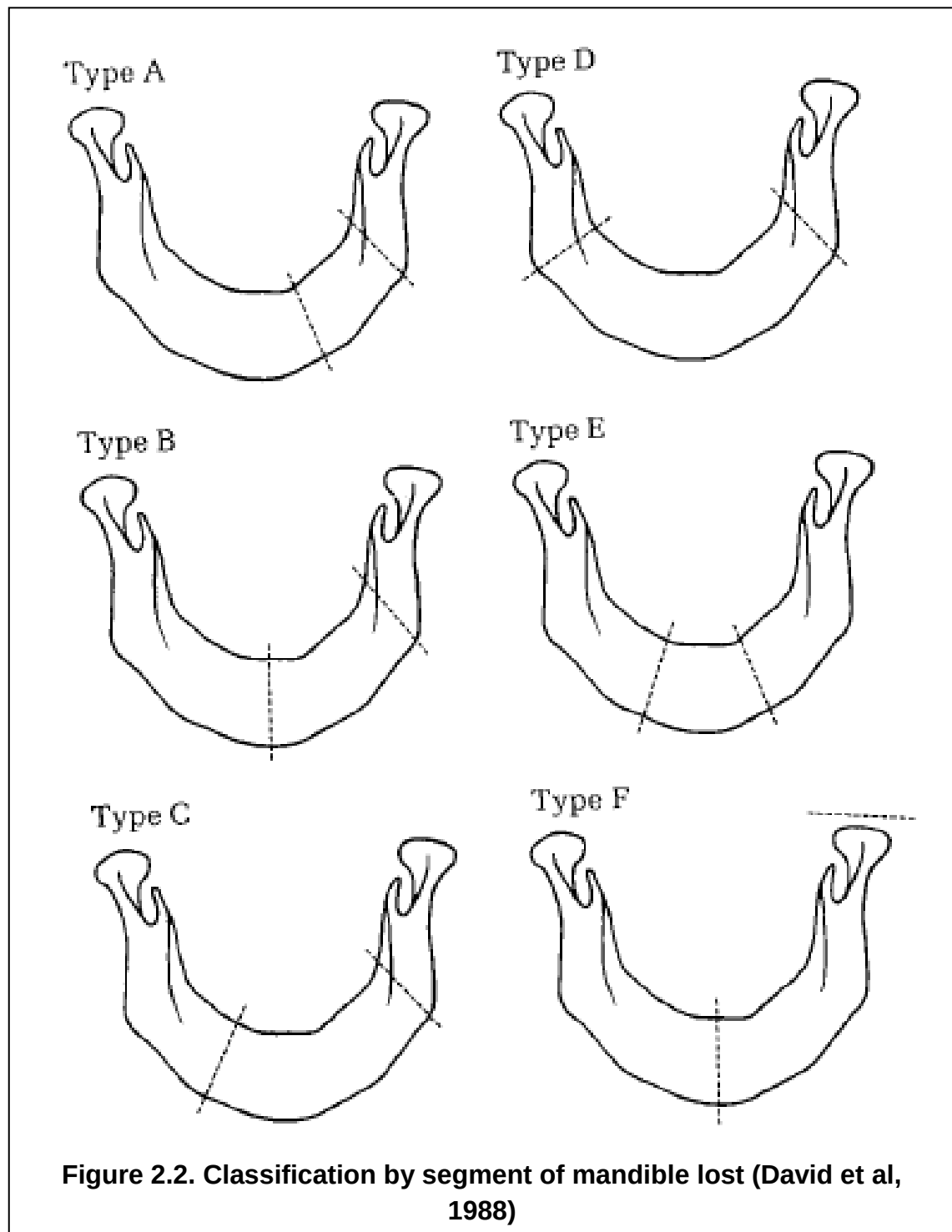
2.2. Classification of mandibular defects

A Pubmed and Science Direct search of the English literature found numerous classifications of mandibular defects. The first classification of mandibular defects was by Pavlov in 1974, who classified mandibular defects by the number of bone fragments that remained after treatment (Brown et al, 2016). (Table 2.1)

Table 2.1. Classification of mandibular defects by Pavlov (Brown et al, 2016)	
Class	Number of remaining bone fragments
Class I	1
Class II	2
Class III	3

Subsequent to Pavlov eight other classification systems have been published. In 1988 David et al proposed a classification which was anatomically based on the margins at either end of the segment of the mandible that was lost (David et al, 1988). (Figure 2.2; Table 2.2)

Table 2.2. Classification of mandibular defects by David et al (David et al, 1988)	
Type	Description
Type A	Short segment confined to one side
Type B	Unilateral angle to symphysis
Type C	Between angle and body on the contralateral side
Type D	Angle to angle
Type E	Symphysis
Type F	Hemimandible, including the ipsilateral mandibular condyle



This was followed by Jewer et al's classification in 1989, a classification most widely cited in the literature, which was based on the extent of the margin of bone loss at each end (Jewer et al, 1989). (Figure 2.3; Table 2.3)

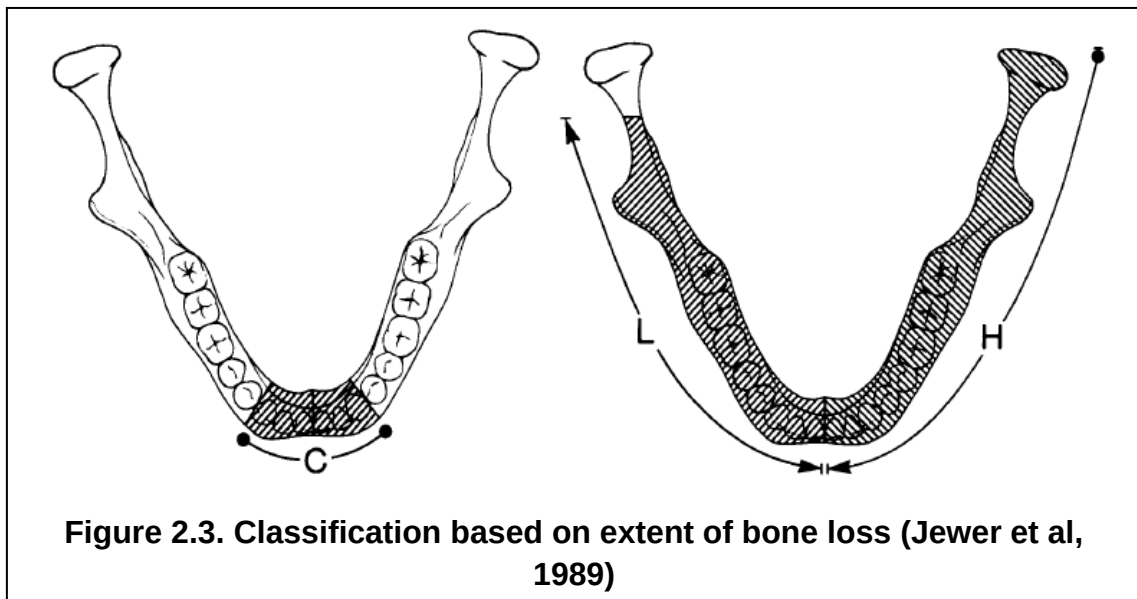


Table 2.3. Classification of mandibular defects by Jewer et al (Brown et al, 2016)	
Reconstruction class	Bony defect
C	Defect includes both canines
L	Unilateral defect, no condyle but can cross midline
H	Unilateral condyle but can cross midline
LC	Lateral defect and both canines
HC	Lateral defect and condyle including both canines
LCL	Bilateral lateral defects including both canines but not condyles
HCL	Condyle, lateral defect, central defect and contralateral lateral defect
HH / HCH	Entire mandible

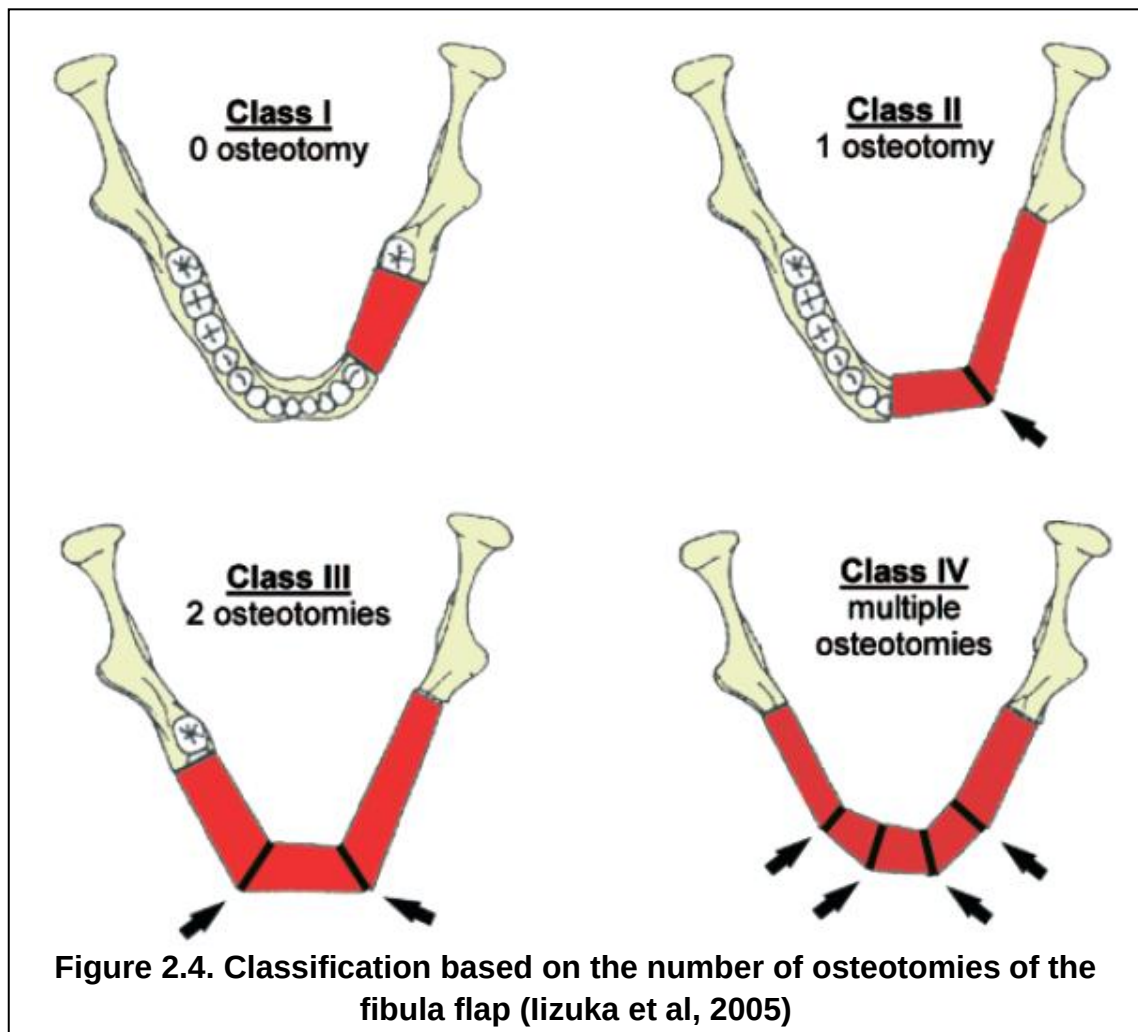
Urken et al in 1991 proposed a purely descriptive classification (Brown et al, 2016). (Table 2.4)

Table 2.4. Classification of mandibular defects by Urken et al (Brown et al, 2016)	
Classification	Description
C	Condyle
R	Ramus
B	Body
S	Symphysis
S ^H	Stops at the midline

In 1993 Boyd et al modified the classification by Jewer et al and added a component denoting the involvement of mucosa and / or skin denoted by a lower case letter added to the HCL classification (Boyd et al, 1993). (Table 2.5)

Table 2.5. Modification of HCL classification by Boyd et al (Boyd et al, 1993)	
Defined as the HCL classification plus one of the lower case letters below	
Soft tissue component	Description
o	Neither a skin nor a mucosal component
s	Skin
m	Mucosa
sm	Skin plus mucosa

A classification based on the number of osteotomies of the fibula flap was published in 2005 by Iizuka et al (Iizuka et al, 2005). (Figure 2.4)



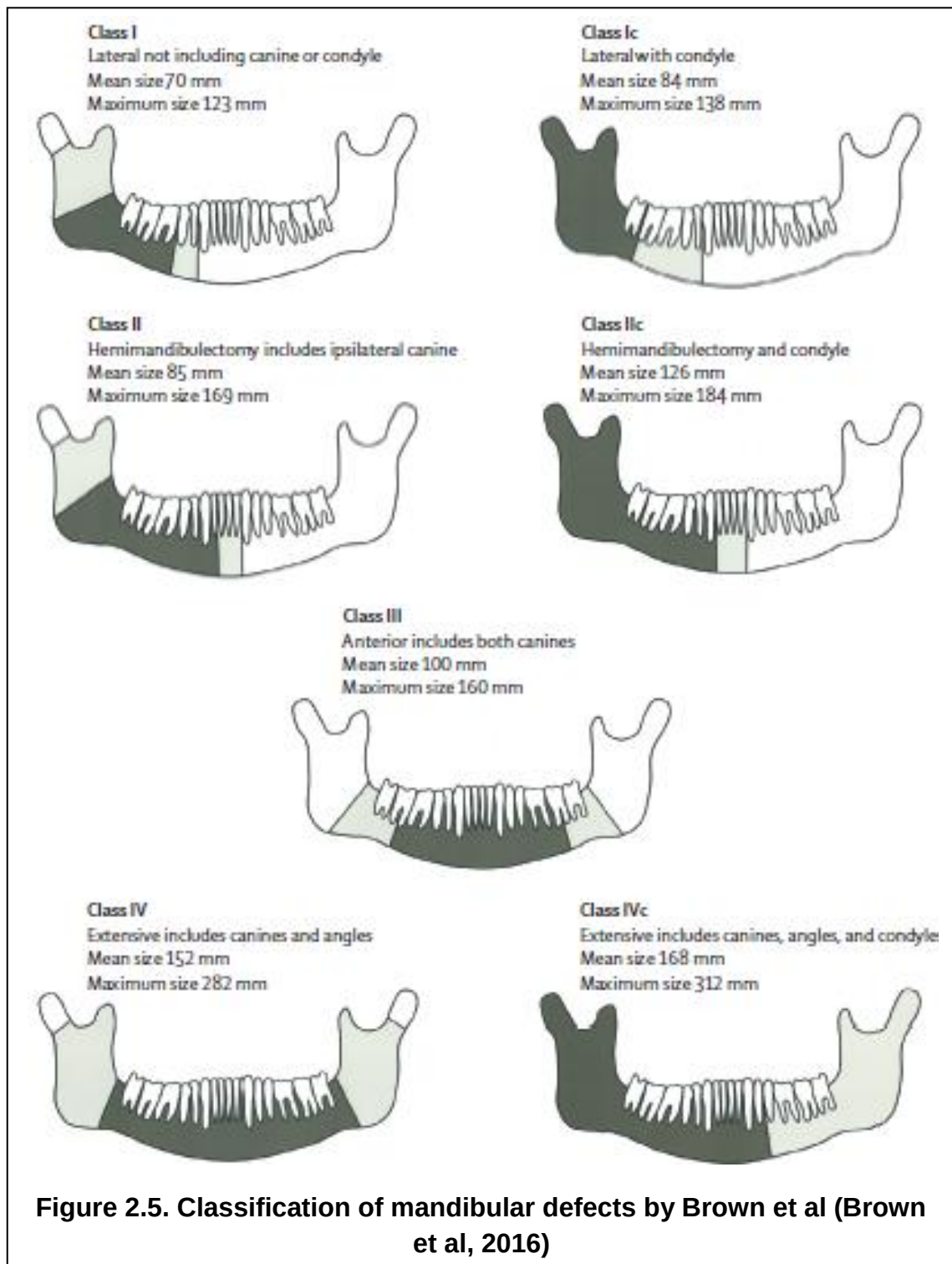
Hashikawa et al's classification in 2008 was based on the anatomical structure of the mandible that is lost (Brown et al, 2016). (Table 2.6)

Table 2.6. Classification of mandibular defects by Hashikawa et al (Brown et al, 2016)	
Classification	Description
C	Loss of condylar head
A	Loss of angle
T	Loss of mental tubercle
CAT	Hemimandible

The absence or presence of the condyle in the lost segment was the system used to classify defects published by Baumann et al in 2011 (Baumann et al, 2011). (Table 2.7)

Table 2.7. Classification of mandibular defects by Baumann et al (Baumann et al, 2011)	
Type	Description
Type Ia	Segmental bony defect, either anterior or lateral, with intact condyle Soft tissue defects limited to intraoral mucosal defects
Type Ib	Segmental mandibular defect plus through-and-through soft tissue defect
Type IIa	Posterior or hemimandibulectomy defects with ramus and condyle removed
Type IIb	Posterior or hemimandibulectomy defects with ramus and condyle removed plus through-and-through soft tissue defect

The latest classification of mandibular defects is that proposed by Brown et al in 2016 which is based on the four corners of the mandible (Brown et al, 2016). (Figure 2.5)



2.3. Anatomy of the vascularised free fibula flap

The fibula has an endosteal as well as a periosteal blood supply, thus having a dual blood supply (Yim et al, 1994; Su et al, 2014; Fichter et al, 2018). The endosteal supply is derived from the nutrient artery while the periosteal supply is provided by various segmentary branches that enter

the periosteum through the muscle insertions (Serra et al, 1991). Both the nutrient artery and the segmentary periosteal branches arise from the peroneal artery which courses parallel to the long axis of the fibula (Futran et al, 1998; Clemenza et al, 2000; Bahr, 1998) and arises as the external branch of the tibioperoneal trunk (Serra et al, 1991; Hoffman et al, 2012). The inner two thirds of the cortex receives its blood supply mainly from the endosteal supply while the outer third is supplied mainly by the periosteal blood supply (Lee et al, 1995) and the two routes are collaterals in that the one increases when the other is compromised (Bahr, 1998). The venous drainage of the fibula is by the vena comitantes (Futran et al, 1998; Clemenza et al, 2000; Lyberg et al, 1991).

If the vascularised free fibula flap is accompanied by a cutaneous component the arterial supply to this is derived from direct cutaneous branches of the peroneal artery and by perforating branches from the circulation of the soleus muscle. (Serra et al, 1991)

This makes the peroneal artery the dominant arterial supply to the vascularised osteocutaneous free fibula flap. Survival is dependent on the abundant periosteal blood supply which is more important than the endosteal blood supply and thus allows the fibula to be osteotomized into multiple segments. The two venae comitantes constitute its venous drainage. (Su et al, 2014)

2.4. The fibula as a suitable donor site for mandibular defects and its comparison with other potential donor sites

Currently mandibular defect reconstruction may be achieved using either synthetic materials (i.e. Silicone or titanium), non-vascularised bone grafts or vascularised bone grafts (Serra et al, 1991; Anthony et al, 1997). Synthetic materials have pitfalls such as frequent infection, rejection and breakage which affect return to masticatory function (Serra et al, 1991). Non-vascularised bone grafts, on the other hand, may undergo resorption and necrosis (Serra et al, 1991). This unpredictable

resorption makes them mainly beneficial for small defects with adequate soft tissue coverage (Behnia et al, 2013).

According to Serra et al, (1991) vascularised bone grafts that can be used to reconstruct mandibular defects should:

- Be strong
- Allow for potential shaping to reconstruct the symphysis
- Have adequate length to reconstruct a hemimandible
- Have a vascular pedicle that is long enough
- Have an easy method of harvesting to shorten the operative time
- Have no sequelae at the donor site
- Allow for harvesting of a potentially needed segment of skin

(Serra et al, 1991)

In addition the vascularised bone graft should, where applicable, be able to accommodate the subsequent placement of dental implants for comprehensive dental rehabilitation and allow for harvesting of required muscle and subcutaneous tissue.

The fibula, the flexor muscles and the overlying skin supplied by the peroneal vessels has been proposed as a suitable donor site for the microsurgical transfer of osteocutaneous tissue (Sieg et al, 1999). Numerous other donor sites have been used for mandibular reconstruction, including, iliac, scapula, radius, metatarsus and rib (Ferrari et al, 2013; Colletti et al, 2014; Kim et al, 2016). These other donor sites have limitations, complications and disadvantages in comparison to the vascularised free fibula flap.

Despite iliac crest (Deep circumflex iliac artery flap [DCIA]) being able to provide significant volumes of bone, harvesting can lead to injury to the femoral cutaneous nerve, pelvic fractures, abdominal herniation and prolonged gait pain (Munoz Guerra et al, 2001; Ishii et al, 2003; Gonzalez-Garcia et al, 2008). Even though it provides a significant volume (Chen et al, 2018), it is primarily cancellous bone that does not

provide acceptable primary stabilization of dental implants (Reychler et al, 1996) and lacks a segmental blood supply (Hidalgo, 1994). Furthermore, contouring is hampered by the predetermined shape (Hidalgo, 1994; Horiuchi et al, 1995; Celebioglu et al, 1998). However, it allows for better temporomandibular joint (TMJ) movement compared to the fibula when used to reconstruct the TMJ (Yilmaz et al, 2008). Lastly, it provides an adequate skin paddle for large composite defects but lacks mobility (Yilmaz et al, 2008; Chen et al, 2018).

The metatarsus provides a limited length of bone and displays greater morbidity due to delayed healing (Lee et al, 1995; Celebioglu et al, 1998; Gonzalez-Garcia et al, 2008).

Although the scapula (Scapula free flap) can provide adequate height for dental implants it is limited in terms of its width and length (Munoz Guerra et al, 2001; Ishii et al, 2003; Gonzalez-Garcia et al, 2008). In addition the bone lacks a segmental blood supply, limiting the number of osteotomies that can be safely performed (Hidalgo, 1994). A longer operative time has also been reported during harvesting (Horiuchi et al, 1995) as it cannot be done during the resection by a second team (Bahr et al, 1998; Punpale et al, 2006; Lopez-Arcas et al, 2010).

The radial forearm osteocutaneous flap has limited length and inadequate volume for placement of dental implants (Munoz Guerra et al, 2001; Ishii et al, 2003; Gonzalez-Garcia et al, 2008) and precarious vascularisation (Reychler et al, 1996). In addition donor site morbidity is relatively high as it can lead to fracture of the donor radius (Ishii et al, 2003; Gonzalez-Garcia et al, 2008; Lopez-Arcas et al, 2010).

The harvesting of a rib carries the risk of development of a subsequent pneumothorax (Serra et al, 1991). It may not be feasible to place dental implants in a rib due to its inadequate thickness (Lee et al, 1995; Punpale et al, 2006; Gonzalez-Garcia et al, 2008). It is not possible to work in two teams and osteotomies may not be feasible (Punpale et al, 2006).

The fibula, due to its cortical bone content, is denser and has superior resistance to torque stress compared to other donor sites (Munoz Guerra et al, 2000), appears to enable effective placement of dental implants and provides a large segment of bone with acceptable blood supply and soft tissue coverage (Behnia et al, 2013; Yilmaz et al, 2008) that is easier to harvest with less blood loss (Yilmaz et al, 2008). The skin paddles of a vascularised free fibula flap are thin and pliable when compared to the bulky skin paddles of other osseous sites (Chen et al, 2018). Compared to other donor sites the ratio of the cortex to the medulla of the fibula is closest to the mandible making it a very suitable site for dental implantation (Dziegielewski et al, 2014; Chuka et al, 2017; Chen et al, 2018). When compared to the scapula and iliac crest, the fibula loses the least volume of bone due to resorption over time (Wilkman et al, 2017). In addition, harvesting is easier and it is associated with reduced donor site morbidity (Munoz Guerra et al, 2000; He et al, 2011). According to Hidalgo there are only two situations where another flap is preferred to a fibula, namely, a mandibular defect that has significant internal and external soft tissue components as in these patients the goal of bone reconstruction is secondary to achieving wound healing and, secondly, lesions involving the retromolar trigone that extend to involve the oropharynx, soft palate and tongue as the bone component is often limited in these cases (Hidalgo, 1994). To address this concern and to make up the soft tissue needed a vascularised free fibula flap and another vascularised flap can be harvested.

In addition, the blood supply in these flaps also differs with the radial forearm and scapula free flaps having only a periosteal supply while the iliac crest and fibula free flaps have both a periosteal and endosteal blood supply (Yilmaz et al, 2008).

2.5. Indications

The vascularised free fibula flap is indicated for:

- 2.5.1. Reconstruction of ablative mandibular tumour surgery (Yim et al, 1994; Salinas et al, 2010; Zavattero et al, 2015) and defects

resulting from trauma, osteomyelitis or osteoradionecrosis (Yim et al, 1994)

- 2.5.2. Reconstruction of the temporomandibular joint with the proximal head of the fibula (Sieg et al, 1999; Wax et al; 2000)
- 2.5.3. Reconstruction of oral and / or pharyngeal mucosal defects and facial or cervical skin defects using the harvest skin flap (Sieg et al, 1999; Avraham et al, 2014)
- 2.5.4. Reconstruction of the floor of mouth or replacement of soft tissue in the neck using the flexor hallucis longus muscle that may be taken together with the fibula as a osteomuscular or osteomyocutaneous flap (Hidalgo, 1994; Sieg et al, 1999; Horiuchi et al, 1995)
- 2.5.5. Secondary reconstruction of the ramus-subcondylar unit in paediatric patients with syndromic and non-syndromic deformities (Salinas et al, 2010)
- 2.5.6. Reconstruction of previous reconstruction failures (Avraham et al, 2014)
- 2.5.7. Reconstruction of an atrophic mandible or after treatment of refractory mandibular osteomyelitis (Salinas et al, 2010)

2.6. Contraindications

The vascularised free fibula flap is contraindicated in patients with:

- 2.6.1. Vascular anomalies (Kelly et al, 2007; Klein et al, 2013; Sugiura et al, 2018)
- 2.6.2. Advance stages of artherosclerosis as the peroneal artery may be the only remaining vessel perfusing the foot (Hoffman et al, 2012; Klein et al, 2013; Sugiura et al, 2018)
- 2.6.3. A blood supply to the lower leg less than 3 patent vessels, namely the anterior tibial, posterior tibial and peroneal arteries (Sugiura et al, 2018)
- 2.6.4. Absence of the peroneal artery (Clemenza et al, 2000; Hoffman et al, 2012)
- 2.6.5. Peroneal arteria magna (Clemenza et al, 2000; Kelly et al, 2007; Hoffman et al, 2012)

- 2.6.6. Short lateral defects who do not wish to undergo osseous reconstruction (Anthony et al, 1997)
- 2.6.7. Conditions making them health compromised (Behnia et al, 2013) or too medically unstable (Anthony et al, 1997)

2.7. Advantages

The vascularised free fibula flap is known to have the following advantages over other potential donor sites:

- 2.7.1. The significant volume of bicortical bone that can be used for reconstruction of defects crossing the midline (van Gemert et al, 2018; Fichter et al, 2018; Chen et al, 2018)
- 2.7.2. The good strength and quality of the cortical bone (Dziegielewski et al, 2014; Sozzi et al, 2017; Cheng et al, 2018)
- 2.7.3. The straight shape (Hidalgo, 1994; Kelly et al, 2007; Gonzalez-Garcia et al, 2008) and its resistance to pressure and torsion (Hidalgo, 1989; Lopez-Arcas et al, 2010)
- 2.7.4. The ability to be contoured to follow the mandibular contour with multiple osteotomies due to its periosteal blood supply (Di Giuli et al, 2018; van Gemert et al, 2018; Fichter et al, 2018; Chen et al, 2018)
- 2.7.5. The ability to accommodate the subsequent placement of dental implants (Sozzi et al, 2017; Di Giuli et al, 2018; Chen et al, 2018)
- 2.7.6. Consistent vascular anatomy (Celebioglu et al, 1998; Garrett et al, 2006)
- 2.7.7. The long vascular pedicle with large-diameter vessels (Bao et al, 2017; van Gemert et al, 2018; Chen et al, 2018)
- 2.7.8. Its rich periosteal blood supply (Lopez-Arcas et al, 2010; Parbo et al, 2013; Fang et al, 2015)
- 2.7.9. The ability to dissect multiple perforators which allows several skin paddles to be harvested (Chen et al, 2018)
- 2.7.10. The possibility for two surgical teams to operate simultaneously, one team operating at the head while the second team harvest the fibula, resulting in cost effectiveness and a shorter operating time (Sozzi et al, 2017; Xu et al, 2017; Chen et al, 2018)

- 2.7.11. The ability to withstand high doses of radiation (Serra et al, 1991; He et al, 2011)
- 2.7.12. The vascularised osteocutaneous free fibula flap provides a greater freedom of motion for insertion compared to other pedicled flaps (Anthony et al, 1997; Horiuchi et al, 1995)
- 2.7.13. The ability to not result in growth retardation (Ferri et al, 1997)
- 2.7.14. Minimal donor site morbidity (Shan et al, 2016; Vittayakittipong et al, 2016; Cheng et al, 2018;)

2.8. Disadvantages

Despite its numerous advantages, the vascularised free fibula flap is known to have some disadvantages, namely:

- 2.8.1. Its limited vertical height particularly in the case of the reconstruction of a dentate mandible (Su et al, 2014; Barber et al, 2016; Chen et al, 2018)
- 2.8.2. The development of undesirable lever forces within the prosthetic supraconstruction as a result of the graft having to be positioned relatively inferiorly to allow for preservation of the facial profile which subsequently creates the need for the use of extended implants to bridge the distance to the occlusal plane (Shen et al, 2012; Shen et al, 2013; Chen et al, 2018)
- 2.8.3. An increased number of osteotomies may lead to decreased vitality of the distal segments (Ferri et al, 1997; Yilmaz et al, 2008)
- 2.8.4. The amount of soft tissue that can be harvested due to the risk of failure of the skin paddle (Hidalgo, 1994; Lopez-Arcas et al, 2010)
- 2.8.5. A hairy lateral distal calf may be disadvantageous for intraoral or pharyngeal tissue reconstruction (Sieg et al, 1999)
- 2.8.6. Aesthetic sequelae along the lateral part of the leg, especially in females (Ferri et al, 1997; Peled et al, 2005; Yilmaz et al, 2008)
- 2.8.7. Rarely, lower limb ischaemia (Clemenza et al, 2000)

2.9. Mandatory preoperative assessments

Standard mandatory preoperative assessments of a surgical patient undergoing significant surgery include haematologic studies for a full blood count and urea and electrolytes, a chest radiograph and an Electrocardiogram (ECG).

In addition to clinical examination and the standard preoperative assessments of a surgical patient it is important to accurately assess the arterial and venous circulation of the lower limb and, although the preferred method is controversial, this is best achieved using Digital Subtraction Angiography (DSA) (Clemenza et al, 2000; Hoffman et al, 2012; Klein et al, 2013) but can also be achieved using Computerized Tomographic Angiography (CTA) or Magnetic Resonance Angiography (MRA) (Hoffman et al, 2012; Wang et al, 2012; Colletti et al, 2014) or Colour Duplex Sonography (CDS) (Hoffman et al, 2012; Wang et al, 2012; Klein et al, 2013).

DSA is expensive, invasive and can be associated with morbidity, namely, haematoma formation, thrombosis, vessel injury, contrast reaction and embolism. CDS can accurately map the flow of the vessels at a low cost and with no morbidity, however, it is not reproducible and does not produce a two-dimensional (2D) or three-dimensional (3D) image. CTA accurately predicts the course and location of the vessels, is able to visualize vessels up to 0.3mm in diameter and provides a 3D image of the artery, however, it is necessary to use radiation and an iodinate contrast medium. MRA is similar to CTA but has difficulty visualizing smaller diameter vessels, however, does not use radiation or a contrast medium. (Hoffman et al, 2012; Wang et al, 2012; Klein et al, 2013)

MRA, however, is expensive, requires a special coil to enhance the image and patients can feel claustrophobic while CDS is less costly and non-invasive (Futran et al, 1998; Clemenza et al, 2000). In addition,

neither angiography nor MRA can indicate the presence and number of cutaneous perforators (Futran et al, 1998).

2.10. Alternative assessments

Despite providing limited information, Doppler probe monitoring is a diagnostic alternative to CTA (Sieg et al, 1999; Lou et al, 2019). Abou-Foul et al, (2017) suggest that vascular mapping at minimal or no additional cost or risk will assist in assessing the adequacy of the perfusion of the foot, the vascular anatomy, the cutaneous perforators and the blood supply of the fibula.

2.11. Surgical techniques for harvesting a vascularised free fibula flap and their comparison

The fibula may be approached via a lateral or medial approach. The lateral approach was first described by Gilbert in 1979 (Sieg et al, 1999; Lopez-Arcas et al, 2010; Rude et al, 2014). With this technique an incision is made along the middle third of the lateral aspect of the leg. (Serra et al, 1991) (Figure 2.6)



Figure 2.6. Lateral approach to fibula

This is followed by blunt dissection between the peroneal and soleus muscles until the fibula is reached. (Serra et al, 1991) (Figure 2.7)

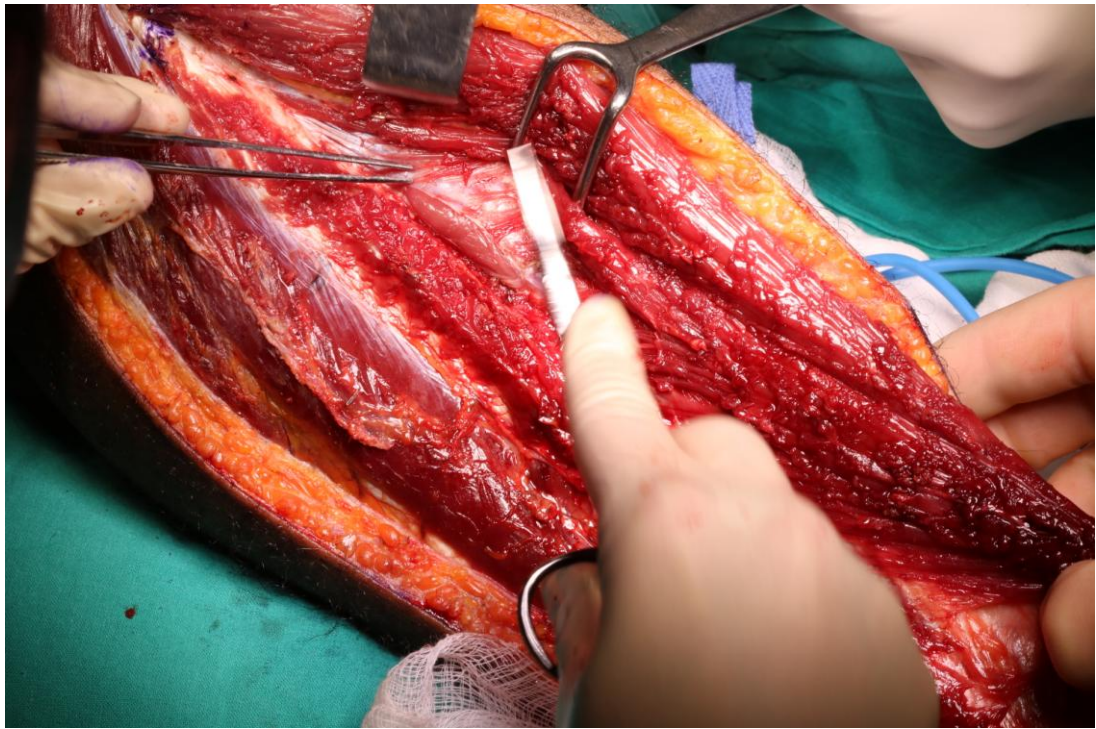


Figure 2.7. Blunt dissection to fibula

A minimum of 1cm of peroneal muscle insertion must be left on the bone to preserve the periosteal blood supply. The fibula is then osteotomized leaving 3cm to 4cm proximally and 10cm distally so as not to interfere with the involved joints and to reduce the risk of common peroneal nerve injury. (Serra et al, 1991) (Figure 2.8)

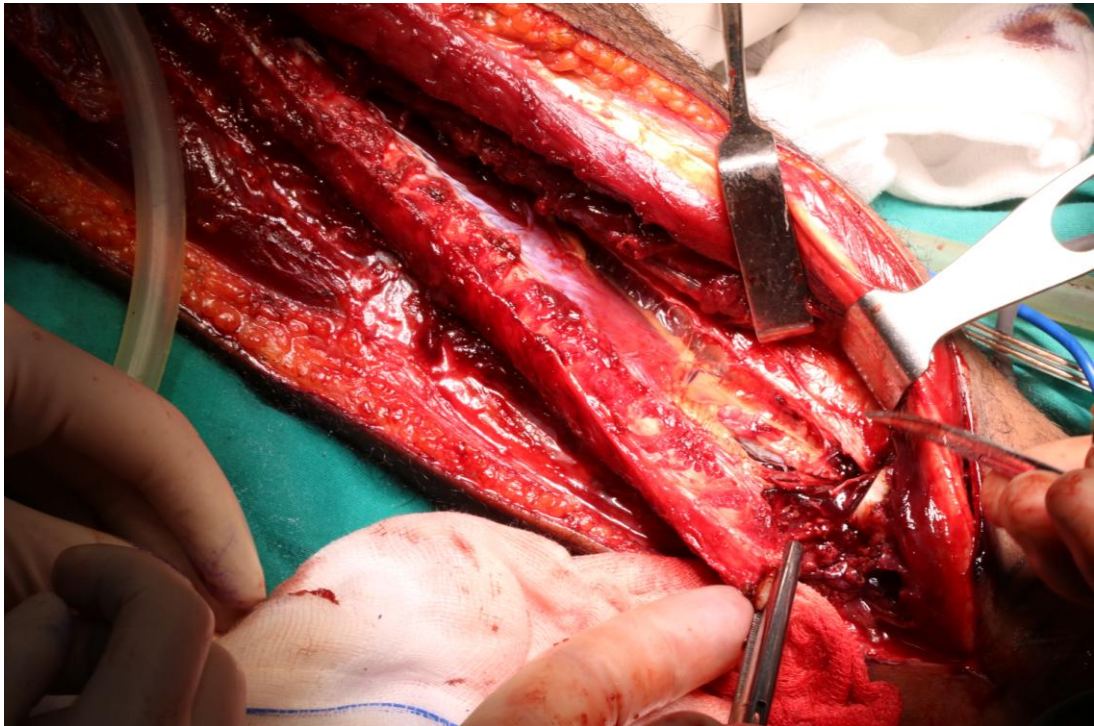


Figure 2.8. Distal osteotomy of fibula

If a cutaneous paddle is required to restore a soft tissue defect the superficial fascia of the peroneal muscles, the soleus and the intermuscular partition is preserved during dissection in order to harvest the greatest number of vessels. (Serra et al, 1991) (Figure 2.9)



Figure 2.9. Harvesting of fibula with cutaneous paddle

Following harvesting closure depends on whether a cutaneous paddle was harvested or not. If only an osseous flap was harvested, primary closure is in layers while if an osteocutaneous flap is harvested, closure will require a skin graft. (Serra et al, 1991)

The medial approach was first described by Blake et al in 2008 (Sieg et al, 1999; Serra et al, 1991; Rude et al, 2014). With this technique an incision is made along the middle third of the medial aspect of the leg. This is followed by blunt dissection between the flexor digitorum longus and soleus muscles until the posterior tibial pedicle is encountered. The posterior tibial artery is then followed superiorly until the point of bifurcation which denotes the origin of the peroneal artery. The peroneal artery is then dissected in a caudal direction to the desired length of the fibula. At this point the peroneal artery is ligated and the fibula osteotomised distally and proximally leaving a length of at least 7cm distally so as not to interfere with the involved joint. (Blake et al, 2008)

The use of the lateral approach has been reported to obstruct the view of the pedicle while the medial approach allows the surgeon to directly visualize and assess the pedicle for any anatomic or vascular anomaly that may not have been identified on pre-operative imaging. However, the lateral approach allows one or more cutaneous paddles to be harvested along with the osseous flap. When compared with a medial approach this is not feasible as preparation of the perforator vessels perfusing the skin is impossible. The medial approach is only beneficial in that the scar is left on the medial surface of the leg, a less conspicuous location, especially in females. Lastly, use of the medial approach allows harvesting of a venous graft from the major saphenous vein, should it be required, because it is located within the operation field. (Catala-Lehnen et al, 2012)

2.12. Previous and current methods of planning for surgery

Prior to 2005 virtual surgical planning (VSP) was not used (Chuka et al, 2017). Contouring of the fibula graft to the mandibular defect was first

performed by the surgeon's clinical experience and clinical judgment (Bao et al, 2017; Zhang et al, 2016). Subsequent to this technique, a reconstruction plate was contoured to the mandible before resection of the involved segment so that it can be used as a template to contour the fibula graft (Thankappan et al, 2008). This technique has limitations in that it is not possible when the hemimandible is either absent or distorted by pathology (Thankappan et al, 2008). In addition, this process is time-consuming and imprecise (Avraham et al, 2014; Sieira Gil et al, 2015). Furthermore, any alteration in the alignment of the reconstruction plate and the remaining mandibular segments could result in aesthetic and functional alterations due to a resultant malocclusional and / or temporomandibular disorder (Tarsitano et al, 2015). In the case of a vascularised free fibula flap this resulted in an extended ischemia time and manoeuvres that are risky and compromised the vascular pedicle (Succo et al, 2015).

Currently virtual surgical planning (VSP) and computer-aided design / computer-aided manufacturing (CAD / CAM) and rapid prototype modelling (RPM) is performed with the aid of three-dimensional (3D) computer planning software. VSP attempts to address the impreciseness of a surgeon contouring a reconstruction plate to a mandibular defect and allows the consideration of the three-dimensional positioning of the flap (Avraham et al, 2014). Avraham et al, (2014) found that VSP allowed precise positioning of dental implants using prefabricated positioning guides. CAD is used to perform the virtual osteotomy and subsequently measure the length and angles of the bone segments required to reconstruct the defect (Shen et al, 2017). CAD / CAM and RPM is used to print a 3D stereolithographic model onto which a titanium reconstruction plate is pre-bent and from which a osteotomy guide for the osteotomy of the fibula graft is designed (Shen et al, 2017). Osteotomy guides are used to achieve accurate osteotomy angles and directions (Bao et al, 2017; Succo et al, 2015; Tarsitano et al, 2015; Zhang et al, 2016) and to allow for translation of the preoperative plan (Toto et al, 2015). The pre-bent titanium plate is used to connect and space the segments according to the correlation of their contour to that of

the shape of the neomandible (Bao et al, 2017) and, further, prevent excessive mental and gonial projection, malocclusion and torque on the condylar head (Toto et al, 2015).

The use of 3D computer planning software, a pre-bent reconstruction plate and a osteotomy guide results in improved planning options, more accurate osteotomies of the linear fibula, a more predictable surgical, functional and aesthetic outcome, a decreased ischemic time of the vascularised free fibula flap and a shortened surgical time (Chuka et al, 2017; Weitz et al, 2018; Prevost et al, 2018). It is proposed that the decreased ischemic time may be due to the ease and speed associated with osteotomy guides and preformed plates and due to the surgeon having the option to conform the fibula to the preformed plate with the flap still perfused at the donor site before transfer to the recipient bed (Culie et al, 2016; Bao et al, 2017). In addition the variability between different surgeons due to experience can be minimized, younger surgeons can be trained to undertake complex surgery and VSP allows interdisciplinary discussions with ablative, reconstructive and dental teams regarding implant positions thus accelerating oral rehabilitation of the patient (Avraham et al, 2014; Ritschl et al, 2017).

However, disadvantages include the time needed to prepare VSP, the considerable additional cost and the absence of flexibility in intraoperative strategy changes (Bao et al, 2017; Ritschl et al, 2017; Weitz et al, 2018). Some argue that the additional cost is offset by the reduced time in the operating theatre due to the use of this technology (Sieira Gil et al, 2015; Succo et al, 2015; Toto et al, 2015). To combat these disadvantages Weitz et al, (2018) have developed a semi-standardized resection and cutting guide for mandibular reconstruction with the vascularised free fibula flap which does not require virtual planning and results in reduced financial costs. Limitations of this guide, however, include the length of the symphysis being fixed at 32mm which could lead to a wide chin contour and that it is only usable for defects classified as L, LC and LCL as per the classification of mandibular defects by Jewer et al (Weitz et al, 2018). This guide will still need to be

tested further in a multicentre study and compared further with the VSP procedure.

The most recent technique for reconstruction of a mandibular defect with a vascularised free fibula flap has been reported by Shen et al (2017). The technique described involves a mandibular fixation device combined with surgical navigation. The mandibular fixation device maintains the width of the mandible, maintains the position of the ramus and condylar segment in the glenoid fossa especially in the absence of a stable occlusion after resection of the tumour. This is achieved while remaining out of the operating field. In addition they are reusable and cheap. Surgical navigation makes use of reference points for the shaping and positioning of the vascularised free fibula flap. This technique has been proposed for use primarily in reconstruction of angle-to-angle mandibular defects where it is difficult to maintain the mandibular width and to position the reconstructed gonion without a reference point. (Shan et al, 2016; Shen et al, 2017)

2.13. Computer simulated planning

VSP and CAD / CAM allow conversion of computered tomographic (CT) scan to a 3D printed model. In the case of a tumour of the maxillofacial region the process begins by uploading Digital Imaging and Communications in Medicine (DICOM) data obtained from a CT scan of the patient taken from the vertex of the skull or base of skull to the hyoid bone into a software program, for example Freeform. The same is done with the CT scan of the patient's fibula. The software program utilizes bony windows from three planes (Axial, coronal and sagittal) and combines them to create a 3D skull and 3D fibula. (Figure 2.10)

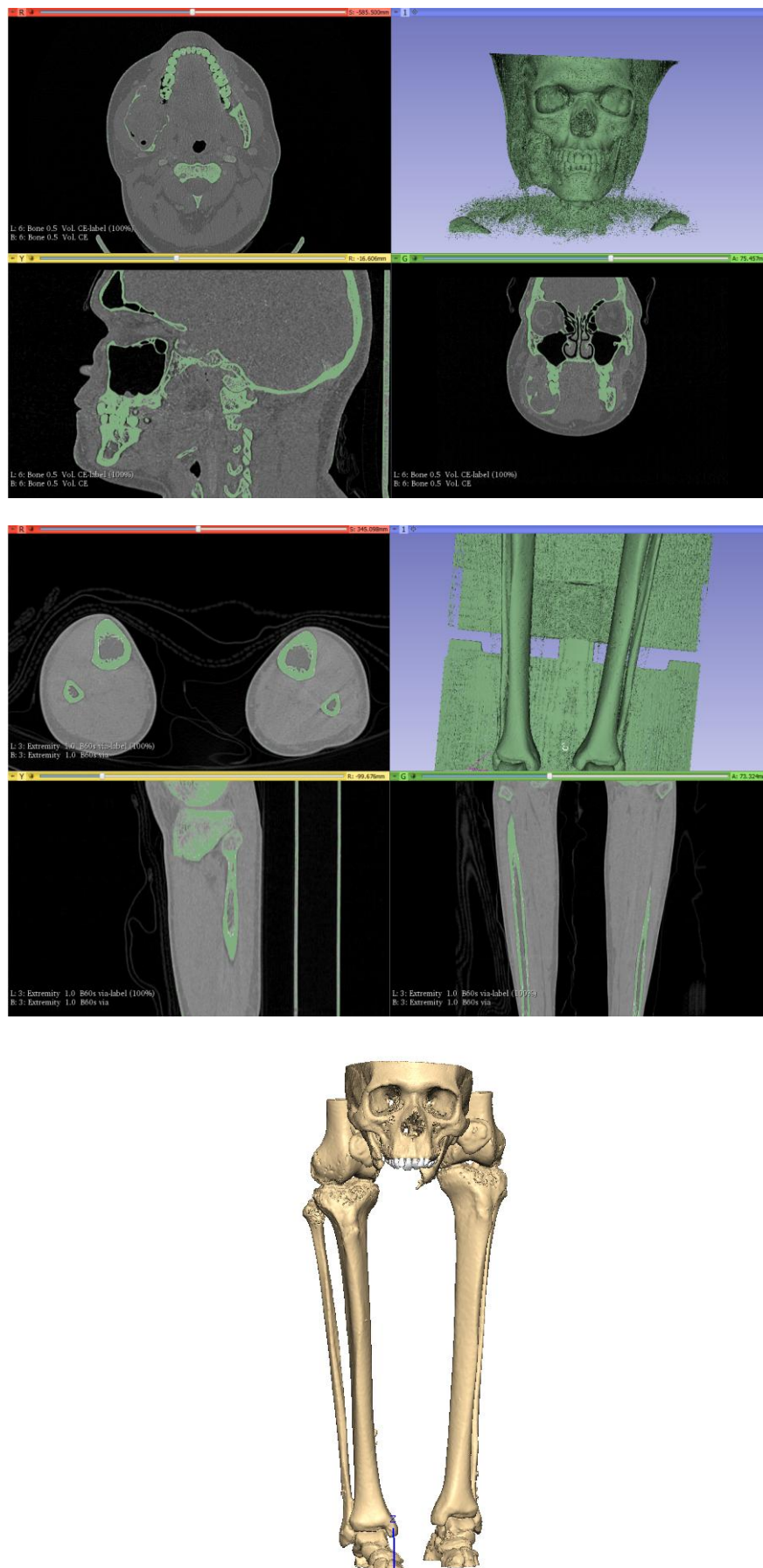
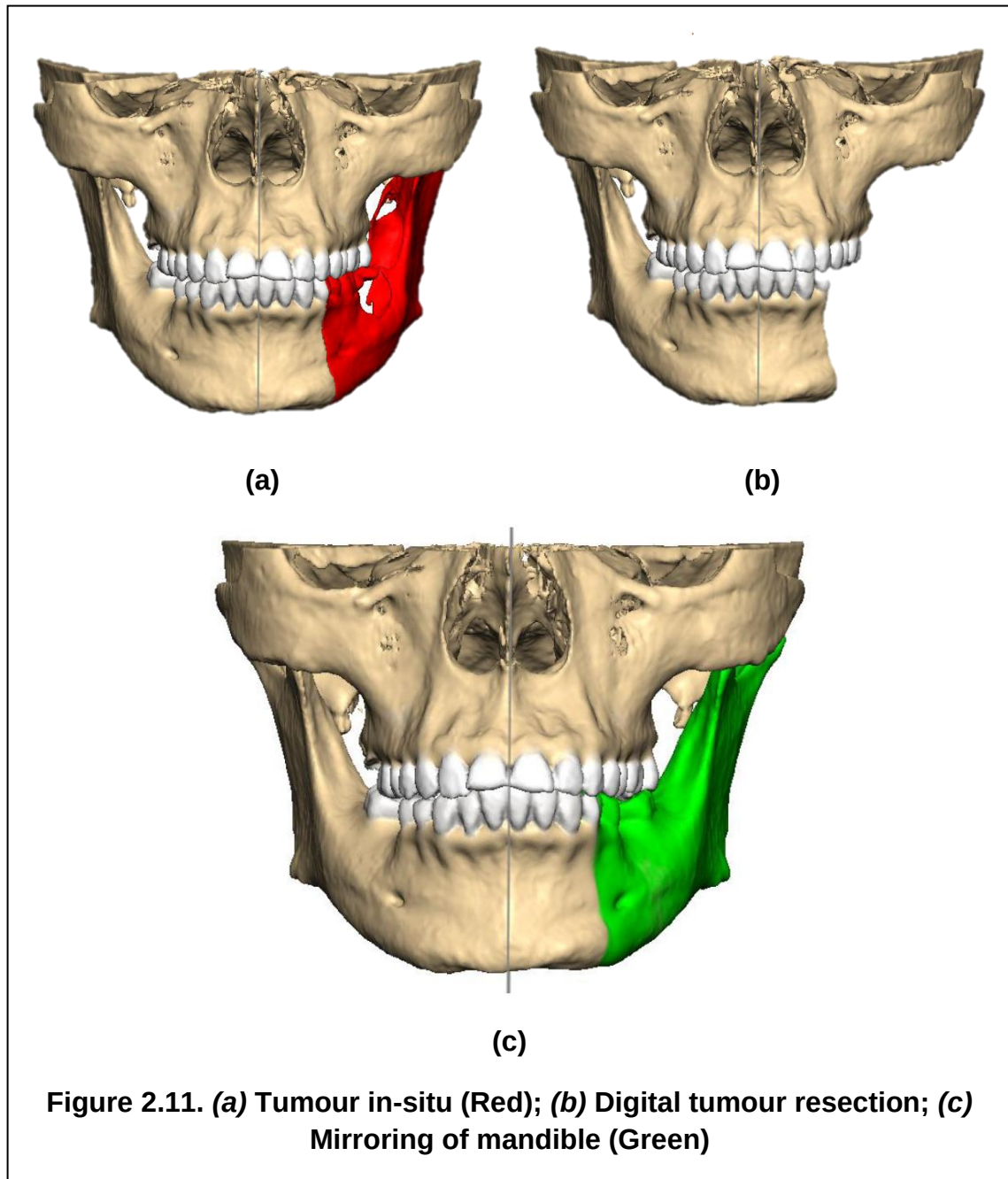


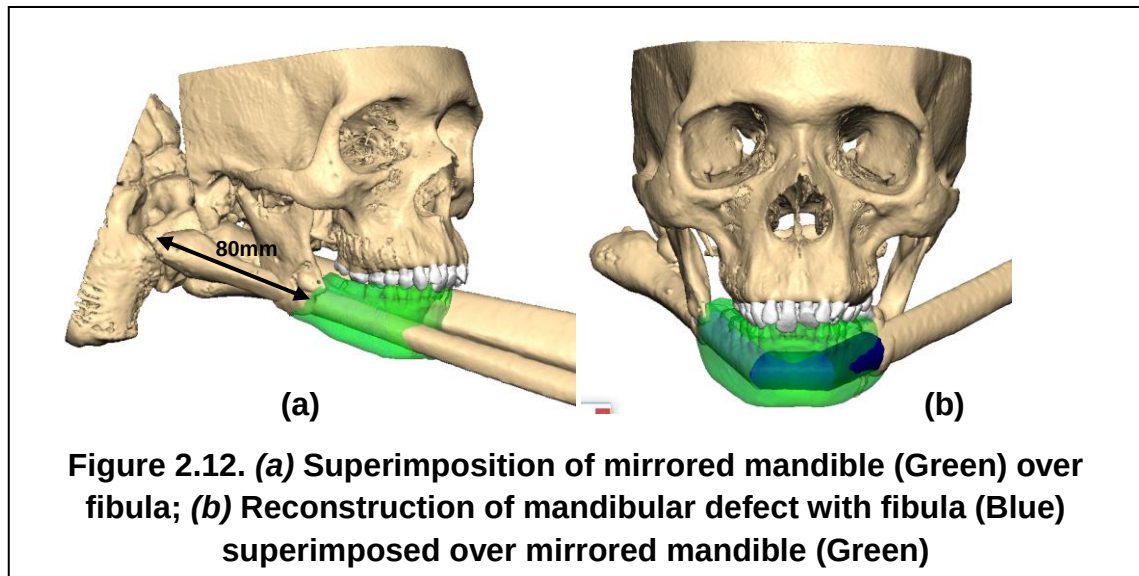
Figure 2.10. Utilization of bony windows from three planes (Axial, Coronal and Sagittal) to create 3D image

These 3D images are then correctly sized in the software program. The tumour is digitally resected (Figure 2.11(b)) and the mandible mirrored (Figure 2.11(c)), in the case of a lateral defect, to digitally recreate the mandible. In the case of an anterior defect, a generic mandible is imported to recreate the mandible. (Figure 2.11)



The 3D skull with the reconstructed (mirrored) mandible is then superimposed over the fibula, always starting 80mm from the ankle. Segments of the fibula are used to reconstruct and follow the contour of

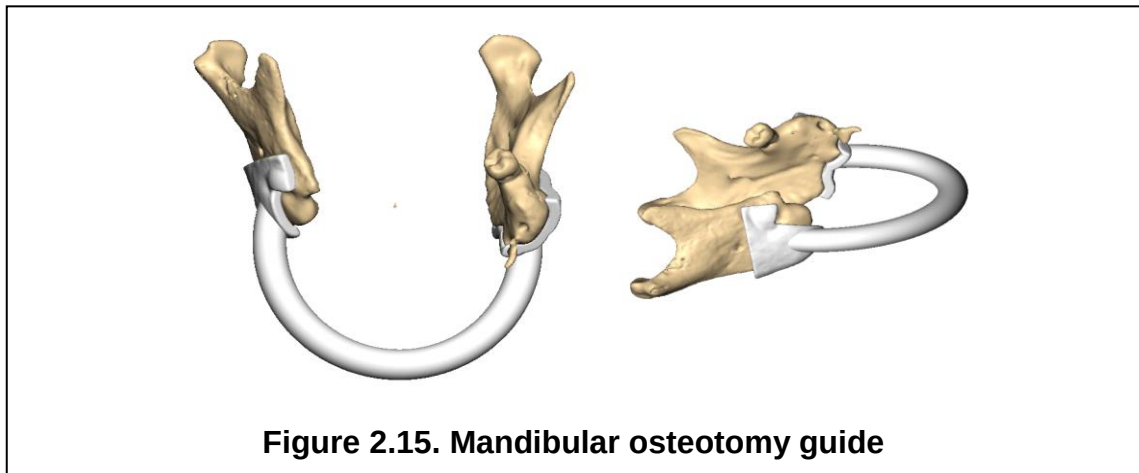
the mandible as closely as possible, ensuring that segments of the fibula are not too small, i.e. not less than 20mm. (Figure 2.12)



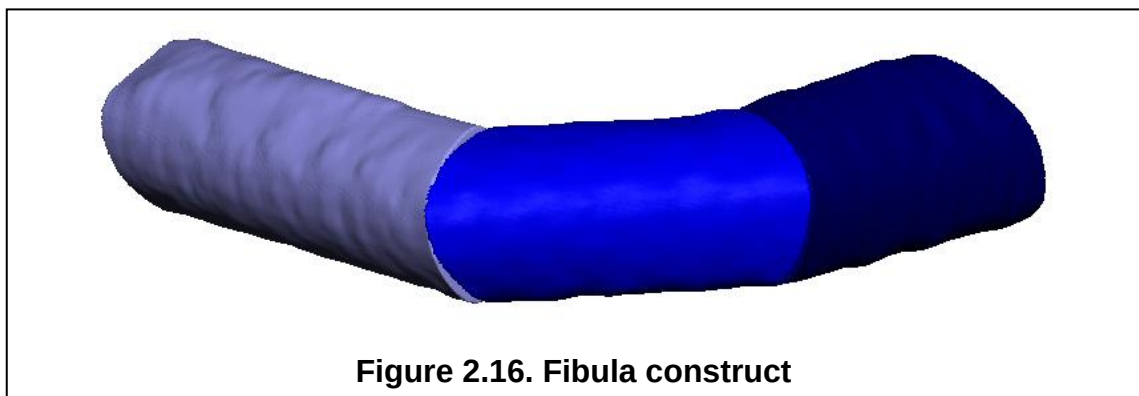
The fibula is digitally osteotomized and placed into the software program and an osteotomy guide is made to fit around the fibula. Slots are placed on both ends of each fibula segment so that the fibula can be osteotomized into the planned segments. (Figure 2.13 and Figure 2.14)



A similar process can be used to create an osteotomy guide to fit around the mandible that can be used intraoperatively for the resection of the tumour. (Figure 2.15)



A fibula construct is the segment of the fibula reconstructed mandible that can be printed separately from the mandible to assist with securing of pre-bent reconstruction plate to the remaining segments of the mandible. (Figure 2.16 and Figure 2.17)



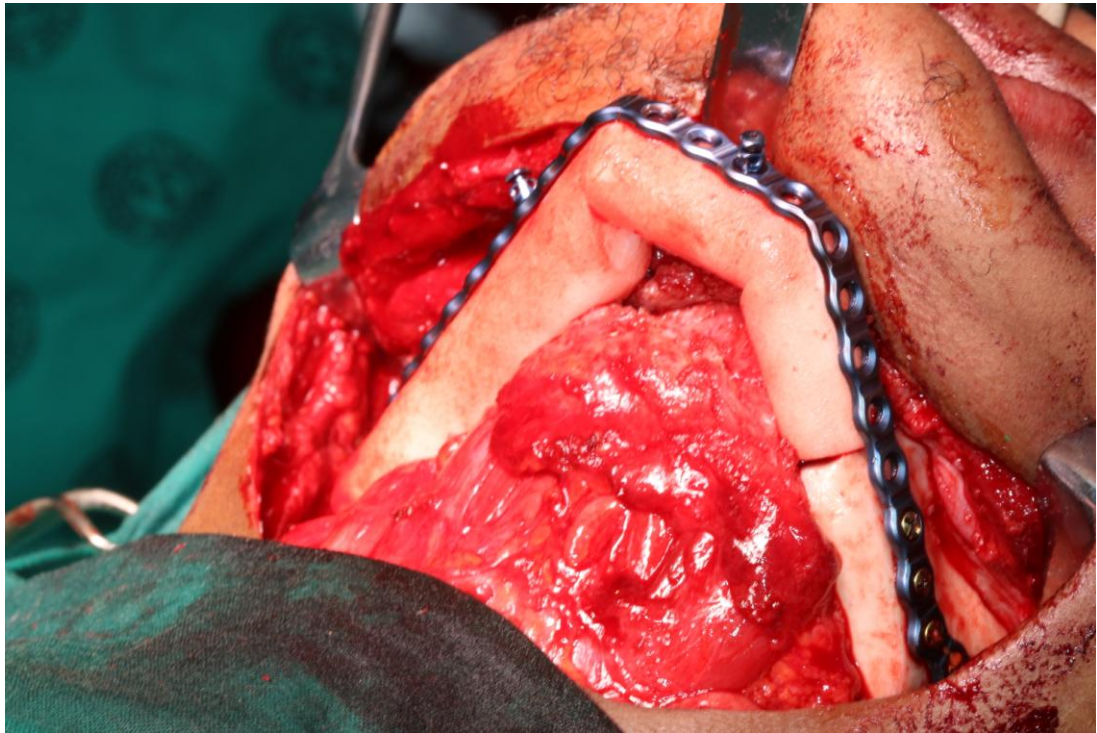


Figure 2.17. Fibula construct utilized to secure reconstruction plate to remaining segments of mandible

The file is then sent to a 3D printer in a “.stl” format to allow the stereolithographic model, osteotomy guides and fibula construct to be printed from a powder resin. A reconstruction plate is then pre-bent on this model. (Figure 2.18)

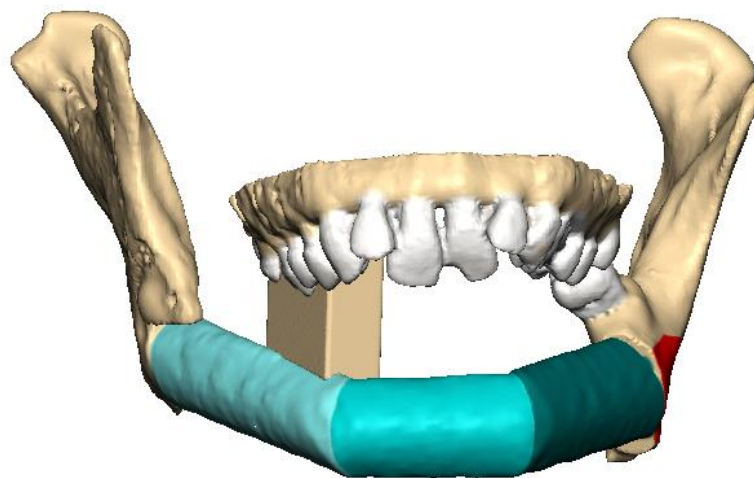


Figure 2.18. Stereolithographic model

2.14. Complications which may arise post grafting

Complications of vascularised free fibula flaps may be divided into complications occurring at the recipient site and complications occurring at the donor site.

2.14.1. Complications at the recipient site

Complications at the recipient site include:

- 2.14.1.1. Loss of the vascularised free fibula flap (Parbo et al, 2013; Wijbenga et al, 2016; Weitz et al, 2016)
- 2.14.1.2. Vascular complications (Colletti et al, 2014; Jackson et al, 2016; van Gemert et al, 2018)
- 2.14.1.3. Haemorrhage (Toto et al, 2015)
- 2.14.1.4. Haematoma (Jackson et al, 2016; van Gemert et al, 2018; Sugiura et al, 2018)
- 2.14.1.5. Local sepsis (Wijbenga et al, 2016; van Gemert et al, 2018; Sugiura et al, 2018)
- 2.14.1.6. Partial or complete necrosis of the cutaneous paddle (Toto et al, 2015; Xu et al, 2016; van Gemert et al, 2018)
- 2.14.1.7. Intraoral or extraoral dehiscence (Ritschl et al, 2017; van Gemert et al, 2018; Sugiura et al, 2018)
- 2.14.1.8. Delayed wound healing (Sieg et al, 1999)
- 2.14.1.9. Oronasal or orocutaneous fistula formation (Jackson et al, 2016; Wijbenga et al, 2016; Weitz et al, 2016)
- 2.14.1.10. Non-union (Toto et al, 2015; van Gemert et al, 2018)
- 2.14.1.11. Hardware failure (Jackson et al, 2016; Wijbenga et al, 2016; van Gemert et al, 2018)
- 2.14.1.12. Displacement of fibula head out of glenoid fossa (Wax et al, 2000)
- 2.14.1.13. Trismus (Parbo et al, 2013; Jackson et al, 2016)
- 2.14.1.14. Peri-implant soft tissue hyperplasia (Bodard et al, 2015; Jackson et al, 2016; Wijbenga et al, 2016)

2.14.2. Complications at the donor site

Complications at the donor site include:

- 2.14.2.1. Foot ischemia secondary to sacrificing the peroneal artery (Blackwell, 1998; Hoffman et al, 2012; Toto et al, 2015)
- 2.14.2.2. Paraesthesia of the skin of the lateral calf and dorsum of the foot (Lison et al, 2010; Catlana-Lehnen et al, 2012; Di Giuli et al, 2018)
- 2.14.2.3. Dysesthesia due to minor nerve impairment (Gonzalez-Garcia et al, 2008; Hoffman et al, 2012; Di Giuli et al, 2018)
- 2.14.2.4. Delayed wound healing (Peled et al, 2005; Catlana-Lehnen et al, 2012; Wijbenga et al, 2016)
- 2.14.2.5. Wound sepsis (Gonzalez-Garcia et al, 2008; Hoffman et al, 2012; Parbo et al, 2013)
- 2.14.2.6. Wound dehiscence (Gonzalez-Garcia et al, 2008; Yilmaz et al, 2008)
- 2.14.2.7. An unsightly scar (Ferri et al, 1997; Riaz et al, 2010; Xu et al, 2016)
- 2.14.2.8. Partial or complete skin graft failure (Hidalgo, 1989; Wax et al, 2000; Jackson et al, 2016)
- 2.14.2.9. Leg oedema (Hidalgo, 1989; Anthony et al, 1997) or compartment syndrome (Hoffman et al, 2012)
- 2.14.2.10. Muscular deficits related to the flexor and extensor hallucis longus muscle (Munoz Guerra, 2001; Garrett et al, 2006; Di Giuli et al, 2018)
- 2.14.2.11. An uncertain gait described subjectively by patients (Wijbenga et al, 2016; Sozzi et al, 2017; Di Giuli et al, 2018)
- 2.14.2.12. Restrictions in ankle and toe movement (Hoffman et al, 2012; Fang et al, 2015; Wijbenga et al, 2016)
- 2.14.2.13. Ankle instability (Di Giuli et al, 2018; Garrett et al, 2006; Hoffman et al, 2012)

2.14.2.14. Toe deformity (Garrett et al, 2006; Lopez-Arcas et al, 2010; Xu et al, 2016; Di Giuli et al, 2018)

2.14.2.15. Rarely, stress fracture of the tibia (Pacifico et al, 2003; Lison et al, 2010)

CHAPTER 3

3. Aims and Objectives

3.1. Aims of the Study

The aim of the study was to retrospectively analyse the reconstruction outcomes of vascularised free fibula flaps in the mandible from 01 November 2010 to the 13 July 2017 at the Department of Maxillofacial and Oral Surgery at the School of Oral Health Sciences, Faculty of Health Sciences, University of the Witwatersrand.

3.2. Objectives of the Study

The objectives of the study were:

- 3.2.1. To determine the reconstruction outcomes of vascularised mandibular fibula grafts
- 3.2.2. To identify factors associated with shortfalls of treatment
- 3.2.3. To establish a protocol to overcome failures

3.3. Rationale for the Study

The Department of Maxillofacial and Oral Surgery of the School of Oral Health Sciences at the University of the Witwatersrand, Faculty of Health Sciences is a tertiary referral centre that treats patients from the Gauteng province and other provinces in South Africa as well as patients from South African Development Community (SADC) countries.

The Department has a Craniofacial unit based at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) that commenced on 01 November 2010 where patients are treated by a multidisciplinary team for resections and reconstruction with microvascular flaps including a vascularised free fibula flap as determined collaboratively and with consensus from all teams involved. The multidisciplinary team includes

the Department of Maxillofacial and Oral surgery, the Department of Ear, Nose and Throat Surgery, the Department of Plastic and Reconstructive Surgery, the Department of Oral Rehabilitation, the Department of Neurosurgery and other allied health disciplines including Radiation Oncology, Psychology, Speech therapy and Dieticians. To date the Department of Maxillofacial and Oral Surgery has performed mandibular reconstructions (post-trauma and tumour ablation) with VFFF but never reported its experience. Against this background, this study is undertaken to report our experience and outcome of mandibular reconstruction with vascularised free fibula flaps. It is envisaged that data generated from this study could provide valuable information for the improvement of clinical outcomes of head and neck reconstruction with VFFF and could serve as the basis for future treatment algorithm.

CHAPTER 4

4. Materials and Methods

4.1. Study Design

A retrospective, descriptive study was conducted where the clinical and radiographic patient records of patients grafted with vascularised free fibula flaps to mandibular defects at the Department of Maxillofacial and Oral Surgery at Charlotte Maxeke Johannesburg Academic Hospital were accessed. The records included and accessed were from the period 01 November 2010 to the 13 July 2017, this being approved by the Human Research Ethics Committee (Medical).

4.2. Ethical clearance and considerations

The Human Research Ethics Committee (HREC) (Medical) of the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg granted ethical clearance (Ethical clearance certificate no: M170521) before the study commenced. The patient's identity was not disclosed in any manner as a study number was assigned to each patient record file. Permission to conduct the study and to use the Charlotte Maxeke Johannesburg Academic Hospital files was granted by the Chief Executive Officer (C. E. O.) of the Charlotte Maxeke Johannesburg Academic Hospital (Reference no: GP_201709_009). Permission to use the Wits Oral Health Centre files was granted by the Hospital Research and Risk Committee of the School of Oral Health Sciences, Faculty of Health Sciences, University of the Witwatersrand (Reference no: HRRR/JUN/02/2017).

4.3. Selection of patients

The clinical and radiological records of patients which satisfied the laid inclusion criteria were included in this study.

The inclusion criteria for the patient records were as follows:

- Completed records of all patients who were grafted with vascularised free fibula flaps to the mandible during the period 01 November 2010 to the 13 July 2017 were included in the study.

The exclusion criteria for the patient records were as follows:

- Incomplete records of patients who were grafted with vascularised free fibula flaps to the mandible during the period 01 November 2010 to the 13 July 2017 were excluded from the study.
- Records of patients who were grafted with vascularised free fibula flaps to the maxilla during the period 01 November 2010 to the 13 July 2017 were excluded from the study.

4.4. Data Collection

All patient records were allocated a study number. Data that was collected from the patient records was divided into 5 broad categories, namely, demographic data, aetiology of the defect, factors related to the vascularised free fibula flap, factors related to placement of dental implants and post-operative factors.

Demographic data such as patient age and gender was collected. All mandibular defects were classified using the classification of Brown et al by assessment of the panoramic radiograph or CT scan of the patient. Data for factors related to the vascularised free fibula flap such as the number of osteotomy segments of the fibula and the administration of radiation was collected from the patient records. Data for factors related to the placement of dental implants such as the immediate or delayed placement of dental implants, the number of implants placed and the number of implants lost, if any, was collected from the patient records. Data for the post-operative factors such as the period of follow-up and complications, if any, was recorded from the patient records.

A data collection sheet which had all the parameters to be investigated was designed (Annexure E). Data obtained from the patient clinical and radiological records was entered onto the data collection sheet and captured using Microsoft Office Excel on a personal computer.

4.5. Criteria for success

A vascularised free fibula flap was considered successful one week post-operatively when adequate perfusion of the flap had been established.

4.6. Statistical Analysis

Data was analysed with the assistance of a statistician. Continuous variables were described using mean, standard deviation, median and interquartile range. Categorical variables were described using frequencies and proportions. The failure/success proportions between two groups were compared using the two-sample proportions test. Fisher's exact test was used to test for association between categorical variables. The Mann-Whitney U test was used to compare two groups with respect to age.

CHAPTER 5

5. Results

The records of nineteen patients who had undergone vascularised free fibula flaps to the mandible during the period 01 November 2010 and 13 July 2017 were included in the study. One patient had had a failure of her first vascularised free fibula flap and had subsequently undergone a second vascularised free fibula flap thus a total of twenty records were included in the study. (Table 5.1)

5.1. Demographic variables

Twelve patients were female (60%) and eight were male (40%) (Figure 5.1). The overall mean age for the patients was 40.85 ± 19.48 , the youngest patient being 17 years and the oldest being 71 years. In total the records of thirteen Africans, five Caucasians, one Coloured (Mixed ancestry) and one Indian patient were included in the study (Figure 5.2).

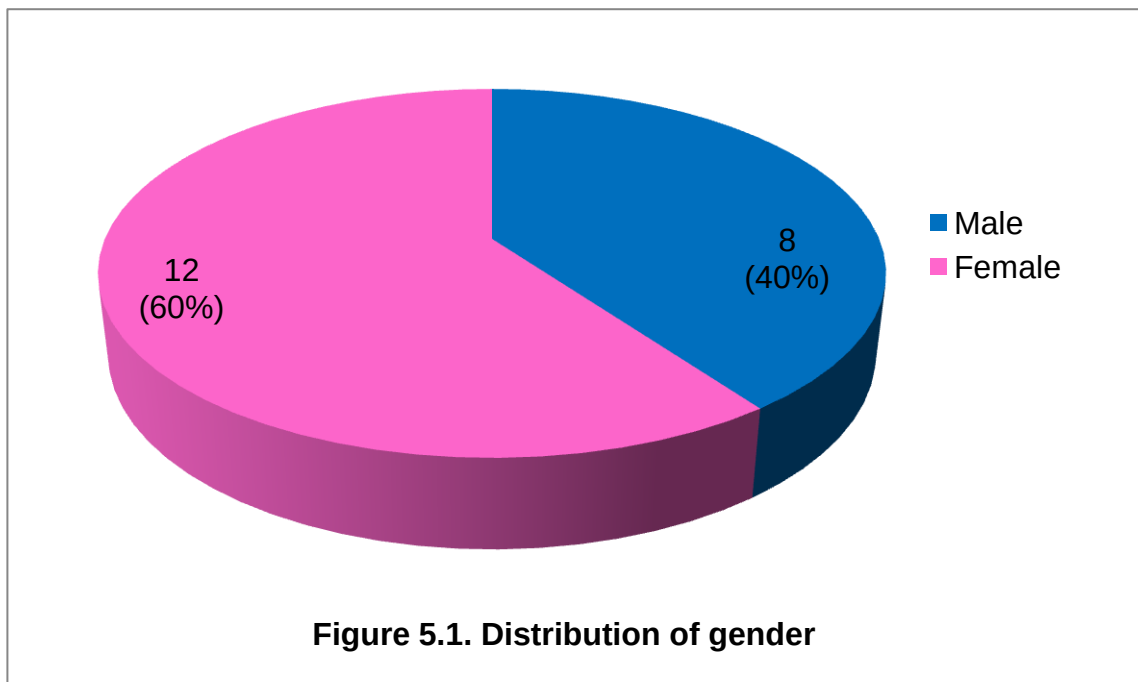
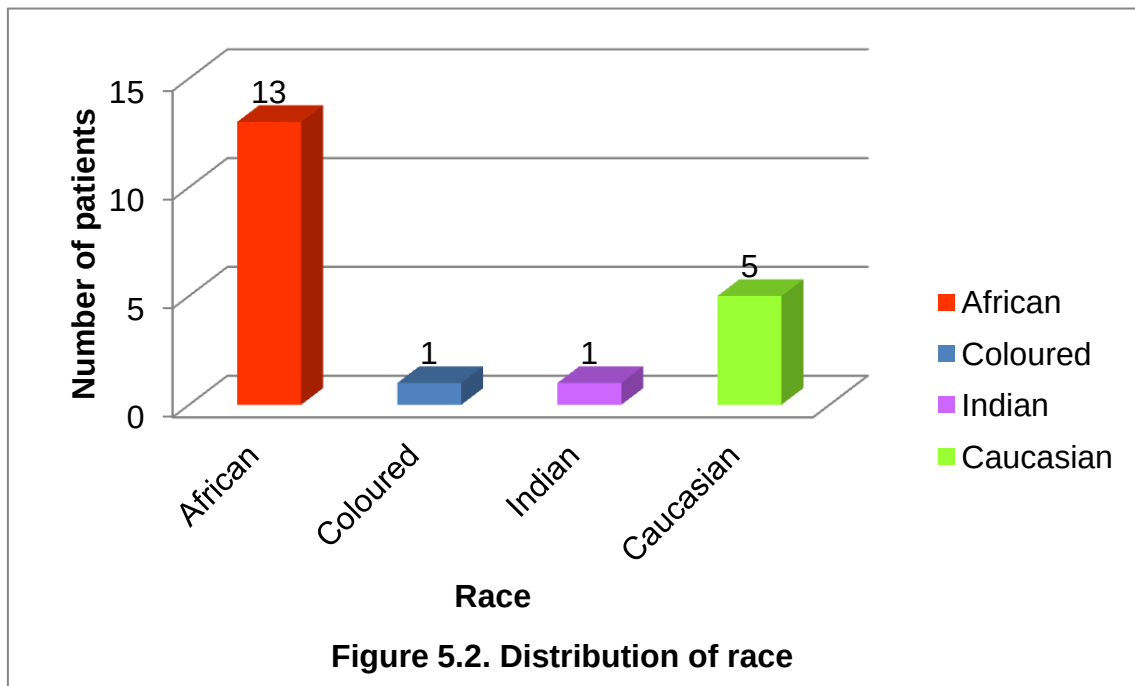


Table 5.1. Baseline demographic and clinical data

Study no	Age	Gender	Race	Aetiology	Classification	No of segments	Outcome	Radiation	Timing of implant placement	Loss of implants	Bony continuity	Complications
1	31	Female	African	Chondroblastic osteosarcoma	Class II	1	Success	No	N/A	N/A	No	No
2	19	Female	African	Ameloblastoma	Class III	3	Success	No	Delayed, 14.5 months	No	Yes	No
3	54	Male	African	Squamous cell carcinoma	Class III	3	Success	Yes, Post grafting	N/A	N/A	No	Yes
4	47	Male	Indian	Squamous cell carcinoma	Class III	3	Failure	No	N/A	N/A	N/A	Yes
5	61	Male	African	Squamous cell carcinoma	Class III	2	Success	Yes, Post grafting	N/A	N/A	No	No
6	21	Male	African	Chondroblastic osteosarcoma	Class II	1	Success	No	N/A	N/A	Yes	No
7	17	Female	African	Chondroblastic osteosarcoma	Class Ic	2	Success	No	Delayed, 36.5 months	No	Yes	No
8	37	Female	African	Odontogenic myxoma	Class IV	3	Success	No	Delayed, 6 months	No	No	No
9	27	Female	African	Ossifying fibroma	Class IVc	3	Failure	No	Immediate	Yes.	N/A	N/A

10	27	Female	African	Ossifying fibroma	Class IVc	3	Success	No	Delayed, 16.5 months	No	Yes	No
11	19	Female	African	Ossifying fibroma	Class IV	4	Success	No	Delayed, 16 months	No	No	Yes
12	23	Female	African	Ameloblastoma	Class III	3	Success	No	Delayed, 13 months	No	Yes	No
13	65	Male	White	Basal cell carcinoma	Class III	2	Success	Yes, Post grafting	N/A	N/A	Yes	Yes
14	64	Male	White	Squamous cell carcinoma	Class III	3	Success	Yes, Post grafting	N/A	N/A	Yes	No
15	71	Male	White	Osteoradionecrosis	Class IVc	3	Success	No	N/A	N/A	Yes	Yes
16	62	Female	Coloured	Squamous cell carcinoma	Class II	4	Success	Yes, Post grafting	Immediate	No	Yes	Yes
17	25	Male	African	Ameloblastoma	Class IVc	3	Success	No	N/A	N/A	Yes	No
18	25	Female	African	Squamous cell carcinoma	Class III	3	Success	Yes, Post grafting	N/A	N/A	Yes	Yes
19	67	Female	White	Squamous cell carcinoma	Class III	3	Success	Yes, Post grafting	N/A	N/A	Yes	No
20	55	Female	White	Gunshot wound mandible	Class III	2	Success	No	Delayed, 12 months	No	Yes	No



5.2. Clinical variables

Neoplasia contributed to 90% of the mandibular defects with the remainder being due to either trauma (5%) in the form of a gunshot wound to the mandible or osteoradionecrosis (5%). Amongst those defects due to neoplasia, seven (38.89%) were due to squamous cell carcinoma; three each (16.67%) were due to ameloblastoma, chondroblastic osteosarcoma and ossifying fibroma respectively and one each (5.56%) were due to basal cell carcinoma and odontogenic myxoma respectively. Thus, 55% of the defects were due to malignant neoplasms, 35% were due to benign neoplasms, 5% were due to trauma and 5% were due to osteoradionecrosis. (Figure 5.3)

The mandibular defects were classified using the latest classification by Brown et al, (2016). Half of the patients (10 patients) had Class III mandibular defects, while four (20%) had Class IVc mandibular defects, three (15%) had Class II mandibular defects, two (10%) had Class IV mandibular defects and one patient (5%) had a Class Ic mandibular defect. (Figure 5.4)

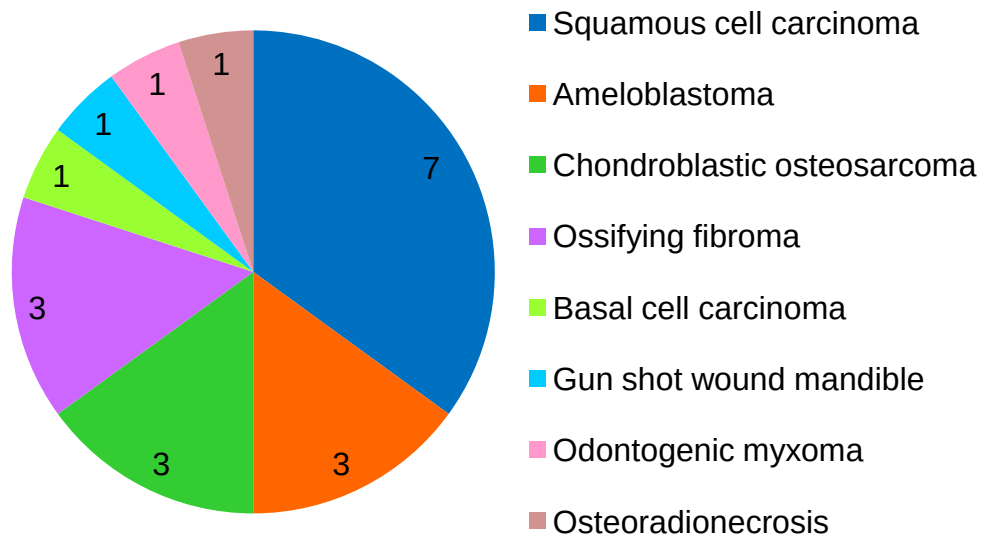


Figure 5.3. Aetiology of mandibular defect

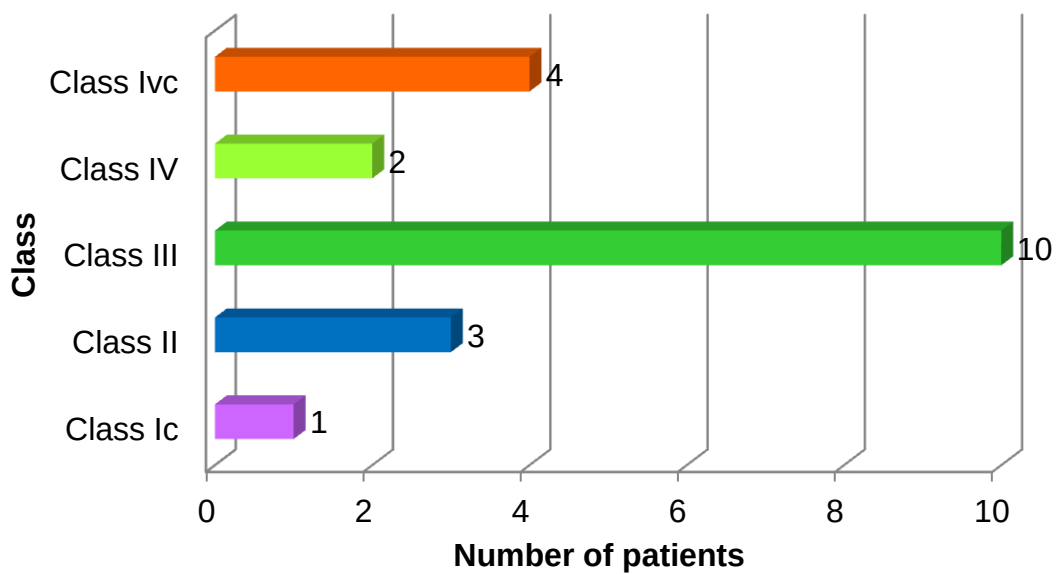


Figure 5.4. Classification of Mandibular Defects according to classification by Brown et al(Brown et al, 2016)

5.3. Reconstruction outcome and its comparison with demographic variables

Reconstruction outcomes of vascularised free fibula flaps were considered to be either successful or a failure. A vascularised free fibula flap was considered successful one week post-operatively when adequate perfusion of the flap had been established. The success rate

of vascularised free fibula flaps to mandibular defects was 90%. (Figure 5.5) No significant associations were found between reconstruction outcome and age, gender and race. Mandibular continuity was deemed to be successful six months after completion of the vascularised free fibula flap when continuity between the native mandible and the grafted fibula was confirmed radiographically. Of the 18 successful flaps 27.78% (5 patients) had lack of mandibular continuity at the interface of the native mandible and the grafted fibula (Table 5.2).

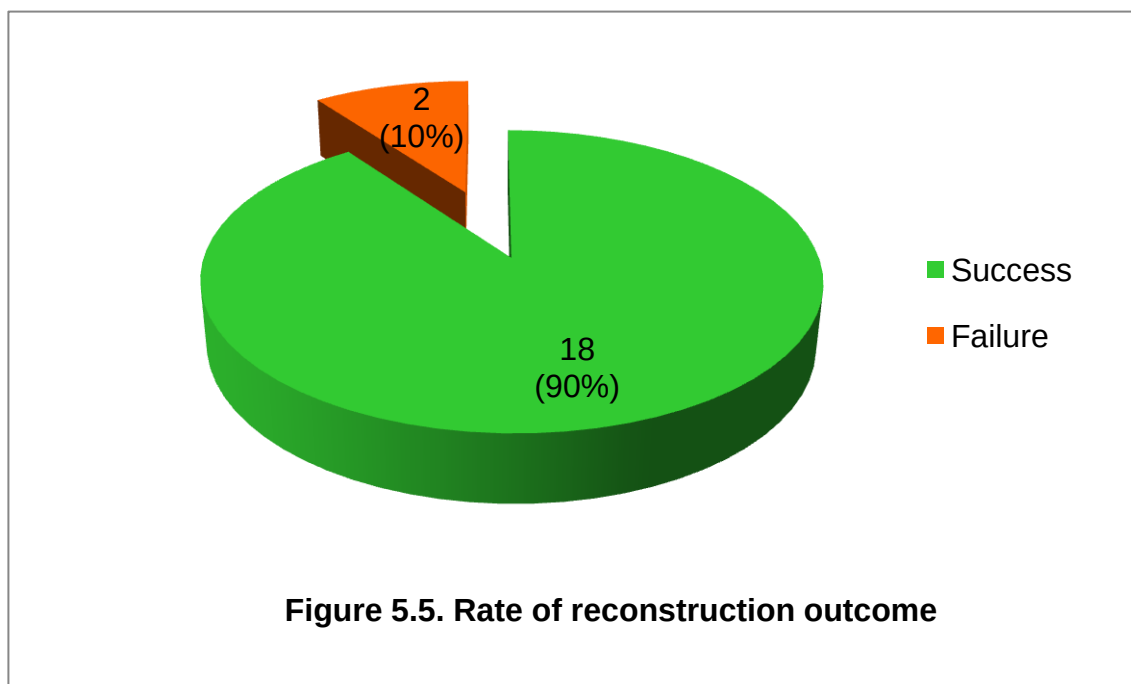
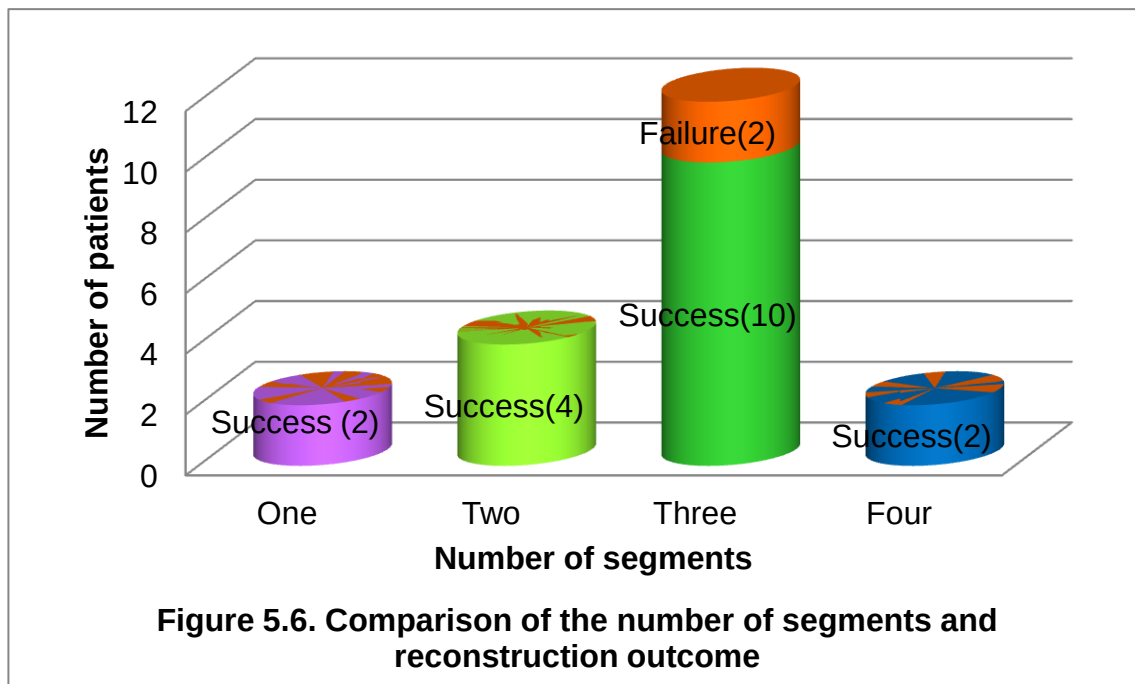


Table 5.2 Comparison of mandibular continuity in successful cases		
Mandibular continuity	Number	Percentage
No	5	27.78%
Yes	13	72.22%
Total	18	100%

5.4. Osteotomy of fibula and reconstruction outcome

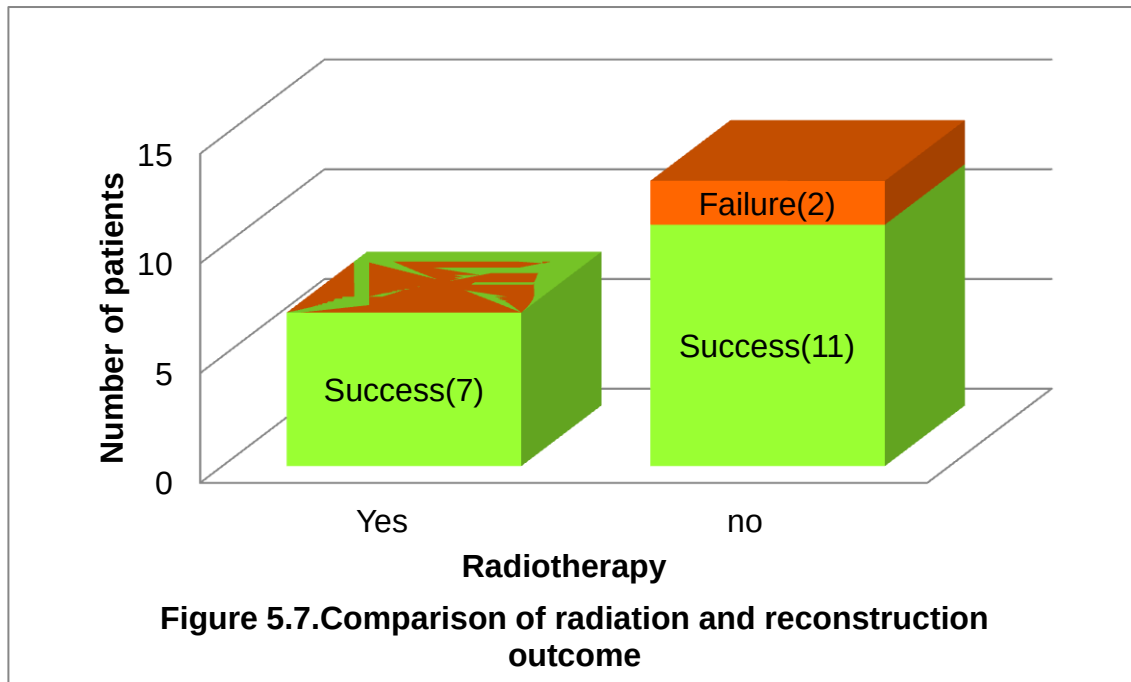
A fibula can be osteotomized into a number of segments in order to reconstruct the defect and to establish a contour of the neomandible that best mimics the patient's own mandible and allows for prosthodontic rehabilitation. A comparison between the reconstruction outcome and

the number of segments the fibula was osteotomized into showed no significant association between these variables. The fibula in our cases had been osteotomized into one (2 patients), two (4 patients), three (12 patients) or 4 (2 patients) segments. Failure of the vascularised free fibula flap was only found in 2 of the 12 patients (16.67%) in whom the fibula was osteotomized into three segments. (Figure 5.6)



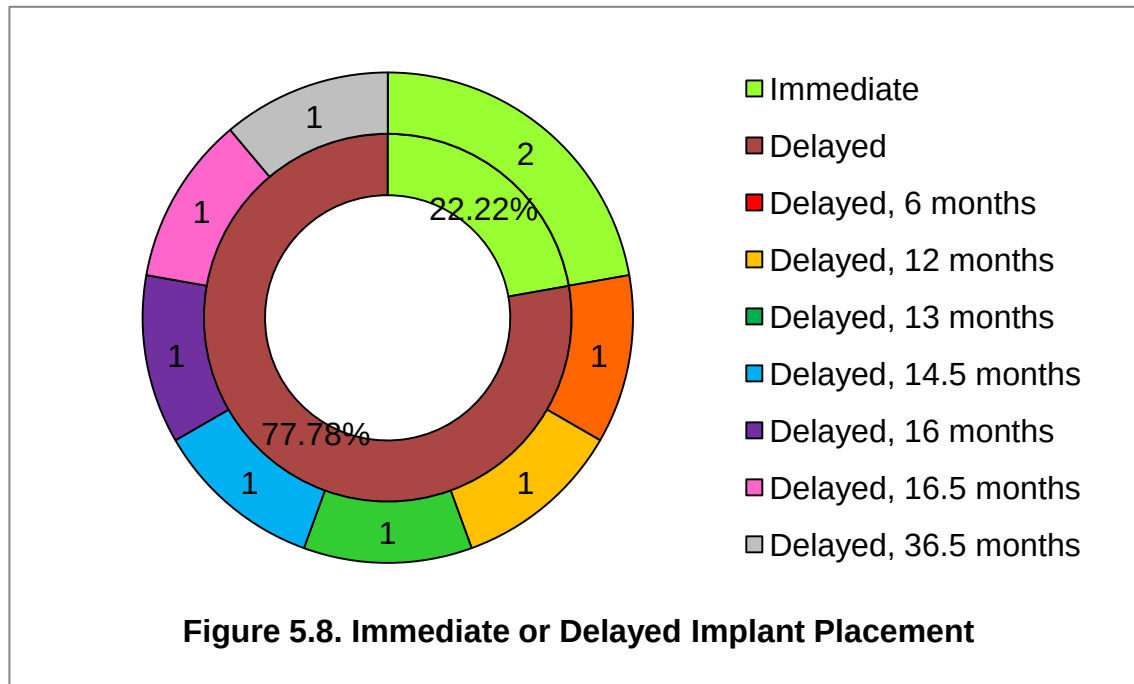
5.5. Radiation therapy and reconstruction outcome

Some patients with malignant neoplasms are treated with adjunctive radiation therapy in addition to ablative tumour surgery. Some of the patients with malignant neoplasms in our study (7 patients out of 11) were part of the protocol where they received adjunctive radiation therapy post-grafting. However, the poor quality of the patient records in this regard resulted in difficulties in determining the dosage and how long post-operatively radiation therapy was commenced. When the reconstruction outcome was compared between the group of patients that received adjunctive radiation therapy and those who did not, two failures were noted in the group of patients who had not received radiation therapy (Figure 5.7). This was, however, not a significant association.



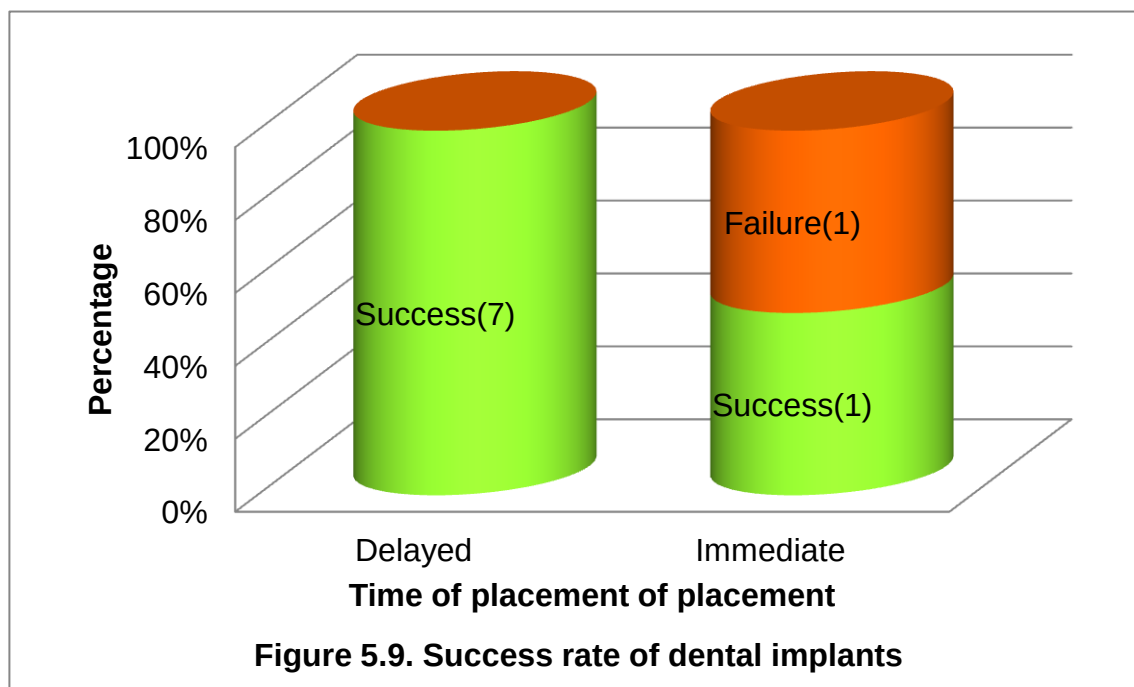
5.6. Immediate versus delayed placement of dental implants

Dental implants may be placed immediately at the time of grafting or as a delayed procedure once the vascularised free fibula flap is successful. Nine patients (45%) in our study that received a vascularised free fibula flap also subsequently received dental implants as part of their comprehensive restoration. Of the nine patients, dental implants were placed immediately at the time of anastomosis of the vascularised free fibula flap in two patients (22.22%) with the remaining seven patients (77.78%) receiving delayed placement of dental implants at time periods ranging from 6 months to 36.5 months (Average 16.36 months). (Figure 5.8)



5.7. Immediate or delayed placement of dental implants and reconstruction outcome

Dental implants can be considered successful upon osseointegration into the fibula three months post placement. The overall success rate of dental implants amongst the nine patients in our study who received dental implants was 88.89%. All dental implants placed as a delayed procedure were successful (7 out of 9 patients) while the implants in one of the two patients who received implants immediately were lost with the failed vascularised free fibula flap (Figure 5.9). In this study, no significant associations were found between the reconstruction outcome and the timing of implant placement.



5.8. Rate of complications and reconstruction outcome

A complication rate of 40% was found in our study. Complications were classified into major or minor complications. Major complications were defined as anastomosis failure. Minor complications included dehiscence and sepsis which ultimately did not lead to failure of the vascularised free fibula flap. Two patients (25%) experienced major complications. Two patients (25%) experienced dehiscence which was subsequently debrided and closed, and four (50%) experienced sepsis and dehiscence which subsequently resolved not affecting the success of the fibula in both instances. (Figure 5.10) A comparison of the reconstruction outcome and rate of complications was also not significant.

One patient developed a delayed complication resulting in necrosis of the skin paddle and subsequent partial necrosis of the vascularised free fibula flap. However, this occurred one year post-operatively following radiation therapy which had resulted in radiation burn of the skin paddle after the vascularised free fibula flap was considered successful. As a result this flap was considered successful, and this did not affect the

overall reconstruction outcome, as the sequelae that followed were considered to be due to radiation injury rather than due to flap failure.

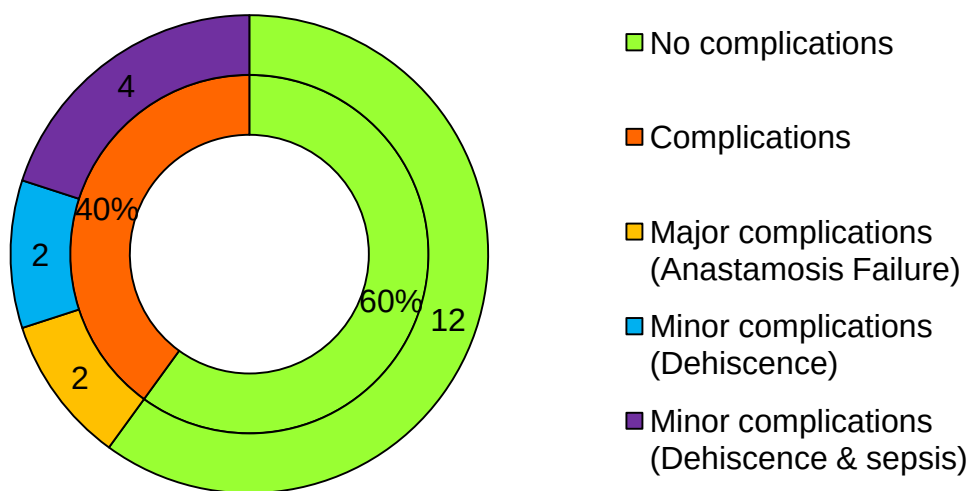


Figure 5.10. Comparison of rate and types of complications

Table 5.3. Tabulation of complications experienced			
Study no	Outcome	Complications	Type of complication
1	Success	No	N/A
2	Success	No	N/A
3	Success	Yes, Minor	Dehiscence, Sepsis
4	Failure	Yes, Major	Anastomosis failure
5	Success	No	N/A
6	Success	No	N/A
7	Success	No	N/A
8	Success	No	N/A
9	Failure	Yes, Major	Anastomosis failure
10	Success	No	N/A
11	Success	Yes, Minor	Dehiscence
12	Success	No	N/A
13	Success	Yes, Minor	Dehiscence
14	Success	No	N/A
15	Success	Yes, Minor	Dehiscence, Sepsis
16	Success	Yes, Minor	Dehiscence, Sepsis
17	Success	No	N/A
18	Success	Yes, Minor & Delayed	Dehiscence, Sepsis, Necrosis of skin paddle and partial necrosis of fibula
19	Success	No	N/A
20	Success	No	N/A

Some patients experienced complications post implant placement which ultimately did not affect the reconstruction outcome of the vascularised free fibula flap. (Table 5.4)

Table 5.4. Tabulation of other complications experienced		
Study no	Complications	Type of complication
1	No	N/A
2	No	N/A
3	No	N/A
4	No	N/A
5	No	N/A
6	No	N/A
7	Yes	Deviation, Soft tissue overgrowth post implant placement
8	No	N/A
9	No	N/A
10	Yes	Soft tissue overgrowth post implant placement, Sepsis post implant placement
11	No	N/A
12	No	N/A
13	No	N/A
14	No	N/A
15	Yes	Dislocation of fibula out of glenoid fossa
16	No	N/A
17	No	N/A
18	No	N/A
19	No	N/A
20	No	N/A

CHAPTER 6

6. Discussion

Available reconstructive options for mandibular continuity defects (post-trauma or ablation of tumours) to rehabilitate these patients include vascularised bone flaps (free vascularised flaps) and non-vascularised bone grafts. This reconstruction is imperative not only for restoration of facial contour and mandibular function, but also for addressing the concomitant psychological problems associated with these deformities. Such reconstructions are frequently insufficient as regards to mastication, speech and swallowing. The latter can be obtained 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.

The VFFF is the most common free flap used for mandibular reconstruction, and is regarded by some as the only choice for defects more than 10 cm in length (Hildago, 1994). This study aimed to evaluate the outcome of mandibular defects reconstructed with VFFF in 20 patients.

The most common aetiology of mandibular defects in the present study was neoplasia. Studies in the English literature have reported a varied distribution of aetiologies for mandibular defects in patients undergoing mandibular reconstruction with VFFF. Most authors have reported a predominance of neoplasia followed by trauma as being predominant causes (Ritschl et al, 2017; Weitz et al, 2018; van Gemert et al, 2018; Fichter et al, 2018) with only a few cases being due to other pathology (Rashid et al, 2012; Ritschl et al, 2017; Weitz et al, 2018; van Gemert et al, 2018; Fichter et al, 2018), namely, cystic lesions, osteoradionecrosis, medication related osteonecrosis of the jaws (MRONJ), osteomyelitis or congenital abnormalities.

The present study concurs with other studies in that the neoplastic cause was attributed more towards malignancy than benign lesion (Avraham et al, 2014; Toto et al, 2015; Ritschl et al, 2017). Gunshot wounds to the face are the main reported

traumatic cause (Anthony et al, 1997; Ferri et al, 1997; Salinas et al, 2010; Shen et al, 2013). Infection has also been reported as a cause for mandibular defects (Yim et al, 1994). The dominance of neoplasia in the aetiology of defects in this study could be attributed to the burden of pathology on the population treated at the institution, with most patients seeking help only when the lesion has reached a grotesque size while others have limited access to the specialized services required to treat such pathology. Possible reasons for late presentation with large tumours include lack of patient awareness, patients being unable to reach tertiary health care facilities and also to patients choosing to seek help from traditional alternative medicine before seeking help from western medicine.

Only 3 elderly patients were included in the present study (patients older than 65 years) when categorised according to Ishikawa et al, (2017)'s definition. Over a 4 year follow-up period, Ishikawa et al, (2017) reported low atrophy rates of VFFF in elderly patients and concluded that even in an elderly patient, fibula bone height is preserved and can afford long-term stability. Thus, age does not appear to be a limiting factor for use of VFFF grafts. Sugiura et al, (2018) (who defined an elderly patient as an individual older than 80 years), also found a success rate of 100% following reconstruction of elderly patients with vascularised free fibula flap. Their finding seem to support that of previous studies that free tissue transfers performed in elderly patients has a high degree of success (Ishikawa et al, 2017). Historically the use and benefit of aggressive surgical treatment in older patients has been questioned and was considered a high risk. Sugiura et al, (2018) however found no significant difference between the rate of complications between the elderly and younger patients and concluded that elderly patients can tolerate free flap surgery just as well as younger patients. All 3 elderly patients in our study healed uneventfully, thus corroborating the findings of Ishikawa et al and Sugiura et al. A bigger sample size would however have given more credence to this conclusion.

Smoking has also been identified as a significant predictor of delayed complications (Chen et al, 2017), presumably because of its vasoconstrictive effects. Diabetes is also identified as a factor associated with failure of hardware in vascularised free fibula flaps in the form of loosening of screws (Liu et al, 2016). In the present study, no significant associations were found between any of the demographic variables,

namely age, gender and the reconstruction outcome or any of the other clinical variables.

There appears to be no universally accepted classification system of mandibular defects. Numerous classification systems for mandibular defects have been published in the English literature since Pavlov's classification in 1974. Most of the current classification systems are purely descriptive and lack the detail required to appropriately describe a defect and guide therapeutic approach. The classification by Jewer et al, (1989) is the most widely cited in the literature. We utilized the classification by Brown et al, (2016) to describe the mandibular defects as it incorporates detail together with the description of the defect and, furthermore incorporates a third dimension into the classification, namely, a numeric range for the defect size.

The overall success rate of vascularised free fibula flaps is reported to be between 90% and 100% (Colletti et al, 2014) despite some studies reporting success rates of less than 90% (Riaz et al, 2010; Weitz et al, 2016; van Gemert et al, 2018). A systematic review by Wijbenga et al, (2016) found a success rate of 99%. Bodard et al, (2015) reported a success rate of 79.9% at 10 years. The success rate in the present study was 90%, at the lower end of the reported range for success, but is comparable to that reported by Sieg et al, (1999) and Lopez-Arcas et al, (2010) (despite these studies having much larger sample sizes, 53 patients and 117 patients respectively). The lower success rate in the present study could be attributed to this being a new unit with lack of surgeons with the required surgical skills and experience to perform vascularised free fibula flaps at our institution as well as the delayed presentation of the patients with massive tumours.

In addition, a single surgeon did not perform the vascularised free fibula flaps in all 20 cases. This introduced surgical variability which could have affected the success rate. As the number of surgeons with the required surgical skills and experience increases, the success rate of 90% is likely to increase.

Good bone union determines the strength of the reconstructed mandible, is necessary for the timely administration of adjuvant therapy, dental implant placement, resumption of the oral intake of food and mastication and the use of the

dental prosthesis by patients undergoing mandibular reconstruction (Akashi et al, 2015). It is essential to confirm bone union prior to placement of delayed dental implants as it may be necessary to remove fixative hardware that may interfere with the placement of dental implants (Akashi et al, 2015). Ferri et al found bone callus at the osteotomy sites of 22 of 29 of their patients as early as 3 months post-operatively (Ferri et al, 1997). Using panoramic radiographs to assess bone union at the osteotomy sites, Disa et al, (1997) reported a bone union of 93% after a mean follow up period of 54 months with no difference between radiated and nonradiated patients. Akashi et al, (2015) compared the rate of bone union assessed on panoramic radiographs and CT scans and reported a bone union rate of 40% six months post-operatively, which increased to 91% two years post-operatively. However no clarification was given by Akashi et al, (2015) as to whether the assessment at two years was on a panoramic radiograph or CT scan. There appears to be no standardization of the method of assessment of bone union with some studies preferring to utilize CT scans while others used panoramic radiographs. Weitz et al, (2016) found significantly greater consolidation at the intersegmental gap between the segments of the fibula when VSP was used compared to the conventional bending of the reconstruction plate according to the surgeon's experience.

In the present study bone union was assessed using panoramic radiographs and CT scans. Five of the 18 (27.78%) patients displayed lack of bony continuity either at the intersegmental gap between fibula segments or between the fibula and the host mandible. Possible reasons for the lack of bony continuity at these interfaces include too large a gap between the segments at the time of the initial grafting procedure, wound dehiscence and minor sepsis (which was treated with local debridement and antibiotics) or excessive pressure on the neomandible during the post-operative healing phase. The lack of bony continuity in these patients, however, did not affect the success of the vascularised free fibula flap. Some of these patients underwent further grafting with particulate corticocancellous bone into these defects which subsequently resulted in bony continuity.

It has long been speculated that the greater the number of segments the fibula is osteotomized into, the more compromised is the blood supply to the distal segment. This is thought to be due to the interruption of both the endosteal blood supply and

detachment of the periosteum disrupting the periosteal blood supply at each osteotomy site. Each osteotomy thus decreases the perfusion of subsequent segments. Fichter et al, (2018) used Indocyanine Green Videoangiography to display lower perfusion to the distal segment as the number of osteotomies increase. Despite the lack of significant association between the number of osteotomies and the reconstruction outcome in the present study, failures were observed in two of the patients in whom the fibula was osteotomized into three segments.

Fichter et al, (2018) also found that segment length is significantly associated with perfusion parameters with longer segments displaying a better arterial flow. This is attributed to a longer uninterrupted endosteal blood supply, an intact periosteum in contact with a longer area of the fibula and a higher probability of a feeder vessel from the peroneal artery entering the segment of the fibula (Fichter et al, 2018). Hidalgo, (1989) found that segments as short as 1 cm received a good perfusion. Bahr, (1998) reported that segments that are at least 2 cm long could be revascularised in the recipient bed while segments 1cm in length could be revascularised but to a lesser extent. Therefore, a minimum segment length of 2 cm is used to avoid the development of non-vascularised segments that could affect the success of a vascularised free fibula flap. The average size of the smallest segment in the present study was not less than 2 cm.

Despite the true risk of delivering radiation on vascularised free flaps being unclear, the rate of flap loss in patients with malignancy receiving radiation therapy reported in the literature varies between 4% and 6% (Choi et al, 2004). Some authors found no significant association between the success rate in irradiated and non-irradiated vascularised free fibula flaps (Jackson et al, 2016; van Gemert et al, 2018) while Avraham et al, (2014) found that radiation therapy was associated with an increased rate of recipient-site-specific complications. Pre-operative radiation therapy may result in anastomotic failure or immediate post-operative complications in the vascularised free fibula flap (Chen et al, 2017). Post-operative radiation therapy does not affect healing of the flap or patency of the anastomosis but is regarded as a significant predictor of delayed complications such as plate exposure (Chen et al, 2017). Choi et al, (2004), however, reported results contradictory to this when none of their patients who underwent vascularised free fibula flaps preceded by or followed by radiation suffered flap loss. It is generally recommended that post-grafting

radiation therapy be commenced a minimum of three weeks post-operatively to minimise the risk of flap necrosis and impaired bone union associated with high-dose radiation. Of the 20 patients in the present study, 7 received radiation therapy post-operatively while none received pre-operative radiation therapy.

Studies have found that a minority of patients with vascularised free fibula flap reconstructed mandibles reach rehabilitation with dental implants (van Gemert et al, 2018) with dental implant placement rates ranging between 25% and 45% and dental rehabilitation rates ranging between 15% and 25% (Avraham et al, 2014). The dental implant placement rate in the present study was 45% which is in keeping with the range reported by Avraham et al, (2014). There appears to be no standardization in the literature regarding the timing for placement of dental implants, with some authors preferring to place them using the two-stage protocol while others prefer to place them simultaneously. It has been argued that simultaneous placement of dental implants is cost-effective and time-effective despite it adding extra time to the free flap operation where ischaemic time is critical (Chang et al, 2004). Jackson et al, (2016) also support simultaneous placement of dental implants, arguing that it allows better access to the grafted bone, eliminates a second procedure, allows for oral rehabilitation in a shorter period of time and improves quality of life. It is suggested that simultaneous placement of dental implants should be considered in patients with benign lesions, where the ramifications of radiation therapy are not a concern (Sozzi et al, 2017; Su et al, 2014). Rude et al, (2014) contend that immediate placement of dental implants, despite involving dissection of a small part of the periosteum, only has a minimal impact on the periosteal blood supply which is crucial for the altered fibula. Avraham et al, (2014) reported that immediate placement of dental implants did not increase the complication rate. Anthony et al, (1997), despite having placed implants simultaneously, preferred to defer implant placement and not to do so during salvage reconstructions. A salvage reconstruction is defined by Anthony et al, (1997) as a reconstruction performed with a VFFF in a patient that has previously undergone mandibular reconstruction that has failed. The benefit of the two-stage protocol is that it allows the surgeon to more precisely determine the position and angulation of the dental implant (Anthony et al, 1997; Reyhler et al, 1994; Reyhler et al, 1996). It also allows an interval for the early post-operative complications, should they arise, and for the definitive pathologic result to be taken into account (Reyhler et al, 1996). Reyhler et al, (1996)

suggested that delayed placement of dental implants be performed 3 months after the reconstruction in the case of a nonirradiated fibula and at least 6 months after the completion of radiation therapy in the case of an irradiated fibula. Carbiner et al, (2012) recommend waiting a minimum of 12 months before implant placement in an irradiated vascularised free fibula flap. According to Duttenhoefer et al, (2015), delayed placement of implants 6 months post grafting had a better survival rate than those placed immediately. The survival rate of implants in a fibula placed with the two-stage protocol was 99% compared to 90% with the simultaneous placement of dental implants (Duttenhoefer et al, 2015). Wijbenga et al, 2016 in their systematic review of the literature found an implant survival rate in a fibula of 95% while Paraque et al, (2011) reported an implant survival rate of 96.1% to 98.6% using Albrektsson's success criteria. This however, included both dental implants placed simultaneously and using the two-stage protocol. Implant survival rate in the present study was 89%.

Two patients in our study underwent immediate placement of dental implants at the time of reconstruction. In one of these two patients, the dental implants were lost with the failed vascularised free fibula flap. Delayed placement of dental implants in this study was performed at various periods ranging from 6 months to 35.5 months and, as a result, it was not possible to compare the immediate and delayed placement of dental implants or to establish the presence of any significant association.

There also appears to be no general agreement on whether dental implants fail more frequently due to radiation therapy or not (Sozzi et al, 2017). While some investigators report that radiation therapy decreases vascularisation, induces fibrosis and results in a decreased resistance to infection, thus resulting in a poor dental implant prognosis (Ferrari et al, 2013; Sozzi et al, 2017; Jackson et al, 2016), others do not consider it a contraindication for placement of dental implants in cancer patients that will undergo subsequent radiation therapy (Sozzi et al, 2017; Reyhler et al, 1994). Salinas et al, (2010) and Jackson et al, (2016) reported no significant association between radiation therapy and failure of dental implants, and concluded that radiation therapy may not be a risk factor for dental implant failure in the irradiated fibula. Some authors propose the uses of Marx's hyperbaric oxygen protocol for the placement of dental implants in an irradiated fibula, i.e. 20 dives

(100% oxygen, 2.4 atmospheres absolute pressure, 90 minutes) before and 10 dives after the placement of dental implants. A concern with Marx's hyperbaric oxygen protocol though is the controversy surrounding the use of hyperbaric oxygen therapy in cancer patients and its purported increased risk of tumour growth in close margins. Stepien et al, (2016) however reported that hyperbaric oxygen therapy inhibited tumour growth. Reychler et al, (1996) reported no complications with placement of dental implants in irradiated fibulas despite their patients not having received hyperbaric oxygen therapy. One patient in the present study had immediate placement of dental implants followed by radiation therapy. All the dental implants in this patient successfully osseointegrated into the irradiated fibula.

Complications of vascularised free fibula flaps have been classified as early or delayed while others classified them as either minor or major complications or recipient-site specific complications or donor-site specific complications. Reported complications rates vary from 26.5% (Lopez-Arcas et al, 2010), 33.3% (Avraham et al, 2014) to 40% (Toto et al, 2015). Some studies reported no complications at the donor site with patients being able to walk one month post-operatively (Ferri et al, 1997; Yilmaz et al, 2008). The rate of complication in the present study was 40%. Complications were classified as major or minor complications, similar to Yilmaz et al, (2008), with major complications being those that affect the success rate of the vascularised free fibula flap such as anastomosis failure while minor complications did not affect the success rate and either resolved spontaneously or with surgical or other intervention. Of the 20 patients in our study, 2 suffered major complications leading to graft loss.

Thirty percent of the patients in this study suffered dehiscence at the recipient site which subsequently resolved. This is lower than the results reported by Weitz et al, (2016) (40%) and Ritschl et al, (2017) (38%). In contrast, other authors have reported much lower complication rates, namely, Jackson et al, (2016) (5%), Shen et al, (2013) (6.67%), Toto et al, (2015) (7%) and van Gemert et al, (2018) (22%).

Four of the 20 (20%) patients in this study developed sepsis at the recipient site post-operatively which subsequently resolved. This is lower than the results of van Gemert et al, (2018) (34%) but significantly higher than the results of Jackson et al, (2016) (1%) and Toto et al, (2015) (3.5%).

Necrosis of the skin paddle is reported to be less than 1% by most studies. One of the 20 (5%) patients in this study suffered necrosis of the skin paddle. This is comparable with the results of Toto et al, (2015) who found that 5% of the participants in their study suffered necrosis of the skin paddle. This is in contrast to the results of Yilmaz et al, (2008), Xu et al, (2017), van Gemert et al, (2018) and Jackson et al, (2016) who all found less than 1% necrosis of the skin paddles in their studies.

The sample size of this study is relatively small by comparison to studies of similar time span in the literature. The low number of vascularised free fibula flaps being undertaken at our institution is attributable to the following factors:

- A shortage of funding limiting the number of cases that can be performed.
- A lack of surgeons with the required surgical skills and experience to perform vascularised free fibula flaps.
- A shortage of Intensive Care Unit (ICU) beds required for patients to be taken care of post-operatively thus leading to cases being cancelled.

Also, delayed presentation with large inoperable tumours results in most patients being referred for radiation therapy. The increased patient load for patients requiring radiation treatment together with the limited financial and equipment resources places more strain on the Department of Radiation Oncology at the institution resulting in long waiting lists for radiation treatment. This also impacts on patients requiring radiation therapy after surgery and negatively affects the 5-year survival rate of these patients.

CHAPTER 7

7. Summary and conclusion

This study sought to retrospectively evaluate outcome of mandibular defects reconstructed with VFFF. Twenty patients (8 Males, 12 Females) were included in the study. Neoplasia, SCC in particular, was the most common indication for reconstruction with VFFF.

There was a 90% fibula graft success rate. No significant associations were found between gender, age and race, or aetiology of defect, the number of segments the fibula is osteotomized into, radiation therapy, timing of dental implant placement and complications and the reconstruction outcome.

The overall complication rate in the present study was 40% and ranged from graft loss to dehiscence and minor sepsis. The minor complications encountered in 6 patients did not influence the success of VFFF bone graft.

Based on this study, we recommend a two-stage protocol for rehabilitation of patients with VFFF, where the initial procedure would be reconstruction of the defect with a vascularised free fibula flap. This will be followed by the delayed placement of dental implants. In the case of trauma or benign neoplasms dental implants may be placed at least six months post operatively. However in the case of irradiated fibulas, the placement of dental implants should be delayed for at least 12 months. This will be followed by delayed loading of the dental implants with a prosthesis once osseointegration of the dental implants has occurred. It is also recommended that stringent patient selection criteria be established for this procedure.

A larger sample size and a standardized follow-up period could have validated the findings in this study. The disproportionate distribution between the number of patients that received the immediate and delayed placement of dental implants and those that were irradiated or not in this study is also a limitation that did not allow adequate comparison between these two groups. Further studies with a larger sample size, standardized follow-up period and similar distribution between the two

groups are necessary to further substantiate and give statistical support to the present trends.

It is hoped that such studies will provide data that will assist in the establishment of evidence-based protocols to improve clinical outcomes of VFFF grafts and hopefully attract funding for these cases.

CHAPTER 8

8. Appendices

8.1. Appendix A: Ethics clearance certificate



R14/49 Dr Priyesh Guvant Hira

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M170521

NAME: Dr Priyesh Guvant Hira
(Principal Investigator)
DEPARTMENT: Maxillofacial and Oral Surgery
Charlotte Maxeke Johannesburg Academic Hospital

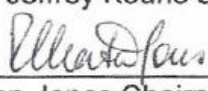
PROJECT TITLE: A Retrospective Analysis of Mandibular Grafting
Using Fibulas at Charlotte Maxeke Johannesburg
Academic Hospital

DATE CONSIDERED: 26/05/2017

DECISION: Approved unconditionally

CONDITIONS: Additional Supervisor (24/07/2017)

SUPERVISOR: Dr Sunita Singh, Dr Jeffrey Kourie and Dr Risimati Rikhotso

APPROVED BY: 
Professor P. Cleaton-Jones Chairperson, HREC (Medical)

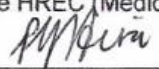
DATE OF APPROVAL: 13/07/2017



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 in Room 10004, 10th floor, Senate House/3rd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand. 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 May and will therefore be due in the month of May each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).


Principal Investigator Signature

Date

02/08/2017

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

**8.2. Appendix B: Permission to conduct the study in the Department of
Maxillofacial and Oral Surgery**



GAUTENG PROVINCE

HEALTH
REPUBLIC OF SOUTH AFRICA

18 May 2017

CEO
Charlotte Maxeke Johannesburg Academic Hospital

Dear Sir/Madam,

RE: PERMISSION TO USE PATIENT WITS ORAL HEALTH CENTRE RECORDS TO CONDUCT A
RESEARCH STUDY – BY DR P HIRA

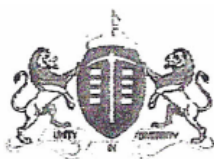
This serves to confirm that I support Dr Hira to conduct his research on “A retrospective analysis of mandibular grafting using fibulas at Charlotte Maxeke Johannesburg Academic Hospital” using data and records for Maxillo-Facial and Oral Surgery Department. All the necessary support will be made available to him to ensure successful completion of the study.

Yours sincerely,

DR E RIKHOTSO
HOD-MFOS

8.3. Appendix C: Permission to conduct study and use patient Wits Oral

Health Centre records



GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

WITS ORAL HEALTH CENTRE

Private Bag X15 Braamfontein, Johannesburg, 2017

Enquiries: Ms Tumelo Marule

Tel: (011)488-4893, Fax 086 406 3196

E-mail: Tumelo.Marule@wits.ac.za

23 June 2017

Dr P Hira
Maxillo-Facial and Oral Surgery
Faculty of Health Sciences
University of the Witwatersrand
Johannesburg

REGARDING: PERMISSION TO USE PATIENT RECORDS TO CONDUCT A RESEARCH STUDY.

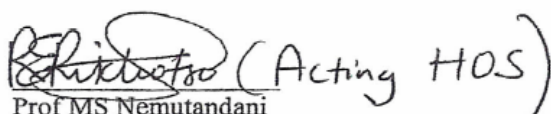
REFERENCE :HRRC/JUN/02/2017

It is my pleasure to grant final approval to utilize resources at Wits Oral Health Centre in order to conduct your research.

The Hospital Research and Risk Committee allocated a unique reference number to this application – Kindly quote this reference number in all future correspondence regarding this research.

Please note that the Hospital Research and Risk Committee should be informed of the estimated date the research will commence, as well as regular status reports until the research has been concluded. Within a month after conclusion of the research project, a written report must be submitted to the Head of School/CEO, summarizing the final result/outcome as well as the recommendations made based on the research concluded.

Regards,


Prof MS Nemutandani
CEO/Head of School

**8.4. Appendix D: Permission to conduct study at Charlotte Maxeke
Johannesburg Academic Hospital and use patient hospital records**



GAUTENG PROVINCE

HEALTH
REPUBLIC OF SOUTH AFRICA

CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC HOSPITAL

Enquiries:
Ms. N. Mzila
Office of the Clinical Director
Tell: (011): 488-3365
Email: Nolwazi.Mzila@gauteng.gov.za
29 September 2017

GP_201709_009

Dear Dr. P. Hira

STUDY TITLE: *A Retrospective Analysis of Mandibular Grafting Using Fibulas at Charlotte Maxeke Johannesburg Academic Hospital*

Permission is granted for you to conduct the above recruitment activities as described in your request provided:

1. Charlotte Maxeke Johannesburg Academic Hospital will not anyway incur or inherit costs as result of the said study.
2. Your study shall not disrupt services at the study sites.
3. Strict confidentiality shall be observed at all times.
4. Informed consent shall be solicited from patients participating in your study.

Please liaise with the HOD and Unit Manager or sister in charge to agree on the dates and time that would suit all parties.

Kindly forward this office with the results of your study on completion of the research.

Supported / ~~not supported~~

**Dr. M.I. Mofokeng
Clinical Director**

DATE: 03/10/2017

Approved / not approved

**Ms. G. Bogoshi
Chief Executive Officer**

Date: 05.10.2017

8.5. Appendix E: Data collection sheet

[illegible]

CHAPTER 9

9. List of references

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