Evaluation of the clinical outcome of curvilinear transport distraction osteogenesis and revascularised fibula free flaps in the reconstruction of large post-maxillectomy defects

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Associate Professor George Vicatos

Supervisor

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DEDICATION

For my beautiful wife and companion Lamiz and our wonderful children Adam, Yasmin, Nazar and Iskandar. Thank you for allowing me to deprive you of our precious family time.

Also with deepest gratitude to my late father Ismail and mother Mariam for instilling in me the attributes to not only persevere, but to also embrace adversity as an opportunity to do better.

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This project had its origins way back in 2010 when I had the privilege of spending some time at the University Medical Center in Groningen, the Netherlands. Professors Ruud Bos and Jerry Raghoebar very kindly offered their expertise and facilities to me so that I could undertake this study in their Department of Maxillofacial Surgery and Prosthetics. However, it would have meant spending a year full-time in the Netherlands which, unfortunately, I could not afford as I was and still am a specialist practitioner in private practice. Nevertheless, their encouragement and guidance provided me with the necessary foundation to tackle this project 'remotely' in Cape Town.

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Most academic pursuits need a home and, as a private practitioner, I needed one too. So I contacted Professor Donald Hudson from the Department of Plastic Reconstructive and Maxillofacial Surgery at the University of Cape Town. With the help of Professors Del Khan (Head of the Division of Surgery) and Anwar Mall (Head of the Departmental Research Committee at UCT), I was allowed to register this project at the University of Cape Town under the auspices of the Department of Surgery. My deepest gratitude goes to these three gentlemen, but it needs to be mentioned that Professor Donald Hudson was the constant driving force behind my progress with this project, and I am indeed grateful to him for not only agreeing to be my co-supervisor, but also making sure that I was given the necessary operating time and facilities to finalise my project. Don, I am indeed deeply indebted to you for the privilege that you bestowed upon me over these years.

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PUBLICATIONS AND PRESENTATIONS ARISING FROM THIS THESIS

Publications:

James Boonzaier, George Vicatos, and **Rushdi Hendricks**. Repair of segmental bone defects in the maxilla by transport disc distraction osteogenesis: Clinical experience with a new device. *Annals of Maxillofacial Surgery* 5.1 (2015): 85.

Presentations:

Post-maxillectomy reconstruction of large segmental defects through transport distraction osteogenesis (oral presentation). Pan-African Division of the International Conference of Oral and Maxillofacial Surgeons, September 2012, Vineyard Hotel, Cape Town, South Africa

Patents:

1. Transport Distraction Apparatus US **WO 2013076693 A1**

Inventors	George VICATOS, **Mogamat Rushdie HENDRICKS,** James Angus BOONZAIER
Applicant	University Of Cape Town

Future publications:

Manuscript submissions are being developed for which the data are available for inclusion (to be submitted within the next 3 – 4 months).

ABBREVIATIONS

#	number
%	percentage
3-D	three -dimensional
ALP	alkaline phosphatase
ASTM	American Society for Testing and Materials
bFGF	basic fibroblast growth factor
bFGF-β	basic fibroblast growth factor - Beta
BIPP	bismuth iodoform paraffin paste
BMP	bone morphogenic protein
cbfa-1	core-binding factor alpha(1)
c-FOS	a proto-oncogene/transcription factor
cm	centimetre
CT	computer-aided tomography
CTDO	curvilinear transport distraction osteogenesis
DO	distraction osteogenesis
ECM	extracellular matrix
ErK	extracellular signal-regulated kinases
et al.	and others
ets-1	ETS proto-oncogene 1, transcription factor
FAK	focal adhesion kinase

FIZ	fibrous interzone
GIT2	cytoskeletal regulatory scaffold protein
Gy	Gray
HBO	hyperbaric oxygen
HIF	hypoxia inducible factor
Hif1α	hypoxia induced 1 Alpha
HIV/AIDS	human immunodeficiency virus/acquired immunodeficiency syndrome
HREC	Human Research Ethics Committee of the University of Cape Town
HU	Hounsfield unit
H-V	Hendricks-Vicatos
IGF	insulin growth factor
IL-1	interleukin-1
IL-6	interleukin-6
ISO	International Organization for Standardisation
kg/f	kilogram/force
LDPE	low-density polyethylene
mRNA	messenger ribonucleic acid
M2	diameter of screw (usually 1.9 mm)
M3	diameter of screw (usually 2.9 mm)
MAP	mitogen-activated protein
MCF	microcolumn formation

Micro-CT	micro-computer-aided tomography
Mm	millimetre
MPa	megapascals
MRC	Medical Research Council
MRI	magnetic resonance imaging
MSC	mesenchymal stem cells
N	newton
Ncm	newton centimetre
Nm	newton metre
NO	nitric oxide
NOS	nitric oxide synthase
OFS	obturator function scale
OPG	osteoprotegrin
P	probability quantifying the strength of the evidence against the null hypothesis in favour of the alternative
$p\leq$	probability equal to or less than
$p\geq$	probability equal to or greater than
PI	principal investigator
Pi3K	phosphatidylinositol-4,5-bisphosphate 3-kinase
PMF	primary mineralisation front
QOL	quality of life
RANK	receptor activator of nuclear factor kappa-b

RANKL	receptor activator of nuclear factor kappa-b ligand
RFFF	revascularised free fibula flap
ROC	radius of a curve
ROCK	rho-associated, coiled-coil-containing protein kinase
ROI	region of interest
SD	standard deviation
Smads	intracellular proteins that transduce extracellular signals from TGF-β ligands to the nucleus
STATA	Statistics and Data Software Package
STL	stereolithography
TDO	transport distraction osteogenesis
TGF	transforming growth factor
TGF-β	transforming growth factor-beta
TNF-2	tissue necrosis factor-2
TrK	tropomycin receptor kinase
UW-QOL	University of Washington − Quality of Life
V1	Version 1
VEGF	vascular endothelial growth factor
VEGFR	vascular endothelial growth factor receptor
Wnt	wingless-related integration site (signalling protein)
αvβ3	The integrin plays an important role in angiogenesis.

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ABSTRACT

Background: Maxillary defects caused by trauma or tumour resection in the head and neck region can be devastating to the patient from a cosmetic and functional perspective. Patients who undergo maxillectomy procedures experience a substantial deterioration in their primary oral functions such as breathing, mastication, salivation, deglutition and phonation, which has a collective adverse influence on their quality of life (QOL). The revascularised free fibula flap (RFFF) has been demonstrated to be most reliable for the reconstruction of maxillary defects, and has been regarded as the 'gold standard.' A novel method of regenerating bone and soft tissue through the process of curvilinear transport distraction oseteogenesis (CTDO) has been developed and compared with the RFFF technique.

Method: A prospective cohort study of 6 post-maxillectomy patients was compared regarding the clinical outcome of function and aesthetics with a group of 6 patients who had undergone RFFF reconstruction. The new bone (regenerate) was compared with the parent bone from which it had been generated. Objective measuring tools were employed to assess pre and post quality of life (QOL) aspects. The RFFF patients were not subjected to any invasive procedures save to undergo a clinical evaluation and undergo a CT scan of their maxillae. A cohort of 6 participants was treated prospectively using CTDO and the results were analysed within that cohort. These results were compared with a retrospective group of 6 participants of similar age and gender distribution who had undergone RFFF reconstruction as an external control. The patented Hendricks-Vicatos (H-V) maxillary transport distractor was applied to all selected participants by the primary investigator under general anaesthesia at Groote Schuur Hospital or a private clinic. The H-V maxillary transport distractor (5 prototypes) was pre-shaped and pre-fitted onto a 3-D model of the participant`s maxilla, in a laboratory. This method reduced clinical installation time. If teeth were present in the area to be distracted, then at least 2 teeth were removed from the maxilla, preferably three months before the date of distraction. In the first few cases, this was the protocol for developing bone stock. This protocol was revised in the last 2 patients of the study, where no teeth were extracted at all. A linear fracture (bi-cortical) was created in the maxilla in a vertical direction (segmentally) to develop a mobile, well-vascularised transport disc. This carrier disc was attached to the metal plate of the 'crawler' via

small titanium screws. The crawler was then moved on the reconstruction plate (Biomet^{TM} Zimmer Biomet, Warsaw, Indiana, USA) as per plate-guided distraction to regenerate new bone and soft tissue. Histological evaluation comprising trephine bone biopsies (2 mm – 3 mm diameter by 10 mm depth) were carried out by the primary investigator in the areas of the test and control regions of interest (ROIs) at the time of removal of the distraction apparatus in the cohort cases. Dental implants were placed into the same osteotomy sites of the trephine biopsy locations.

Results: The **width** of the alveolar bone was computed based on the measurements taken from study models. When comparing all three areas of interest, namely A, B and C collectively, it was noted that the newly formed bone possessed anatomical and physiological characteristics commensurate with the control (parent) bone. The measurements of the **depth** of the alveolar vestibule were taken at three different points as described above. When all three areas, namely A, B and C, are taken as an average, there was no statistical significance between the control and the parent bone (A: $p \geq 0.99$; B: $p=0.25$; C: $p \geq 0.99$). The **width** of the new bone compared most favourably with that of the **fibula** bone. In the areas of A, B and C, there was no statistical difference between the new bone and the fibula bone. In area A, the **depth** of the fibula sulcus was about half that of the new bone. In area B, the depth of the fibula sulcus was less than half of that produced by the new bone (regenerate). In area C, the depth of the fibula sulcus was almost one-third that of the alveolar bone created by the regenerate. The comparison between the fibula sulcus depth and the new alveolar bone showed clearly that the vestibule produced by the new alveolar bone was **superior** to that generated by the fibula bone. When comparing Hounsfield units over a period of nine months between the regenerate and the parent bone, the Wilcoxon matched-pairs signed rank test was employed to compare the median bone densities. The latter showed no significant difference between the regenerate and the control bone ($p>0.05$). The result indicated clearly that the regenerate bone was as good as the parent bone. The results showed no significant difference in bone density between the regenerate bone and the fibula bone. When comparing the regenerate bone method to that of the fibula bone, the Mann-Whitney test showed that there was no statistical difference between the new bone (regenerate) and the fibula bone at three months. In terms of QOL, there was (1) a significant increase in the patient's ability to participate in **recreational activities** ($p=0.03$) post surgery;

(2) a marked improvement in the patient's **mood** post surgery (*p*=0.03); and (3) a significant decrease in **anxiety**, **avoidance** and **difficulties** (*p*=0.03, *p*=0.03 and *p*=0.03 respectively) post surgery. Additionally, when comparing the accumulative QOL score pre and post surgery, there was a significant improvement in QOL (***p<0.0001).

Regarding histological results, the **quality** and **strength** of the distraction bone appeared to be better than that of the control sample. The volume of regenerate was far more copious, and the **new cancellous bone was considerably thicker than the control cancellous bone.**

Discussion: The project comprised two main objectives: (1) the development of the device including subsequent improvements which led to the production of five prototypes that were used successfully to create an excellent quality and volume of new bone and soft tissue; and (2) to establish the biological responses to the CTDO technique. When the CTDO technique was compared with the current gold standard of RFFF, it produced a quality of bone and soft tissue that was in most respects equivalent, and in other respects superior, to the latter technique.

Conclusions: The results of the present study show that the method of CTDO compares favourably to the RFFF method and appears to be superior in several further aspects. It was found that the new alveolar bone had a vestibular depth **almost double** that created by the fibula bone. This was indeed a **highly significant clinical finding** as it determined the functional and aesthetic value of the new alveolar bone.

CHAPTER 1. LITERATURE REVIEW

1.1 Historical background to limb lengthening

Limb lengthening was attempted as early as the 19th century, as surgeons struggled to treat the debilitating outcomes of war injuries, mainly malunion of femoral shaft fractures, and also deformities following on poliomyelitis.

The pioneers of limb lengthening who performed a single-stage lengthening osteotomy were surgeons such as Von Langenbeck (1869) [1], Hopkins and Penrose (1889) [2], and Von Eiselsberg (1897).[3] However, modern techniques of limb lengthening found their origin in the early 1900s with the work of Alessandro Codivilla, an Italian orthopaedic surgeon in Bologna, Italy. He investigated novel ways of managing many complicated orthopaedic conditions, such as clubfoot, scoliosis, congenital dislocations of the hip and the residual of poliomyelitis. He initially reported his work on the use of external pin fixation and traction for bone lengthening in the Italian literature in 1903.[4] In June 1904, he gave a presentation at the Annual Meeting of the American Orthopaedic Association and the first English-language report in 1905.[5] Codivilla acknowledged that others had previously attempted limb lengthening, and wrote the following:

> The greater number have applied constant traction, after having separated the bone; others have used great stretching under narcotics, followed by constant extension of the muscles, by means of weights; others again, after the stretching have applied the plaster apparatus.[5]

However, Codivilla astutely noted that the choices of the technique by most surgeons were often empirical, without much clinical evidence to support their methods. He presented two separate approaches. For relatively small degrees of short legs, he recommended acute forced lengthening under narcotic sedation. However, for larger increments of short legs, he offered a method called 'continuous extension' (Figure 1.1). This approach meant that he applied moderate traction by way of placing a pin in the calcaneal bone. He made an oblique osteotomy in the femur using a chisel, followed by the application of a medium amount of traction (25 kg – 30 kg). He then placed the patient in a 'plaster jacket', encompassing the thorax, pelvis and leg, and incorporating the calcaneal pin. If the lengthening was not sufficient, he then cut the cast at the level of the osteotomy and added more traction in stages (however, not exceeding 25 kg – 30 kg per stage).

He found that, by using this technique, the desired length could be obtained within a period of 20 days but that he could also continue for 30 – 35 days without any pin complications. Codivilla presented his results in 1905 wherein he treated 26 patients with limb shortening secondary to a variety of causes.[5] All his patients achieved the desired lengthening, ranging from 3 cm to 8 cm. Complications of this technique included the following: severe nerve lesions, skin complications, and persistent uncontrollable convulsions. Despite these difficulties, Codivilla wrote as follows: 'The method has borne the very best results, correcting the deformity, and diminishing, or completely removing, the shortness of the limb.'

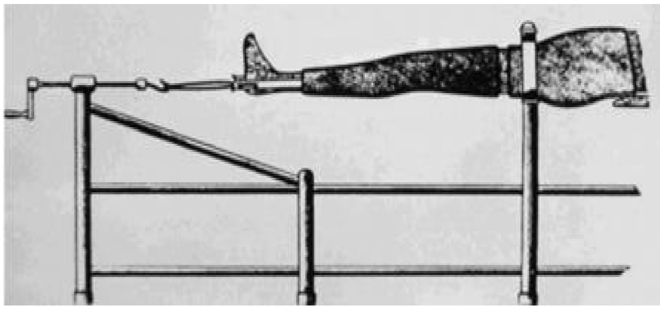


Figure 1.1: Schematic representation of Codivilla's 'continuous extension' technique.[5]

Over the ensuing few years, Codivilla's technique was adopted and implemented throughout the United States and Europe. In Chicago in 1908, Magnuson performed the first experimental studies of this technique. By utilising a dog model, Magnuson carried out the first empirical studies to demonstrate that single-stage lengthening of 5 – 7.5 cm could be effected successfully without damaging the soft tissues. Magnuson advised a Z-shaped osteotomy after making several drilled holes and dividing the periosteum longitudinally, reporting that this method would minimise damage to the underlying periosteum and endosteum.[6]

For the following few years, Magnuson carried out this process in humans and performed 14 limb-lengthening procedures. However, he encountered serious complications, including shock, both before and after surgery in all of his patients. Unfortunately, one patient died during or after the operating procedure.[6]

Codivilla's technique indeed created much excitement. Hence, many surgeons sought to advance the science of limb lengthening by improving on his method.

In Cincinnati in 1911, Freiberg attempted the bone lengthening method over several sessions to overcome the problem of shrinking of the soft tissues. Freiberg operated mainly on poliomyelitis patients. He designed and created an operating table with a built-in sidepiece resembling a saddle to exert sufficient counter-traction force. He produced a pulling force in a distal direction using a screw and a spring as a dynamometer. He found that the force necessary for lengthening ranged between 25 kg and 50 kg.[7]

In 1913, Ombredanne modified the technique of Codivilla further by recommending an oblique osteotomy with a slow, gradual lengthening.[8] He attached one pin above and one pin below the osteotomy line, using an apparatus fitted to the side of the thigh. In this way, he managed to achieve up to 4 cm of bone lengthening. Unfortunately, however, the operation was frequently followed by osteomyelitis, and he abandoned the method.[9]

In Seattle in 1913, Fassett developed a single-stage procedure whereby he lengthened the femur by approximately 3 cm. He controversially inserted bone chips into the osteotomy site and stabilized the osteotomy with a plate. However, he too noted many serious complications. Fassett subsequently wrote: 'With modern surgical technique, almost everything is possible, but not everything which is possible is necessarily worthwhile.'[10]

In 1916, Taylor presented his decade-long experience to the American Orthopaedic Society in performing bone lengthening operations to the femur. Taylor`s technique comprised a Z-shaped osteotomy, which he encircled in plaster. He proceeded to section the plaster longitudinally and, over a period of 10 days, distracted the two halves of the bone by using threaded rods with blocks of magnesium or ivory bolted into the distraction gap. Severe infection seriously complicated his technique, and he subsequently came to favour the method of shortening the unaffected healthy limb.[9]

In 1912, Putti succeeded Codivilla as director of the Rizzoli Institute of Bologna. He pursued the work of Codivilla on leg lengthening.[11] Putti lectured to the American Medical Association in Boston in 1921, reporting on several cases of femoral lengthening. He stressed the need for an osteotomy involving minimal trauma and also for a gradual, controlled lengthening of bone.

Putti's method required one or two pins inserted into the proximal and distal ends of the osteotomy in both cortices of the femur. This procedure was carried out with a Z-shaped osteotomy, but without pre-drilling.[12] Putti used a telescopic tube (Figure 1.2) which he termed an osteoton, mounted to one side, that provided a continuous distraction for up to 30 days.[12, 13] This device resembled the modern unilateral external fixator. The mean length gained by using this technique was 8 cm. Unfortunately, however, it was not widely received owing to the impossibility of controlling the axial positioning with this insufficiently rigid apparatus.[3] Also, as the force was increased, the pins protruded out of the bones. When he converted the structure into a more rigid, three-dimensional fixator, the method became more practical. Putti substituted his technique for the distraction method performed, with the use of piano wires, and a stationary extension device fitted to the bed of the patient. [13] However, he was not the first to employ wires for limb lengthening. Klapp first used this method in 1913 during the Balkan War.[3]

Figure 1.2: The osteoton described by Putti in 1921.[12]

In 1918, Herzberg again applied traction to wires using a frame and demonstrated that he could, without the risk of infection, carry this out for quite a long time.These devices enabled the surgeon to reposition the fragments freely and obtain controlled axial correction.[3]

1.1.1 Advent of the latency period

Abbott and Crego in 1921 attended Putti`s lecture and subsequently adopted the osteoton and began performing limb-lengthening operations in St. Louis in 1924.[3] The two workers improved on the main weakness of the osteoton –its lack of unilateral fixation. They inserted drill wires proximally and distally to the osteotomy site throughout the entire cross-section of the tibia.[4] They connected the wires on both sides to telescopic tubes or threaded rods, thereby creating a stable frame construction. After performing the osteotomy, Abbott carried out an intraoperative distraction of between 1 cm and 2 cm. After waiting for 7 – 10 days post surgery, he began a gradual distraction of 1.5 cm – 3 cm daily. **The waiting period is the first record of a latency period used before distraction osteogenesis.**

By the 1930s, Abbott and Crego had performed their procedure on 73 patients; however, they noted numerous complications.[14] Equinovalgus deformity of the foot resulted from dissociation in the tibiofibular joint and a disproportionate lengthening of soft tissue in the lower leg. They also observed restriction in movement within the hip joint, flexion contractures of the knee joint and procurvatum or recurvatum of the distracted tibial fragments. There were also weakening of the muscles of the lower limb, paralysis of the peroneal or tibial nerves, infections of the pins, pressure necrosis of the skin, aseptic and septic necrosis of the fragments with associated osteomyelitis, and delayed fracture formations.[15] Abbott performed extensive anatomic studies and made modifications to his original technique in an attempt to stem these complications. He tried to solve the problem of soft tissue shrinking using excessive dissection of the fascia, periosteum and interosseous membrane. Abbott separated all of the muscle origins on the proximal part of the tibia initially by subperiosteal dissection and performed the actual lengthening procedure in a second operation. Also, he waited up to 2 weeks after the osteotomy (latency) before commencing the process of lengthening. Abbott successfully made lengthening procedures acceptable to both patients and surgeons throughout the United States. Many other professionals adopted his method on many different levels.[3] However, the widespread implementation of Abbott`s plan lacked proper patient selection and was carried out without sufficiently safe operative protocols and methodologies. This indiscriminate use of Abbott`s method led to leg amputation, septicaemia, and even death. Abbott eventually condemned the operation, and in 1939 he wrote, 'We believe that this is not an operation for the uninitiated and should be reserved for those whose experience renders them competent to perform this technically difficult and delicate procedure.'[15] And, even though Abbott himself remained loyal to his method, he suggested contralateral leg shortening for the 'uninitiated.' Throughout the 1930s, modifications were made to Abbott's plan. The main problem that emerged from Abbott`s work was the lack of qualified surgical instrument manufacturers to construct his complicated apparatus.[3]

1.1.2 Advent of ambulation during distraction

In Dallas in 1928, Carrell advocated a more conservative osteotomy in which he preserved the periosteum, and the cortical bone was broken through to the opposite side.[16]

White, in 1930, used Steinmann pins which he incorporated into an encircling plaster cast.[17] After dividing the plaster, White attached two threaded rods and performed distraction along these rods. His method required 30 days for a lengthening of approximately 5 cm. **It was the first time that the apparatus was portable, allowing the patient to get out of bed.**

In Kansas City in 1932, Dickson and Divelet used Kirschner wires stretched between half-stirrups.[18] This modification resulted in better control of the fragments in the axial plane.

In Seattle, Roger Anderson similarly used a horseshoe shaped half-stirrup for each pin, thereby providing improved control in rotation.[18]

In New York in 1932, Haboush and Finkelstein reported some complications arising from the use of Abbott's technique.[19, 20] They found that radical dissection of the deeper structures did not prevent foot deformity and contributed to infections and failure of the regenerate. They conducted numerous cadaveric experiments and developed a new model, advocating a more conservative approach to dissection of the deep rigid structures and consequently recommended performing the exploration distant from the circular incision of the periosteum. This method allowed the regenerate to develop within a tube or a sleeve of periosteum.

In 1936, Compere also outlined the many complications of leg-lengthening procedures.[21] He pointed out that every surgeon had encountered numerous difficulties and that patients were often more severely compromised after their treatment than before. His work significantly dampened enthusiasm for the procedure. However, his paper was also the first to recognise the problem of devascularisation and established a protocol to avoid devascularisation.[3, 21]

1.1.3 Advent of bone distraction

Bosworth worked in New York throughout the 1930s to improve the concept of limb lengthening.[9, 13] He was the first to introduce the term 'bone distraction', and emphasised the importance of using a 'rigid frame'. He wrote that the level of the osteotomy did not influence the outcome and suggested that a second osteotomy site be performed to divide the distraction factor between the two locations. He also warned against radical dissection of the fascia. He reported his results from 24 patients, and again he described numerous complications. These included three infections and delayed unions, four non-unions, five cases of recurvatum, and eversion of the foot in six patients. However, he found that, in all of the uncomplicated cases, **a new marrow cavity** had developed within six months after the operation. He had made an astute finding.

In Chicago in 1941, Moore critically analysed leg-lengthening surgery. He performed 52 limb-lengthening operations and found that, in most cases, the shortening of the affected limb had been corrected, and the limbs were of the same length. However, he too noted an alarmingly high rate of complications, including deformities of the foot. Foot eversion was the biggest problem, and internal rotation at the knee joint induced by the procedure led to altered gait. In summary, the method failed to improve ambulation in most cases. He also found that this approach tended to result in attenuation of muscle power. Moore opted for the importance of function over cosmesis.[22]

In Los Angeles in 1942, Brockway and Benjamin performed 105 limb-lengthening procedures using Abbott's apparatus and method in its original form.[3, 23] Their results were found to be 'good' or 'satisfactory' in 87% of their patients. However, within their 'successful group' were delayed unions, sequestrations as well as foot and knee deformities. Outcomes in the remaining 13% were worse than the preoperative states. Also, osteomyelitis occurred in 22% of their patients.

1.1.4 Advent of the ring fixator

In 1944, Wittmoser developed a ring fixator for the lengthening of the tibia and fibula. His device resembled the fixator system in current use worldwide. However, his teacher **Bohler failed to recognise the brilliance of the underlying idea and could see no link with earlier studies.** He convinced Wittmoser not to publish reviews on his device.[24]

In 1950, Allan presented his results for limb lengthening in 105 patients in Birmingham. He emphasised that, while most patients strongly desire limb lengthening, they were not eager to accept a shortening procedure on the contralateral limb. He stated that a lengthening procedure restored the height and confidence of the patient, whereas the alternative method compromises the patient through deformation and disproportionate shortening. Allan created a relatively atraumatic osteotomy line, breaking through the bone after making a unilateral chisel osteotomy on the contralateral side. He immobilised and secured the fragments with tensioned Kirschner wires along several planes to provide control in the axial plane. Allan also used threaded rods to produce controlled and progressive distraction. He performed daily distraction at a rate of 1.6 mm per day, and lengthening was interrupted if discomfort and pain occurred. Allan also maintained that excessive soft-tissue dissection was not necessary, believing that soft-tissue contraction or shrinkage could be obviated with slow, gentle distraction. **With this technique, Allan was able to achieve bony union in all patients.**[25]

While these techniques were undergoing staged development in the United States, European surgeons were also developing their modifications to the limb-lengthening procedure. In Edinburgh in 1933, Cochrane adopted Abbott's technique and established a link between the United States and Europe.

In 1952, Anderson and Green introduced further improvements.[26] The problem of malpositioning of the foot led to the development of a screw synostosis of the distal tibiofibular joint. When a new fracture complicated the lengthening procedure, a less traumatic percutaneous osteotomy technique was embarked upon.[3]

1.1.5 Osteogenic potential of the fracture haematoma

Bier first described the osteogenic potential of a fracture haematoma. In 1905, he expressed his ideas on the fracture haematoma as follows: ‘It is these accumulations of blood that constitute the natural conditions for the healing of a fracture’.[27] He understood that the occurrence of a fracture haematoma provided the infrastructure to stimulate bone metaplasia. Bier also postulated that new bone was built up in layers like an onion around the central haematoma and that the bone ends had little or no part in the formation of the regenerate. **He was unable to appreciate the osteogenic potential offered by the periosteum and the endosteum**.[27] He reported his results with femoral lengthening where he cut through the periosteum, cortical bone and cancellous bone. He waited a few days (latency) before commencing distraction to exploit the stimulus of the fracture haematoma. He applied traction and counter-traction on the same bone. Bier reported six out of seven successful attempts at femoral lengthening, in spite of the fact that severe pain and sciatic nerve lesions complicated his bone lengthening.[28]

1.1.6 Tension stresses promote bone formation

In 1942, Glucksman carried out *in vitro* experiments and found that the application of tension stresses tends to promote bone formation in tissues with osteogenic potential. He also determined the pattern of osseous architecture.[29]

In the 1950s, Krompecher introduced the principle of ‘direct desmoids ossification’, referring to the direct formation of new woven bone created by the process of osseodistraction.[30] As understanding of the basic biological principles of limb lengthening improved, the methods of leg lengthening gained acceptance.

In 1963, Wagner developed a new approach to limb lengthening through the introduction of his technique that he staged as three sequential operations. The index procedure involved an osteotomy to the diaphysis and application of a monolateral external fixator that served as the lengthening device. Immediately, the osteotomy was distracted by 5 mm. **There was no latency phase**, and distraction was begun immediately at a rate of 1.5 mm – 3 mm per day. The regenerate was often of poor quality, requiring additional procedures. During the second procedure, the distraction gap was bone grafted, and a plate was applied. A third operation was necessary to remove the plate (Figure 1.3).

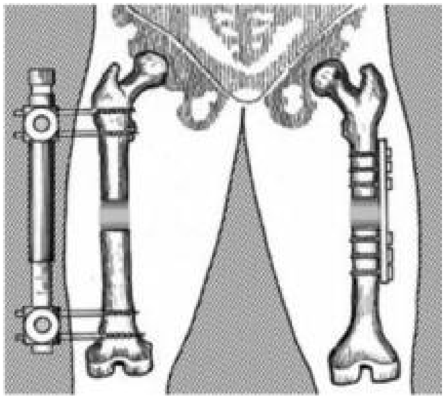


Figure 1.3: Posterior view of schematic representation of a left femur undergoing the first phase of Wagner's technique and a right femur after the second period.[31]

This method was technically simple and in keeping with contemporary ideas. Thus its use became prevalent across the United States and Western Europe.[31] However, the method offered no significant advantages regarding early mobilisation of the patient. It also disregarded the soft tissues and the core biological principles of distraction osteogenesis and involved several major operations. Also, the technique had a high rate of complications including acute hypertension at the time of the distraction procedure, infection, as well as early and late fracture.[32] Despite these significant disadvantages and difficulties, Wagner's technique gained ground in Germany, and eventually the method was adopted in the United States.

1.2 The seminal work of Gavril Ilizarov

While Wagner advanced his technique in the West, Ilizarov, working in Kurgan, Siberia, introduced the methodology and biological principles that would successfully unite the operational principles of limb lengthening with the biology of distraction histogenesis. He first used his method in 1951 for the treatment of a bone defect caused by tuberculosis. Ilizarov developed a circular external skeletal fixation device that attached to the bone with tensioned transfixion wires. Threaded rods connected the rings of the apparatus to each other. The technique was designed to stimulate and harness the biological potential of the tissues.

In 1952, Ilizarov introduced the modular ring fixator.[9, 33] This stable device facilitated greater precision in the technique of osseodistraction while rendering predictable results. In 1954, Ilizarov used this method to heal pseudoarthroses and fibrous nonunions, using a combination of local compression followed by distraction.[34] He underpinned the stimulatory effect of compression on bone healing and distraction on new tissue formation. Following on from osseodistraction, he utilised the compression concept again to transform the cartilaginous interface into new bone.

In 1956, Ilizarov observed new bone formation within a distraction gap while he was correcting an ankylosed knee flexion deformity by open osteotomy. He followed this by distraction with an external fixator and bone grafting.[33] In 1969, he reported on lengthening without the use of bone graft;[35] he wrote: '... living tissue, when subjected to slow, steady traction becomes metabolically activated in both the biosynthetic and proliferative pathways.'[36-38] Ilizarov performed an osteotomy of the cortical bone, referred to as a corticotomy, carefully preserving the vascularity to the medulla of the bone. He then carried out pure distraction and, by using this method, he was able to induce the formation of new bone at the lengthening site. He stated that the application of these principles would allow the physician to achieve bone formation in various applications.[36]

The Ilizarov technique embraces a straightforward set of principles.[39] The principles emphasise and focus on the superior biological quality of the regenerated bone following on the creation of a percutaneous corticotomy that reduces trauma to the periosteum and bone marrow while at the same time maximising the preservation of bone marrow and periosteal blood supply. **The technique also emphasises the importance of a postoperative waiting or 'latency' period.** Cardinal principles included multistage, incremental distractions totalling an amount of 1 mm per day and the use of a compression and distraction procedure involving full weight-bearing.

The method uses a ring fixator with fragments that are held securely by Kirschner wires under tension. This configuration enables the surgeon to exert planned control in all possible planes while allowing the correction of multidirectional deformities. Ilizarov developed the technique of **transport distraction** for defects of the bone shaft. He also emphasised the promotion of good tissue nutrition and joint mobility using a mobile device that allows full weight-bearing and physiotherapy.

The development of Ilizarov's concepts and methods decreased reservations attached to older procedures.[33] Initially, Ilizarov was largely unknown outside Russia.

Contemporaneously, Wagner's flawed technique was still widely employed in German-speaking countries and also in the United States. However, valid and ethical concerns over the number of procedures required and the attendant high rates of complications with the Wagner technique caused the focus to shift towards the Ilizarov technique. Subsequently, more than 2000 publications have been issued by the Ilizarov Institute in Kurgan, describing the favourable clinical results, biological concept studies, and technical protocols related to the use of transosseous compression and distraction osteosynthesis.[37]

Since 1983, more than 15 000 patients have been successfully treated at the Institute. Currently, about 9000 patients are treated there annually, and more than 300 000 have been successfully treated worldwide.[33]

The clinic was started in 1949 in a modest log cabin and has now developed into a research institute with 60 full-time PhD graduates. There is also a 1000-bed clinic staffed by 300 orthopaedic surgeons with more than 100 machinists on the grounds of the Institute, who fabricate the components of the Ilizarov apparatus.

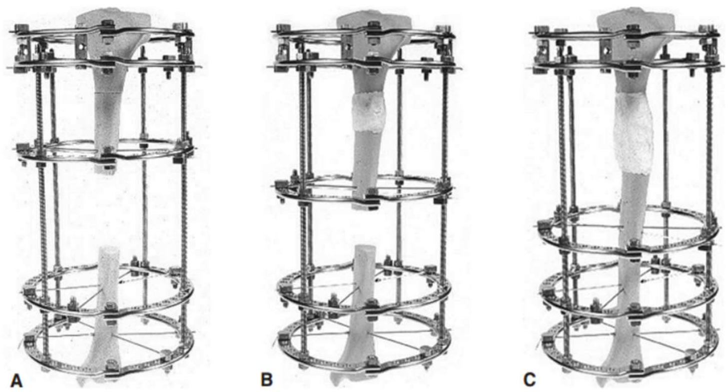


Figure 1.4: The phases of distraction osteogenesis: A, latency, B, distraction, and C, consolidation.[33]

1.3 The concept of distraction osteogenesis

The term **distraction osteogenesis** is used to describe the production of new bone between corticotomy surfaces undergoing gradual distraction (Figure1.4). New bone forms by a process akin to intramembranous ossification.[35, 40] Within this intramembranous ossification, areas of endochondral ossification may also be present.[40] Whether or not these areas of endochondral ossification within the regenerate are typical, remains a matter of controversy. Some investigators propose that cartilaginous occurrence is inherent to the standard process of regenerate formation.[41, 42] However, Ilizarov and others have argued that the presence of cartilage is indicative of instability or localised ischaemia.[39, 43-45] The site where the transported segment meets the target segment at the end of bone transport is termed the docking site.[46, 47] There is an appreciable difference in the histological appearance between the regenerate and the docking site. It is well documented that endochondral ossification predominates over intramembranous ossification in this region. There is a progressive increase in the quantity of bone tissue seen here accompanied by a concomitant decrease and ultimate disappearance of necrotic tissue and haematoma. This region displays a variable contingency of blood vessels. The histological findings at the docking site do not differ significantly from the standard process of secondary consolidation seen in a healing fracture but appear in a slower manner.[40] The direction of consolidation of the regenerate is another area of some controversy. Ilizarov and others make mention of **zone growth**.[39, 44, 46, 48] Zone growth assumes that the process of regenerate ossification is usually in tandem with similar regions adjacent to the osteotomised surfaces. A physis-like structure ossifies in both the proximal and distal directions from a central growth zone during the distraction process. The fibrous interzone, a collagen-rich central region, is usually the last area to undergo the ossification process. Under optimal conditions, this growth region is hardly visible during the distraction phase. During the neutral fixation period following distraction, the central growth area undergoes gradual ossification. Fibroblast-like cells become metabolically active and secrete collagen. The collagen eventually forms fibres that align themselves parallel to the force of distraction. Osteoblast activity results in osteoid production and eventually new bone formation. The new bone formation presents mainly at the proximal and distal ends of the regenerate. Another group of investigators argues that ossification of the regenerate site progresses in a uniform direction accompanying the transported segment of bone.[40] This directional growth has only been seen in animal models.

1.3.1 The corticotomy

One of the core principles of Ilizarov's technique is the use of a percutaneous corticotomy that reduces trauma to the periosteum and maintains the blood supply of the marrow and periosteum.[39] By opting for the utilisation of a corticotomy instead of an osteotomy, Ilizarov emphasises the importance of the blood supply to the process of osteogenesis. By cutting only within the cortex, both the periosteal and medullary blood supplies can be preserved. Aronson found that by conservatively displacing the edges of the corticotomy, the highly elastic spongiosa within the medulla could be maintained along with its medullary blood supply.[48]

Significant retardation of osteogenesis has been observed in animal studies when damage to the intramedullary nutrient vessels was created in osteotomised bones.[44] On the contrary, animals treated by corticotomy and preservation of the nutrient vessel demonstrated a more significant rate of bone formation.[39, 44]

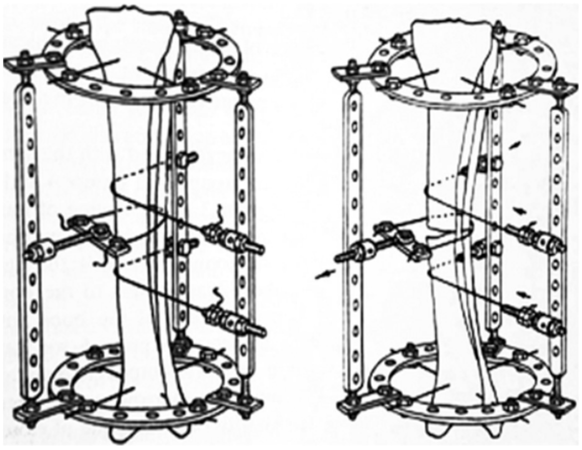


Figure: 1.5 Closed osteoclasis.[33]

Ilizarov developed the procedure known as ‘closed osteoclasis,’ whereby wires are placed around the bone and attached to the frame so that tensioning of the ligatures would produce a three-point bending force with a subsequent fracture of the bone (Figure 1.5).

Another accepted and traditional technique involves making a corticotomy by transecting approximately two-thirds of the cortex. The corticotomy is completed by deploying the method of osteoclasis which involves rotating the external fixation rings in opposite directions.[35, 44] Others have described a method of inserting the osteotome into the corticotomy site and rotating it by 90° until the remaining cortex fractures.[44] Further modifications of the technique described the use of a complete transverse osteotomy to ensure the division of the entire cross-section of the bone or connecting several drill holes with an osteotome. It is also acceptable to perform the corticotomy by means of a Gigli saw.

A 1994 animal study demonstrated that there was no significant difference in histology and bone density or in perfusion between the new bone formed in dogs that underwent corticotomy with osteoclasis and the new bone in dogs that underwent osteotomy using the drilling of many small holes in the bone.[44, 49] However, an increased rate of delayed consolidation was noted in the group that underwent osteotomy performed with an oscillating saw. The investigators postulated that this was secondary to thermal necrosis. Yasui found that a transverse osteotomy was as reliable as a corticotomy in rabbits as long as the periosteum was protected.[50] Again, this consideration reiterates the importance of maintaining a healthy blood supply.

1.3.2 The distraction process

Before the initiation of distraction, Ilizarov insisted upon a period of postoperative waiting.[39] The duration of this required **latency period** depends on the preoperative regional blood and the amount of trauma done during the corticotomy procedure. [41] This latency period usually lasts from 3 to 7 days and allows for neovascularisation before the initiation of distraction.[48] Ilizarov's experiments with distraction osteogenesis confirmed that both the rate and the rhythm of distraction affected the quality of the regenerate.[36, 39, 44]

Ilizarov performed his experiments in canine tibiae. He found that 0.5 mm of distraction per day often resulted in the premature consolidation of the regenerate, while 2 mm of distraction per day produced a poor regenerate, often with intervening fibrous tissue.[36, 39]. When distraction of 0.25 mm was carried out 4 times per day, this provided an excellent quality of regenerate and also allowed organisation of early mesenchymal growth into parallel bundles of collagen (Figure 1.6).

Figure 1.6: Electron micrograph showing healthy regenerate organised into parallel columnar collagen bundles.[36]

However, he found that the results were further enhanced when distraction was carried out unabated using an auto distractor that divided the millimetre daily lengthening into 60 equal steps. The distraction period usually proceeds until the desired length of gap formation is obtained. Collagen bundles begin to undergo mineralisation from both lateral corticotomy sites towards the centre.[46, 48] As long as the distraction continues uninterruptedly; the central region remains fibrous, thereby allowing viscoelastic lengthening. Mineralisation initially protects through the entire cross-section of the gap. At the completion of the distraction process, this solid cylinder of new bone remodels into the cortex and medullary canal.[46]

1.4 Distraction osteogenesis in the maxillofacial region

The literature has been extensively reviewed by Swennen *et al*. in 2001 with two elaborate articles covering the expanse of topics relating to distraction osteogenesis (DO) in general.[51] Further, systematic reviews were carried out on protocols for distraction rates in animal models by Djasim *et al.* in 2009 [17] and on alveolar distraction by Saulacic *et al* in 2008.[52] Most of the publications referred to mandibular and alveolar distraction; however, not much has been written about transport distraction as a subject dedicated entirely to the maxilla.

In 1973, Snyder *et al* introduced the application of DO in the maxillofacial complex by experimenting on maxillary elongation in dogs.[53] In 1992, for the first time in the western literature, Joseph McCarthy *et al.* reported on the clinical application of mandible elongation by gradual distraction in patients with hemifacial microsomia and Nager syndrome, first and second pharyngeal arch deformities.[54]

In humans, DO has been used for the surgical expansion of the hard palate[55] and elongation of the mandibular symphysis.[56] Also, DO has been used for the correction of congenital facial abnormalities,[57] and the management of cleft patients[58] while repairing continuity defects of the mandible by transport distraction. Lastly, DO was also used for effecting vertical alveolar crest augmentation,[59] and lower jaw reconstruction after tumour resection.[59, 60]

DO has become an established modality of treatment, and scientific evidence supports it as a practical and sound technique. DO provides a useful new tool for correcting osseous deformities while still respecting the basic principles of surgery.

1.4.1 The advent of transport distraction in mandibles

In 1993, Peter Costantino reported on the use of gradual distraction to grow bone by creating experimental defects in segments of the bony mandible. He closed these bony defects using DO of a bifocal nature. In his canine model, Costantino reported that his dogs exhibited normal oromandibular function for 12 months following segment regrowth and external fixator removal. In his article, he wrote:

> Macroscopic and histologic evaluation of the regrown segments revealed a re-formation of the cortical and medullary architecture. Stress testing demonstrated the average ultimate strength of the regrown segment at 53 MPa, which corresponded to 77%±5.7% of normal mandibular bone. The data suggest that clinical trials applying this technique to segmental mandibular reconstruction are warranted. The regenerated bone had a similar diameter to the preexisting mandible, and the inferior alveolar artery and nerve were found to recannulate through the regenerated bone.[61]

This seminal work on transport distraction in dogs later gave rise to the placement of dental implants into regenerate bone.[61]

Bone transport DO which arose from the concept of DO has shown great promise in reconstructing segmental bone defects in the extremities.[62-64] This concept involves the gradual transport or movement of an osteotomised bone segment (transport disc) along a carriage track spanning the existing bone defect (bifocal transport). The advantages of this technique, especially in difficult cases in which traditional grafting procedures are unfeasible or have failed, have been well documented in case reports.[65]

In 1995, Costantino *et al.* reported the first clinical case of transport distraction. The patient had a surgical defect of 4 cm after resection of a malignant tumour which did not require radiotherapy. However, owing to the use of an external device, anchorage pin track scarring was an issue as well as possible damage to the marginal mandibular nerve.[66]

In 2003, Kuriakose *et al.* reported a case series of four patients who had undergone transport distraction for the treatment of lateral defects of the mandible ranging from 3·5 cm – 6·5 cm. These patients had no need for radiotherapy. Two patients underwent bifocal distraction successfully while the other two patients who underwent trifocal transport had some complications. In one patient, the device failed and, in the other patient, there was only partial bone formation owing to loss of the posterior transport disc.[67]

Although these results were encouraging, there were still unresolved issues. External devices caused scarring along the pin tracks, and patients were at risk of injury to the marginal mandibular nerve.

1.4.1.1 Types of transport distraction

Transport DO takes place when the incremental movement of one (bifocal), or two (trifocal) or three (tetrafocal) transport disc/s moves across a surgical defect.[68] The diagram below (Figure 1.7) illustrates the concept.

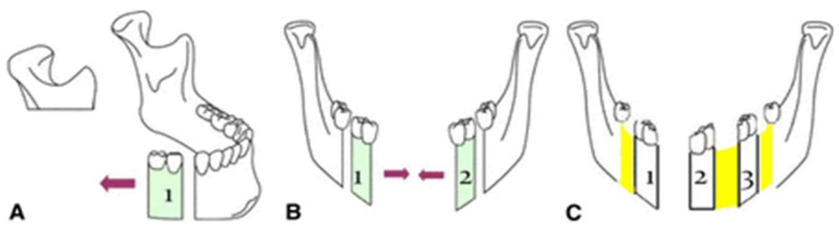


Figure 1.7: A is bifocal; B is trifocal and C is tetrafocal. The numbers 1, 2 and 3 refer to the number of transport discs.[68]

The process of transport distraction induces tensile stretching of the osteoblast-like cells that alter the local regulation of bone formation and thereby increases the expression of the growth factors. While the entire process is dependent upon a rich blood supply, it also requires the maintenance of a continuous blood supply to the regenerate during distraction.[69] In 1999, De Coster *et al.* performed transport distraction in an animal model and carried out angiography to study the arterial response of the bone undergoing the process of distraction. They found that the segment under transport had a healthy arterial supply after completion of the osteotomy cut and also after the commencement of transport distraction.[70]

1.4.2 Applications of transport distraction

1.4.2.1 Formation of a neo-condyle

Bifocal distraction is used in cases of congenital or acquired hypoplasia of the mandibular condyle. In 1999, Stucki-McCormick reconstructed a neo-condyle of the mandible by using transport distraction to lengthen the vertical ramus. She stated that the concept of functional remodelling could be utilised for the creation of a neo-condyle as the jaw could keep moving while the bone grew.[71]

1.4.2.2 Closure of segmental defects in the mandible

Mandibular defects can range from isolated segmental defects to extensive areas of bone loss involving almost the entire jaw. There are six cardinal goals in the reconstruction of mandibular defects:

1. restoration of osseous continuity
2. recovery of bone bulk
3. restoration of alveolar height
4. restoration of arch form, width and alignment
5. maintenance of the bone graft/graft durability
6. acceptable facial contour and appearance.

Adherence to the principles will yield a patient with an acceptable cosmetic and functional result.[72]

Nanjappa *et al.* in 2011 published a case report of 4 patients where segmental mandibular defects ranging from 10 mm – 30 mm were closed with transport distraction. The surgical bone defects were created by the removal of benign odontogenic tumours. All patients were successfully restored by the process.[73]

1.4.3 Closure of segmental defects in the maxilla

In 2002, Castro-Nunez and Gonzalez performed a partial maxillectomy of the anterior maxilla for the removal of an aggressive odontogenic cyst. Five months later, they placed two bone distractors in the first and second quadrants to grow bone in a posteroanterior direction (trifocal distraction). They subsequently produced 11 mm of bone in an anterior direction and stopped the distraction. They left the distractors *in situ* for three more months, at the end of which, because they could not achieve union in the midline, they placed a third distractor to bridge the gap. They completed the reconstruction by means of an iliac bone graft with mini-plates. Three months later, they removed the hardware and placed six osseointegrated dental implants into the premaxilla. In 2013, they reported a nine-year follow-up of the same patient, showing the healthy bone and soft tissues.[74]

Transport distraction can be used to treat patients who have already undergone radiotherapy. Also, there is a group of patients who have had ablative surgery, and would subsequently need adjuvant radiotherapy. It has been experimentally shown by Girod *et al.*, in 2005, that bone consolidation and mineralisation of the regenerate was possible in mandibular distraction with irradiation at the stage of consolidation in the third post-operative week.[75]

In 1995, Hibi *et al.* reconstructed a large mandibular segmental defect in a 45-year-old patient who had received 60 Gy of radiation therapy to the mandible as well as preoperative chemotherapy. During the distraction phase, hyperbaric oxygen (HBO) therapy was administered twice daily (2 atmospheres for 60 minutes in the morning and 3 atmospheres for 90 minutes in the afternoon). In this patient, the segmental mandibular defect measuring about 60 mm was reconstructed by trifocal distraction. Radiologically, the consolidation of the lengthened area in this patient seemed to occur later than that in their younger patients who had undergone lengthening of their congenitally hypoplastic mandibles.[76] Histological examination of the bone suggested that the lengthened bone did not possess a mature structure about seven months after the cessation of distraction. This slow consolidation of the bone might have been owing to the effects of the age of the patient or the consequences of irradiation. In spite of this, however, the clinical hardness and radiological calcification in the lengthened area seemed to provide sufficient stability. Also, a small bone graft from the iliac crest was required for bone bridging.

A year before the work of Hibi *et al.*, Gantous *et al.* performed transport distraction in an irradiated canine model. Five mixed-breed dogs were given external beam irradiation of 50 Gy. After 6 months, a 2 cm segmental mandibular defect was created and distracted using an external device. Within a period of 30 days, the defects were filled with regenerate in 4 of the 5 dogs. Histological and fluorochrome microscopy confirmed the presence of new cortical bone.[76,77] This critical study upheld the possibility of bone formation in previously irradiated bone.

In 2005, Rubio-Bueno *et al.* also published results of transport distraction in a radiated setting. They presented a case series of 5 patients undergoing internal transport distraction. Three of the 5 patients had a radical dose of 60 Gy – 64Gy. In the patient who did not receive radiotherapy, a successful distraction of 80 mm was achieved. Two of the 3 patients had successful transport distraction of 35 mm and 37 mm respectively. In the third patient, distraction was not completed as a result of extensive intraoral exposure. Of the 2 patients with successful distraction who had undergone radiotherapy, one received two osseointegrated dental implants in the regenerate. This seminal study illustrated the success of transport distraction with dental implants in irradiated tissue in the largest series reported at that time.[78]

1.4.4 Transport distraction-assisted rapid orthodontic canine retraction

Rapid orthodontic tooth movement facilitated by distraction osteogenesis has proven to be very efficient especially in cases involving severe malocclusion. By employing the dentoalveolar DO technique, the canines can be retracted within 8 to 14 days, as compared to the regular rate of orthodontic tooth movement during canine retraction (a distance of about 1 mm per month). The indications for rapid orthodontic treatment in individual patients may include the following:

1. those who have had compliance problems for social and professional reasons
2. adult patients requesting orthodontics
3. moderate and severe crowding
4. Class II severe overjet
5. bimaxillary protrusion
6. preoperative dental decompensation for orthognathic surgery
7. short-rooted teeth
8. periodontal problems
9. patients with an ankylosed tooth.

The anchorage teeth are usually able to withstand the retraction forces with no resultant loss of anchorage. Also, there is no clinical or radiological evidence of complications, such as root fracture or resorption, ankylosis and soft-tissue dehiscence. Some authors believe that reduced bone density and osteopenia may mitigate the decreased risk of root resorption. In contradistinction, however, denser adjacent bone accentuates or exacerbates resorption in orthodontic tooth movements.[79]

Rapid orthodontic tooth movement assisted by DO is efficient because it reduces the overall orthodontic treatment time by about 50% with no need for extraoral or intraoral anchorage devices and with no unfavourable long-term effects in periodontal tissues.[80, 81]

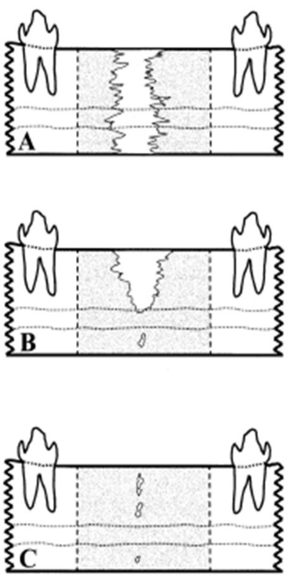
1.4.5 The application of transport distraction to close cleft palates

As most articles relating to transport distraction refer to work done in the mandible, this area is of interest to the present study. The review is as follows: The evolution of transport distraction as a means to close small segmental defects in the maxilla, e.g. in the case of cleft palate defects, has led to the development of small bifocal distractors. The latter have met with much success. Unilateral and bilateral clefts measuring up to 12 mm per side were successfully obturated (Liou *et al*., 2000).[82] Mitsugi *et al*. in 2005 confirmed the same idea by closing cleft palate defects ranging between 10 mm and 12 mm.[83] They used bifocal distractor appliances in 22 patients and successfully placed dental implants into the regenerate after a consolidation period of 3 months.

1.4.6 The regenerate

In 1999, Jason Cope stated that the consolidation period is the most critical phase in DO. During the term of consolidation, newly formed collagenous tissue begins to mineralise to culminate in parallel oriented bony trabeculae within the distraction gap.

Mineralisation and remodelling of the regenerate have been investigated experimentally by many authors, mainly via the medium of radiography,[84, 85] ultrasound,[86] computed tomography,[87-89] light microscopy,[90-94] and electron microscopy.[94-96] Cope stated in 2000 that too little was understood about the correct timing of removing the distraction apparatus. If the removal were premature, this could lead to bending or fracture[97] of the regenerate.[96] Whereas, if the consolidation were left too long, this could result in stress shielding also potentially weakening the regenerate.[35, 98]



Three histologic types of mandibular distraction regenerates

A – Type I: regenerate with intact interzone from superior crest to the inferior cortex.

B – Type II: regenerate with 2 dissimilar interzones. The superior aspect of the interzone is moderately wide and mostly fibrous, whereas the inferior\aspect of the interzone is narrower and mostly cartilagenous when present.

C – Type III: regenerate with varying degrees of interzone obliteration.[98]

Figure 1.8: The three histologic types of mandibular regenerate, namely A, B and C.[98]

In his publication of 2000, Cope states:

> Interestingly, three types of relatively mature regenerates were observed during consolidation. Type I corresponded to the classic three zonal regenerate seen as two mineralizing zones separated by an intervening fibrous Interzone. For the Type II regenerate, most of the crestal part of the Interzone was present, but the central and cortical Interzone areas were mostly obliterated. The Type III regenerate was characterized by almost complete obliteration of the interzone with few isolated islands of fibrous or cartilage tissue. Although these regenerate types were evident at different time periods, they likely represent a continuum of individual regenerate maturation. For example, the classic three zonal regenerate (Type I) may progress to a Type II regenerate with obliteration of the inferior aspect of the Interzone, but with patency of the superior aspect of the Interzone. The Type III regenerate would represent the last stage of regenerate maturation when Interzone obliteration is almost complete and remodeling activities supersede bone formation.[99]

The seminal study that led to this project was the work done by Cheung in 2003. He created small maxillectomy defects in the posterior maxilla of 14 rhesus monkeys and developed prototype tubular distractors to obturate these surgically created defects at a rate of 1 mm of osseo-distraction per day.[100] Cheung not only confirmed the real possibility of recreating an alveolar ridge, a palatal vault and vestibule, but also went further to test the quality of the regenerated bone, also referred to as 'regenerate'. He published sections of bone histology subjected to various types of staining and immunohistochemistry. Cheung also released radiological proof of the regenerate in late 2003. He used microcomputer tomography to qualify and quantify the mineralisation and remodelling of the regenerate during the consolidation phase.

1.5 Quality of life assessment

All patients who undergo maxillectomy procedures experience a substantial deterioration in their primary oral functions such as breathing, mastication, salivation, deglutition and phonation. According to Silveira *et al.* in 2010, the senses of hearing, taste and smell, along with possible aesthetic changes, have a collective adverse influence on the quality of life (QOL) of both patients and their relatives.[101] A questionnaire was developed by the University of Washington (UW-QOL) (Appendix III). The detailed survey was adjusted for obturator patients and internalised most parts of the obturator functioning scale (OFS) described below by Kornblith and co-workers in 1996[102] and employed in a study by Riaz and Warriach in 2010.[103] Hassan and Weymuller first described the UW-QOL in 1999.[104] The current version (4) consists of 13 questions including the following items: the disease-specific items, namely appearance, recreation, pain, activity, chewing, speech, swallowing, taste, mood, saliva, shoulder problem, anxiety and three other general items measuring global health-related QOL. Each patient is tallied as 0 (worst) to100 (best) using a Likert-type scale giving a maximum summary score of 1200.[267]

1.6 Advantages and disadvantages of revascularised fibula free flaps

1.6.1 Benefits of RFFF

The first revascularised free fibula flap (RFFF) was used by Hidalgo *et al*. in 1989 to reconstruct a mandibular defect.[105] Subsequently, the RFFF has been demonstrated to be most reliable for the reconstruction of maxillary defects following on the ablation for benign or malignant tumours or osteoradionecrosis of the maxillo-mandibular complex. Morbidity was acceptable in all the treated patients, with limited postoperative pain and gait disturbances.[106] The following unique advantages make the RFFF the ideal choice for maxillary reconstruction:

1. the long vascular pedicle
2. the wide diameter of the peroneal vessels
3. the availability of a composite flap consisting of bone, muscle tissue and skin
4. the relatively straightforward harvesting procedure resulting in minimal donor morbidity
5. the distant donor site from the head and neck region makes a two-team approach feasible
6. the anatomical three-dimensional shape of the fibula makes a simulation of the maxillary alveolar process possible
7. the high density of the fibula bone is conducive to placement of osseointegrated dental implants.[107]

The survival rates of fibula flaps in a case series by Chiapasco *et al.* in 2006 was 94.9%[108] and consistent with those reported by other authors.[109-117]

1.6.2 Disadvantages of RFFF

A significant problem of the RFFF is that skin does not do well with dental implants owing to the hyperplasia and inflammation that leads to pain and bleeding. Also, the maximum height of the fibula bone is 14 mm and presents problems in the aesthetic zone of the mouth.[118, 119] In particular, patients treated by partial resection of the maxilla have residual dentition on the healthy side. In these cases, despite a successful reconstruction, an inappropriate step at the graft-to-residual stump level may be present.

In mandibular reconstruction, the fibula is amenable to vertical distraction to increase vestibular depth.[120, 121] However, in the maxilla, this would not be a feasible proposition. From a functional perspective, the implants would support very high prosthetic superstructures to approximate the occlusal plane. These superstructures pose the risk of unfavourable bending moments and also implant overload. The latter may jeopardise the long-term survival of dental implants.[122, 123] Also, the aesthetic appearance of very high crowns is most undesirable.

Additionally, the shape of the palatal vault is a major problem because this area lacks a hard bony support and is usually obturated by the musculocutaneous portion of the composite flap. It is quite unaesthetic in the sense that it has a flattened shape and hence no natural curvature.[124]

CHAPTER 2. GENERAL METHODS AND DEMOGRAPHIC DATA

2.1 Study design and ethical considerations

The design of the study was cross-sectional. The Ethics Committee of the University of Cape Town's Human Research Ethics Committee (HREC) approved the study (*vide infra* Appendix I). A prospective cohort study of 6 post-maxillectomy patients was compared regarding clinical outcome of function and aesthetics with a group of 6 patients who had undergone RFFF reconstruction. Also, the new bone was compared with the native bone from which it was generated. Informed consent was obtained from all study participants as per UCT HREC guidelines. Ethical issues to be considered at all times were patient confidentiality and privacy, the latter of which was ensured, and patient dignity was protected. Given the sensitive nature of this kind of work involving patient aesthetics (gross deformity) and function, the needs of the patient were taken into account. The study was designed to optimise the dentofacial anatomy, especially by using dental implants to rehabilitate aesthetics and function. Informed consent to publish the results of the study was obtained from the participants (*vide infra* Appendix II). Objective measuring tools were employed to assess pre and post quality of life (QOL) aspects (*vide infra* Appendix III). The RFFF patients were not subjected to any invasive procedures save to undergo a clinical evaluation and have a CT scan performed of their maxillae by independent radiologists Morton and Partners in Claremont, Cape Town. The patent of the distraction device does not bestow any financial benefit or conflict of interest concerning the research team. The intent of the patent was to prevent any potential misuse of the concept and to allow the study to proceed unhindered (*vide infra* Appendix IV).

2.2 Participant selection and recruitment

2.2.1 Study population

Patients of both sexes, irrespective of age, who had undergone partial maxillectomy procedures for tumour ablation or trauma or congenital defects, were eligible for the study. The surgical defects were anatomically classified according to Brown *et al.* (in 2010) and limited to classes II, III and IV with subclasses (b) to (d) in any combination.

2.2.2 Sample size

A cohort of 6 participants was treated prospectively using curvilinear transport distraction osteogenesis (CTDO), and the results were analysed within that cohort. These results were compared with a retrospective group of 6 participants of similar age and sex who had undergone RFFF reconstruction as an external control.

2.2.3 Inclusion criteria

All patients conforming to Brown Classification classes II, III and IV (b) to (d) were eligible for the study. It was critical that both groups of participants to be analysed (CTDO and RFFF) fall within the same Brown classification groupings for accurate statistical comparison as was analysed in the postoperative or post reconstruction stage.

2.2.4 Exclusion criteria

Patients who were immunologically compromised owing to either systemic disease (e.g. uncontrolled diabetes mellitus, HIV/AIDS) or being administered immunosuppressive agents or who had undergone radio/chemotherapy, were not eligible for the study; i.e. any pre-existing possible impediment to healing or predisposition to infection was taken into account and the patient would not qualify for the present study.

2.3 Study procedures

2.3.1 Participant evaluation

Participants were seen and followed up by the primary investigator (MRH) in his private maxillofacial clinic and the Department of Plastic and Reconstructive Surgery at Groote Schuur Hospital.

2.3.2 Participant education

The aim and purpose of the study were explained in simple terms and in detail to participants and use was made of visual aids to inform them of their problem and the treatment method/s.

Prospective participants were duly informed about the experimental nature of the study, as well as possible alternative treatment modalities.

2.3.3 Informed consent

Signed informed consent for participation in the proposed study was obtained in the patients' first language before the commencement of any treatment. If a patient was unable to understand either English or Afrikaans, a translator was employed (Appendix II).

2.4 Quality of life evaluation

A psychometric instrument to measure the QOL in head and neck tumour patients has been developed by the University of Washington (UW-QOL) and it has incorporated aspects of the Obturator Functioning Scale (OFS) developed by Kornblith *et al*. in 1996. All patients in the study were assisted in the completion of the questionnaire. The same questionnaire was repeated 6 months after the CTDO procedure (Appendix III).

2.5 Preoperative radiological evaluation

Preoperative and radiological imaging including plain radiographs as well as computer-aided tomography (CT) and stereolithography (STL) were used throughout the study.

2.6 Installation of distraction apparatus

The patented Hendricks-Vicatos (H-V) maxillary transport distractor (Appendix IV – Registration of patent document) was applied to all selected participants by the primary investigator under general anaesthesia at Groote Schuur Hospital or private clinic. The H-V maxillary transport distractor was pre-shaped and pre-fitted onto a 3-D model of the participant`s maxilla, in a laboratory. This method reduces placement time during the operation in theatre. If teeth were present in the proposed osteotomy line and in the area to be distracted, then at least 2 teeth were removed from the maxilla, preferably 3 months before the date of distraction. In the first few cases, this was the protocol for developing bone stock. This protocol was revised in the last 2 cases of the study, where no teeth were extracted at all. A linear fracture (bi-cortical) was created in the maxilla in a vertical direction (segmentally) to develop a mobile, well-vascularised transport disc. This carrier disc was attached to the metal plate of the 'crawler' via small titanium screws. The crawler was then moved on the reconstruction plate (Biomet^{TM} Zimmer Biomet, Warsaw, Indiana, USA) as per plate-guided distraction described in par. 1.5.1. The use of a plate-guided distractor (PGD) designed by Herford (2004) solved the problem initially of negotiating maxillary curves, but further developments had to be made.

The PGD followed the curve of the plate but, as the distractor moved along the curve, the regenerated tissue straightened in the manner of a rubber band. When this occurred, a dental model was constructed with the desired ideal final location of the regenerated tissue. A surgical acrylic splint was then fabricated to maintain the desired curve intra-orally. The splint was secured in place by wiring it to the remaining teeth or by means of titanium screws into the hard parent palate. The splint was put into place before activation of the distractor and helped to guide the transported bone superiorly and, more importantly, to maintain the desired curve. Alternatively, the splint was placed after distraction, when the regenerate could still be moulded before ossification. After a latency period of 5 days, CTDO was commenced under the direct supervision of the primary investigator (MRH). CTDO was carried out once daily from a minimum of 1 mm to a maximum of 1.5 mm per day.

2.6.1 Process of distraction

Distraction was carried out on the participant under the supervision of the primary investigator. Serial radiographs were used to monitor progress. While under distraction, patients were fed via nasogastric feeding tubes either in hospital or as outpatients. While new bone and soft tissue grew, the nasogastric feed continued until the participant could swallow unhindered.

2.6.2 Postoperative radiological evaluation

Evaluation of the new bone (regenerate) was done by CT scanning (independent radiologists Morton and Partners). Evaluation of the new bone formation regarding quality and quantity (densitometry) was computed in Hounsfield units (HU) according to Hashemi and Javidi in 2010. An independent radiologist monitored the capturing of the radiological data after a period of three, six and nine months post-distraction. Three particular regions of interest (ROIs) (lateral incisor, first premolar and first molar areas) measuring an area of approximately 0.1 square cm were pre-selected in the native or existing bone (control group). The same three ROIs were selected on a juxtaposed mirror image selected in the regenerated bone (test group) as well as in the bone of the six RFFF cases.

2.6.3 Histological evaluation

Trephine bone biopsies (2 mm – 3 mm diameter by 10 mm depth) were carried out by the primary investigator in the areas of the test and control ROIs as stated above at the time of removal of the distraction apparatus in the cohort cases. The specimens were analysed by Professor J.J. Hille after decalcification in 2.5% formic acid solution for 3 days. Decalcified specimens were processed and embedded in paraffin wax. Axial sections of 6 micrometres in thickness were cut horizontally with a microtome and stained with haematoxylin and eosin and also Masson/trichrome stain for polarised light microscopic examination.

The trephine bone biopsies took place at the same time as the placement of the dental implants. The dental implants were placed into the same osteotomy sites of the trephine biopsy locations. The trephine depth for biopsy (10 mm) was between 3 mm and 5 mm less than the depth required for the dental implants.

2.7 Statistical analysis

The following tests were proposed after consultation with the Department of Statistics, University of Cape Town.

2.7.1 Test for paired (matched) data or non-parametric test (Wilcoxon signed rank test)

The Wilcoxon signed rank test was used to compare numerical values in a cohort of 6 cases of the regenerated bone via CTDO by analysing the bone density (densitometry) of the parent (existing) bone of the maxilla (using Hounsfield units with standard deviation (SD) and comparing the figures with the new bone.

There were 13 questions with weighted scoring, according to the Likert Scale, totalling 1200. The scores for each patient were analysed so that the pre- and postoperative clinical data from the QOL questionnaire could be statistically compared.

2.7.2 Test for two independent means or non-parametric (Mann-Whitney test)

The Mann-Whitney test was used to compare the binary outcome in bone densitometry between a group of 6 patients (similar age and sex grouping) who had undergone maxillectomy reconstruction with RFFF with the regenerated bone in the cohort of 6 cases after CTDO. Again, standardised CT scanning with Hounsfield units was used. The Mann-Whitney test was also used to compare the clinical measurements of width, height and depth of fibula-reconstructed maxillae with the cohort of 6 CTDO patients.

Note: Parametric tests (the paired and unpaired *t* test) were only be implemented if numerical values were 'normally distributed'. The Shapiro-Wilk test was used to determine if numerical outcomes were usually spread or not. Data analysis was computed using the STATA package (Statacorp LP 2009 Texas) and MRC. The deviation from the protocol reducing the number of patients from 10 to 6 patients was based upon the statistical power calculations performed by Mr Henri Carrara from the Department of Biostatistics, University of Cape Town (See APPENDIX V).

CHAPTER 3. PHYSIOLOGY AND THE BIOLOGICAL BASIS FOR DISTRACTION OSTEOGENESIS

3.1 Introduction

Bone possesses the unique ability to repair and regenerate itself when subjected to injury or surgical intervention. The processes of repair and regeneration involve a complex integration of growth factors, cells and the extracellular matrix (ECM). During this process of healing, only the continuity of the injured bone is restored, without contributing to an increase in the resultant volume of bone. The process of regeneration, however, involves the formation of new bone tissue through a process of cellular differentiation that culminates in an overall increase in the volume of new bone tissue.

Distraction osteogenesis (DO), in contrast, uses mechanical strain to enhance the biological responses of the injured tissues to create new bone by employing a controlled surgical procedure. This surgical model is currently used worldwide with great success in bridging gap defects such as non-healing fractures, and treating disease conditions such as osteomyelitis, with the concomitant net destruction of the bony tissue. Also, DO can be used for creating and augmenting lost alveolar bone, and correcting congenital or acquired dentofacial deformity seen in the facial skeleton. It will be shown later that both these biological processes employ complex molecular mechanisms that involve local and systemic factors that may interact with many types of cells. These factors are attracted and deployed to the site of injury or site of surgery from the surrounding tissues and microcirculation.[125]

In DO, an osteotomy is created, and the surgical defect is gradually distracted to elicit a mechanical strain. This tension, in turn, induces the integration of growth factors, cells and extracellular matrix to form and create bone. While DO mainly creates an environment that suppresses the formation of cartilage, it also promotes angioneogenesis with subsequent formation of intramembranous bone tissue.[45] The three distinct phases of DO are latency, distraction and consolidation.[126, 127]

3.2 Phases of distraction osteogenesis

3.2.1 Latency phase

Almost immediately following the creation of the surgical osteotomy, the primary inflammatory response begins – a process not dissimilar to that seen in the repair process of fractures. This latency phase allows the stage to be set as seen in the initial response to trauma. It commences immediately following the creation of the osteotomy and continues until the onset of active distraction. However, usually, by the time the active distraction phase has been set in motion, the primary inflammatory processes have subsided. This period allowed for settling of the inflammatory response during latency is clinically determined by the patient's healing potential. Latency may last from three to ten days on average.[32, 128, 129]

3.2.2 Distraction phase

During the process of DO, the callus is subjected to mechanical forces, which creates a fibrous interzone (FIZ),[45, 130, 131] characterised by active chondrocyte-like cells, osteoblasts and fibroblasts. The forces applied to the callus are tensile in nature, and the application thereof is carried out at a particular rate and rhythm. The FIZ is rich in fibroblasts, chondrocyte-like cells and oval cells (Figure 3.1 below). The latter is morphologically intermediate between fibroblasts and chondrocytes.[97, 130, 131] Osteoid is deposited alongside the collagen bundles at the FIZ by the differentiating osteoblasts. When osteoid undergoes mineral crystallisation and is laid down parallel to the collagen bundles, a zone is formed called the area of microcolumn formation (MCF). An area referred to as the primary matrix or the mineralisation front (PMF) forms between the FIZ and the microcolumn formation. This area consists of highly proliferating cells.[132] The onset of the consolidation phase begins at the cessation of the destruction process, once the desired bone length is achieved. At this stage, bone as well as extensive amounts of osteoid undergo a process of mineralisation and eventual remodelling. Upon radiographic examination during the process of distraction, callus formation is usually seen within three to six weeks after the commencement of distraction.[133]

It is of critical importance that the duration of the latency phase, and the rate and rhythm during the distraction phase, are taken into account as these can influence the balance between nonunion and premature consolidation. Therefore, attentive clinical and radiographic follow-up is central to using the concept of DO to achieve the desired correction.

3.2.2.1 The distraction gap

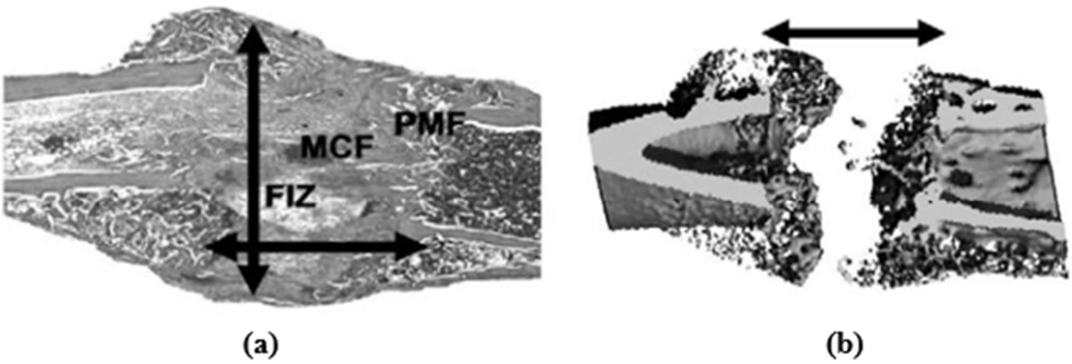


Figure 3.1: (a) The gradual stretching of the callus creates the central fibrous interzone (FIZ). When osteoid undergoes mineral crystallisation and is laid down parallel to the collagen bundles, an area is formed called the zone of microcolumn formation (MCF). An area referred to as the primary matrix or the mineralisation front (PMF) forms between the FIZ and the microcolumn formation. This zone consists of highly proliferating cells. (b) The distraction gap as seen on micro-CT.[138]

3.2.3 Consolidation phase

During this critical phase, mineralisation and remodelling will occur, resulting in ossification within the distraction gap. The time required for complete consolidation can be variable. It is dependent upon the age and health status of the patient. For example, in the paediatric population, consolidation may only require one month per centimetre of lengthening whereas, in the adult group, this period may need 1.5 to 2 months of consolidation per centimetre of bone lengthening.[128] Although the initial healing after osteotomy is not dissimilar to fracture healing, there is evidence to suggest that the osteogenic responses exist throughout the distraction period. Also, considerable time has been spent on elucidating the basic science that dictates the variable healing potential throughout the three phases of DO.

Central to bone formation is the preservation of blood supply to the periosteum, which affects the planning and placement of the surgical osteotomy.[134, 135] After gradual distraction takes place, new bone forms between the vascularised bone surfaces. The cellular and molecular processes are summarised below in Table 3.1. It is thought that mechanical strain applied longitudinally to the healing callus is responsible for the regeneration of bone during the process of DO. The exact mechanism by which tension stimulates osteogenesis remains unclear. One theory suggests that living tissues become metabolically activated by slow, steady traction during a process called ‘mechanotransduction’, characterised by the stimulation of proliferative and biosynthetic cellular functions.[35] Also, investigations carried out recently suggest that there is a meaningful relationship between induced strain and bone regeneration. It is accepted that the molecular signalling cascade is central to this relationship. Although the distraction process creates new bone tissue formation using a process entirely different to that of a healing fracture, it is interesting that the molecular signals driving the regenerative process are indeed similar. The latter includes the pro-inflammatory cytokines, the transforming growth factor beta superfamily, as well as angiogenic factors.

Table 3.1: Summary of the stages of distraction osteogenesis (DO) and the associated molecular regulator The different stages of DO are denoted in the top cells and subdivided into early and late stages. The number of arrows indicates the intensity of expression. Based on the results of the following investigators: [17,32,34,35]

Signalling molecules	**Latency**		**Active distraction**		**Consolidation**	
	Early	**Late**	**Early**	**Late**	**Early**	**Late**
Cytokines						
IL-1	↑↑↑					
IL-6	↑↑↑		↑↑↑	↑↑↑		
TNF-α						↑↑↑
RANKL		↑↑↑	↑↑↑			
OPG		↑↑		↑↑↑		
TGF-β superfamily						
BMP-2	↑↑		↑↑↑	↑↑↑	↑↑	↑
BMP-4	↑↑		↑↑↑	↑↑↑	↑↑	↑
BMP-6		↑↑↑	↑↑↑	↑		
TGF-β		↑↑↑	↑↑↑	↑↑↑		
bFGF			↑↑	↑↑	↑	↑
IGF			↑↑	↑↑		
Angiogenic factors						
VEGFA			↑	↑	↑	
VEGF B			↑	↑	↑	
VEGF C	↑↑		↑	↑	↑	
VEGF D		↑↑	↑	↑		
Angiopoietin 1			↑	↑		
Angiopoietin 2			↑	↑		

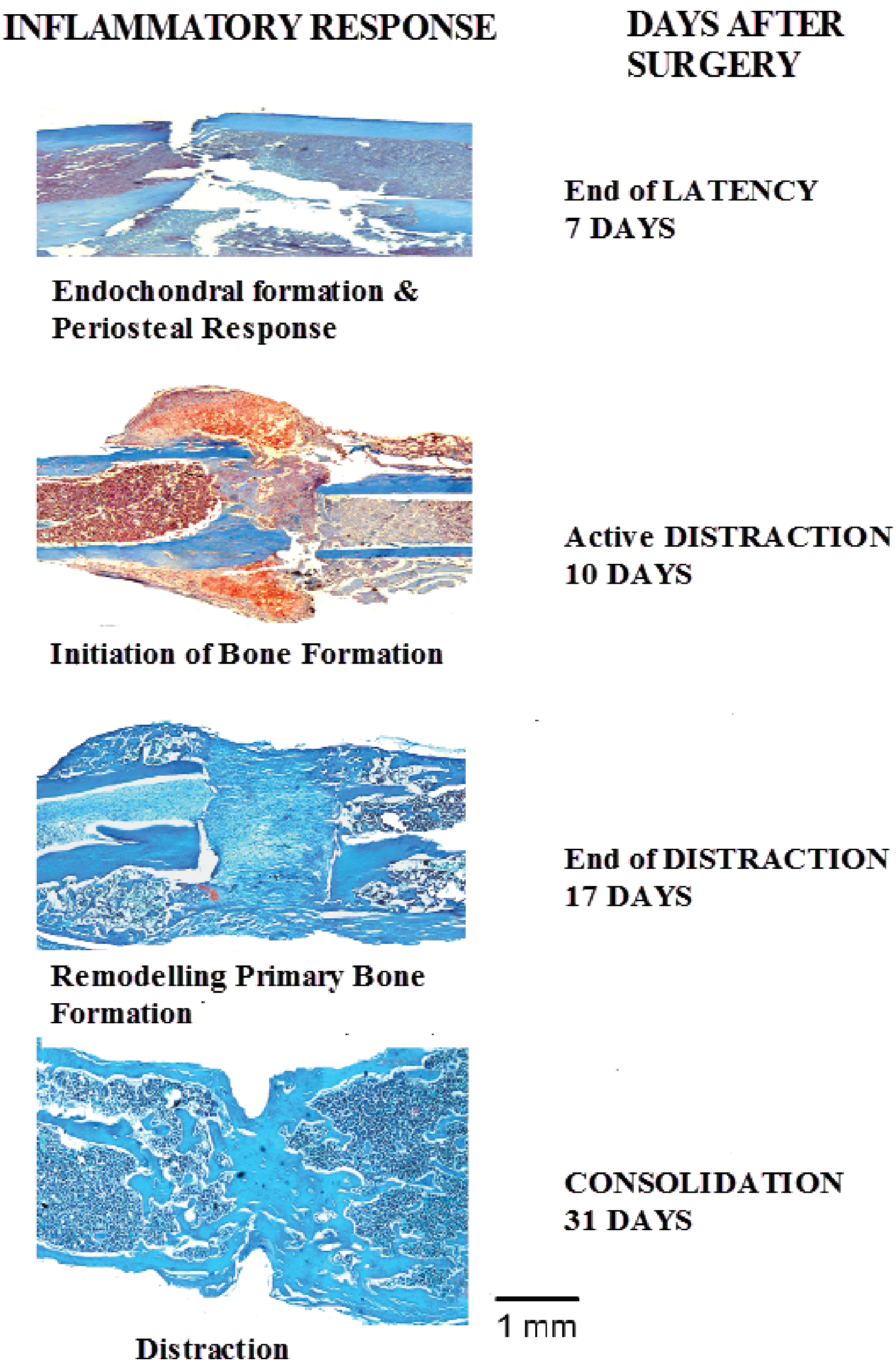


Figure 3.2: The tissue prepared from the distraction gap of murine tibiae at various time intervals. Each different stage of bone formation and healing is given. Representative histologic specimens stained with Safranin-O/fast green appear in bright cartilage red. On the lower right is a scale bar of 1 mm for all panels.[139]

3.3 The role of pro-inflammatory cytokines in distraction osteogenesis

After the initial osteotomy, pro-inflammatory cytokines are implicated in escalating the repair cascade. Initially, Interleukin1 and IL-6 levels are elevated during the latency period and subsequently return to baseline quite rapidly, while IL-6 remains elevated into the distraction phase (Figure 3.3 below).

The raised level of IL-6 is thought to help stimulate the process of intramembranous ossification as well as furthering the differentiation of cells already in the osteoblastic lineage.[136] Once distraction commences and mechanical strain is applied to the callus, the expression of IL-6 increases for the second time. During this phase, IL-6 is expressed by the oval cells within the FIZ, at the area where the tension strains are the highest, as well as by osteoblasts and chondrocytes. Insulin growth factor-1 (IGF-1) assists osteoprogenitor cells to differentiate and proliferate.[137]

During the early stage of distraction, IGF-1 levels have been found to increase, with a subsequent drop after cessation of the distraction process. It is therefore strongly suggested that IGF-1 plays a relevant role in the formation of new bone.[138]

The expression of TNF-alpha was thought to remain silent throughout the distraction process, suggesting that its expression is induced only by more substantial trauma.[136] However, these findings were contradicted by Al-Aql *et al.* in 2008, who reached a different conclusion when he examined the temporal patterns of the expression of TNF-alpha superfamily (Figure 3.2 above). She found that during the distraction process in mouse tibiae, TNF-alpha mRNA levels were markedly increased towards the end of the consolidation stage.[139]

It is well documented that TNF-alpha as well as IL-1, usually known to regulate inflammation and immune function, both participate in the healing of fractures and are therefore expressed in both the early and late phases of the repair process. These cytokines, therefore, are known to play a central role in the repair process and also during remodelling and intramembranous bone formation.[140]

Additionally, the expression ratio of RANKL/OPG is increased at the beginning of the distraction phase and subsequently decreased by the end of the consolidation period. These results compare favourably with those from the study conducted by Wang *et al*. in 2005 on DO in the mandible.[141]

It was suggested by Gerstenfeld *et al*. in 2003 that the resorption of mineralised cartilage within the external callus areas takes place adjacent to the ends of the bone tissues.Within the distraction gap, the latency period is more dependent upon the levels of RANKL and OPG and less so upon the levels of other cytokines.[142] On the contrary, it is the activity of TNF-Alpha that promotes cartilage removal and bone remodelling in the fracture healing process. Temporal genetic expression of various molecules in DO influences the maintenance of osteogenic potential. Latency, distraction, and consolidation constitute unique molecular environments.[143].

Figure 3.3: Molecular signalling in distraction osteogenesis.[142]

3.4 Molecular and cellular mechanisms of DO

During DO, the molecular and cellular activities are quite distinct from the typical bone-healing process and underscore the adaptability of skeletal bone healing. Although there is a close resemblance between the latency phase and early fracture healing within the osteotomy site, there is an expression of an array of bone-active proteins which occurs at the onset of distraction. The latter alters the local environment of the distraction gap and further influences the mechanisms of consolidation and remodelling. The temporal expression of these proteins is tightly controlled throughout each phase of DO.[139]

In distraction, the trauma created by the surgical osteotomy increases the concentration of cytokines, namely interleukin-1 (IL-1) and IL-6. In a study of rat tibial distraction osteogenesis, it was showed that IL-6, specifically, is usually expressed beyond the initial latency phase of healing and well into the distraction phase by cells not only in the FIZ but also by osteoblasts and chondrocytes.[136] IL-6 hence responds to tensile strain in the distraction gap, thereby inhibiting the differentiation of mesenchymal cells into mature osteoblastic lineage cells. This inhibition strongly suggests that IL-6 is the key in delaying maturation of the callus.[139]

3.4.1 The function of angiogenic factors in DO

The successful regeneration of bone requires the constant production of a concomitant neovasculature to provide growth factors and metabolic needs to the cellular matrix.[144-146] During the process of DO, blood flow is increased, thereby creating a fertile infrastructure for osteoneogenesis, as is the case in the repair of fractures. DO exerts a demand on the surrounding tissues to increase blood flow so that the successful induction of new bone regeneration can occur.[97, 144] However, under hypoxic conditions, as seen commonly at the sites of trauma or decreased vascularity, the angiogenic factor is activated by the expression of hypoxia-inducible factor (HIF)[147] which increases the oxygen supply at the sites of skeletal trauma. There is evidence to suggest that, under an hypoxic environment, osteocytic phenotypes will prevail, while under normoxic conditions, osteoblastic differentiation and bone formation will occur.[148]

HIF mediates tissue oxygenation by recruiting neovascularisation and thus directly influences bone cell differentiation by modulating oxygen tension and the availability of nutrients.

The detection of all the key vascular endothelial growth factor (VEGF) ligands as well as interactive molecules, namely neuropilin and placental growth factor, in both DO and fracture repair, emphasises their importance in healthy bone regeneration.[149-152] It is well documented that VEGF receptors (VEGFRs) 1 and 2 are fundamental to both new blood vessel formation as well as new bone formation through the process of cellular differentiation. It has also been well established that a partial blockade of the VEGF pathway will select for chondrogenesis, while a complete barrier causes the failure of both osteogenesis as well as chondrogenesis.[153]

During DO, the induction of angioneogenesis is stimulated by VEGF-A and neuropilin, an alternative receptor for VEGF. Also, during DO, the expression of other VEGF ligands and receptors is less than that of VEGF-A and neuropilin1, and therefore difficult to quantify. VEGF-D is the only factor which peaks at the end of the period of latency and continues into the early stages of active distraction. However, the latter displays reduced expression at the later stages.[144] The expression of VEGF-A is peculiar to osteoblasts that mature at the primary mineralisation front, and also to osteoclasts located in the zone of microcolumn formation.[154] The localisation of VEGF-A to the primary mineralisation front suggests that a tight spatial co-ordination exists between the areas of neovascularisation and osteoneogenesis.[152]

3.4.2 Angiopoietins

The angiopoietins are a family of angiogenic factors expressed during the distraction process. The simultaneous appearance of angiopoietin-1 is quickly followed by angiopoietin-2, which again is followed by a profound expression of VEGF-A. The latter was demonstrated in a distraction model. However, angiopoietin-2 *per se* is antagonistic to angiopoietin-1. Pacicca *et al*. in 2003 postulated that the combination of angiopoieten-2 and VEGF-A is responsible for the formation of new vessel formation, as well as the enhancement of the plasticity of existing larger vessels, and contributes to the process of neovascularisation. Also, it has been reported that an upregulation of the expression of hypoxia-induced factor 1 alpha (Hif1α) is associated with the increase of VEGF-A and angiopoietin-1 expression. Hif1α is known to be one of the key transcription factors responsible for regulating genes usually associated with an angiogenic response, namely, VEGF-A and angiopoietin-1.[144, 152]

3.4.3 The function of transforming growth factor-beta superfamily in DO

Of the most widely studied group of growth factors, the bone morphogenic proteins (BMPs) have gained much attention. BMPs subscribe to the TGF-beta superfamily and play a pivotal role in bone formation. BMPs are multifunctional growth factors which stimulate cellular proliferation and further differentiation down the osteoblastic lineage.[155, 156] The expression of BMPs during each phase of DO tends to vacillate.[91, 157-159] During the distraction phase, the up-regulation of group 1 BMPs such as BMP-2 and BMP-4 is most significant. Also, the expression of BMPs 2, 4, 6 and 7 are also up-regulated locally within the distraction gap. However, these levels tend to taper off during the consolidation phase.[157, 160] Throughout the entire period of distraction, higher levels of BMPs are maintained.

During late latency, BMP-6 is strongly expressed and usually diminishes during distraction.[157] The transient expression of BMP-4 is also observed in the late latency phase.[91, 159, 161] However, in a study of DO in the rat, the uninterrupted bone formation was seen to be owing to the high expression of BMP-2 and BMP-4 in chondrocytes and osteoblasts and also their precursors throughout the process of distraction.[157] During DO, different BMPs exhibit different temporal patterns of expression.

In the early latency phase, the expression of BMP-2 and BMP-4 rises, probably to stimulate the production of precursor cells which then differentiate into osteogenic or chondrogenic cells. During the distraction phase, the application of mechanical tension strongly enhances the expression of BMP-2 and BMP-4. These growth factors are produced by chondrogenic cells involved in the formation of cartilage and osteogenic cells at the primary mineralising front. The oval cells found in the FIZ produce BMP-2 and BMP-4, which may form bone in response to strain.[91, 138, 157, 158, 162, 163], Once the distraction process ceases, the expression of BMP-2 and BMP-4 gradually resolves.[91, 158, 159, 161, 164] It has also been reported that this BMP expression could last for up to two weeks once a distraction has been stopped, implying that they perform a central function in the production of cells required for bone healing to be completed.[164, 165] While BMP-2 has been known to have osteoinductive properties, the administration of exogenous BMP-2 has been used with much success to shorten the treatment time during DO. The latter does this by accelerating bone formation during the consolidation stage.[166]

It has been well recognised that the effect of exogenous BMPs alone is limited;[167] however, BMP-6 peaks during the late phase of latency and into the early stage of distraction. BMP-6 then declines toward the late phase of distraction. During this phase, the mode of ossification changes from endochondral to intramembranous, thereby reflecting its role in the endochondral phase.[157, 158, 163]

While it has been mooted that BMP-7 plays a role not dissimilar to that of BMP-2 and BMP-4,[158] most experiments have detected trace levels or nil expression of BMP-7 during this process of DO.[157, 159, 165]

Wang *et al*. concluded in 2004, however, that while endogenous BMP-2 plays a pivotal role in the initiation of stem cell differentiation, that supplementation with exogenous BMP-alpha would only partially enhance cellular differentiation and proliferation.[168]

3.4.4 Transforming growth factor beta

TGF-beta plays an integral role in the regulation of bone formation by influencing the regulation of cell differentiation.[169] It has been found that during the early phase of distraction, the levels of TGF-beta mRNA rose to three times that of the usual level.[170] Furthermore, TGF-beta also inhibits osteoclastic activity and stimulates osteoprogenitor cellular activity, thereby promoting new bone formation.[91]

Towards the end of the latency period, TGF-beta expression is increased well into the distraction phase. Furthermore, the diffuse expression of TGF-beta is carried out throughout the distraction gap.[138]

It has been found in a canine distraction model that an inverse relationship exists between TGF-beta and osteocalcin where elevated levels of TGF-beta were accompanied by lower levels of osteocalcin after the onset of DO.[162] These observations suggest that by delaying the differentiation of osteoblasts, TGF-beta suppresses osteoblastic maturation.

It has also been found during mandibular DO in a rat model, that TGFβ1 expression was increased at the onset of the distraction process and subsequently remained elevated for up to four weeks after the completion of the distraction phase and the beginning of consolidation.[171] Although TGF-b1 is known to stimulate osteoblastic proliferation, high levels thereof tend to suppress osteocalcin expression and thereby induce osteoclastogenesis. This phenomenon may delay mineralisation in the process of DO.[147, 172, 173]

3.4.5 Neurotrophins

Neurotrophins are a family of proteins concerned with the development, function and survival of neurons. Neurotrophins are growth factors, responsible for the signalling of particular cells to differentiate, grow and survive.[174] Neurotrophin expression during the distraction process exceeded the levels found in fracture models during an experimental rat femoral DO model.[175, 176] While peak neurotrophin levels occurred during the process of distraction, these levels tapered rapidly at the commencement of the consolidation period.[177] The expression of neurotrophin-3, by osteoblast-like cells and concomitant tropomyosin receptor kinase (Trk) receptor expression, may also suggest that an autocrine loop function could exist within the process of DO.[178]

3.4.6 RANK/RANKL

The receptor activator of NF (nuclear factor)-kappa-b (RANK)/RANK ligand (RANKL)/osteoprotegerin (OPG) system is fundamental for homoeostasis of the bony skeleton. RANK/RANKL also regulates resorption and remodelling of bone cells.[179] Control of cellular differentiation, proliferation, and apoptosis is fundamental to repair and remodelling of osseous tissue.[180] During the distraction process, osteoclast-inhibitory OPG messenger RNA (mRNA) peaks and remains high for up to two weeks of consolidation.[181] At the same time, there is a profound tissue inhibition by metalloproteinase-1 which is an extracellular matrix turnover regulator. The outcome of the latter ultimately favors the deposition of new bone.[182] RANKL, an osteoclastogenic cytokine, steadily increases in concentration during the period of consolidation and remains in high expression up until three or four weeks after consolidation has transpired, thus confirming that remodelling activity is taking place within the distraction gap (Figure 3.3).[183]

Initial inflammation, cytokine expression and cellular recruitment are the key activities within the latency phase. However, a complex interaction of multiple cascades follows to form the malleable bone regenerate found within the distraction gap. During the period of consolidation, bone remodelling is inhibited until the process of distraction is complete, as can be seen by the cellular reaction to changes that take place within the distraction gap.[54]

3.4.7 Smads

Smad proteins play a significant role in transducing or carrying BMP signals intracellularly.[184, 185] Smads were found to be maximally expressed in fibroblasts and chondrocytes during the periods of distraction as well as consolidation.[177, 186] It was also found that receptor-activated as well as common-partner Smads (transducing molecules in the BMP pathway) were strongly expressed during the process of distraction while the expression of inhibitory Smads (antagonists of the BMP pathway) was increased during the period of consolidation, thereby inhibiting the signalling of BMP. It is well documented that the expression of BMP-2 and BMP-4, as well as Smad proteins during the distraction phase, is associated with bone deposition. During the consolidation phase, these proteins taper down as the callus matures from mineralisation to remodelling.[177, 186, 187]

3.5 The mechanical mechanisms of DO

The mechanical strain applied to the distraction gap influences cellular activities and gene expression, ultimately altering healing and osteogenesis. Mechanical tension is implemented by choosing an appropriate distraction rate and rhythm for each patient. It is integral to maintaining a balance between nonunion and premature callus formation. Mechanical tension during distraction osteogenesis affects synthetic cellular processes. It also affects the differentiation of pluripotent cells in the distraction gap.[188, 189] It has been shown in vitro that osteoblasts that are subjected to cyclic stretching stimulated not only proliferation but also the increased production of additional mitogens, such as TGF-β.[173] The mechanical tension in the distraction gap is directly related to the rate of distraction. A balance needs to exist between the rate of distraction and the regeneration of muscle development and angiogenesis. Slower rates of 0.3 to 0.7 mm/day are best for muscle generation and angiogenesis, as well as type-I collagen production [173, 190, 191], whereas a rate of 1.0 mm/day is most favorable for osteogenesis.[192] The rate of distraction influences the distribution of collagen within the callus.As the distraction rate increases, the number of cells expressing type-II collagen mRNA increases, thereby correlating with the generation of chondrofibrous tissue in the distraction gap.[131, 192] It is therefore implied that the slowest rate of distraction required to produce regenerate tissue without inducing premature consolidation should be used during distraction osteogenesis. Weight-bearing during distraction osteogenesis may alter overall mechanical strain. A study on rat femoral distraction osteogenesis showed stimulation of blood vessel formation in physiologic weight-bearing compared with none weight bearing.[193] The mechanical stress may be a determinant factor for chondrogenesis and inhibition of the osteoblastic lineage.[194, 195] It is also well known that distraction osteogenesis increases the production of other extracellular matrix proteins namely, osteonectin, osteopontin, and osteocalcin.[179]

Table 3.2: Summary of the biological processes seen during the various stages of distraction and the expression of signalling molecules. Based on the results of the following investigators:[17,32,34,35]

Stage of DO	Biological process	Signalling molecules expression and their functions
Latency	Haematoma Inflammation Recruitment of mesenchymal stem cells Periosteal callus and cartilage formation	IL-1 and IL-6 upregulate post osteotomy, then return to baseline. BMP-2 and BMP-4 rise during the early phase of latency to accelerate differentiation of precursor cells into chondrogenic/osteogenic cells. RANKL/OPG ratio increases by the late latency period about cartilage resorption. BMP-6 and TGF-β expression rise during the late period of latency, owing to the role they play in endochondral ossification.
Active distraction	Callus stretches Cartilage resorption and endochondral bone synthesis. Formation of a central FIZ comprised of fibroblast cells and collagen fibres aligned parallel to the vector of elongation. Neo-angiogenesis between collagen fibre bundles. Osteoblast recruitment and arrangement along the new vessels, followed by intramembranous ossification and bone column formation.	IL-6 rises again during this period to contribute to intramembranous ossification by stimulating the production of cells committed to the osteoblastic lineage. RANKL/OPG ratio remains high during the early distraction period to promote resorption of the remaining mineralised cartilage formed during the latency phase. BMP-6 expression remains high during the initial distraction phase. BMP-2, BMP-4 and TGF-β expression peak during this period to stimulate uninterrupted bone formation in response to strain caused by distraction. IGF-1 and bFGF are induced during this period.VEGF and angiopoietin-1 and -2 are up-regulated to stimulate new vessel formation and enhance the plasticity of existent larger vessels.
Consolidation	Bone columns interconnect. Osteoclast recruitment Remodelling	BMP-2, BMP-4 and bFGF expression gradually disappear. TNF-α markedly increases toward the end of the consolidation period, suggesting that it regulates bone remodelling.

3.6 The effects of mechanotransduction on stem cells

The process of self-renewal is peculiar to stem cells; as undifferentiated cells within the appropriate environment, they have the ability to differentiate into designated cells of a particular phenotype.[196] The 'stem cell niche' is the local microenvironment that provides the differentiation and self-renewal of stem cells.[197] This 'niche' is composed of various support cells including mesenchymal stem cells (MSCs), haematopoietic progenitor cells and their progeny. The latter includes fibroblasts, endothelial cells, adipocytes and osteoblasts. The latter encompasses the osteocytes embedded in bone.[198] The stem cell niche can also be defined as a particular location in a tissue where stem cells hibernate for an undefined period of self-renewing while still producing progeny.[199] While within this niche, stem cells remain undifferentiated. Cellular behaviour within this niche is thought to hinge on three factors: (1) mechanical perturbation; (2) altered extracellular matrix (ECM) stiffness; and (3) altered cell stiffness (Figure 3.4).[197]

Any alteration within these three factors will result in a loss of the stem cell niche and will most likely trigger for cellular differentiation. Also, owing to the interdependence between these three factors, any change in one factor can effect a change in the other two factors.[200]

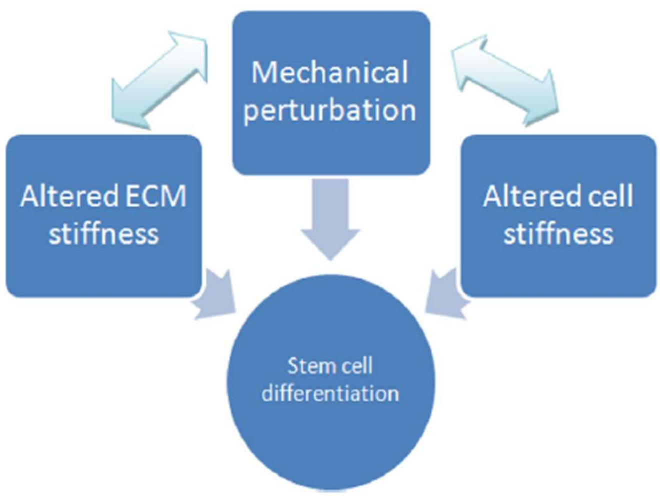


Figure 3.4: The stem cell mechano-niche concept.[196]

Stem cells have been known to respond and interact with their surrounding environment by being sensitive to changes in the external mechanical pressure. They employ a range of signalling molecules, of which the majority reside in the cell membrane. It remains to be explained how exactly the mechanism works for these external mechanical signals to eventually manifest as intracellular changes in gene expression, and also how they influence the production of growth or biological molecules from the existing osteoblasts and osteocytes within the fracture callus.[201]

It is thought that this significant translation of mechanical forces is central to the initiation of stem cell differentiation. Stem cells employ a diverse group of membrane-anchored mechanosensors such as cell membrane-spanning G-protein-coupled receptors, stretch-activated ion channels, and integrins to sense mechanical loading.[197, 202]

3.6.1 Models of mechanotransduction in bone formation

In 1942, Pauwels suggested that mechanical stresses and strains could influence differentiation in cellular pathways and thereby control tissue differentiation. Moreover, Carter expanded upon this idea in his theory of mechanobiological principles. He proposed that mechanical stimuli were responsible for phenotypic alteration in cells.[203]

In 2003, Pavalko *et al.* proposed a model of mechanotransduction in bone cells. Their theory suggests that deformation of the bone as a result of mechanical force causes deformation of proteins within the cell membrane. The latter subsequently triggers a cascade of signals within the cell, culminating in the release of mechanosomes (these are multi-protein complexes consisting of focal adhesion-associated or adherens junction-associated proteins). Mechanosomes conduct external mechanical information towards and into the nucleus, thereby effecting altered gene activity.[204]

3.6.2 The role of mechanosensitive molecules in cell signalling

The role played by the extracellular matrix(ECM) is vital in converting the external mechanical forces into intracellular signals.[205] Guilak *et al.* in 2009 found that the transmission of these mechanical signals influences the commitment of undifferentiated stem cells.[206]

Furthermore, any deformation of the ECM resulting in a structural change of the arrangement of the surface matrix proteins subsequently alters the local concentrations and gradients of matrix-bound growth factors and also adhesion sites.[201]

In 1995, Swartz *et al.* suggested that integrins play a fundamental role in transmitting signals between the ECM and the cytoskeleton of the cell. They showed that integrins could be seen to act as direct mechanosensors.[207] When a force is applied to the tissues, it results in a change of conformation in the integrins and subsequent transmission of the mechanical signal. Campbell *et al*. also confirmed this concept in 2011.[208] The outcome is evidenced in the release of load-related signalling molecules, namely PI3K, MAP and extracellular signal-related kinase (ErK) with resultant prevention of cellular apoptosis.[209] Furthermore, integrin receptors are also physically linked to the actin cytoskeleton using intermediate proteins.[210] The most important integrin is AlphaV beta 3, which is abundantly expressed on osteocytes and plays a vital role in initiating mechano-sensing along the calcium influx pathway.[211]

In 2003, Tong *et al.* identified an integrin protein called focal adhesion kinase (FAK), which is the central regulator of the integrin-mediated pathway. FAK immunolocalisation occurs only in distraction osteogenesis and not in any other bone defect repair processes. The latter suggests that FAK expression is peculiar only to distraction osteogenesis and thereby emphasises a possible unique role of the integrin pathway in the physiology of DO.[212] It is also well documented that undifferentiated stem cells remaining within the stem cell niche express high levels of surface integrins. These integrins are responsible for the integrin-mediated pathway of signal transduction and therefore the primary route by which mechanotransduction occurs. Hence it is believed to play a central role in the differentiation of stem cells (Figure 3.5).[202, 213]

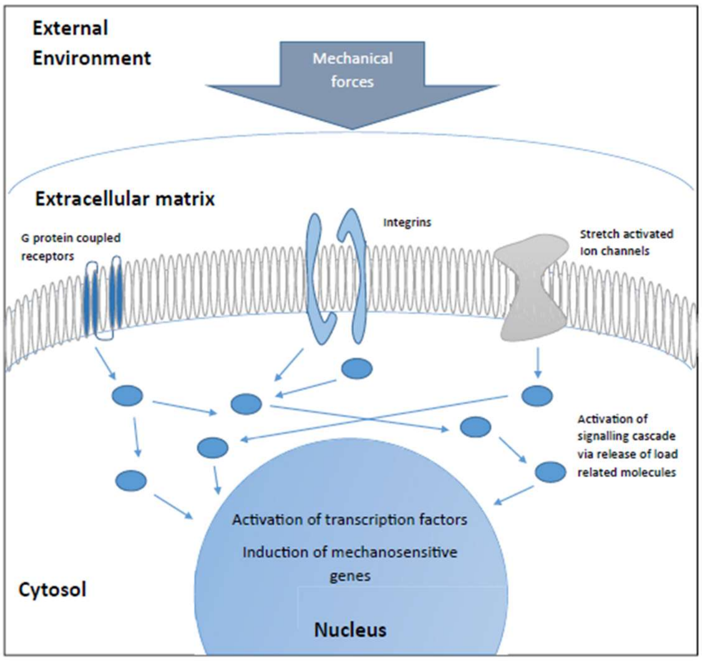


Figure 3.5: A schematic representation of the intracellular signalling cascade triggered by mechanical stimulation.[201]

It has also been demonstrated that the cytoskeletal architecture of cells affects the differentiation of stem cells and the formation of new bone. In 2012, Wang *et al.* showed that if cytoskeleton regulatory scaffold protein GIT2 is absent, then bone synthesis is affected significantly. It is well understood that GIT2 plays a significant role in the differentiation of osteoblastic cells and therefore, when absent, there is a reduction in the number of mature osteoblasts, with attendant reduction in osteoblastic activity. The latter eventually culminates in the formation of a low-density bone of an osteoporotic nature and quality.[214]

It is therefore conclusive that mechanical strain affects the cellular cytoskeleton, cytokine expression, and cellular growth. During the process of osseodistraction, the mechanical loading of the bone by the appliance stimulates an increase in the production of ECM proteins via osteoblasts already within the callus and the surrounding region. The result is an up-regulation of mRNA production that encodes for ECM proteins, such as collagen I and osteocalcin.[170] Furthermore, it is known that mechanical strain behaves as a key regulator of extracellular signal-related kinase (ErK) one and two expressions. Hence, it has been shown that the ErK protein levels only increase during the distraction phase of the procedure. Conversely, it has also been demonstrated that there is no change in the levels during normal fracture healing, which confirms that mechanical strain is the key regulator of bone formation.[215]

3.6.3 Fluid flow theory and signalling molecules

In 2012, Varghese and Engler proposed a theory to explain how the mechanical loading of bone translates into biological signals that will result in bone remodelling. Their fluid flow theory suggests that the loading of bone forces interstitial fluid to flow around the bone microarchitecture, thereby creating a shear strain.[216] Hence, the effect of the applied load on the bone causes a decrease in the size of the lacuna and subsequently forces fluid through the lacuna-canalicular system. This flow of fluid stimulates an intracellular response by way of signalling molecules.[217, 218] Numerous signalling molecules have been identified in displaying a pertinent role in the transduction of mechanical stimuli. The most fundamental of these identified are nitric oxide (NO), prostaglandins and Wnt.[219]

The primary response of the cell to a mechanical stimulus is the influx of calcium ions. When the calcium levels increase, this activates the calcium-dependent proteins such as nitric oxide synthase (NOS) as well as subsequent NO release to promote active bone remodelling.[220] Wnts are a group of signalling peptides that modulate the adaptive response of bone to mechanical stress.[221] They play a central role in the fluid flow theory. Shear stress up-regulates the mRNA expression of Wnt[219]. Shear stress also activates the surrounding osteocytes to undergo a cellular response, thereby releasing other signalling molecules, namely prostaglandins, which are capable of recruiting osteoblasts. Ultimately, not only is new bone formed, but the osteoclastic formation is also inhibited.[222] Vezeridis *et al.* in 2006 found that those osteocytes can sense changes in the environment directly by detecting shifts in the cell morphology and the distribution of actin fibres within the matrix.[223]

Numerous other studies corroborate the notion that osteocytes play a relevant role in detecting this fluid shear strain with its resultant cellular response.[218, 224-226] However, it is not entirely clear how exactly mechanical loading is sensed by these cells.[227] Some researchers appear to think that the fluid flow induced by mechanical loading applies a type of strain to the osteocyte cell membrane. This tension subsequently deforms the cells with their dendritic processes. Drag forces are finally created which then cause an amplified strain on the actin bundles inside the osteocyte cell process. This in turn again stimulates the signalling molecules, which eventually culminates in cellular signalling and cytoskeletal reorganization.[228] Burra *et al.* in 2010 as well as Cherian *et al.* in 2005 were able to identify the location of the load sensors as the hemichannels.[229, 230] These hemichannels reside within the osteocyte cell body. They are involved in the exchange of signalling molecules as well as communicating with the extracellular environment.[230] These hemichannels are induced to open whenever there is a mechanical load applied to either the cell body of the osteocyte or to its dendritic processes.[229]

The above concept confirms that the osteocyte is a mechanosensing organelle which plays a pivotal role in the response of bone tissue to loading.

3.6.4 The effects of mechanical stress on mesenchymal stem cell (MSC) osteogenic differentiation

It is not yet fully understood what the role of mechanical forces is in the differentiation of MSCs and also their underlying cellular mechanisms. It is also speculated that mechanotransduction may act simultaneously with other cues to regulate or modulate MSC differentiation and subsequent cell behaviour.[203] Presently, there is evidence to suggest that mechanical stress causes osteogenic MSC differentiation, thereby ultimately producing intramembranous bone formation in the area of osseo-distraction.

For bone healing to take place, MSCs must undergo osteogenic differentiation. It is not yet entirely clear what the cellular details of this process are. However, several studies have suggested a possible mechanism. New bone formation is an essential ingredient of successful osseo-distraction. Guilak *et al.* in 2009 suggested that the mechanical stress applied to the bone of the mandible enhances the formation of a microenvironment that in turn increases the expression of certain bone growth factors. The latter in turn causes the differentiation of MSCs into osteoblasts.[206]

Friedl *et al.* in 2007 reported that MSCs are highly sensitive to mechanical strain.[231] As far back as 1996, Stein *et al.* indicated that C-Fos (FOS) belongs to a gene family encoding for nuclear proteins that are known to be involved in the regulation of osteoblast-related genes.[232] FOS plays a central role in the physiological response to mechanical forces, and human MSCs are stimulated within the cyclic tensile strain-up-regulated FOS expression.[233] The stiffness of the matrix also plays a role in MSC differentiation. Stiffer matrices were found to up-regulate levels of mechanotransducers such as rho kinase (ROCK), FAK and ErK1/2.

It has also been discussed in par. 3.6.3 that mechanical strain induces differentiation of MSCs down an osteogenic lineage by way of up-regulation of BMP-2 expression from surrounding cells.[234] It has also been mentioned that the expression of IL-6 and IL-8 is also up-regulated by cyclic tension strain. However, Sumanasinghe *et al.* in 2009 showed that IL-8 up-regulation is dependent upon the presence of dexamethasone, suggesting that interleukins also act as autocrine signals during the differentiation of MSCs.[235]

In 2011, Santos *et al.* reported that only BMP-7 production is up-regulated by mechanical stress, and not BMP-2. Currently, this is the first time that such a finding has been made. The authors also suggested that, in tandem with BMP-2, BMP-7 also plays a central role in the mechanotransduction process seen in osteocytes, thereby establishing the hypothesis that they act in synergy. The inference is that while BMP-2 presents the initial cue for osteoblastic differentiation and is germane to bone formation in general, BMP-7 production enhances osteoblastic differentiation of cells that are already committed and hence play a vital role in local bone formation.[236]

Also of importance is that Qi *et al.* found in 2008 that mechanical strain caused an increase in alkaline phosphatase (ALP) activity and subsequent up-regulation of transcriptional factors cbfa-1 and ets-1 in rat mesenchymal cells. These transcription factors have a vital role in the osteogenic differentiation of MSCs.[237] However, it was found that this effect of up-regulation was only contemporaneous (40 minutes); after that, up-regulation of transcription factors was no longer maintained. During DO, because the load is maintained over a protracted period, this process may result in a sustained up-regulation of growth factors, thereby resulting in prolonged osteoblastic differentiation. To corroborate these findings regarding the latter, Kanno *et al*. in 2005 also found that mechanical strain applied to human mandibular periosteal cells induced the up-regulation of cbfa-1 expression.[238]

In summary, the preceding studies confirm that mechanical stress can have a direct osteogenic effect on MSCs during the process of DO. It was further corroborated by Park *et al.* in 2011 who showed that mechanical stress *per se* is sufficient, in the absence of chemical stimulation, as a stimulus to drive the differentiation of MSCs down an osteoblastic lineage.[239] Further experimental studies have also shown that the properties of the stress applied to the bone are also considered to be an integral denominator. It is postulated that the direction of the tension used may also determine the cell lineage and differentiation of MSCs.[240] Koike *et al.* further confirmed in 2005 that the magnitude of the stress correlated with the expression of transcriptional factors. Hence it was further postulated that lower levels of stress had a greater effect on the up-regulation of salient bone factors as compared with higher levels of stress. However, regarding the magnitude of the strain, it appears that small tensile stress favours bone formation as compared with high tensile strain which results in fibrous tissue formation.[241] In DO, it is the continuous and increasing tension that is applied to the bone in a controlled fashion that is thought to be responsible for osteoneogenesis, as compared with fibrous tissue formation.[241]

Mechanical strain on cells has also compared the healing of dynamic to static bone. During both types of healing, when a mechanical load is placed upon healthy bone, an increase in the osteoid volume results. However, in contradistinction to adequate bone healing, Amir *et al.* in 2009 showed that, during the process of static bone healing, there are lower levels of cytokines and transcriptional factors to promote cell osteogenic differentiation and proliferation.[242]

While the above studies illustrate that mechanical stress is pertinent to MSC differentiation, it remains unclear, however, what the exact mechanism is that determines the differentiation of stem cells. While it is assumed that mechanical signals may act directly upon stem cells to induce differentiation, this finding is in contrast to another proposal that mechanical signals could exert their influence indirectly, for example by way of regulating angiogenesis and thus altering the local oxygen concentration at the level of the regenerating tissue. The latter is according to Burke *et al*. in 2012.[243]

It is therefore abundantly clear from earlier reports that the microenvironment or 'niche' is modulated in the main by the mechanical forces applied to the area. According to Birmingham *et al.* in 2012, it has been shown that the osteoblast-osteocyte network is known to play a central role in providing the natural cues for osteocytic differentiation.[244] In this way, the process of DO creates the perfect environment for MSC differentiation.

DO has therefore been shown to create the appropriate local mechanical environment or conditions to mitigate and modulate the process of bone regeneration. Korossis *et al*. in 2005 coined the term 'bioreactor' by referring to a system in which the conditions are strictly controlled to permit or induce certain behaviours in living cells or tissues. DO also behaves as an *in vivo* bioreactor that promotes osteoblastic differentiation and subsequent bone formation.[245]

CHAPTER 4. ASSESSING THE NEED FOR A BIOLOGICAL SOLUTION TO POST-MAXILLECTOMY DEFECTS

4.1 Maxillectomy defects and their implications

The midface is central to facial cosmetics and the essential human functions of eating, speech, deglutition and facial expression.[246] Accordingly, any damage to the region may compromise the patient's ability to function normally and enjoy a meaningful quality of life. Common causes of midfacial ablation include surgically removed tumours, congenital defects such as cleft lip and palate, as well as acute trauma such as gunshot wounds and vehicular accidents.[247] Surgical tumour removal is the most prevalent cause of maxillofacial defects, owing to its high incidence and severity. In the USA, 22 000 new cases of oral cancer are diagnosed annually, for which treatment usually involves removal of both hard and soft tissues of this region.[248]

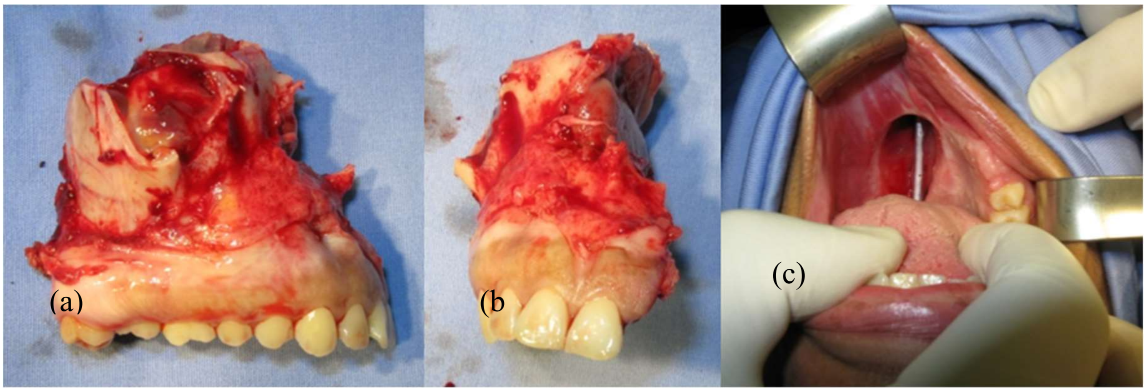


Figure 4.1: (a) Typical maxillectomy specimen. (b) The excised bone segment. (c) The resultant defect.

4.1.1 Existing methods of treatment

The main aim of maxillofacial reconstruction is to optimise function and aesthetics.[248] In the maxilla, the ideal treatment should restore:

- sensibility of the mucosa
- sufficient alveolar height and thickness to support dental implants
- lip competence

- physiological function, e.g. chewing, swallowing and speech
- correct geometry and symmetry
- aesthetic appearance of the reconstructed soft tissues.

The conventional treatment for reconstruction of the major maxillary defects is the re-vascularised free fibula graft (RFFF). This involves the transplant of a living bone segment, including an intact vascular network, usually from the fibula. While other bones such as the scapula or ilium could also be used, the fibula is the most popular. While RFFF is used successfully to restore maxillofacial defects, it has five major shortcomings:[246, 248]

1. failure rate of 5%
2. highly demanding technique, requiring specialised personnel and clinical environment
3. significant morbidity and complications arising from the donor site
4. Grafted bone does not always match native bone in structure and physical dimensions, limiting prospects for dental prosthetic implantation. The latter problem is one of the main reasons why the restoration of the occlusal plane in partially dentate patients is a problem.
5. In comparison with non-vascularised bone-grafting, RFFF patients spend, on average, 3 more hours in surgery, 12 more days in the hospital, and lose 500 ml more blood. According to Elsalanty *et al*. in 2009, high rates of complications and the limited applications of grafting methods necessitate the development of new and effective alternatives.[248]

In South Africa, there are only a few treatment centres that are capable of performing RFFF procedures. In contrast, there are more than 100 maxillofacial surgeons in the RSA alone who are capable of executing the transport distraction technique. Also, the technology of CTDO can be used in the rest of Africa, Asia and any country where inadequate financial means for RFFF makes this service financially untenable.

4.1.2 CTDO as an alternative

Bone generated by transport distraction mimics the parent bone in both physical dimensions and mechanical properties, and involves a less invasive surgical procedure than bone grafting. With a growing understanding of its capabilities, transport distraction is becoming an increasingly compelling alternative to conventional grafting techniques for the following reasons:[246, 249]

- surgical trauma is reduced: no donor site needed
- reduced operating time
- CTDO involves a comparatively simple surgical protocol
- The regenerated bone quality and geometry are comparable to the parent bone of the maxilla, making it ideal for restorative dental implantation.
- The surrounding mucosa, nerves and blood supply are regenerated in tandem, restoring physiological functionality to the oral region.

Prosthetic rehabilitation is the ultimate goal in maxillary reconstruction, and this demands sufficient bone bulk for the successful placement of dental implants. A randomised controlled trial by Elsalanty *et al.* in 2009 concluded that CTDO techniques produced far superior results to grafting. CTDO in the mandible created an alveolar regenerate with an average height and width of 96% and 87.5% of the parent bone respectively, compared to 26% in height in the case of treatment by RFFF.[248]

However, CTDO to date also has inherent shortcomings:

- failure of devices during treatment
- need for two distinct surgeries for device installation and removal
- reliance of patient compliance, given that CTDO requires home activation of the apparatus
- requires adequate healthy bone stock for harvesting the **bone transport disc** and anchoring the distraction device (this requirement became less significant towards the end of the study).

These shortcomings are, however, mostly peculiar to the distraction device in question, and are relatively superficial in comparison to the overall physiological benefits of CTDO.[247, 249]

In summary, the literature has demonstrated that CTDO may indeed offer a viable method of treating large maxillofacial bone defects, both in theory and in practice. It is implied in the literature that the extension of the CTDO technique to the repair of maxillary defects is restricted primarily by the lack of suitable devices.[247]

4.2 CTDO – understanding the physical environment

4.2.1 The distraction vector

The trajectory followed by the bone transport disc is known as the distraction vector. Zapata *et al*. (2010) classified this vector as follows:

- unifocal, if the distraction vector follows a one-dimensional linear path
- bifocal, if the distraction vector is curvilinear within a flat plane, i.e. two direction components
- multifocal, if the distraction vector incorporates a third spatial dimension.[247]

The activation mechanisms employed by most intra-oral devices limit their application to unifocal distraction. Such devices do not cater for craniofacial deformities that require a curvilinear distraction vector,[250] such as defects of the maxilla. Hence, methods have been developed that make use of a malleable rail that can easily be customised by the surgeon to suit the geometry of a particular patient.[246, 247] These curvilinear devices cater for curvilinear CTDO in the mandible.[247]. However, as discussed in subsection 4.4.3, the characteristics of these devices are not suited to CTDO applied to the maxilla.

4.2.2 Distraction rate and rhythm

Manually activated distraction, the current standard for craniofacial applications, involves two main components: (1) the rate of distraction, i.e. the total displacement of the bone transport disc per day; and (2) the rhythm, or frequency, of activations. According to Zapata,[247] rates vary from 1 mm to 2 mm per day at frequencies of up to 5 activations per day for craniofacial transport distraction osteogenesis (TDO). Maintaining the correct rate and rhythm is crucial. If the osteotomy is separated too rapidly (>2 mm per day), bone will not heal. Instead, fibrous scar tissue will form in the distraction gap. However, if the gap is separated too slowly (<0.5 mm per day), the regenerate will consolidate prematurely, hence impeding further distraction.[249, 250] The same applies if the latency period is too long. There is a consensus in the literature that 1mm per day, activated twice daily, is satisfactory.[249]

Continuous distraction is considered the ideal mode of distraction, as it minimises acute trauma in the healing gap by distributing the distraction over a greater period, while still achieving the required overall strain rate. However, attempts at constant distraction involving actuation by small motors, hydraulics or stored spring energy have proved impractical for reasons of size, patient comfort, and reliability.[247, 251]

4.2.3 The callus stretching force

In CTDO, tensile forces in the healing callus and surrounding soft tissue provide the only resistance to distraction. The distraction apparatus must overcome the resistance in the fracture gap to acquire optimal strain. Actual mandibular distraction forces reported in the literature ranged from 20 N to 60 N, with an average of approximately 35 N.[252, 253] In an entirely different application, a study by Burstein[254] concluded that resorbable midface distraction devices provide a safety factor of 4.4 over the maximum expected distraction load of 60 N. However, this large safety factor is owing to the relatively unpredictable nature of the polymeric materials used. Furthermore, the fact that resorbable materials weaken over time must be compensated for by an initial overdesign.

According to Meyer *et al.* in 2004, the distraction force is proportional to the cross-sectional area of the healing callus.[255] As the cross-sectional dimensions of the maxilla are marginally higher than those of the mandible, the forces required by maxillary CTDO are likely to be proportionally less than those in the mandible. It is thus reasonably assumed that the maximum mandibular distraction force of 60 N presented by the literature provides a safe benchmark for the design of a maxillary CTDO device.

Romanyk *et al.*[251] models the distraction force as a stepwise relaxation function (Figure 4.2). Daily activation of the distraction produces a displacement of the bone transport disc that is effectively stepwise. The visco-elastic behaviour of the stretched tissues generates resistive forces in the callus that peak at the instant of activation and decay exponentially as the callus tissue relaxes.

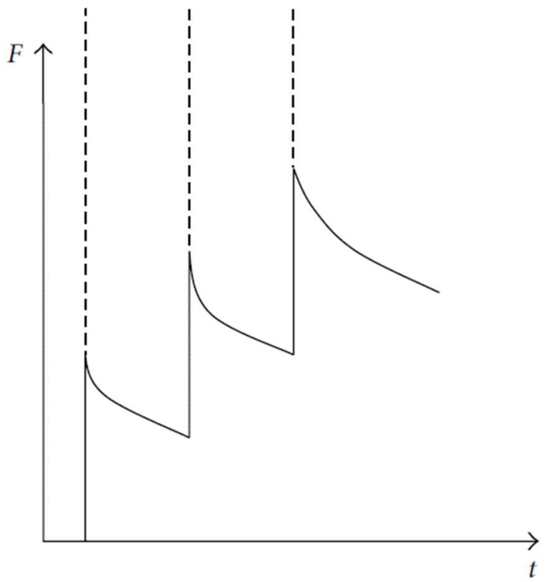


Figure 4.2: Stepwise relaxation of distraction force during CTDO.[250]

A study by Suzuki *et al*. in 2011 supports this model, finding that distraction force increases over the course of the procedure, rising to a local peak at the moment of activation and then decreasing until the next activation, owing to increasing consolidation of the regenerate.[253] Meyer *et al.* found in 2004 that, at a rate of 2 mm per day, mandibular distraction force remains relatively constant throughout the distraction process, implying that distraction of up to 2 mm per day remains within the elastic range of the distracted tissues.[255] Consequently, devices for transport distraction must withstand cyclic force spikes of the order of 60 N, with moderate residual loads.

4.2.4 Accidental disturbance owing to lingual forces

The stability of the bone transport disc is largely dependent upon external forces that might disturb the healing fracture, i.e. micromotion at the fracture site. Repetitive movement at the fracture site can lead to fibrous healing rather than proper bone formation. Forces owing to the tongue have been investigated in various studies. For the force exerted by the tongue in the vertical direction, Trawitzki *et al*. in 2011 found a maximum force of approximately 13 N for the anterior tip and 18 N for the dorsum of the tongue (Figure 4.3). In both cases, the maximum applied lingual force was measured in male test subjects.[256]

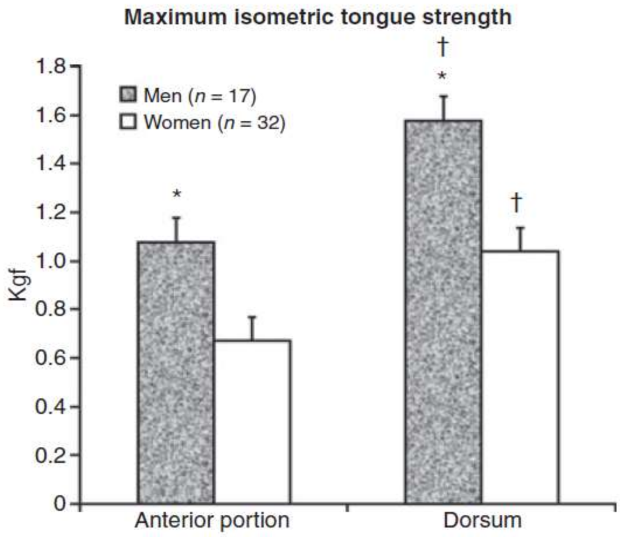


Figure 4.3: The mean maximum vertical tongue force exerted by the anterior portion and dorsum of the tongue (conversion 1 kgf=9.8 N).[255]

Valentim *et al.* in 2012 presented a summary of various studies on tongue force in the anterior and lateral directions.[257] A maximum lateral force of 16 N was found in a study by Dworkin *et al.* in 1980.[258] Other studies presented lateral lingual forces in the region of 12 N. The maximum tongue force in the anterior direction was approximately 26 N.[257]

4.2.5 The bone transport disc: Size and stability

The geometry of the regenerated bone is largely dependent upon aspects of the initial bone transport disc, illustrated in Figure 4.4. The literature suggests that the bone transport disc should be approximately 20 mm long[246] and that more than four screws should be used to stabilise the carrier disc.[248] The screws should run perpendicularly to the vector of distraction to obviate loosening during the process of distraction.

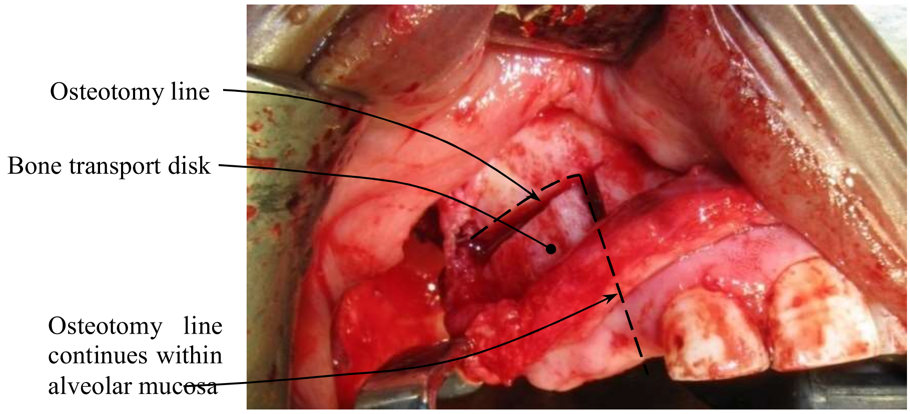


Figure 4.4 Intra-operative photograph of the surgically produced bone transport disc.

It is of paramount importance that the palatal mucosa remains attached to the bone transport disc to preserve the blood supply, and also that it be subjected to the least amount of trauma during creation of the carriage disc. This method ensures that revascularisation to the regenerate will occur.

4.3 Ergonomics: Patient compliance and comfort

For exceptionally large defects, the active distraction period can last up to 2 months (Figure 4.5). Many maxillofacial CTDO protocols, therefore, allow patients to return home within a few days after the initial surgery. In such cases, daily distractions are carried out by the patients themselves or by a trained nursing aide; the rate and rhythm of distraction are prescribed by the surgeon.

Figure 4.5: Patient activation of extra-oral mandibular distractor.

In general, patient compliance has been satisfactory, but in 2012 Romanyk *et al*. suggested that patient involvement during treatment should be minimised to eliminate potential risks and to reduce inconvenience caused to the patient.[247, 251]. However, in the absence of automated distraction mechanisms, patient-activated devices currently offer the only practical solution. As such, activation of distraction devices must be simple, intuitive and produce repeatable results, despite the lack of experience and training of users.

Intra-oral devices should minimise the presence of voids that might provide traps for food, detritus and infection, as this leads to unpleasant smells and taste and can provide a nidus for infection. To this end, the ISO7153-1 standard specifies that this category of device has smooth contours and highly polished surfaces that are easy to clean, resist corrosion and tend not to accumulate adherent debris. However, it should be noted that highly reflective surfaces can cause glare under operating lights. Where appropriate, non-glare finishes are preferable. Newson *et al*.(2002) recommend a final anti-glare finish using a polishing mop.[259]

4.4 CTDO device design: Existing concepts

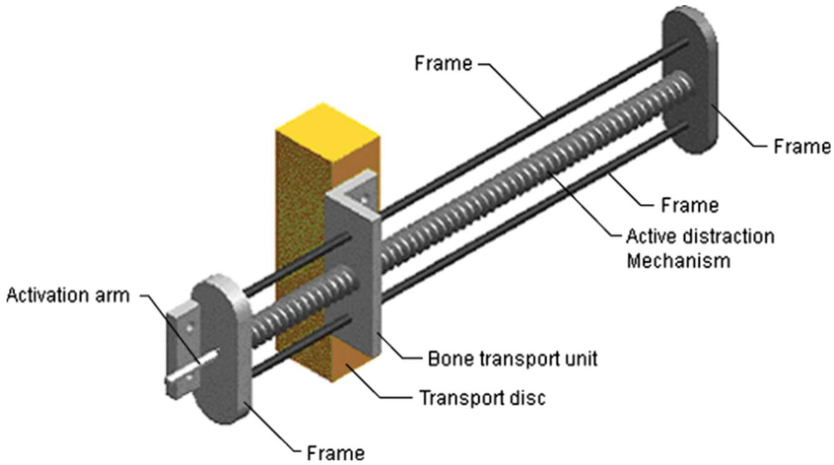


Figure 4.6: Typical format of existing CTDO devices.[246]

Transport distraction devices consist of the following fundamental components (Figure 4.6):

1. The **frame** supports the elements of the apparatus and designates the trajectory to be followed by the bone transport disc.
2. The **transport disc carriage** supports the bone disc while navigating the trajectory/path.
3. The **traction mechanism** translates the operator's activation torque into a displacement force along the path.

Zapata *et al.* (2010) make several pertinent suggestions for maxillofacial distraction devices.[247]

1. CTDO devices should be intra-oral, to lessen scar formation, and be small, to improve patient comfort and reduce stress on the soft tissues.
2. Devices should be stable, with a sturdy frame, and attach directly to the bone to diminish shear stresses within the newly formed callus.
3. The devices should follow the desired vector of distraction.
4. Device customisation and installation should be as simple as possible to minimise operating time.

5. Devices should be capable of **bifocal** or **multifocal** distraction to mimic the natural curvilinear continuity in the newly formed bone when reconstructing the facial contours.

The following subsections analyse aspects of existing maxillofacial CTDO devices regarding the above suggestions.

4.4.1 Intra-oral v. extra-oral distraction

Depending on the clinical application, intra-oral and extra-oral distraction methods possess individual benefits and shortcomings. In brief, intra-oral distraction is superior in the context of the maxilla. Extra-oral distraction methods are preferred when complicated three-dimensional bone reconstruction is required.

Table 4.1: Comparison of extra-oral v. intra-oral distraction devices.[246, 251]

INTRA-ORAL	EXTRA-ORAL
× Only capable of bifocal distraction	✓ Capable of multifocal distraction
✓ Excellent stability of anchorage pins	× More susceptible to loosening of anchorage pins
✓ Relatively small: good patient comfort	× Relatively large: poor patient comfort
✓ Intra-oral: no scarring	× Transcutaneous protrusions: scarring
✓ Low infection rate	× Pin tract infection common
✓ No activation arm extension: less error	× Long activation arm extension: greater error

It can be seen that extra-oral devices are bulky and generally inconvenient for patients to tolerate (Figure 4.7). The methods of fixation must consider the surrounding anatomy regarding installation, **distraction activation** and eventual removal of the device. Access at all stages of treatment is a critical consideration.

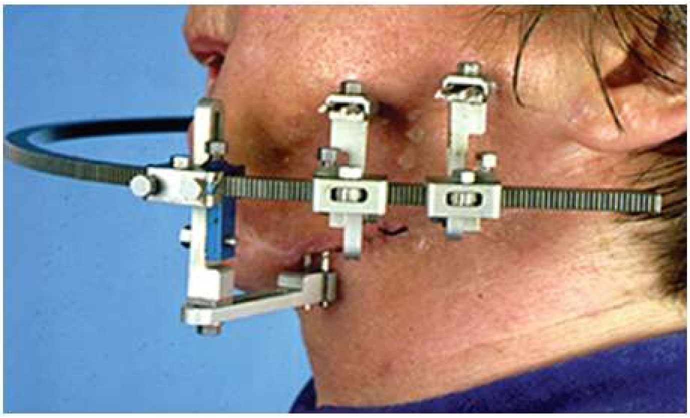


Figure 4.7: Example of an extra-oral mandibular CTDO device.[246]

4.4.2 Anchorage of the device and stability

The primary factors affecting mechanical integrity and stability of the distractor are the following:

1. The manner in which the device frame is **anchored** to the surrounding bone.
2. The number, length and diameter of the anchorage **screws**.
3. The **orientation** of the various components of the device and the effect thereof on the distraction vector.
4. **Material** properties of the apparatus.

Anchorage of maxillofacial CTDO devices is commonly achieved in one of three ways: bone borne, tooth borne, or a hybrid of the two. Tooth-borne and hybrid fixation are less secure and can damage the teeth and gums. Bone-borne anchorage, which uses fixation screws placed directly into the parent bone, provides the most stable anchorage condition.[247]

Fixation screws are of two types: The anchoring screws (2.0 mm – 2.5 mm) that secure the distractor to the surrounding native bone; and the **bone transport disc** fixation screws (1.5 mm) used to fix the distracted bone segment or transport disc to the mobile part of the device. Depending on the application and the integrity of the surrounding bone, Elsalanty *et al.*

recommend using more than four screws in the bone transport disc to mitigate tipping of the disc during distraction.[248]

The **orientation** of the device during installation dictates the distraction vector to be followed by the **bone transport disc**. Thus, the ideal device should provide the surgeon with maximum versatility in device placement and adjustment of the vector after device installation.[255]

A review of **materials** is presented in Section 4.5.

4.4.3 Activation mechanisms: Case studies

The literature offers four types of activation mechanism used historically in CTDO:[247,248]

- screw-type with or without a traction wire
- rack-and-pinion, or worm-rack
- spring-type
- hydraulically driven

For intra-oral CTDO in the maxilla, the literature suggests screw-type and traction cable devices as the most appropriate solutions. Spring and hydraulic appliances are impractical for reasons of size, reliability and limitations on the extent of distraction.[246, 247]

Romanyk *et al*. cites the main benefit of screw-type devices as the straightforward and well-understood mechanics.[251] The pitch of the screw defines the relationship between rotation and axial displacement, and thus the strain induced. As distraction-induced healing is strain- rather than stress-related, it is preferable that the operator has control over the distance by which the callus is stretched (strain), rather than the force applied (stress); while on the contrary, spring devices provide control of the force applied.[255] A significant benefit of screw-type devices is that they can be easily scaled to suit the size and loading requirements of a range of applications, whereas the scalability of spring-type devices is limited.

Hydraulically powered devices have been found to be large and impractical and require an auxiliary device to pressurise and meter the working fluid.

In the past, screw-type devices have been supplemented with a **traction wire**. A power screw mechanism, equal in length to the distraction trajectory, is situated at least partially outside of the mouth. This device is known as the **activation arm**. It generates a displacement which is transmitted to the **transport disc carriage** by the **traction wire**. Such devices require protrusion through the skin and are thus prone to infection and scarring. In the case of mandibular appliances, where the bulk of the device is submerged in the tissues, where it cannot be accessed directly, it is desirable that the activation arm is available extra-orally (Figure 4.8).

Figure 4.8: Traction-wire device.[247]

For power-screw type devices, the literature reports distraction lengths of up to 50 mm with or without the **traction wire** adaptation and, by incorporating a customisable guide-rail, both formats have facilitated **bifocal** distraction in the mandible.

In the case of individual screw-type devices, the screw actuation mechanism and the guide rail can be incorporated into a single unit, substantially reducing the size of the apparatus. Elsalanty *et al*. proposed one such method for mandibular distraction.[248] The device consists of a guide rail, formable to the desired trajectory, and a transport disc carriage. The guide rail features a toothed rack (A) on the outer surface. A worm screw housed within the carrier disc carriage engages with the toothed rack, providing the traction mechanism (Figure 4.9).

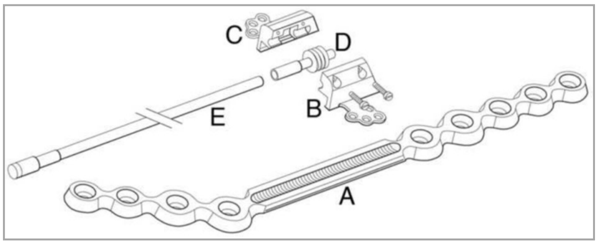


Figure 4.9: Exploded view of the device proposed by Elsalanty *et al.*2009 [248]

In a study of 13 beagle dogs, Elsalanty *et al.* in 2009 reported that the toothed guide rail mechanism provided adequate stability of the bone transport disc and accurate control of distraction.[248]

4.5 Implantable materials: A review

The choice of suitable materials is a critical consideration in the design of implanted medical devices. Materials must be suitable for close and prolonged contact with human tissue in warm and saline conditions.[259]

According to Elias *et al.*[260] the most important criteria for medical implant materials are biocompatibility and corrosion resistance. The most commonly used biomaterials are titanium alloys, stainless steel alloys, and polylactide resorbable polymers.

4.5.1 Titanium alloys

Titanium offers the highest level of biocompatibility and corrosion resistance, causes minimal image scatter in CT scanning, and is compatible with ultrasound and magnetic resonance imaging.[261] Five grades of titanium have been developed specifically for dental implant applications, specified according to their ASTM grades as 1 to 5.[260] More recently, Grade 23 has been introduced, as a higher-purity version of grade 5, and is considered the ultimate material for dental implantation owing to its high biocompatibility and excellent fatigue strength.

4.5.2 Stainless steels

Stainless steels for medical applications are specified in ISO 7153-1 standards for non-implant devices and ISO 5832-1 and 5832-9 for implants. Stainless steels are desirable for their excellent corrosion resistance but, with the development of highly biocompatible titanium alloys, stainless steel is seldom used for long-term implants.

4.5.3 Resorbable materials: Polylactide

The use of resorbable materials is growing in maxillofacial reconstruction, as this often removes the need for secondary surgery to remove plates and screws. The literature reports cases of distraction systems that can be eliminated non-invasively after treatment, by making use of resorbable materials.

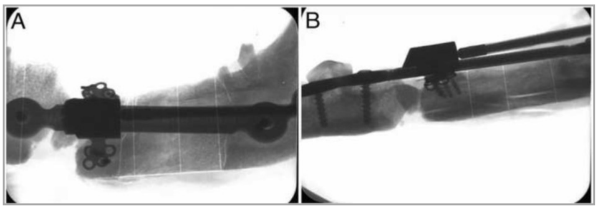


Figure 4.10: Radiographic images of implanted device: straight vector and high profile.[247]

Polylactide is the most widely used of these materials in maxillofacial applications. It begins to dissolve within 6 weeks and is fully absorbed within 12 months; with chemical modification, the material can be engineered to last several years. It has been utilised in maxillofacial transport distraction procedures where the forces present are similar to those in the mandible and maxilla.[261] However, polylactide loses strength long before it loses volume,[254] leading to ongoing concerns about the reliability of resorbable materials for distraction applications. Also, it is reported that during the resorptive process, these materials can fragment into large particles, which are often extruded through the skin, causing severe irritation and discomfort.[254]

In a randomised controlled trial in 2004 of resorbable v. titanium alloy distraction devices, Cheung *et al.*[261] found that:

1. there was a high incidence of broken screws and fixation plates in the resorbable group only
2. customisation of devices in the resorbable group was more time-consuming than that in the titanium alloy group
3. placement of resorbable screws took twice as long as in the titanium-alloy group
4. resorbable screws required pre-tapping of the drilled hole, whereas the titanium alloy screws were self-tapping.

4.6 Defining and formulating the design problem

4.6.1 Problem definition

According to the author, no device currently exists for CTDO in the maxilla that is capable of anterior-to-posterior distraction along a three-dimensional curvilinear vector, for repair of segmental defects of the maxilla. Maxillary CTDO is a pioneering method of treatment never before applied in humans. While new theories regularly add insight into the underlying mechanisms of CTDO, the exact mechanical requirements are not entirely understood. Furthermore, the literature only discusses cases in the mandible, with no reference to CTDO in the maxilla. While the biomechanics of mandibular and maxillary CTDO are similar, there are distinct practical differences between the two procedures, particularly in the ergonomic requirements of the devices that facilitate each procedure.

Given the lack of definite information about maxillary CTDO, the present project involved the parallel evolution of both the physical design of the new device and its functional requirements, both considerations being clinically and patient related. Clinical observations, patient feedback and recommendations from expert collaborators provided valuable insight into the diverse needs of both the surgeon and patient.

Over the course of the present project, the various design considerations were distilled and formulated into a coherent set of requirements – both quantitative and qualitative. The latter is presented in the form of a product requirement specification (PRS) in Section 4.8.

4.7 The surgical environment

It was a priority of the present project to develop a solution that can be readily adopted by all surgeons and is compatible with the medical environment. It was therefore necessary to consider the practicalities of surgery, existing technology and tooling, and how the device affects the experience of the patient. The following is a discussion of the problem as it was understood at the outset of the design process. The concepts were based on the literature and in consultation with the engineers involved.

4.7.1 Surgical installation of the device

While the application of CTDO to the maxilla is unprecedented, it has been used successfully in the mandible. The primary surgical protocol for installation of mandibular CTDO devices involves the following procedure:

Pre-operatively: By utilising life-sized models (stereolithography) of the patient's skull, the critical aspects of the surgery are planned, including customisation of the device (subsection 4.7.2).

Intra-operatively:

1. The accuracy of any pre-operative planning is checked and adjusted if necessary.
2. The locations of bone anchorage screws are demarcated as well as the osteotomy line for the transport disc.
3. The transport disc osteotomy is performed, creating a distinct vital bone segment.
4. The device is installed, anchored to the parent bone using bone screws.
5. The transport disc segment is affixed to the bone transport unit using bone screws.
6. Once installed, the distraction device is activated to ensure that there is visible separation at the transport disc osteotomy.
7. The distraction device is reversed to bring the osteotomy surfaces back into forced contact so that healing can begin.

The osteotomy is allowed to heal at the discretion of the surgeon (latency period, usually about 5 days) to allow the formation of healthy callus.

4.7.2 Pre-operative planning and preparation

Maxillofacial reconstruction demands accurate reconstruction of both facial functionality and geometry, where even the slightest disparities can compromise the aesthetics of the result.[250] In CTDO, this objective relies upon the anatomical accuracy of the distraction trajectory prepared by the surgeon. Also, the points of anchorage to the parent bone must be stable and structurally sound to prevent excessive micromotion at the fracture site.

Modern computed tomography (CT) and rapid prototyping technology (Figure 4.11) provide accurate full-scale cranial models, facilitating detailed preoperative surgical planning and device customisation, thereby enhancing the predictability of surgery. This facility separates the planning aspect from the surgical installation procedure, reducing operating time, patient trauma and cost, while affording the surgeon additional time for hardware customisation.[246, 254, 255]

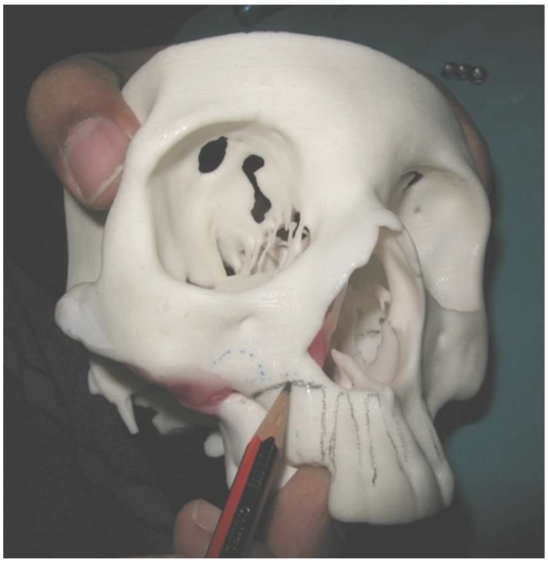


Figure 4.11: Pre-operative planning of surgery facilitated by CT imaging and rapid-prototyped cranial models (case report 1).

4.7.3 Design factors

The surgical protocol in subsection 4.7.1 hints at the diversity of factors to be considered:

1. case-specific customisability – adapting the device to the individual case
2. intra-oral access – the device must be installed and activated within the oral confines
3. stability – the influence of the intra-oral environment
4. patient experience – comfort, compliance and postoperative oral hygiene.

4.7.3.1 Case-specific customisation

Maxillofacial geometry can vary considerably between patients, depending on gender, age and ethnicity. Furthermore, the invasive and unpredictable nature of maxillofacial neoplasia produces defects that differ widely in severity and location. Consequently, the ideal CTDO device should cater for a variety of facial geometries and defects, provided that adequate bone stock is available adjacent to the defect, from which to harvest a substantial and viable bone transport disc.

To be accessible to a wide range of users, the device should be customisable by the surgeon according to the needs of the individual. The latter can be achieved by employing modular and customisable components; however, such customisation poses the risk of damage. Moreover, to mitigate such risks, the customisation should be isolated to the relevant part, thereby ensuring that other critical components are not inadvertently affected. Installation of the device should be user-friendly, and individual customisation should not demand highly trained personnel.

The present project focuses on segmental defects in the maxillary alveolar ridge. These defects can be 20 mm or more, measured circumferentially along the outer surface of the alveolar ridge, and can extend to the nasal floor (Figure 4.1(c)). It was believed that a two-dimensional curvilinear trajectory was sufficient to reproduce the typical functional geometry of the maxilla, i.e. an arch within a flat plane. The minimum curvature of the maxillary alveolar ridge varies from 25 mm to 30 mm.[1] The device should cater for a 25 mm minimum radius of curvature along the plane of occlusion.

[1] 25 mm - 30 mm curvature is based on measurements from CT images in various publications and stereolithographic models sourced from the author.

4.7.3.2 Intra-oral access

The installation, activation and ultimate removal of intra-oral devices require manipulation of various components and tools within the oral cavity. The design of the apparatus, and its position and orientation, must consider the tight constraints of the surrounding facial anatomy. The effect of trismus exacerbates poor intra-oral access. In maxillofacial surgery, the leading causes of trismus are prolonged contact with foreign bodies, radiotherapy and infection. Trismus can be reduced by administering a muscle relaxant and is therefore not a prohibitive problem.

During its working life, the device should be accessed through the mouth without any protrusion through the skin. According to the literature, extra-oral activation may provide easier access, but this benefit is far outweighed by the reduced scarring and patient comfort offered by intra-orally activated devices.

4.7.3.3 Stability

For the apparatus to function satisfactorily, it must provide a stable mechanical environment that promotes proper bone formation. The device must therefore be capable of withstanding individual loads within the mouth, which arise primarily from the actions of the patient. Given the large magnitude of bite forces, a level of patient co-operation must be expected, trusting that the patient will take due care not to behave in any way that could compromise treatment or cause damage to the device. Such assumptions are common in any long-term medical care. Nonetheless, the device should withstand disturbance from the tongue, as this is very often unconscious and therefore inevitable. Also, traumatic forces onto the apparatus or regenerate can be obviated by the fabrication of a sectional acrylic bite splint that can fit onto the lower teeth. This bite appliance frees the device from contact with the teeth of the lower occlusal plane (see Figure 9.52).

4.7.3.4 Patient experience

Patients are required to live with the device installed for up to six months, making comfort a primary concern. For hygiene reasons, the prevalence of food-trapping voids in or around the device should be minimised, as they provide sources of infection and foul odours. In general, the treatment protocol includes a thorough hygiene regimen, involving oral brushing, rinsing and the use of water-jet oral cleaning systems such as the Waterpik,™ (Tri-star marketing 3444 S Westshore Blvd., Tampa, Fl 33629, United States) if necessary. Considering the long duration of treatment, the presence of the device within the mouth should not compromise standard functions, including eating, drinking, breathing, speaking and sleeping. Furthermore, any potentially abrasive or intrusive surfaces should be eliminated. In the interests of social interaction, it is highly desirable that the device is not visible externally.

4.8 Product requirement specification

This section presents a summary of the design needs of the maxillary CTDO device. These requirements were based on a review of the literature, a survey of existing appliances, and consultation with the engineers. While initially qualitative, concerning ergonomics and basic functionality, these requirements evolved to define quantifiable force and strength requirements as the project progressed.

Quantitative criteria were included for the purpose of verifying power and reliability of the device. In general, these were not considered to be formal design standards from the outset, as the early design was based on ergonomic qualitative requirements, i.e. dimensions were originally based on user convenience, rather than optimised for strength. It is shown in Section 8.2 that the dimensions of the device, as determined by ergonomics, are also sufficiently large regarding its distraction force and reliability criteria.

4.8.1 Scope statement

The present project involves the development of a device that achieves stable and controlled intra-oral transport distraction of a bone fragment along a three-dimensional curvilinear vector for reconstruction of unilateral defects of the maxilla in adults.

Treatment of uni- or partially bilateral, or lateral maxillary tumours, usually requires the removal of the entire posterior segment of the maxilla, resulting in a void at the rear of the affected side of the maxilla. This void implies a lack of bone on which to anchor the posterior end of the device, which must be accounted for by the method of anchorage of an effective distraction system.

The CTDO system should address the requirements of each stage of treatment, from pre-operative planning, through installation and daily operation, to removal of the device. The availability of auxiliary tooling has to be considered. The installation and removal of the device can be accomplished by any skilled surgeon.

4.8.2 Functional capabilities

The device should accommodate patient-specific three-dimensional curvilinear[2] geometry, such that:

- a distraction path of up to 100 mm length can be achieved.
- a minimum radius of curvature of 25 mm can be followed.
- the device must secure the bone transport disc with at least four bone anchorage screws.
- installation and removal must be as simple as possible.
- the device must make use of existing installation/activation tooling, wherever possible.
- the device should permit adjustment of the distraction vector at any stage during the surgical installation procedure.
- the device should be capable of being driven along the trajectory in both the forward and reverse directions.
- actuation of the device should require a torque of no more than 20 N.cm.[3]
- the appliance should produce an axial distraction force of at least 60 N.(subsection 4.2.3).
- the device must endure a cyclic distraction force for at least 100 cycles.
- the device must withstand erratic tongue forces of up to 12 N vertically and 16 N laterally (subsection 4.2.4).

4.8.3 Safety, user interface and patient experience

A review of existing devices and recommendations in the literature suggests the following:

1. The device should attach directly to parent bone, with minimal intrusion on the local anatomy, such as disturbance of dental roots or irritation of soft tissue.

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[2]Three-dimensional curvilinear refers to a curved line on a flat plane.
[3]20 N.cm value is based on the activation torque of existing devices and provides a benchmark.

2. The device should be manually activated intra-orally, requiring no penetration of the skin. Activation should be simple enough to be carried out by the patient or the patient's minder, in a non-clinical environment such as in their home.

3. Primary oral function must not be hindered, i.e. the device must not interfere with:

- the passage of air and food
- movement of the tongue
- movement of the mandible.

4. The device should not be visible externally.

5. The device should not protrude more than 10 mm from the outer maxillary contour.[4]

6. Suitable implantable materials should be used for all tissue-submerged components.

7. The device must withstand normal sterilisation procedures.

4.8.4 Maintenance

1. The implanted device must endure a working life of at least six months.
2. The device should require no maintenance during its working life.

[4] 10 mm dimension is based on qualitative comfort testing by author on consenting subjects.

CHAPTER 5. SURGICAL ABLATION AND TEMPORISATION OF BONY DEFECTS

5.1 Case overview

The current chapter discusses all six cases where surgical removal of the tumours or pathology was performed by the same surgeon (MRH). All cases were classified according to the Brown classification (2010) of maxillectomy and midfacial defects.[262]

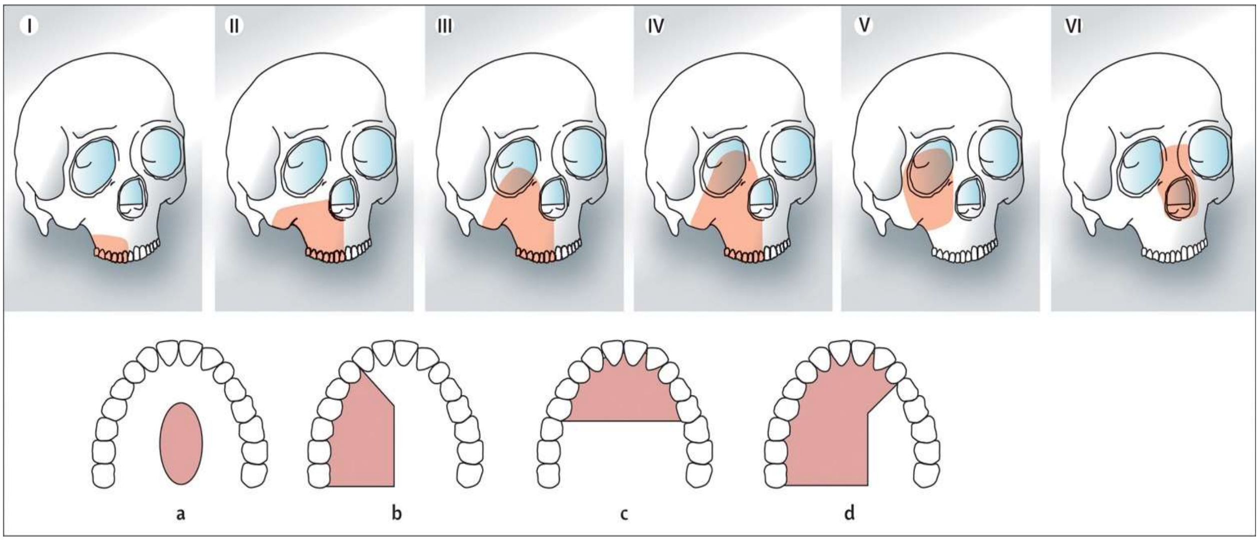

Figure 5.1: Classification of vertical and horizontal maxillectomy and midface defects.[261]

Vertical classification: I—maxillectomy not causing an oronasal fistula; II—not involving the orbit; III—involving the orbital adnexae with orbital retention; IV—with orbital enucleation or exenteration; V—orbitomaxillary defect; VI—nasomaxillary defect.

Horizontal classification: a—palatal defect only, not involving the dental alveolus; b—less than or equal to 1/2 unilateral; c—less than or equal to 1/2 bilateral or transverse anterior; d—greater than 1/2 maxillectomy. Letters refer to the increasing complexity of the dentoalveolar and palatal defect, and qualify the vertical dimension.

The presentation of these 6 cases is in the chronological order of the surgical procedures, as the development of the device prototypes was prompted by the reconstructive challenge provided by these cases.

5.2 Case report 1

Patient VT was referred to our private maxillofacial clinic on 19 February 2010 by her general practitioner for a palatal swelling. The age of the patient was 37 years and the swelling in her palate had been noticed for a week.

5.2.1 Clinical examination

There was a soft fluctuant swelling in the palatal region of tooth #16 and #17. The swelling was asymptomatic. All the teeth in the first quadrant were vital and non-tender to percussion. Aspiration of the swelling revealed no pus or fluid. Incisional biopsy revealed a low-grade adenocarcinoma. A computerised tomography (CT) scan on 24 February 2010 showed early erosion of the hard palate, alveolar bone and floor of the nose.

5.2.2 Radiological examination

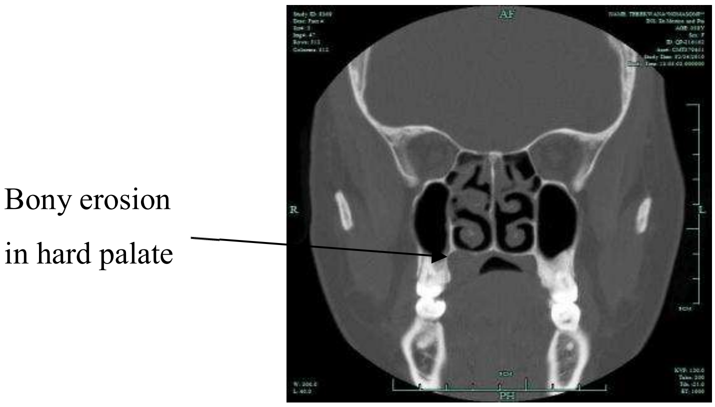

Figure 5.2: A coronal view of the vault of the palate shows erosion of the posterior alveolar bone on the right side.

5.2.3 Treatment plan

The patient consented to undergo a partial maxillectomy followed by distraction osteogenesis (Brown II b resection).

5.2.4 Surgical ablation

A general anaesthetic was administered on 10 March 2010 in a private hospital. A partial maxillectomy was performed (Fig. 5.3(a)), tooth #15 was extracted and the osteotomy was carried through at a low Le Fort I level via a circumvestibular approach. The transverse osteotomy was extended into the hard palate to the 2nd quadrant, ensuring a clearance level of 10 mm all round. The tuberosity was separated from the pterygoid plates. The tumour and all teeth were removed *en bloc* and sent for histology (Fig. 5.3(b)). The surgical defect (Fig. 5.3(c)) was packed with bismuth iodoform paraffin paste (BIPP) (Orion Laboratories Pty Ltd 85 Brigg Street, Welshpool,Wa 6106 Australia) and a prefabricated acrylic baseplate was inserted and secured to the palate with 3 x 20 mm Biomet^{TM} titanium screws. The surrounding cheek and soft palate were sutured to the baseplate with 5-0 Vicryl^{TM} suture (Ethicon Inc, Johnson & Johnson , Brunswick, New Jersey, USA) (Fig. 5.3(d)).

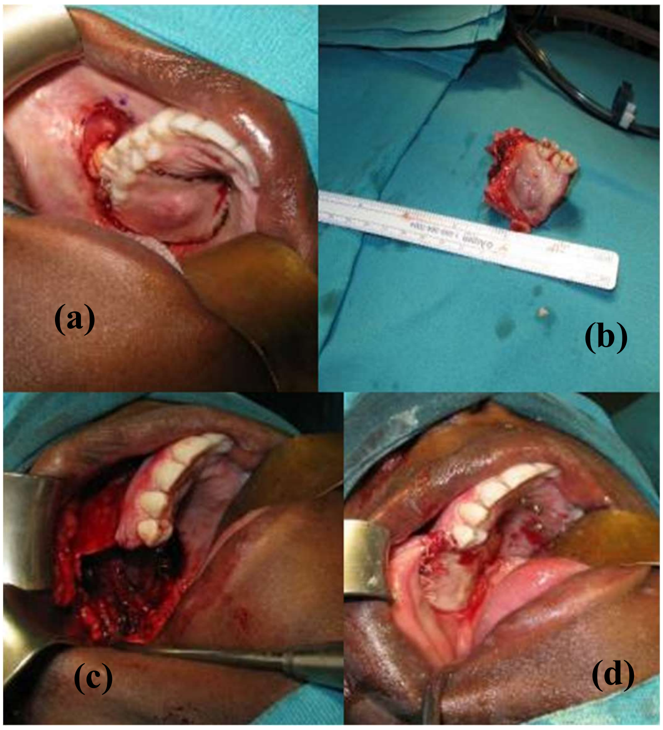

Figure 5.3: (a) The tumour in the palate and the excision line. (b) The excised tumour with a wide margin. (c) The large surgical defect. (d) The obturator plate with screws, holding the BIPP in place.

5.2.5 Postoperative course

The patient was nursed in high care for the first 2 days postoperatively under continuous nasogastric feeding until swallowing was satisfactory. The patient was discharged 3 days later and could feed orally.

5.2.6 Temporisation of surgical defect

After 3 weeks, on 7 April 2010, under general anaesthesia, the obturator plate and the BIPP pack were removed. The defect (Fig. 5.4(a)) was irrigated and an alginate impression was made by a prosthodontist for fabrication of a formal obturator. The obturator plate was replaced using Viscogel^{TM} Dentsply International, USA) soft reline (Fig. 5.4(b)).

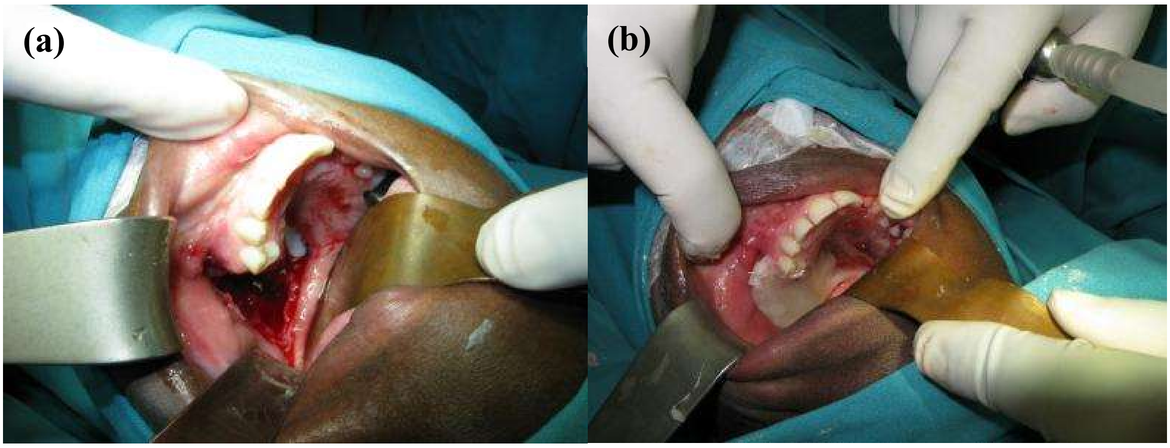

Figure 5.4: (a) The surgical defect after healing of 3 weeks. (b) The Viscogel^{TM} reline in the obturator plate.

5.3 Case report 2

5.3.1 Clinical background and examination

Patient LH was referred to our maxillofacial clinic on 2 July 2009 for a swelling on the right and anterior maxilla (extending from tooth #17 to #21). The swelling had been present for about 32 weeks and had been asymptomatic for most of the time period. Clinically, there was only labial expansion of the lesion to be seen, and all affected teeth were tested to be vital. The lesion appeared to have a cystic nature. Figure 5.5 shows a 3-D stereolithographically generated model exposing the position of the tumour within and involving most of the right maxillary antrum.

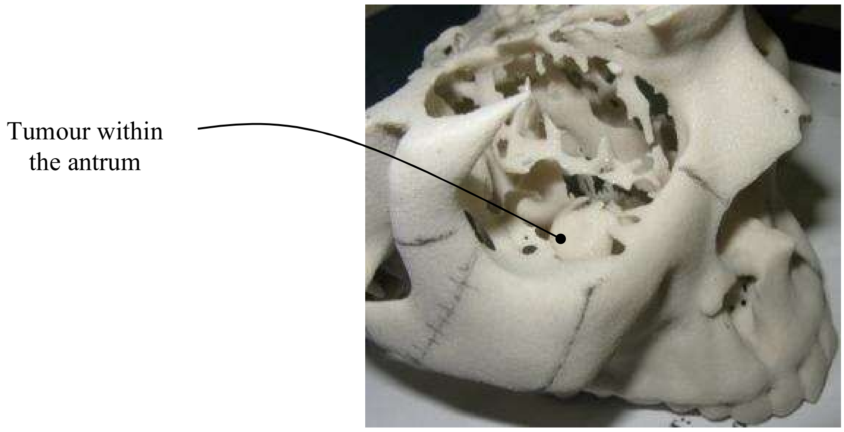

Figure 5.5: Position of the tumour within and involving the right maxillary sinus.

5.3.2 Radiological examination

A CT scan on 12 June 2009 showed a radiopaque extension of the lesion from the complete right maxillary sinus into the floor of the nose as well as the floor and medial wall of the bony orbit (Fig. 5.6). An axial CT view showed that the radiopacity extended from tooth #17 to #21 (Fig. 5.7).

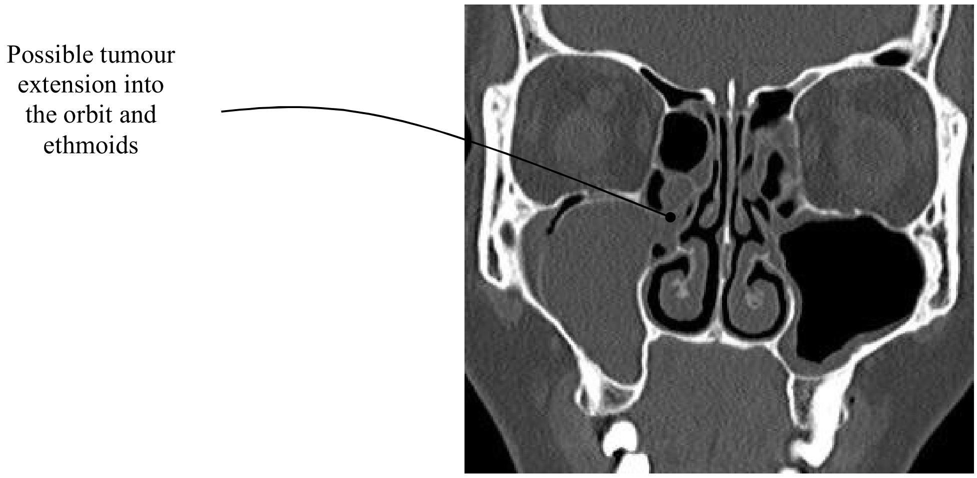

Figure 5.6: The radiopacity extension from the right maxillary sinus to the orbital floor and ethmoidal air cells.

Figure 5.7: The tumour involvement of the right maxilla from tooth #17 to #21.

5.3.3 Incisional biopsy

The patient was admitted to a surgical facility where, under general anaesthesia, an incisional biopsy of the tumour was performed. At surgery, the lesion appeared to have a multi-lobulated appearance not unlike that of an ameloblastoma or odongenic keratocystic tumour. A histological diagnosis of an ameloblastoma indicated that the patient had to undergo a maxillectomy.

5.3.4 Complication of pregnancy

At the time of referral, the patient revealed that she was on a regimen of fertility drugs to facilitate a pregnancy. Unfortunately, it was clinically too late to curtail the process of fertilisation. It subsequently transpired that the pregnancy did materialise, and hence the surgery for the maxillectomy was postponed until the post partum period.

The challenge to curtail further growth of the tumour became a priority. It was decided to marsupialise the tumour and pack the cavity of the tumour with BIPP to stunt further growth and expansion. At the same time, after removal of the BIPP (14 days), the tumour was expected to involute to some extent.

5.3.5 Initial surgery

Under local anaesthesia and sedation in a clinical facility, an operculectomy was performed and as much as possible of the tumour lining was removed. The defect was packed with BIPP and marsupialisation to the oral mucosa was performed. The BIPP pack was left *in situ* for 2 weeks. While good granulation of the defect lining was seen, the defect was repacked with clean BIPP which was incrementally removed in the clinic.The pregnancy was monitored regularly and the tumour was checked with magnetic resonance imaging (MRI) on a 12-week basis to monitor for base of skull expansion. The repeated MRIs showed no further activity.

5.3.6 Post partum

A few weeks after childbirth, a repeat CT scan indicated that the extent of the tumour had not deteriorated further since the marsupialisation process. The patient was counselled and informed consent was taken for a maxillectomy (Brown class III d).

5.3.7 Ablative surgery

Under general anaesthesia in a private surgical facility, a submental intubation was performed by the author. A Weber-Ferguson-Dieffenbach incision was performed to gain access to the tumour, orbit and posterior maxilla (Figure 5.8(a)).

Figure 5.8: (a) The surgical approach and submental intubation. (b) Soft-tissue dissection to the facial skeleton.

An incision was made with a #15 blade along the lines indicated in Figure 5.8(b) and blunt dissection was carried inferiorly onto the underlying facial skeleton. The upper lip was sectioned through its entirety and the dissection was carried into the pyriform fossa of the nasal floor and alveolus. The right infra-orbital nerve was identified, sectioned and marked for later reconnection. The right facial skeleton was degloved from its overlying muscle and skin to the level of the zygomatic arch (Figure 5.9 (a)).

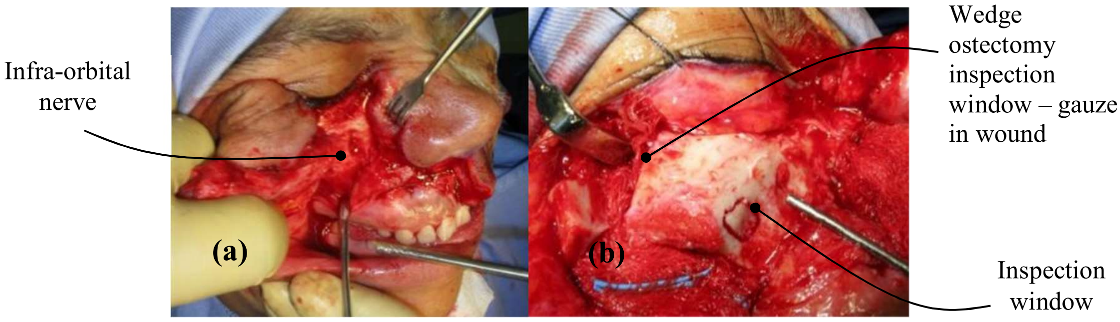

Figure 5.9: (a) Degloving of the right cheek and exposure of the infra-orbital neurovascular bundle. (b) Inspection windows as described for access into the infratemporal fossa and antrum respectively.

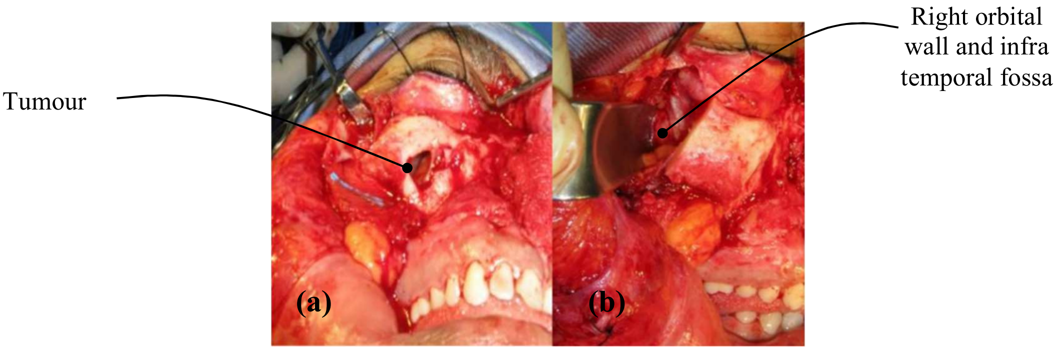

Figure 5.10: (a) The tumour within the right maxillary antrum. (b) Access to the right lateral orbit and infra temporal fossa.

After exposure of the malar corpus, two inspection windows were made (Figure 5.9). On the left side of Figure 5.9(b), a wedge osteotomy was performed by means of a reciprocating saw. This was done to inspect and gain access to the lateral and posterior aspects of the right orbit and infra-temporal fossa region. On the right of Figure 5.9(b) is the second inspection window for visual access to the right antrum to study the posterior extent of the tumour.

Figure 5.10 shows the position of the tumour within the right antrum. The posterior and lateral wall of the right orbit were inspected and found to be free of tumour invasion. This allowed preservation of the lateral wall of the orbit.

In Figure 5.11(a), the vital structures of the infratemporal fossa can be seen. This vista also allows access and control of the terminal portion of the internal maxillary artery. To preserve the corpus of the right malar bone, the latter was removed and brushed with cytology for tumour involvement. This was found to be clear of tumour and could therefore be re-used during reconstruction. Figure 5.11(b) shows the extent of the tumour within the maxilla after removal of the corpus malar. The orbital floor was inspected and found to be involved with tumour and therefore it was included in the resection. The right infraorbital nerve was mobilised and removed from its canal through a proximal pull-through approach and marked with a suture for later repair.

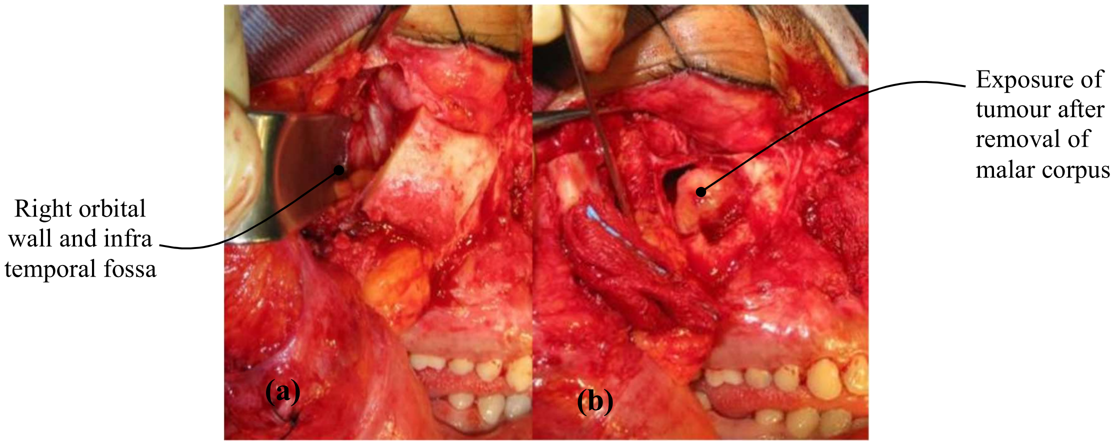

Figure 5.11: (a) Access to the right lateral orbit and infra temporal fossa. (b) The extent of the tumour within the maxilla after removal of the corpus malar.

The lacrimal duct was identified and sectioned with a #11 blade and prepared for Crawford tube recannulation (as per dacrocystorhinostomy). Figure 5.12(a) shows sectioning of the right lacrimal duct. Further inspection of the medial orbital wall and ethmoidal air cells confirmed the presence of tumour extension (Figure 5.12(b)) and hence the inferior section of the medial orbital wall was included in the resection.This was effected by use of a 701 burr and osteotomes. Tooth #22 was extracted and a paramedian osteotomy through the socket of tooth #22 was carried out. This was extended through hard palate and alveolar bone (Figure 5.12(c)) by means of a reciprocating saw and osteotomes. At all times, a clearance margin of about 10 mm was observed. The right tuberosity and posterior margin of the maxilla was dismembered from the pterygoid plates by means of a curved osteotome and mallet (Figure 5.12(d)). This allowed mobilisation of the complete complex in its entirety. The naso-orbital-ethmoidal-maxillary complex was carefully removed and the tumour bed was brushed for cytological examination. All margins were clear of tumour and no base of skull involvement was seen. The large surgical defect was packed with gauze for haemostasis, and all bleeding points were tied off or cauterised.

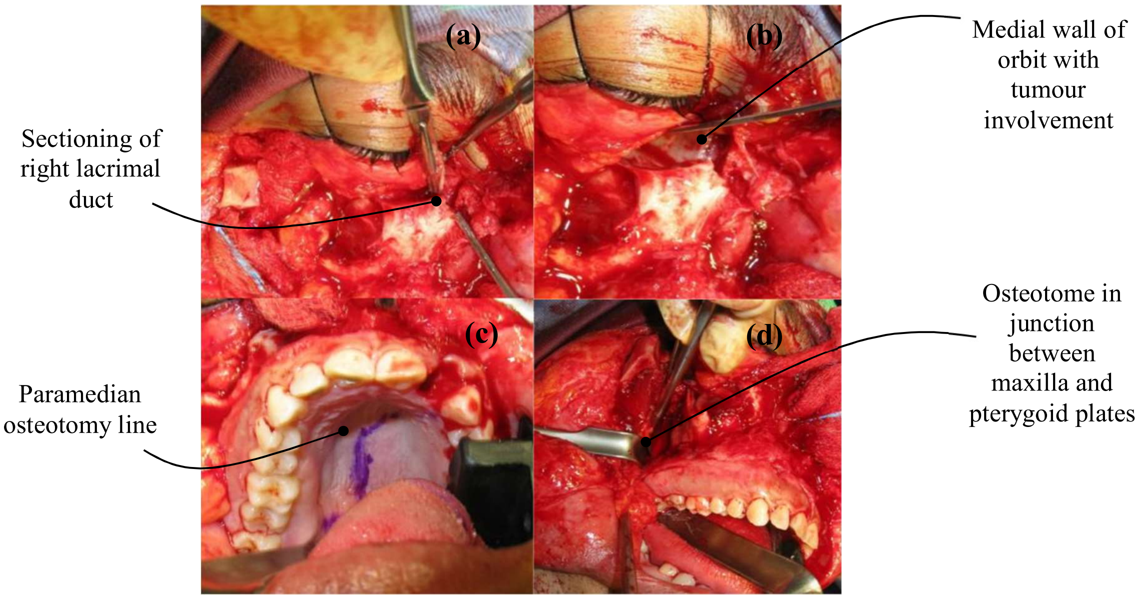

Figure 5.12: (a) Sectioning of the right lacrimal duct. (b) Extension of the tumour into the medial orbital wall. (c) The hard palate and paramedian osteotomy line. (d) Removal of the maxilla from the pterygoid plates.

The complete right maxilla with orbital floor, the premaxilla, all three nasal conchae and nasal septum were outfractured *en bloc* and removed (Figure 5.13(a)). All the margins of the resected specimen (Figure 5.13(b)) were tested via frozen section and the resected surgical defect was brushed for cytology. All margins were reported to be negative.

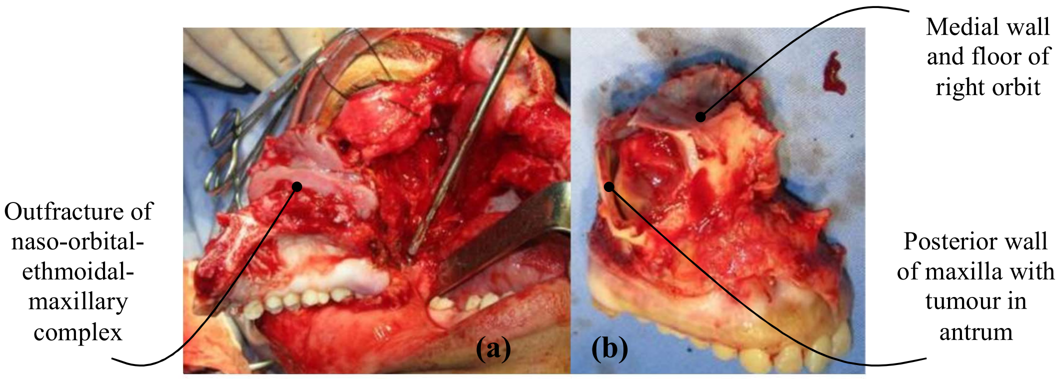

Figure 5.13: **(a)** Outfracture of naso-orbital-ethmoidal-maxillary complex.(b) Resected specimen of naso-orbital-ethmoidal-maxillary complex.

5.3.8 Immediate temporary reconstruction

Crawford tubes were placed into the lacrimal apparatus from the ocular side and attached to the nasal septum with a 4-0 Vicryl™ suture, to allow drainage of tears from the lacrimal sac into the nasal cavity and prevent subsequent epiphora (Figure 5.14(a)). The resected malar corpus was replaced in its original position and secured with 0.6 mm titanium plates and screws (Biomet™) (Figure 5.14(b)).

A new infra-orbital rim was made from cortical bone harvested from the right external oblique ridge region of the horizontal ramus of the mandible (Figure 5.14(c)). Once the infraorbital rim was in place, it would provide support to the titanium orbital plate (Biomet™) used for reconstruction of the orbital floor (Figure 5.14(d)). The orbital floor was subsequently reconstructed by securing the prefashioned titanium orbital floor plate to the infra-orbital rim via the placement of screws into the lug extensions.

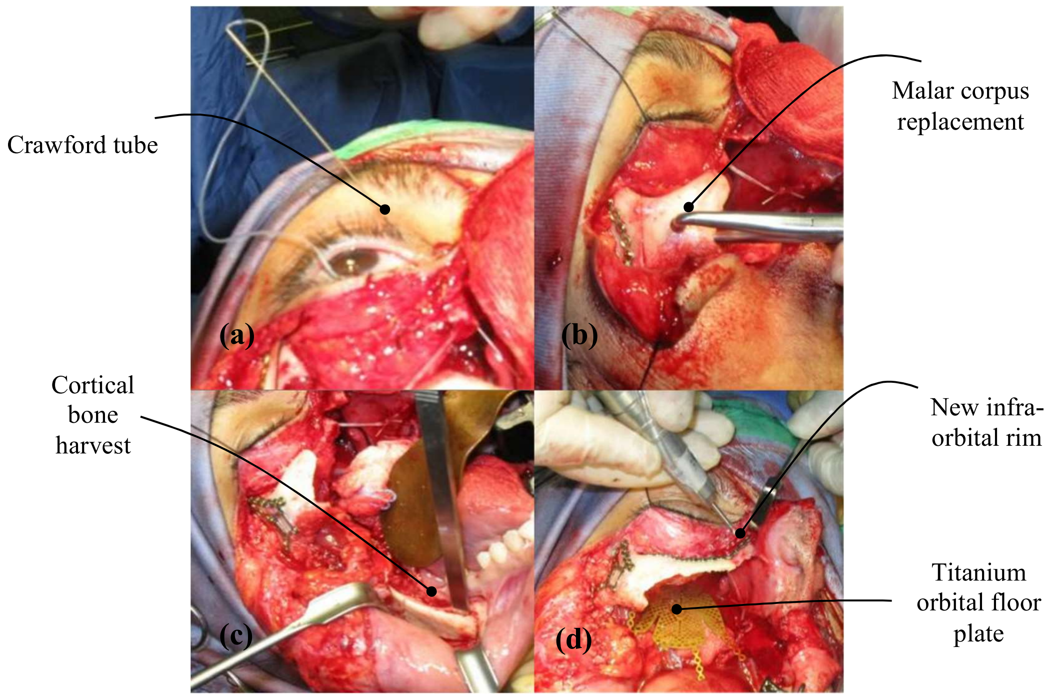

Figure 5.14: (a) Insertion of Crawford tube. (b) Replacement of malar corpus and securing of Crawford tube. (c) Harvest of bone graft from the mandible. (d) Reconstruction of a new infraorbital rim.

The right infra-orbital nerve was repaired with three 9-0 Nylon™ (Ethicon) perineural sutures (Figure 5.15(a)). Buccal fat pad tissue was used as a flap to cover the titanium orbital floor as far as possible to reduce the potential for infection of the titanium plate (Figure 5.15(b)). The facial skin wound was closed in layers (Figure 5.15(c)) and potential ectropion of the lower eyelid was obviated by the use of a Frost suspension suture (Figure 5.15(d)), which was left *in situ* for 10 days.

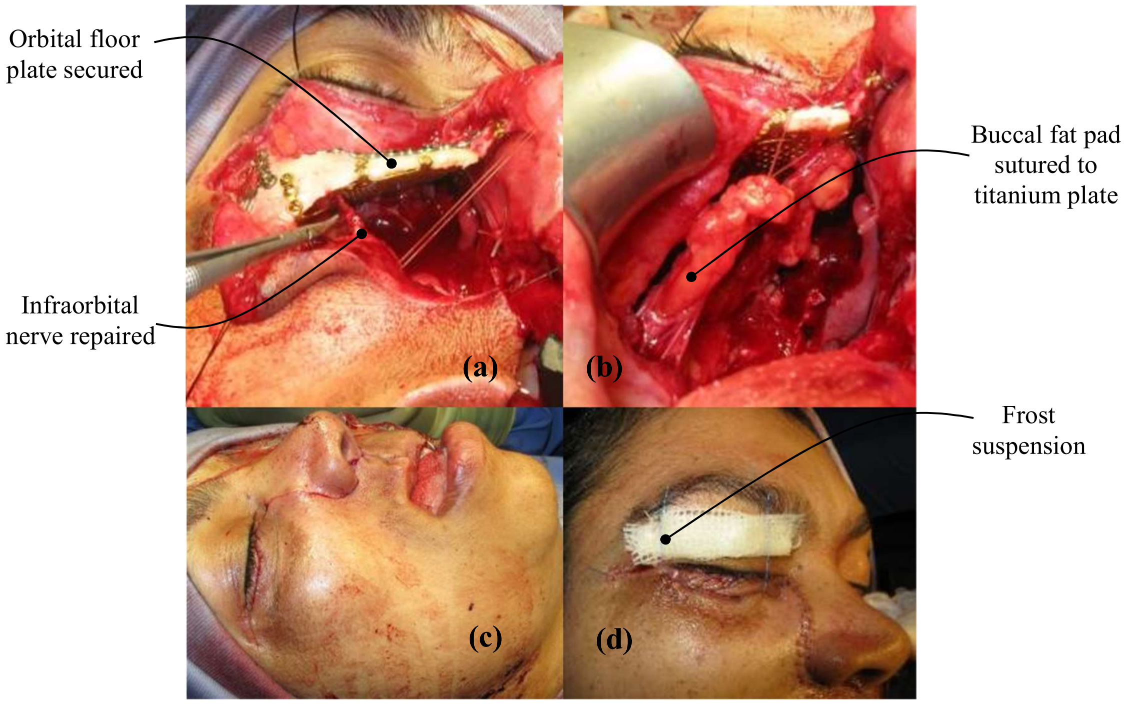

Figure 5.15: (a) Reconstruction of orbital floor and repair of infraorbital nerve. (b) Titanium orbital plate covered by buccal fat tissue.(c) Layered closure of the muscle and skin. (d) Frost suspension sutures to the lower eyelid.

5.3.8.1 Temporisation of surgical defect

The large oral defect was temporarily obturated by means of a prefabricated clear acrylic baseplate (Figure 5.16(a)). The surgical defect was packed with BIPP (Figure 5.16(b)) which was left in situ for 10 days. The acrylic obturator plate was secured to the non-operated palatal shelf by means of intra-osseous titanium screws (Biomet ™). The surrounding soft tissue of the cheek (buccinator muscle and mucosa) as well as the soft palate was sutured to the obturator plate to ensure hermetic closure of the hard and soft palate.

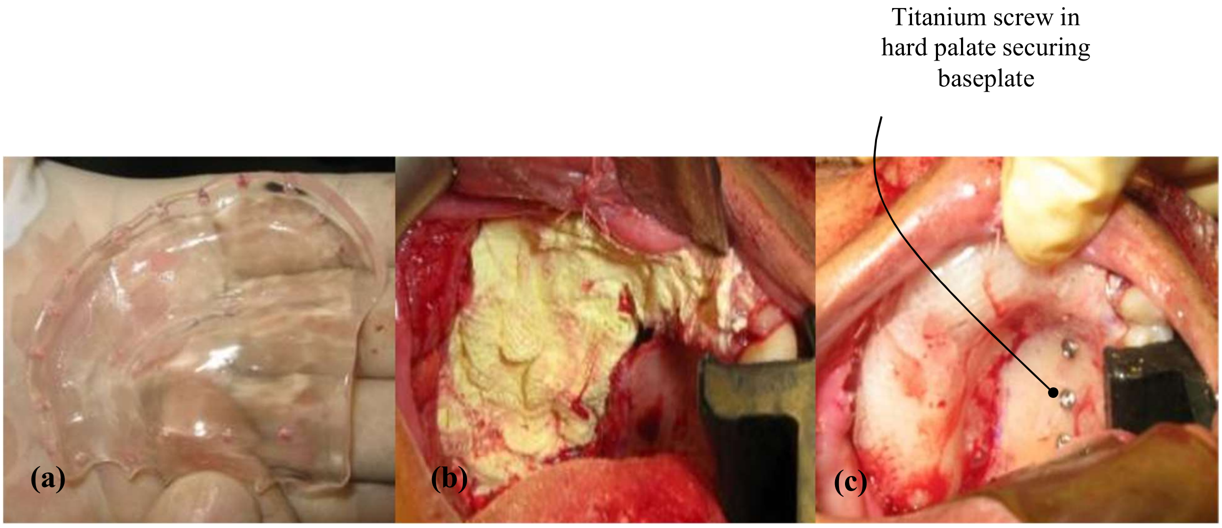

Figure 5.16: (a) The obturator plate. (b) BIPP packing in defect.(c) Titanium screws supporting the obturator plate.

5.3.8.2 Postoperative course

The healing of the operative site proceeded without event. The BIPP and obturator plate were removed after 10 days. Impressions of the surgical defect were taken by a prosthodontist for the fabrication of a formal obturator (Figure 5.17). This obturator was worn for about 12 weeks while the planning of the distraction process was under way.

Figure 5.17: (a) The aesthetically pleasing wound healing and facial support provided by the obturator. (b) The obturator *ex vivo* (consent obtained).

5.4 Case report 3

5.4.1 Clinical background and examination

Patient TK was referred to our maxillofacial clinic by the Military Hospital for the investigation and management of a palatal swelling in the left posterior maxilla.The patient was a 25-year-old woman who complained about a swelling in the left maxilla which had been present for about 2 months. The swelling was uncomfortable to palpation.

Clinical examination revealed a firm reddish lesion in the posterior mucosa with a sessile base and the typical clinical appearance of giant cell granuloma. A CT scan at the time showed erosion of the tuberosity region caused by the tumour. Incision biopsy confirmed central giant cell tumour (Figure 5.18).

Figure 5.18: The sessile-based tumour in the left maxilla.

5.4.2 Treatment plan

The patient consented to undergo a partial maxillectomy followed by CTDO (Brown II a resection).

5.4.3 Surgical ablation

A general anaesthetic was administered on 18 June 2012 at the military hospital, and a partial maxillectomy was performed (Figure 5.19(a)). An osteotomy of the left maxillary alveolus and hard palate was created between tooth #26 and #27 with a 701 burr and osteotomes. The osteotomy was carried through at a low Le Fort I level via a circumvestibular approach. The transverse osteotomy was extended into the hard palate to the 2nd quadrant ensuring the palatal mucosa was spared. The tumour and all teeth were removed *en bloc* and sent for histology (Figure 5.19(b)). A Piccolo drain was placed to obviate haematoma formation. A BIPP pack was put into the left nasal/antral defect to eliminate dead space. The pack was secured to the left nostril via an intranasal antrotomy. Buccal fat pad tissue was also used to facilitate primary closure (Figure 5.19(c)).

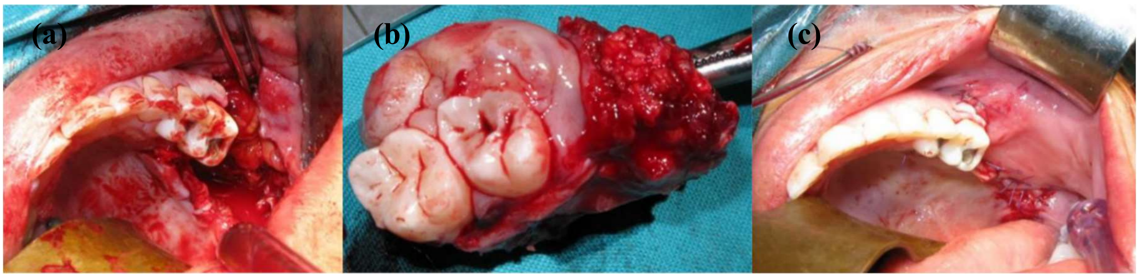

Figure 5.19: (a) The left post-maxillectomy defect and buccal fat pad. (b) The surgical specimen with the tumour, teeth and pterygoid muscle. (c) Primary closure of the surgical defect.

5.4.4 Postoperative course

The patient was discharged from the hospital two days later and could feed easily. The Piccolo drain was removed after 24 hours and the BIPP pack was left *in situ* for 10 days.

5.5 Case report 4

5.5.1 Clinical background and examination

Patient PG was referred to our maxillofacial clinic on 12 November 2002 for a swelling in the left maxilla from teeth #26–#28 (Fig. 5.20). She was unaware that her left eye had been proptotic for the previous 3 months. She was referred by her dental practitioner, who extracted tooth #27, and was surprised to find tumour tissue exuding from the dental socket. Upon clinical examination on the same day, the author referred the patient for a CT scan.

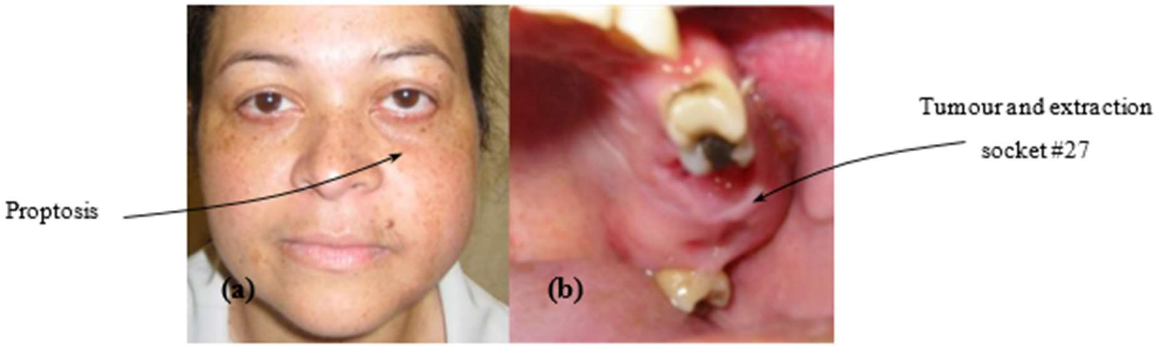

Figure 5.20: (a) Swelling of left cheek and proptotic left eye. (b) Intra-oral presentation of the tumour with buccal-palatal expansion and obliteration of vestibule (consent obtained).

5.5.2 Radiological examination

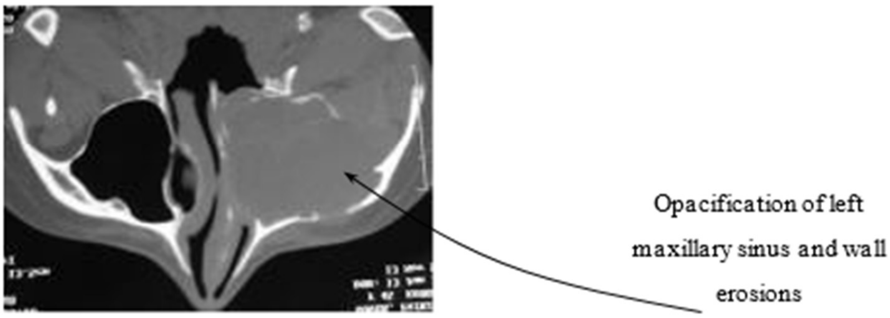

Figure 5.21: CT scan showing extent of opacification of the left maxilla.

The CT scan (Fig. 5.21) showed opacification of the left maxillary sinus indicative of extensive involvement of tumour from #24–#27. There was also an extension of tumour tissue towards the base of the skull involving posterior ethmoidal sinuses and erosion of the left orbital floor. In addition, there was erosion of the left posterior maxilla, the left nasal wall and the anterior wall of the maxillary sinus.

5.5.3 Incisional biopsy

The patient was admitted to a surgical facility where, under general anaesthetic, an incisional biopsy of the tumour was performed. At surgery, the lesion appeared to have a firm multilobulated appearance not unlike that of an ameloblastoma. A histological diagnosis of an ameloblastoma with desmoplastic change was made. The patient was indicated for a high maxillectomy (Brown III b).

5.5.4 Ablative surgery

On 18 November 2002, under general anaesthesia in a private surgical facility, a Weber-Ferguson-Dieffenbach incision was performed to gain access to the tumour, the orbit and the posterior maxilla (Figure 5.22). The tumour was exposed and excised *en bloc*. A detailed description of the methodology of the surgery has already been given in Section 5.3.1. The left infra orbital nerve was included in the tumour and had to be excised.

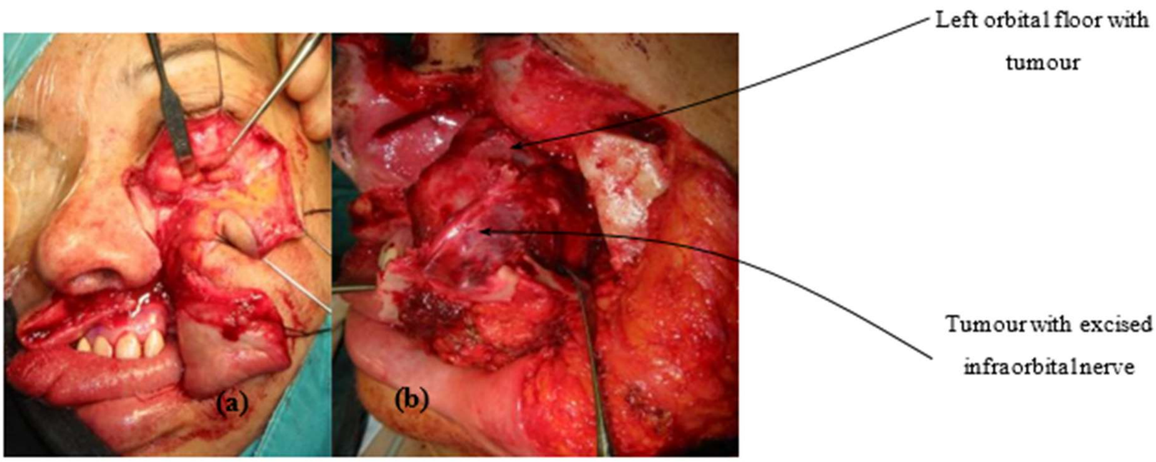

Figure 5.22: (a) The Weber-Ferguson-Dieffenbach approach. (b) Removal of the tumour and infraorbital nerve.

5.5.5 Immediate reconstruction

After all frozen sections were revealed to be negative, immediate reconstruction of the left orbital floor, the left hard palate and the left malar corpus was performed using calvarial bone grafts (Figures 5.23 (a) and (b)).

5.5.6 Postoperative course

Approximately 10 days after surgery, a small fistula developed between the oral cavity and the bone grafted region in the #28 area, resulting in pain and discomfort. This event led to infection of the metal plates and screws and also the free calvarial bone grafts.

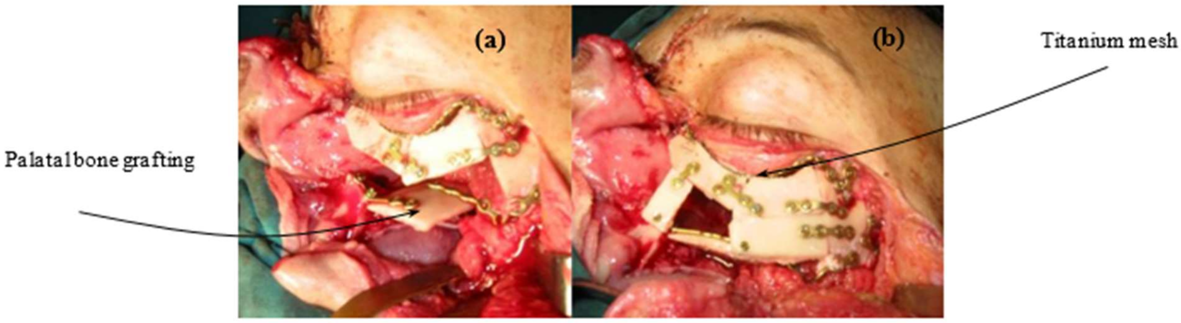

Figure 5.23: (a) The palatal reconstruction with calvarial bone. (b) The malar- maxillary bone grafting with titanium mesh on the floor of the left orbit.

5.5.7 Removal of non-vital bone grafts and plates and screws

On 4 February 2004, via a circumvestibular intra-oral approach, all non-vital palatal grafts were removed, as well as the titanium plates and screws. The anterior wall of the maxilla had resorbed. The orbital floor bone graft was also removed and reconstructed with MEDPOR™ (Stryker 2555 Davie Rd, Davie, Florida, USA) implant material. The removal of these bone grafts resulted in collapse the of the left malar-orbital-palatal complex.

5.5.8 Postoperative course

While primary closure was achieved, there was a lack of bone support in the 2nd quadrant for the teeth as well as the cheekbone.

5.6 Case report 5

5.6.1 Clinical examination

Patient LD was referred to our maxillofacial clinic on 5 February 2014 for investigation of pain and swelling in the right cheek and upper jaw that was not settling on antimicrobial therapy. Extraoral examination was non- contributory. Intraoral examination revealed a loss of soft tissue around teeth #15 and #16 with draining sinuses around teeth #13 and #16 (Fig. 5.24). There was also expansion of the palatal and buccal mucosa. Teeth #17 to #23 responded as non-vital to ethyl chloride.

Figure 5.24: The exposure of bone and loss of keratinised soft tissue around teeth#15 and #16 as well as a draining sinus in the area of tooth #14.

5.6.2 Radiological examination

Radiologically, there were areas of opacity and radiolucency indicative of a fibro-osseous lesion. Incision biopsy revealed chronic sclerosis osteomyelitis. A CT scan revealed the massive extent of the lesion involving the complete maxilla on the right and crossing the middle to the region of tooth #23. Additionally, the superior aspect of the lesion extended to the orbital floor and ethmoid air cells.

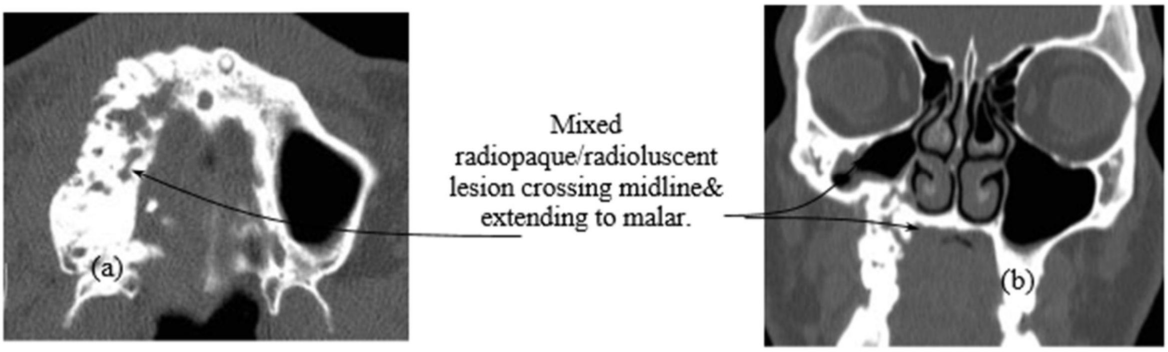

Figure 5.25: (a) The mixed radiopacity/radiolucency in maxilla. (b)The vertical and horizontal extent of the lesion in the maxilla.

5.6.3 Treatment plan

The condition was explained to the patient in detail and a high maxillectomy (Brown III d) with sparing of the palatal mucosa was planned.

5.6.4 Ablative surgery

Under general anaesthesia in a private surgical facility, a submental intubation was performed by the author.

Figure 5.26: Submental intubation.

A Weber-Ferguson-Dieffenbach incision was performed to deglove the lower eyelid, and expose the malar and maxillary skeleton. The incision was made using a #15 blade along the lines indicated in Figure 5.27(a), and blunt dissection was carried inferiorly onto the underlying facial skeleton. The upper lip was sectioned through its entirety as well as the right nostril, and the dissection was carried into the pyriform fossa of the nasal floor and alveolus. The infra-orbital nerve was sectioned and marked for later repair. Further blunt dissection was carried out towards the pterygoid plates, and the complete right maxilla and malar complex was exposed.

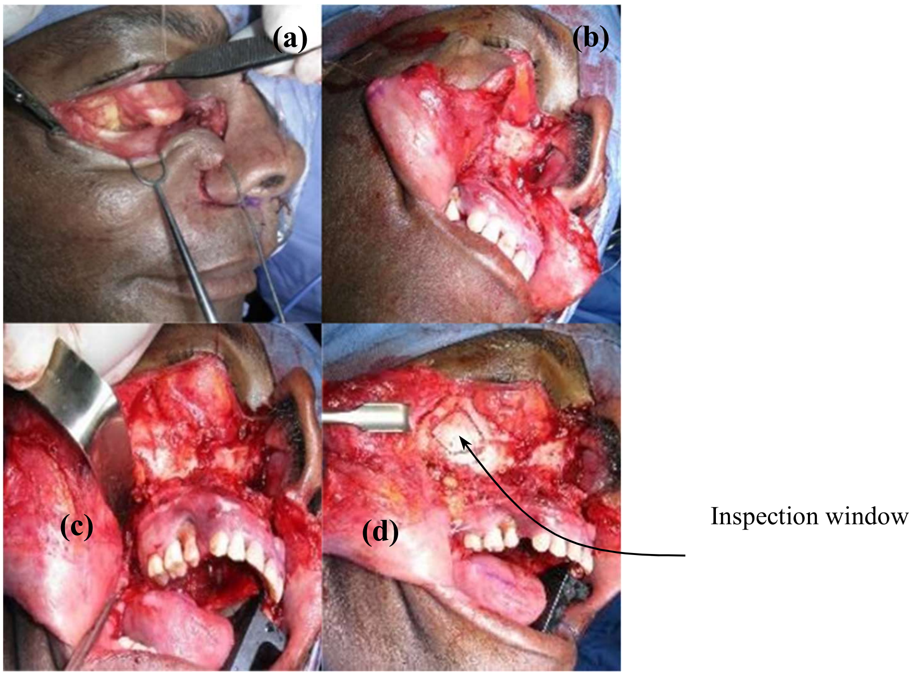

Figure 5.27: (a) Degloving of the lower eyelid. (b) The anterior wall of the maxilla is exposed. (c) The exposed maxilla to the level of the pterygoid plates. (d) The inspection window exposing the sclerotic bone which affected the complete maxilla up to the pterygoid plates and across the midline.

An inspection window was made into the corpus malar to follow the extent of disease. A considerable amount of bone constituting the corpus malar was affected by the disease (Figure 5.27(d)).

The infra-orbital nerve was freed from the floor of the orbit (Figure 5.28(a), sectioned and marked for later repair. The explanted specimen is shown in Figure 5.28(b). Most of the unaffected palatal mucosa was spared for later closure of the defect.

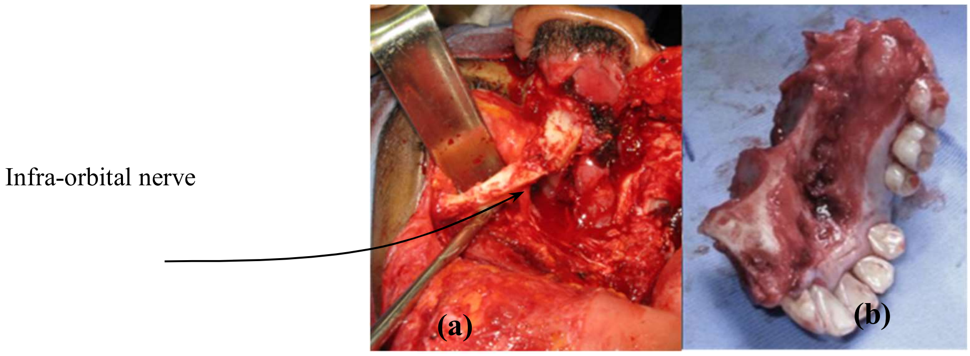

Figure 5.28: (a) The post maxillectomy tissue bed and the infraorbital nerve. (b) The maxillectomy specimen without palatal mucosa.

5.6.5 Immediate temporary reconstruction

In this particular case, the infra-orbital nerve was spared, and a mandibular ramus graft (Figure 5.29(a)) was used to recreate the malar complex and maxillary bone. The mandibular ramus graft was split to increase the usage of the bone (Figure 5.29(b)). A new orbital floor was reconstructed using 0.8 mm thick titanium orbital floor plate (Biomet^{TM}), and the malar corpus as well as the anterior wall of the maxilla was reconstructed. Nasal septal bone was also used for the reconstruction, and Biomet^{TM} 1.5 mm titanium plates were used for fixation of the grafts (Figure 5.29(c)).The right infra-orbital nerve was repaired with three 9-0 Nylon^{TM} epineural sutures (Figure 5.29(d)). The upper lip was repaired and the palatal mucosa easily approximated with the cheek mucosa. A BIPP pack was used for obliterating dead space.

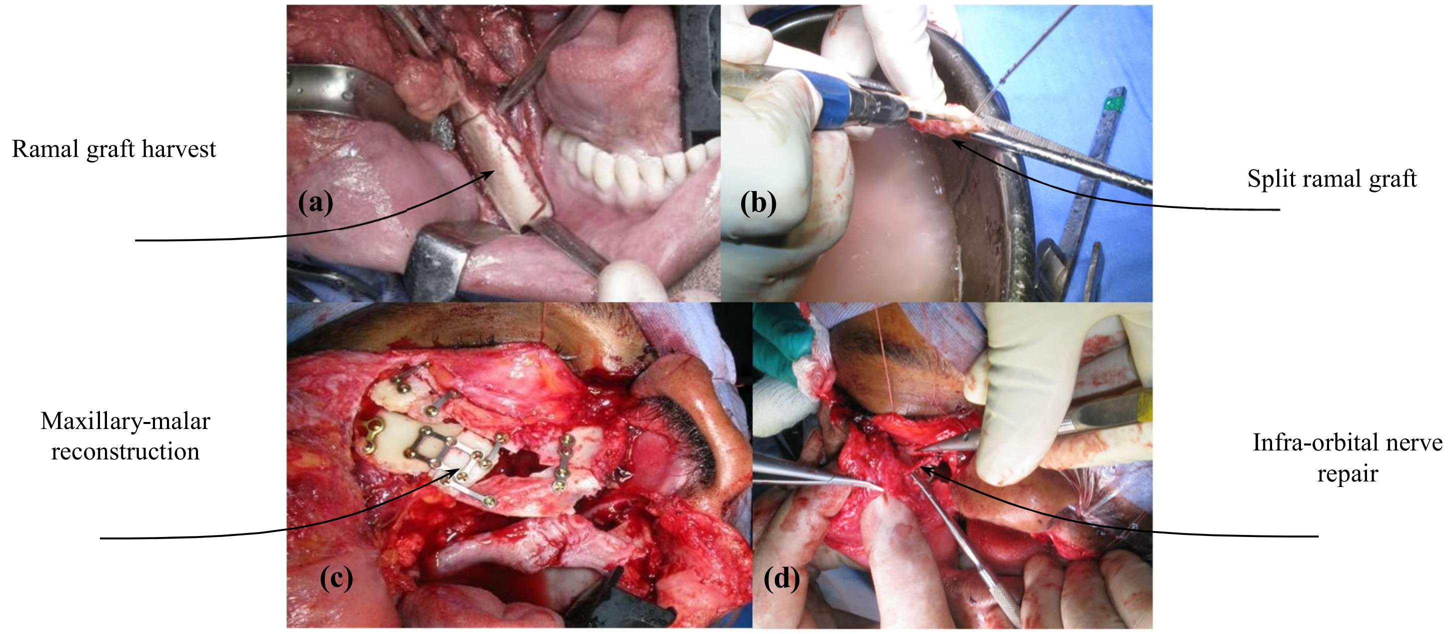

Figure 5.29: (a) A mandibular ramus graft is harvested. (b) The graft is split to create a new malar corpus and maxilla.(c) The malar-maxillary complex with titanium miniplate osteosynthesis. (d) Infraorbital nerve repair.

In this patient, the palatal mucosa could be used to close the surgical defect between the oral and sinonasal cavities, and hence hermetic closure was achieved for the hard palate as well as the upper lip (Figure 5.30(a) and (b)). This facilitated the wearing of a temporary upper denture while the distraction osteogenesis was being planned. The facial skin wound was closed in layers (Figure 5.30(c)), and potential ectropion of the lower eyelid was obviated by the use of a Frost suspension suture (Figure 5.30(d)). The Frost suture was removed after 10 days.

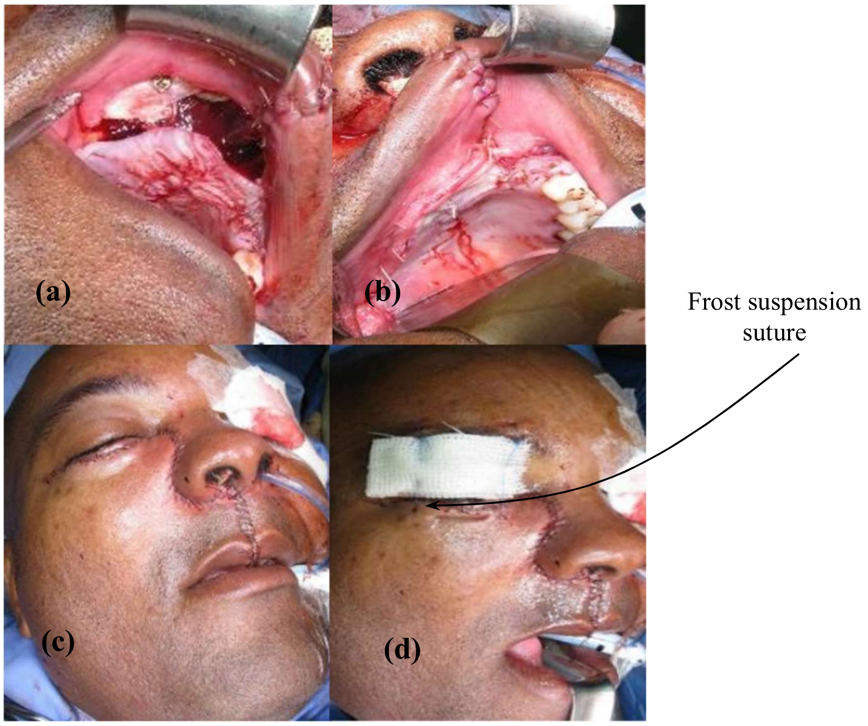

Figure 5.30: (a) The approximation of the palatal to the buccal mucosa.(b) Optimal closure of the sinonasal-oral defect as well as the upper lip.(c) External appearance of the skin closure.(d) Frost suspension suture attached to the lower eyelid to prevent ectropion contraction.

5.6.6 Postoperative course

While healing was mostly uneventful, a small oro-nasal fistula appeared about two weeks later. For patient comfort and to prevent unnecessary infection of the bone grafts, it was decided to close the fistula. This was accomplished using a distally based tongue flap (Figure 5.31(a) and (b)) carried out on 19 February 2014. The tongue flap healed well and provided the hermetic seal needed for patient comfort, good oral hygiene and adequate masticatory function (Figure 5.31(d)).

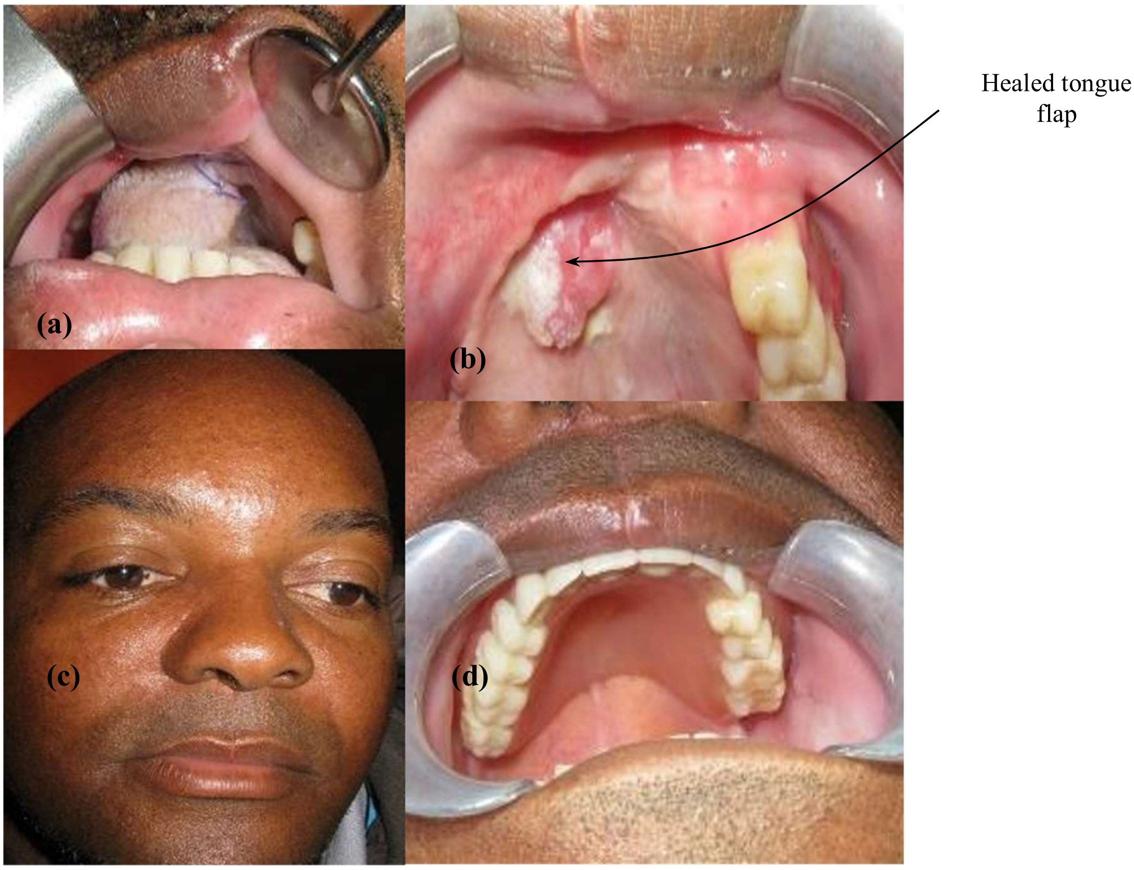

Figure 5.31: (a) The attached tongue flap pedicle.(b) Successful closure with the healed tongue flap after release and inset. (c) The pleasing extra-oral scar on the face of the patient. (d) Comfortable fit of the upper partial denture, providing an aesthetic appearance and good function (consent obtained).

5.7 Case report 6

Patient KB, age 37 years, was referred to our maxillofacial clinic by his general practitioner. He complained of swelling of the right maxilla with associated pain and odour.

5.7.1 Clinical examination

Extraoral examination was non-contributory. The intraoral examination revealed a loss of soft tissue around teeth #16 and #17 with exposure of alveolar bone (Fig. 5.32). The alveolar bone appeared to be non-vital. There was also expansion of the hard palate and mobility of teeth #16 and #17. Teeth #14, #15, #16 and #17 were non-vital to ethyl chloride testing.

Figure 5.32: Exposure of alveolar bone (necrotic) and loss of keratinised soft tissue around teeth #16 and #17.

5.7.2 Radiological examination

CT scan of the maxilla revealed a mixed radiopaque/radiolucent lesion indicative of fibro-osseous pathology and hence consistent with chronic osteomyelitis (Fig. 5.33). A provisional diagnosis of diffuse sclerosing osteomyelitis was made. The lesion extended from the right pterygoid plates in an anterior direction to tooth #14.

Figure 5.33: CT scan with radiopaque lesion in the right posterior maxilla.

5.7.3 Treatment plan

The condition was explained to the patient in detail and a high maxillectomy (Brown II a) with sparing of the palatal mucosa was planned.

5.7.4 Ablative surgery

Under general anaesthesia in a private surgical facility, an intraoral approach was taken for the performance of a partial maxillectomy. Tooth #14 was extracted. A mucoperiosteal flap was raised from #13 to #18 region. A vertical osteotomy was made with a reciprocating saw through the socket of #14 and a horizontal extension at the low Le Fort I level extending posteriorly towards the pterygoid plates (Figure 5.34(a)). The palatal mucosa was reflected and another osteotomy was carried through horizontally at the para-median region towards the posterior aspect of the hard palate (Figure 5.34(b)). The maxilla was mobilized and dismembered from the pterygoid plates (Figure 5.34 (c)). The palatal mucosa was spared. The maxillectomy was now completed. Primary closure could be achieved by approximating and repairing the buccal and palatal mucosa.

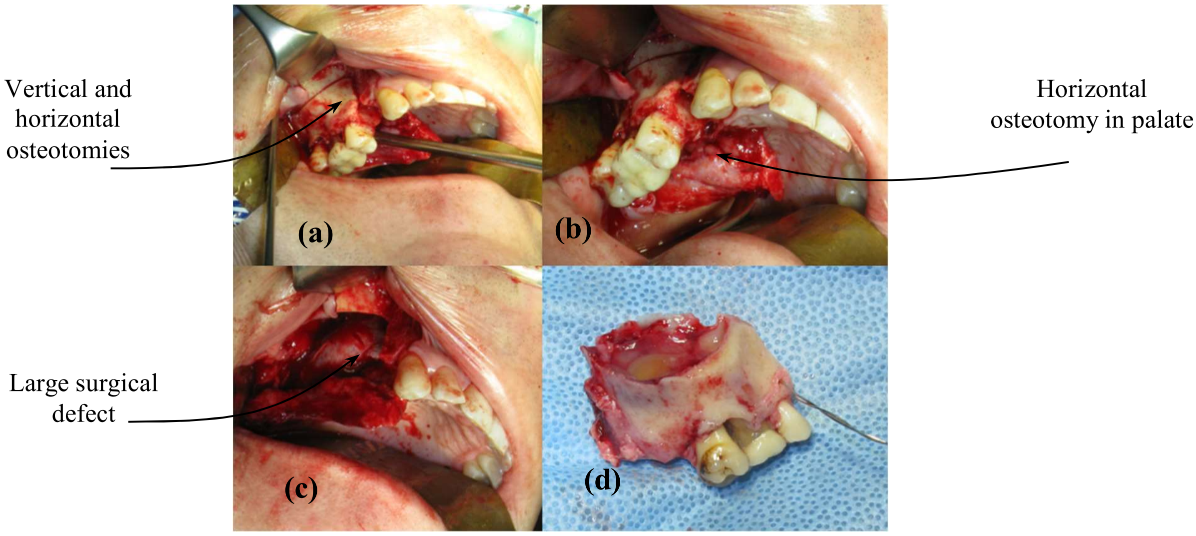

Figure 5.34: (a) Vertical and horizontal osteotomies in the right maxilla. (b) Horizontal osteotomy of the hard palate.(c) Post maxillectomy surgical defect. (d) Explanted specimen.

5.7.5 Immediate temporary reconstruction

The defect was packed with BIPP gauze secured in the right nostril via an intra-nasal antrostomy (Figure 5.35(a)). Primary closure was effected with Vicryl 3.0 ™ sutures (Figure 5.35(b)).

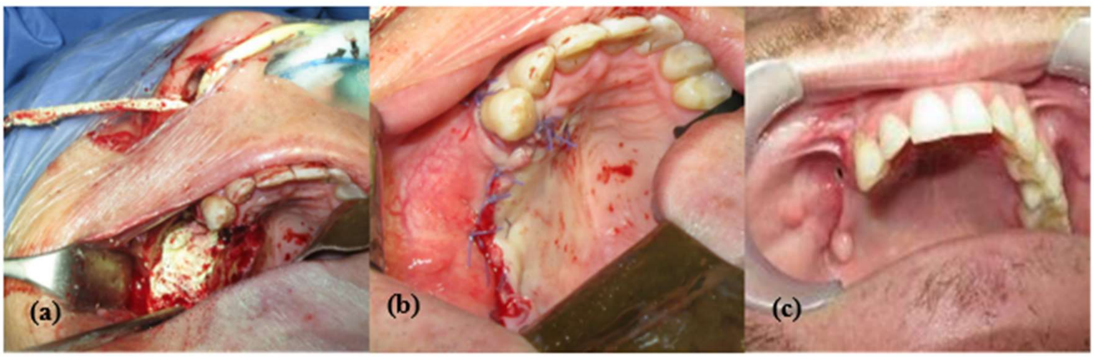

Figure 5.35: (a) BIPP pack in antral and nasal cavities with intranasal antrostomy. (b) The primary wound closure of the hard palate and cheek. (c) Well-healed wound with small oro-antal fistula.

5.7.6 Postoperative course

The patient healed uneventfully and wore an obturator/denture for a short period to seal off a small oro-nasal fistula (Figure 5.35(c)). The fistula was well tolerated in the longer term by the patient who did not see the need for a temporary denture.

CHAPTER 6. DEVELOPMENT AND APPLICATION OF THE FIRST PROTOTYPE DISTRACTOR (V1)

6.1 Introduction

Described below is the first recorded attempt at closing a Brown II b surgical defect using curvilinear transport distraction osteogenesis. The employment of transport distraction concepts and principles have thus far been limited to the mandible and therefore there is no previous literature or experience about applying this technology to the maxilla. The anatomy of the maxilla is vastly different from that of the mandible, and so is the bone tissue biotype and the physiological functions related thereto. The animal model reported by Cheung in 2003 provided the inspiration to embark on this project in humans.[100]

Figure 6.1: Post-surgical ablation CT scan illustrating the large defect in the first quadrant.

6.2 Planning for the version 1 (V1) distractor

6.2.1 3-D model print

A postoperative CT scan was taken and a 3-D stereolithographic model was printed from the scan to show the detail of the defect. By means of mirror imaging, the defect could be 'filled in' to facilitate contouring of the trajectory rail of the distraction appliance (Figure 6.2). As there has been no attempt in the past to distract a transport disc in the anterior-to-posterior direction in the maxilla, and there are no bony structures on which to anchor a distraction device, no device has been available for such a procedure, save for the linear distractor used in animals by Cheung in 2003.[100]

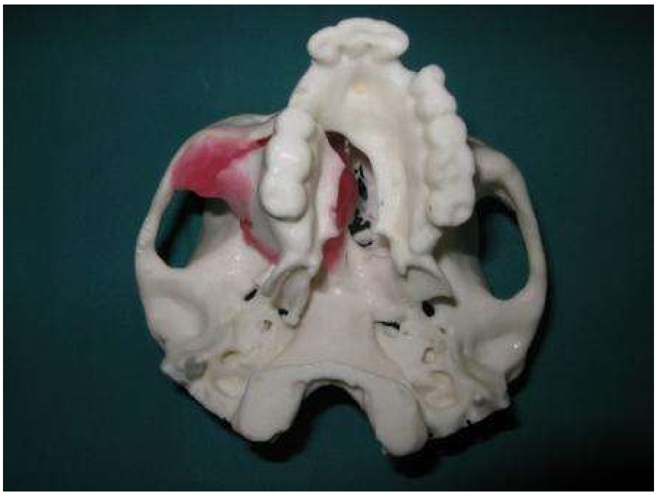

Figure 6.2: The mirror imaged section taken from a duplicate model and secured with pink wax onto the presurgical 3-D stereolithographic model.

6.3 Engineering design concepts of version 1

In collaboration with Dr George Vicatos (Ph.D, Pr.Eng.) and Mr James Boonzaier (MSc.), the following design of the first prototype distraction device was conceived and fabricated.

6.3.1 Design and development

The design and development process aimed to produce a fully functional device, encompassing the various mechanical and ergonomic requirements as defined in the product requirement specification in Section 4.8. This was achieved through an iterative process of design, manufacture, testing and refinement.

The development and refinement process comprised the design and fabrication of three successive prototypes:

1. Version 1 (V1): self-cutting traction mechanism (Section 6.4)
2. Version 2 (V2): metallic worm-rack traction mechanism (Section 7.2)
3. Version 3 (V3): metallic worm-rack traction mechanism with baseplate (Section 8).

Each of these devices was implemented clinically to treat large defects of the maxilla. During each case, observation of the surgical procedure and the device in practice provided crucial insight, by the engineers, into the needs of the patient and surgeon, thus directing iterative refinement of the device in both form and function. Coupled with ongoing research into the details of maxillofacial CTDO, these clinical observations provided a robust understanding of the mechanical and ergonomic requirements of the CTDO procedure.

The following section sets out the development of the distraction device from a basic concept into the fully-functional V3 device, via the intermediate V1 and V2 prototypes. The key design decisions, successes and failures are documented, as well as the observations and outcomes of clinical treatment.

6.3.2 Basic format of the device

Based upon various recommendations in the literature (section 4.2.), a survey of existing maxillofacial TDO devices, and consultation with medical and engineering specialists, it was established that the device should include the following basic elements:

1. a transport disc carriage (or locomotive*)* that supports and guides the transport disc
2. a traction mechanism that actuates distraction of the transport disc carriage
3. a trajectory rail that defines the path of the transport disc carriage.

6.3.3 Traction mechanism: Solution concepts

Guided by the principles described in Section 4.6, various solution concepts were generated for the basic actuation (or traction) mechanism. The section below presents a brief summary of the three most promising solution concepts considered.

6.3.3.1 Simple worm-rack mechanism

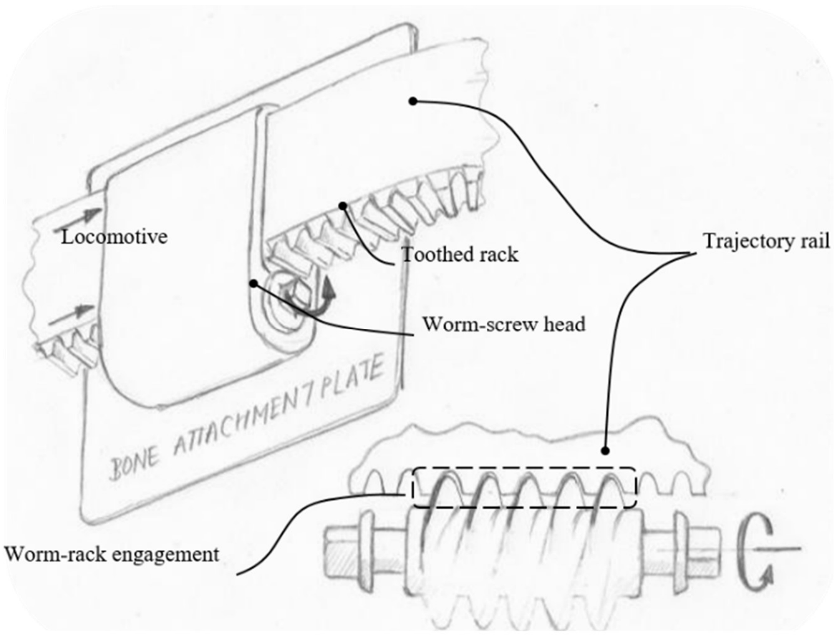

Figure 6.3: Sketch of a worm-rack solution concept, with detail of the worm-rack engagement (hand drawing by Mr James Boonzaier).

The worm-rack concept, illustrated in Figure 6.3, involves a worm-screw that engages with a toothed rack on the narrow edge of the trajectory rail. The worm-screw is housed within the locomotive. By rotating the worm-screw, the locomotive is propelled linearly along the trajectory rail. The trajectory rail can be bent and trimmed to form the desired distraction vector according to the geometry of the individual case. Aside from the rack teeth, the trajectory rail has a continuous rectangular cross-section along its length.

It was foreseen that ending of the trajectory rail would distort the rack teeth, causing the tooth spacing to widen on the outside of bends and narrow on the inside. In order to tolerate this distortion, the profiles of the engaged worm and rack would require a suitable amount of intentional play to be incorporated.

6.3.3.2 Self-cutting worm and plastic track

This mechanism utilises a sharp-toothed worm-screw that cuts notches into a closely coupled plastic track, thereby progressively forming a corresponding ‘rack’ in the previously virgin plastic (Figure 6.4). When rotated, the worm ‘crawls’ along its track in the manner of a hose clamp. The plastic track is bonded to a metallic trajectory rail, which provides the necessary rigidity to support the locomotive. The trajectory rail and plastic track can be bent and trimmed to form the desired distraction vector, according to the requirements of the individual case.

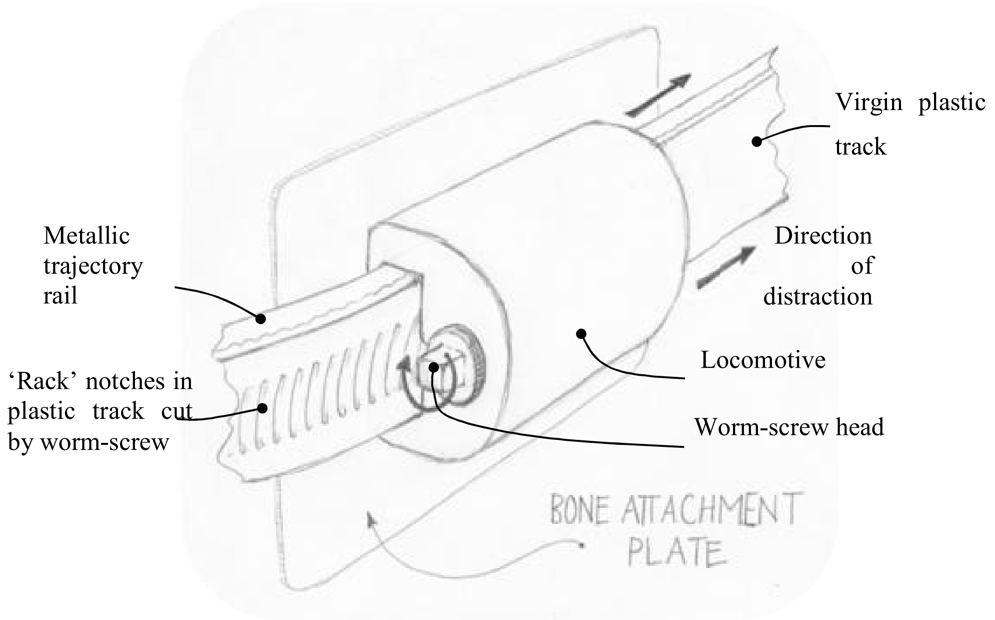

Figure 6.4. Sketch of self-cutting worm solution concept (hand-drawing by Mr James Boonzaier).

In principle, the capability of the self-cutting concept to progressively form a unique corresponding rack in the plastic track accommodates potential irregularities in the trajectory rail and elegantly overcomes the trajectory rail distortion issue described in subsection 6.3.3.1

6.3.3.3 Dual rail and straddled worm

This concept involves a pair of parallel metallic trajectory rails with a worm-screw housed between the two, as illustrated in Figure 6.5. One of the trajectory rails incorporates a toothed rack for engagement with the worm-screw, and the second rail provides additional stability and guidance. A variation of this concept utilises the plastic self-cutting mechanism described in subsection 6.3.3.1.

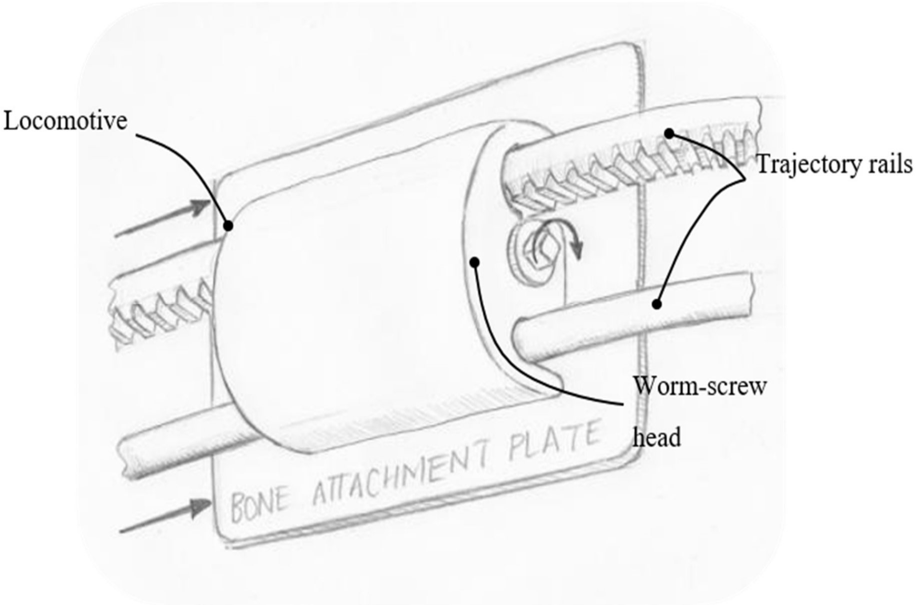

Figure 6.5: Sketch of dual-rail solution concept (hand drawing by Mr James Boonzaier).

The benefit of this arrangement over the single trajectory rail is that the spaced trajectory rails provide a wider footprint for more stable constraint of the locomotive. On the other hand, this mechanism poses several significant problems: it requires accurate matching of the two trajectory rails, incurs the additional cost of more components and a more complex design, and the second rail implies a bulkier device than the two alternative concepts.

6.3.3.4 Chosen concept: Self-cutting worm and plastic track

The 'self-cutting' concept originated in an undergraduate proof-of-concept study,[5] where a basic prototype was made, and elementary strength tests yielded positive results. Having thus established the design's feasibility, it was decided that the versatility of the self-cutting concept warranted further investigation. The following text demonstrates the evolution of the first prototype device, which employed the self-cutting concept.

[5]Available from Mr James Boonzaier (MSc.) on request: 'Device for maxillary transport distraction osteogenesis'.

6.4 Version 1 prototype: Self-cutting concept

The V1 prototype focused on developing the self-cutting traction mechanism (subsection 6.3.3.2) into a prototype device that would provide the required distraction force, adequate control and navigate the tight curvature of the maxillary anatomy. At this stage, ergonomic issues were not explicitly addressed as it was felt that these might detract from the primary focus on the traction mechanism.

6.4.1 V1: Prototype design and development

During the first phase of development, the design of the V1 distractor evolved considerably, as illustrated by the initial and final designs in Figures 6.6 and 6.7, respectively. In all its forms, the V1 prototype consisted of the following core elements:

1. a metallic trajectory rail – subsection 6.4.5
2. a plastic track that attaches to the trajectory rail – subsection 6.4.1.1
3. a locomotive, which secures and directs the bone transport disc along the trajectory rail and houses the worm-screw traction/cutting mechanism – subsection 6.4.2
4. two buttress plates, which support the posterior end of the trajectory rail – subsection 6.4.5.

The following sections present the refinement of these elements during the first phase of the development.

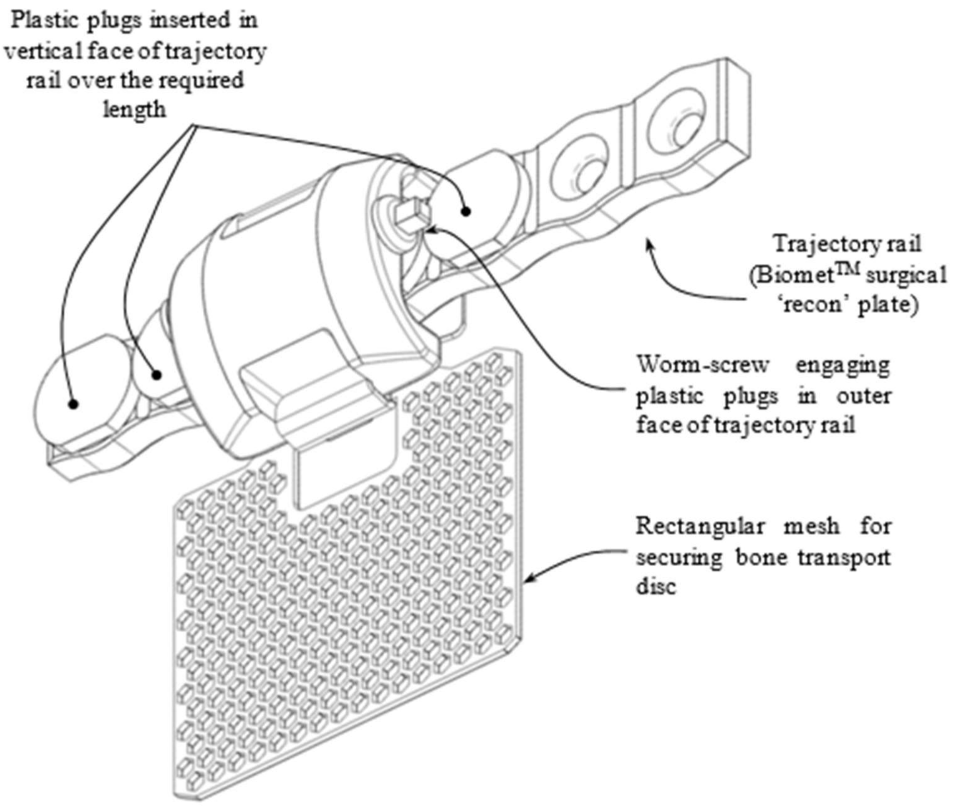

Figure 6.6: First conceptual version of the V1 distractor as developed in Mr James Boonzaier`s proof-of-concept project.

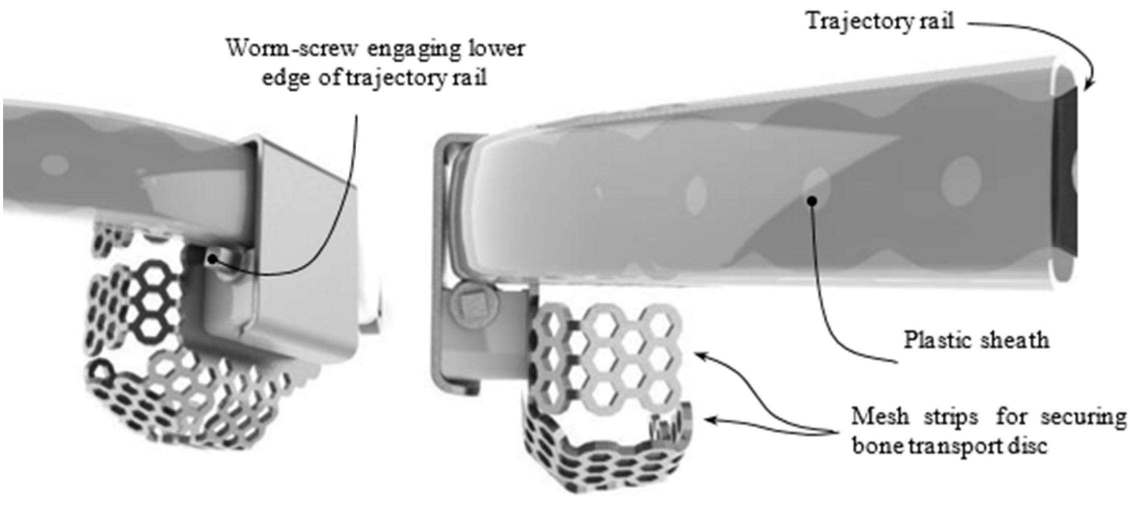

Figure 6.7: Final version of the V1 distractor.

6.4.1.1 Plastic track: Low-density polyethylene

The plastic self-cutting concept employed a plastic track, in the form of a low-density polyethylene (LDPE) sheath, which was reinforced with a titanium trajectory rail. The LDPE track was problematic, as the material is susceptible to mechanical and thermal effects. The CTDO treatment protocol exposes the device to both of these in the form of:

- high-temperature sterilisation by autoclave
- forceful customisation of the device by bending and cutting.

It was therefore made a requirement that any plastic components should be separate items, but attachable after customisation and sterilisation of the device. To this end, two distinct formats of plastic track were considered, both of which can be attached to the trajectory rail intra-operatively:

1. numerous plastic plugs embedded in a metal rail (Figure 6.8)
2. a single, continuous plastic tube on a metal rail (Figure 6.9).

Figure 6.8 shows a photograph of a test model that was used to prove the viability of the self-cutting concept. This test model was used to establish the required depth of cut to produce the required traction force. The trajectory rail was provided by an existing mandibular reconstruction plate supplied by Biomet^{TM}.

High- and low-density polyethylene (HDPE and LDPE, respectively) specimens were tested to establish whether the mechanism could produce the required distraction force. At this stage, the only known study of maxillofacial distraction force specified that a traction force of 35 N was adequate in mandibular TDDO.[263] Using this figure as a benchmark, it was found that both HDPE and LDPE were suitable: HDPE provided a traction force of 100 N, and LDPE provided a traction force of 65 N before failure.

Although HDPE provided a significantly higher traction force than the LDPE, it had two shortcomings that made it impractical for the desired application:

- HDPE was found to be too rigid to accommodate the required curvilinear trajectories.

- HDPE offered particularly high resistance to rotation of the worm-screw, which raised concerns about the forces on the device and the bone transport disc during activation. LDPE was therefore specified.

The initial design of the V1 distractor engaged the worm-screw on the vertical face of the trajectory rail (Figure 6.6). In this orientation, the worm-screw was located outboard of the trajectory rail, causing the device to intrude significantly on the adjacent cheek. In the interests of patient comfort, the design was revised so that the worm-screw engaged the trajectory rail on the inferior edge of the rail (Figure 6.7) rather than its outer vertical face. This modification places the bulk of the device below the trajectory rail, in a less intrusive area.

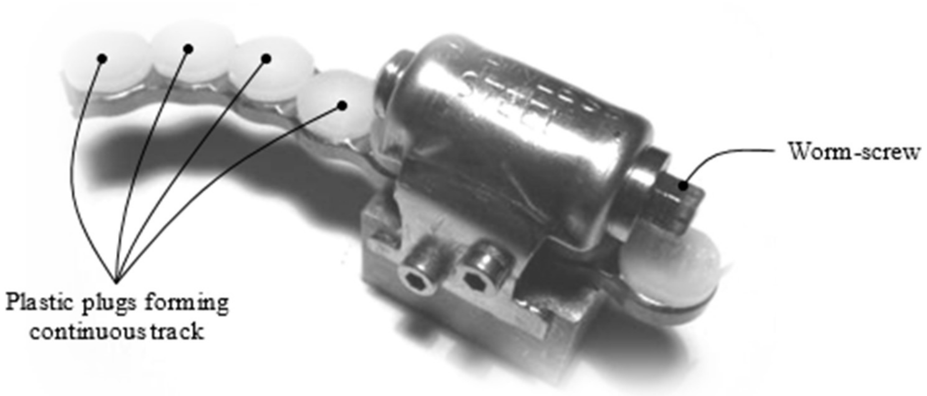

Figure 6.8 Apparatus for quantifying traction force of plastic self-cutting mechanism.

To accommodate this modification, the format of the plastic track was revised, abandoning the numerous plugs in favour of a single sheath (Figure 6.9). The sheath, of LDPE tubing, can be slipped over the trajectory rail after it has been finally customised. Experimentation showed that, in this format, both the LDPE tube and trajectory rail could accommodate the necessary bend radius of 25 mm. The use of a single tubular track rather than numerous plastic plugs eliminated from the design the need for these small components and reduced the intricacy of the surgical installation procedure.

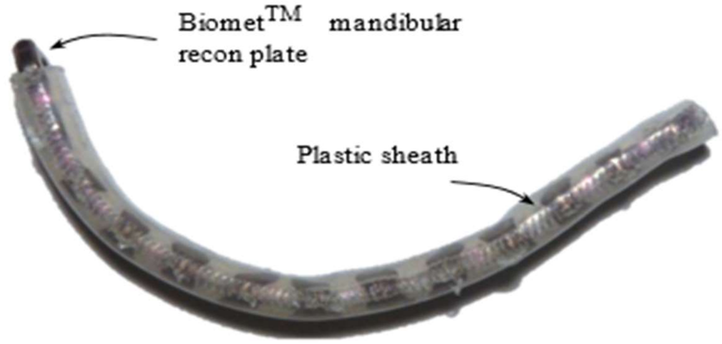

Figure 6.9: Biomet^{TM} mandibular recon plate with LDPE 'sheath'.

6.4.2 Locomotive – housing

The locomotive is the mobile element of the device that supports and guides the bone transport disc along the trajectory rail. The locomotive houses and constrains the worm-screw against the trajectory rail, ensuring that the thread of the worm-screw traction/cutting mechanism is reliably engaged with the plastic track.

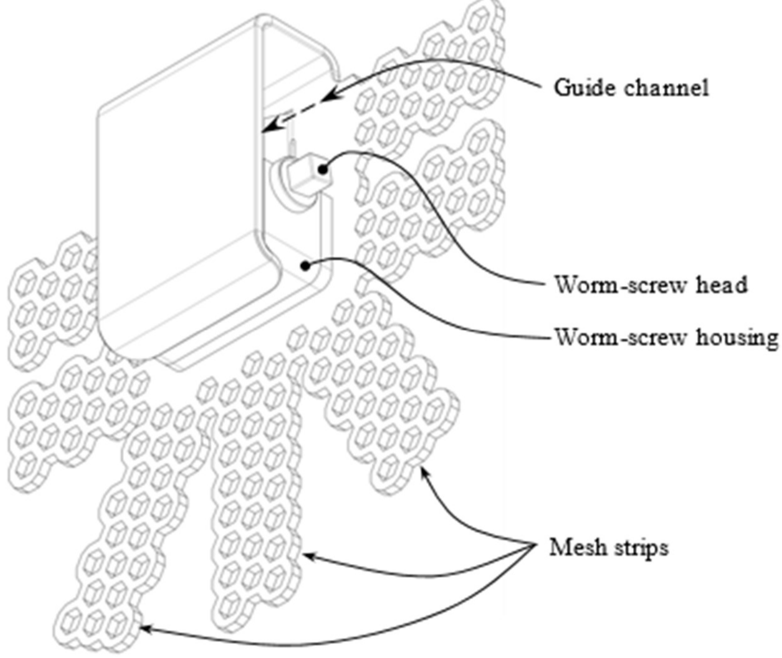

Figure 6.10: Labelled components of the V1 locomotive assembly**.**

The bone transport disc is secured to the locomotive by forming the integrated mesh strips (Figure 6.10) into a cradle, as shown in Figure 6.7. This mesh cradle thus envelops the bone fragment so that it can be firmly secured by screws from various angles.The locomotive is stabilised by close contact with the trajectory rail that feeds through the guide channel (Figure 6.10). According to the design specifications, the device must accommodate a radius of curvature of 25 mm. For the locomotive to navigate along a trajectory rail with such tight curvature, the constraints between the locomotive guide channel and trajectory rail were relaxed. The sketches in Figure 6.11 illustrate an early study of locomotive stability using a protrusion on the inner surface (labelled A) which accommodates tight curvature, while maintaining at least two points of contact between the locomotive and the trajectory rail.

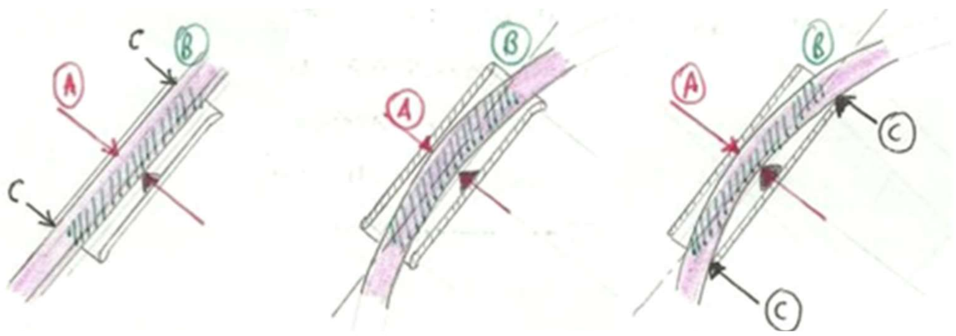

Figure 6.11: An early investigation of locomotive constraint and stability (hand-drawings by Mr James Boonzaier).

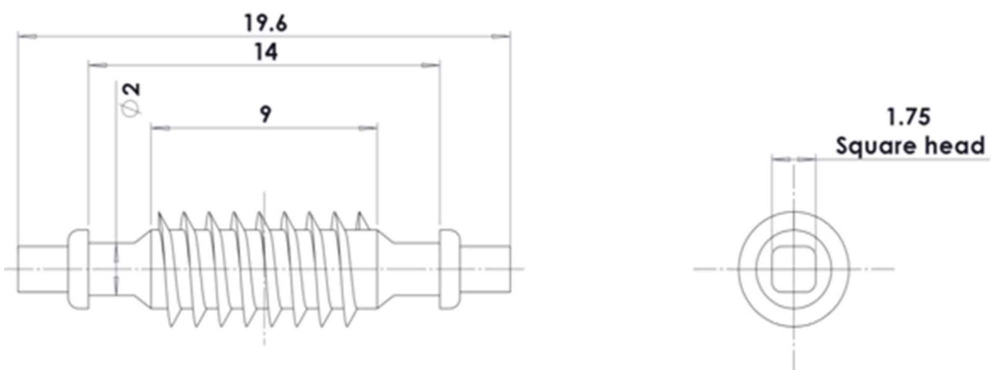

Figure 6.12: The V1 worm activation head design and overall dimensions in mm (hand drawing by Mr James Boonzaier).

6.4.3 Worm activation head: Compatibility with existing tools

In an effort to utilise existing tools and to minimise cost, the worm activation head was designed to be compatible with an existing Biomet™ distraction driver, which prescribed a 1.75 mm square head (Figure 6.12). These distraction drivers were developed specially for activation of existing non-maxillary distraction devices, e.g. mandibular or midface distractors, and are commonplace in surgery. The screwdriver in Figure 6.13 below produces a 'click' every 180° to promote accurate control.

Figure 6.13 Biomet™ 'click' distraction screwdriver

6.4.4 V1: Device anchorage and stabilisation

The device was supported and anchored using a scaffold of metallic plates and bone screws (Figure 6.14), all of which were commercially available. These components had three distinct functions:

1. The trajectory rail supports and guides the locomotive along the desired path.
2. Buttress plates support and stabilise the trajectory rail.
3. Various sizes of bone anchorage screws anchor the device to the parent bone.

6.4.5 Trajectory rail – Biomet™ mandibular plate

At this early stage, not enough was known about the rigidity, anchorage and patient comfort requirements of the trajectory rail to underpin the development of a unique proprietary rail. Consequently, the V1 device utilised the existing Biomet™ titanium mandibular reconstruction plate. A compelling benefit of Biomet™ reconstruction plates is their 'locking head' feature, which binds the head of the bone anchorage screw to the plate, thereby locking its orientation. Locking head screws incorporate a tapered multi-start thread at the neck below the head of the screw. This threaded head engages with a corresponding internal thread at the entrance to the holes in the plate. By locking the screw to the plate, the screw is prohibited from shifting its orientation or position, so improving the overall integrity of the bone–screw anchorage.

6.4.6 Stability of the trajectory rail – zygomatic and alveolar buttress plates

Figure 6.14: Various Biomet^{TM}plates and anchorage screws used in the V1 distractor.

As mentioned in subsection 4.8.1, treatment of unilateral maxillary tumours usually involves total removal of the posterior segment of the maxilla, leaving a void in the bony anatomy at the rear of the mouth. In such cases, there is no intact bone onto which anchorage of the posterior free end of the rail can be effected. To provide stability and prevent a cantilever effect, two 1.5 mm Biomet^{TM} plates were introduced to buttress the posterior end of the rail against the adjacent zygoma and the opposite alveolar ridge (Figure 6.15). These plates are referred to as the buttress plates. The zygomatic buttress resists vertical, and the alveolar buttress resists

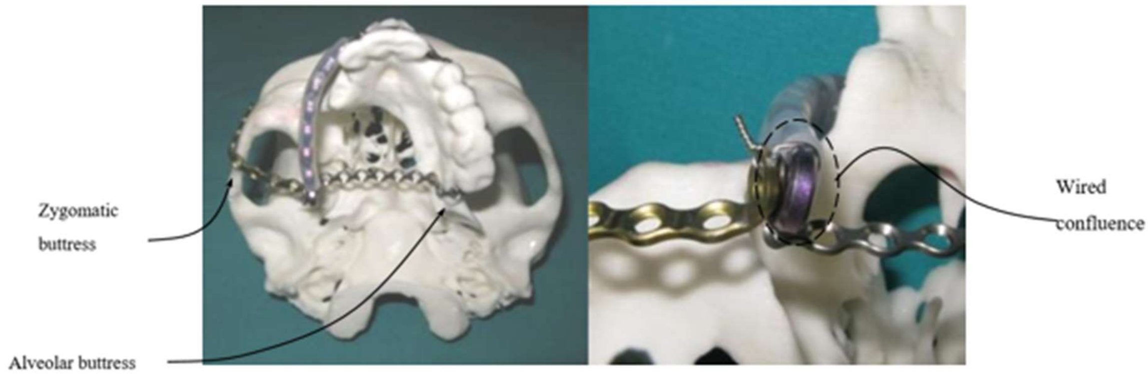

Figure 6.15: Trajectory rail and buttress plates installed on a stereo-lithographic patient model with a detailed view of the wired confluence.

horizontal, deflection of the trajectory rail at its posterior end, providing three-dimensional stability.

For the V1 prototype, the trajectory rail and buttress plates were linked by a simple wired joint using 0.6 mm titanium wire (Figure 6.15), fed through the holes in the buttress plates and rail, and tightened by twisting. Titanium wire is commonly used in maxillofacial surgery, and the wired confluence technique was endorsed by the author for its simplicity and the relative ease-of-use within the confines of the posterior oral cavity.

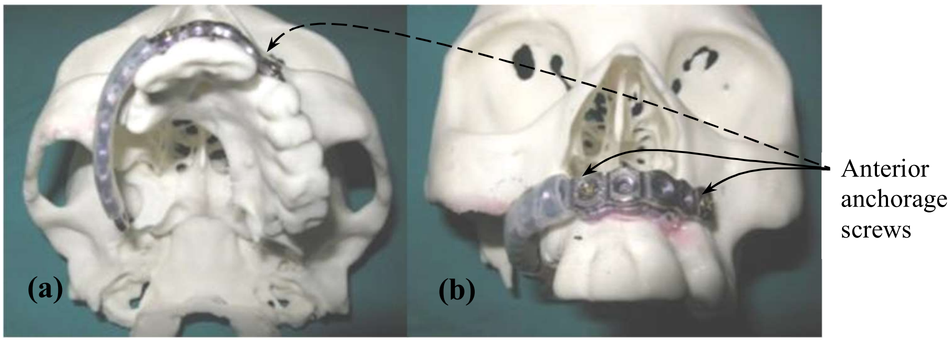

Figure 6.16: (a) Inferior and (b) frontal view of customised Biomet™ recon plate installed on a cranial model.

Figure 6.16 (a) and (b) above show the trajectory rail anchored to the maxilla on a cranial model of a maxillectomy patient. The device is anchored at its anterior end. It was found postoperatively that these titanium plates were well tolerated by patients and did not interfere with mastication or speech.

6.4.7 V1: Laboratory testing

Despite the encouraging results of preliminary testing (see subsection 6.3.3.4), there were concerns about the strength of the LDPE track. Laboratory testing of the manufactured V1 prototype attempted to evaluate the effects of loading on the plastic track by simulating the basic aspects of the clinical distraction environment, namely:

1. distraction along the worst-case curvilinear trajectory with the minimum expected bend radius of 25 mm
2. distraction against a load of 60 N, representing the maximum callus stretching force.

6.4.7.1 Test distraction on worst-case trajectory

The V1 device performed satisfactorily on the worst-case trajectory, encountering no significant mechanical interference. The distracted length was 40 mm with a radius of curvature of 25 mm. As expected, the sharp-threaded worm produced distinct ridges in the edge of the plastic track as it progressed. In general, these ridges were left intact, though some debris was observed: 0.2 mm to 0.5 mm thick and up to 3 mm long. At some points, the worm cut through the LDPE track material completely. The stability of the locomotive on the trajectory rail was unsatisfactory. Play between the two components permitted the locomotive to rotate around the axis of the rail by ±10°. To address this stability concern, the constraint of the locomotive on the rail was tightened by removing the spacer shown in Figure 6.17. The rotational play was thus reduced to less than ±5°. Patient comfort was improved by countersinking the assembly screws and removing any protrusions or sharp edges. Figure 6.17 presents the prototype before and after refinement.

6.4.7.2 Traction force tests on a linear trajectory

A linear distraction of 10 mm was carried out under a load of 60 N, activated in increments of 2 mm (equivalent to 2 turns), allowing an hour between each activation. To achieve the desired 10 mm distraction, the device was then activated 5 times. The 60 N load represented a safety factor of 1.7 above what was then considered to be the maximum expected distraction load of 36 N.

For the sake of brevity and conciseness, full details of these tests are not presented here, but similar tests are described in detail in subsection 8.4.1, which describes testing of the most recent device version.It was expected that 5 activations of 2 mm each would displace the locomotive by a total of 10 mm. However the actual displacement of the locomotive proved to be 9.1 mm, i.e. 9% less than the intended distraction extent. This suggested that the LDPE track deformed under the load or that there was a degree of slippage of the traction mechanism. The clinical implication of this discrepancy is that, in the worst case, the daily distraction rate would be 9% less than that intended, e.g. an intended distraction rate of 1.5 mm, would actually generate 1.37 mm per day. This was deemed acceptable by the author. Nevertheless, concerns were noted about the accuracy of control offered by the self-cutting concept.

Having satisfied the engineering aspects of laboratory testing, the V1 device proceeded to clinical implementation.

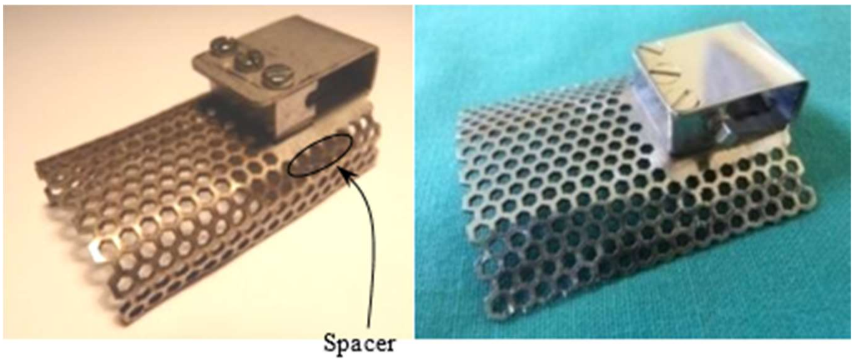

Figure 6.17: V1 locomotive before and after refinement.

6.4.8 V1: Clinical evaluation

The first clinical case involved the repair of a 45 mm defect on the right side of the maxilla (Figure 6.19), which was the result of the surgical excision of a low grade adenocarcinoma. This surgery led to a defect that included a section of the hard palate and nasal floor, and the posterior segment of the alveolus but left the zygomatic complex intact (Brown II b).

A craniofacial stereolithographic model was produced which facilitated pre-operative customisation of the device and planning of the surgical installation procedure (Figures 6.15 – 6.18). This model was produced by the University of Cape Town based on CT images of the patient.

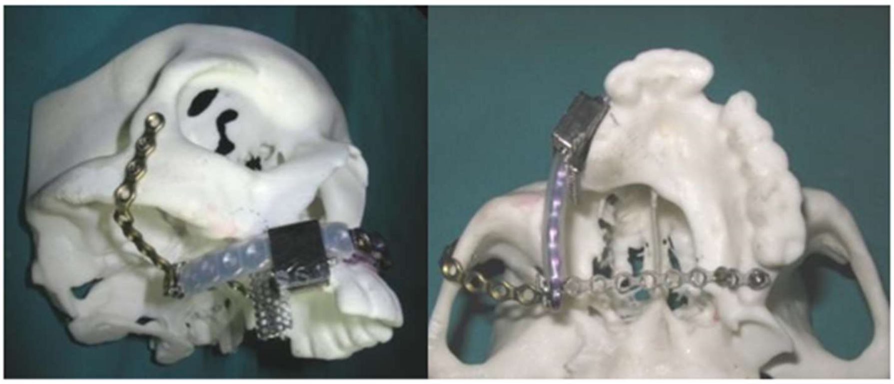

Figure 6.18: Oblique and inferior view of V1 distractor installed on a cranial model.

6.4.9 Preparation of bone stock for transport disc

Two teeth (#13 and #14) were extracted under local anaesthesia to create bone bulk for the transport disc. This was allowed to consolidate for 3 months (Figure 6.19).

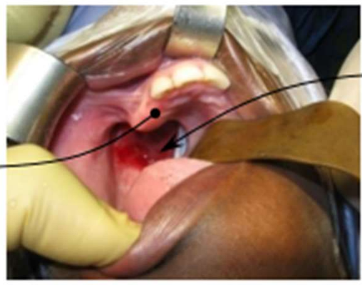

Figure 6.19: The defect before treatment.

6.4.10 Surgical installation of distraction apparatus

Figure 6.19 displays the 45 mm surgical defect (Brown II b). A circumvestibular incision was made to expose the roots of the existing teeth in the anterior maxilla as well as the transport disc. Care was taken not to interfere with the blood supply from the palatal region (Figure 6.20(c)).

6.4.10.1 Creation of transport disc

The trajectory rail was pre-attached to the maxillary bone to ensure correct adaptation and secured with 2.0 Biomet^{TM} titanium screws (Figure 6.20(b)). This was done before the transport disc was created. Once the horizontal position of the trajectory rail was adjusted and made parallel to the occlusion plane, the complete apparatus was removed and only the transport disc was surgically created. A vertical and horizontal osteotomy was made using a reciprocating saw (Figure 6.20(c)). Once the transport disc was mobilised with osteotomes ensuring no injury to the palatal mucosa, the distraction apparatus was re-applied to the bone and four (1.5 mm diameter x 8 mm deep) titanium fixation screws were placed through the mesh holes of the cradle, at right angles to each other, to ensure three-dimensional retention and stability of the transport disc.

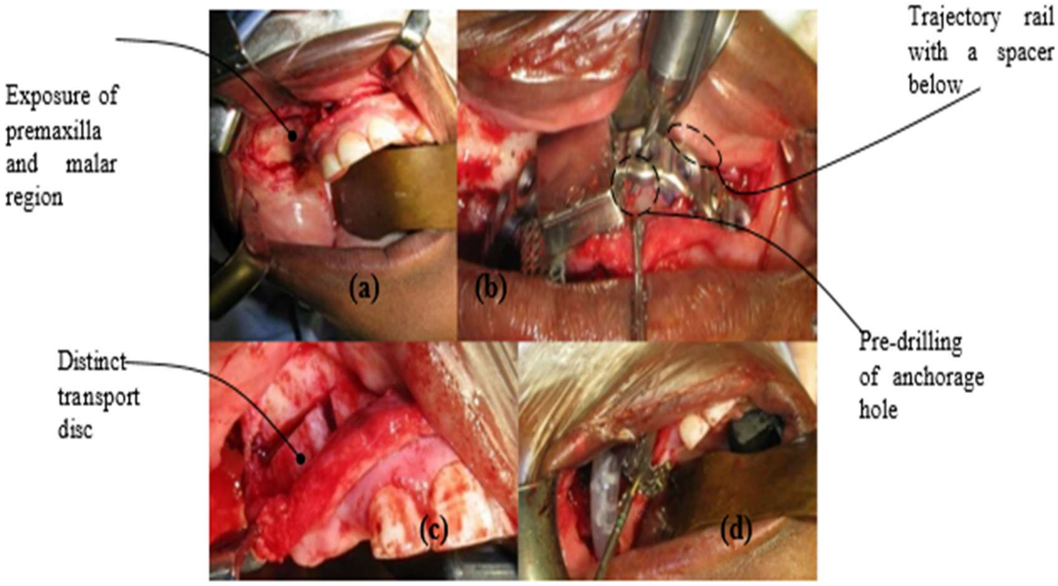

Figure 6.20: (a) Surgical exposure of anterior maxilla and malar region. (b) Placement of trajectory rail spacers, and drilling holes for bone anchorage before osteotomy to transport disc.(c) Surgical osteotomy to create transport disc.(d) 1.5 mm diameter x 8 mm deep titanium fixation screws are placed through the mesh holes of the cradle to secure the transport disc.

In the posterior region, the transpalatal and zygomatic plates were placed to provide stability to the end of the trajectory plate. The confluence of the three plates was secured with a 0.18 mm stainless steel wire ligature. Figure 6.21(a) shows the transport disk fixed to the locomotive and cradle as well as the stabilisation by the transpalatal and zygomatic plates. Once secure, the locomotive is tested by advancing the worm clockwise for about 2 mm – 3 mm and then reversing it back to the original position. The latency phase can now begin after suturing of the soft tissue to cover all exposed key areas; wherever a problem of lack of soft tissue presents itself, the buccal fat pad can be used as covering tissue.

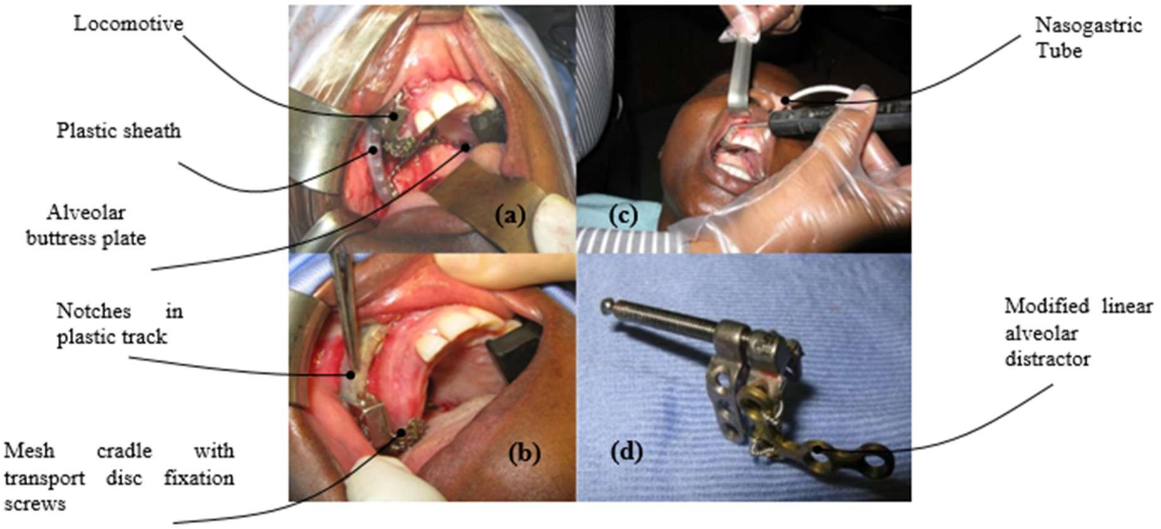

Figure 6.21: (a) Installed V1 distractor. (b) Failure of the device owing to stripping of the plastic track; 26 mm of healthy tissue regenerate. (c) Activation of distractor outside the hospital. (d) Alveolar distractor modification with attached titanium plate and wire.

6.4.11 Distraction phase

After a latency period of 5 days, distraction was commenced on 14 September 2011, at a rate of 1.5 mm per day. The rhythm was carried out at 1 mm in the morning and 0.5 mm in the afternoon. The patient was discharged with a nasogastric tube to facilitate feeding. However, it was found that this assistance was not needed after a few days at home, and subsequently the tube was removed.

6.4.12 Failure of distraction apparatus

After 15 days of distraction (amounting to approximately 26 mm of distraction), the carriage was found to be slipping owing to creep of the plastic sleeve.

6.4.13 Installation of auxiliary distractor

As the amount of regenerate was deemed to be insufficient, it was decided that distraction should continue if possible. It was decided to place a second alveolar distractor as an auxiliary to assist the first distraction device (Figure 6.22).

This required some innovative modifications to accomplish (Figure 6.21(d)). A linear alveolar 15 mm distractor (Biomet^{TM}) was used with a 2 mm titanium plate and wire to the trajectory rail and locomotive. Thus, the locomotive was pushed forward and the distraction process was successfully continued for a further 9 days (Figure 6.22 (a), (b) and (c)). The distraction process was continued until completion, which amounted to an additional regenerate of 13 mm in length.

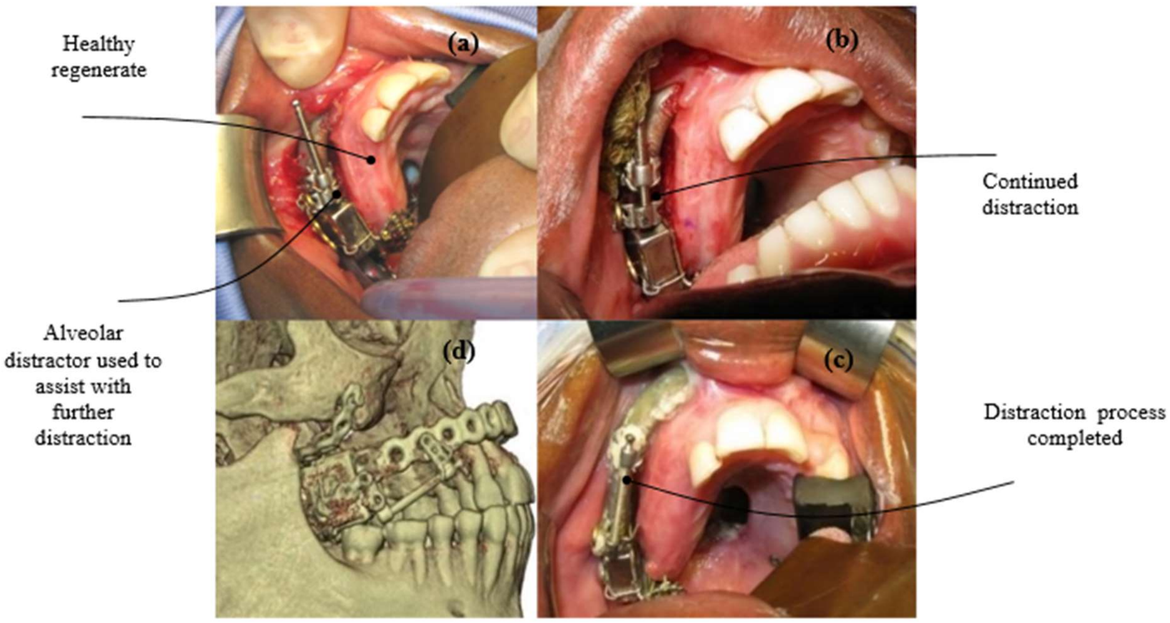

Figure 6.22: (a) Auxiliary assistance using alveolar distractor. (b) Enhancement of distraction process.(c) Completion of the distraction process with both distractors in tandem. Note the thick regenerate and the extruding basket and screws. The patent oronasal defect is evident.(d) The 3-D CT scan shows attachment of the linear distractor to the locomotive on the rail.

6.4.14 Consolidation period

The consolidation phase was 12 weeks. During this period, the distraction devices were left *in situ* and no callus-enhancing supplements or other modalities of callus manipulation were administered. Figure 6.22(d) shows a 3-D CT scan with the distraction devices *in situ* and the mature regenerate in the patient. It is interesting to note in Figure 6.22(c) that the transport disc basket and screws were almost completely extruded from the bone owing to the counter-traction of the maturing regenerate.

6.4.15 Removal of distraction devices

After the consolidation phase, general anaesthesia was administered. The V1 distraction device, as well as the linear distractor, were removed. A thick neo-alveolus could be seen after reflection of the gingival mucosa (Figure 6.23(a)). Although almost cantilevered from the parent bone in its entirety, this new bone was found to be quite robust and well mineralised.

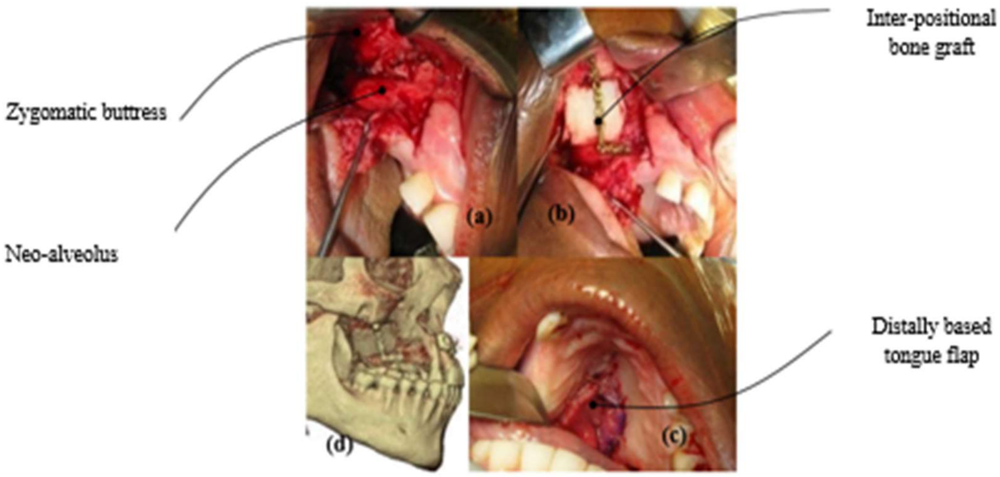

Figure 6.23: (a) The exposed mature regenerate and the zygomatic buttress. (b) The inter-positioned cortico-cancellous bone graft secured by a 1.5 mm Biomet^{TM} titanium plate. (c) The anteriorly based tongue flap closing the palatal defect. (d) A 3D CT scan of the graft and plate.

6.4.16 Placement of interpositional bone graft

Owing to the intention to ultimately place dental implants, it was decided to stabilise the regenerate against the zygomatic buttress. This was effected by placing a cortico-cancellous iliac bone graft between the neo-alveolus or regenerate, and the zygomatic buttress (Figures 6.23(b) and (d)). The bone graft was secured by means of a 1.5 mm Biomet™ titanium plate and screws (Figure 6.23(b)).

6.4.17 Closure of oronasal fistula

During the same surgical procedure as above, the patent oronasal fistula was obturated by means of a distally based tongue flap. This flap was allowed to revascularise over a period of 8 days. Thereafter, the flap was released and inset. The tongue was released and repaired. The tongue flap was successfully integrated into the defect and established hermetic closure of the palatal defect (Figure 6.23(c)). After maturation of the tongue flap, the patient was ready for removal of the titanium plates and screws and the placement of dental implants. The clinical image below clearly illustrates the value of transport distraction in creating bone and soft tissue bulk for reconstructive purposes (Figure 6.24).

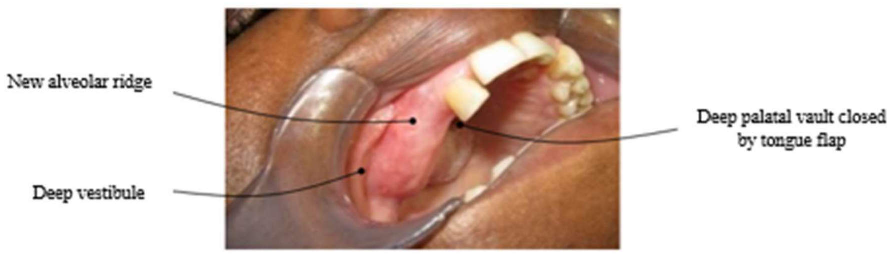

Figure 6.24: The impressive new alveolar bone ready for the placement of dental implants. Note the deep vestibule and palatal vault replication.

6.4.17.1 Bone density of regenerate and parent bone

After a period of 52 weeks since the commencement of the distraction process, a CT scan was done to evaluate the bone density of the regenerate, as the intention was to place dental implants into the newly created bone. The scan below (Figure 6.25) shows the Hounsfield unit count which confirmed the suitability of the new bone for dental implant placement. Also shown is a comparison between the new and the parent bone. It can be seen that the new bone compares most favourably with the parent bone (cf. Chapter 10).

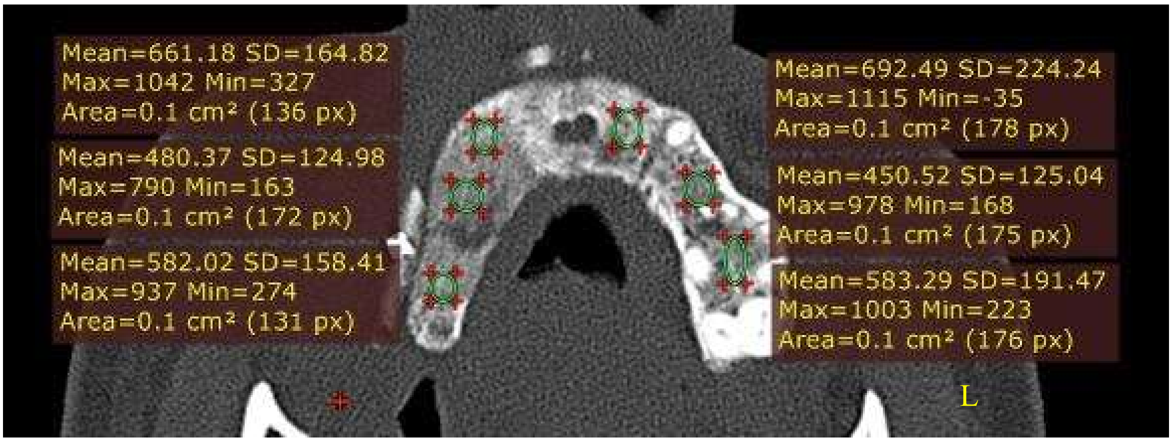

Figure 6.25: CT scan of maxilla 12 months post distraction with bone density of regenerate (right-side) v. parent bone (left-side) expressed in Hounsfield units (ROI = 0.1 $cm^{2)}$.

6.4.18 Placement of dental implants

After a period of 24 weeks following placement of the inter-positional bone graft, the patient was returned to the operating theatre for removal of the titanium plate and screws. This was done through a separate vestibular incision. A prefabricated acrylic stent was used to determine the placement of the dental implants. This was done via a flapless method to preserve as much blood supply to the regenerate as possible (Figure 6.26).

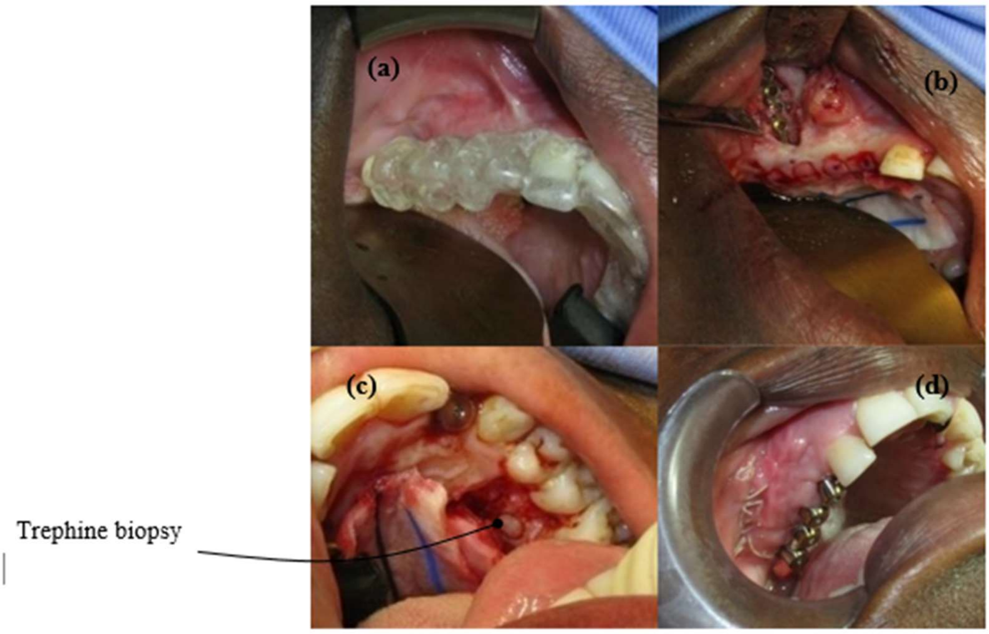

Figure 6.26: (a) The acrylic splint for dental implant placement.(b) The conservative incision for removal of the plate and screws. Also note the flapless punch-outs.(c) Trephine biopsy of bone being taken. (d) Dental implants with transmucosal abutments.

At the same time as the placement of the dental implants, bone trephine biopsies were done at selected areas for the purposes of histological examination. These trephine biopsies were done not only on the regenerate, but also on the corresponding side within the parent bone. The dental implants were placed within the same osteotomies made for the trephine biopsies. Figure 6.26(d) shows the placement of four Nobel Active^{TM} (Nobel Biocare, Kloten, Switzerland) dental implants with transmucosal abutments at the one-week postoperative stage. A fifth dental implant was placed in the tooth #22 bone area to complement the dentition.

6.4.19 Final prosthodontic rehabilitation of post-maxillectomy patient

After allowing osseo-integration of the dental implants to take place over a 12-week period, the dental occlusion was restored with a temporary hybrid bridge. However, the patient never returned for further assessment and is no longer contactable.

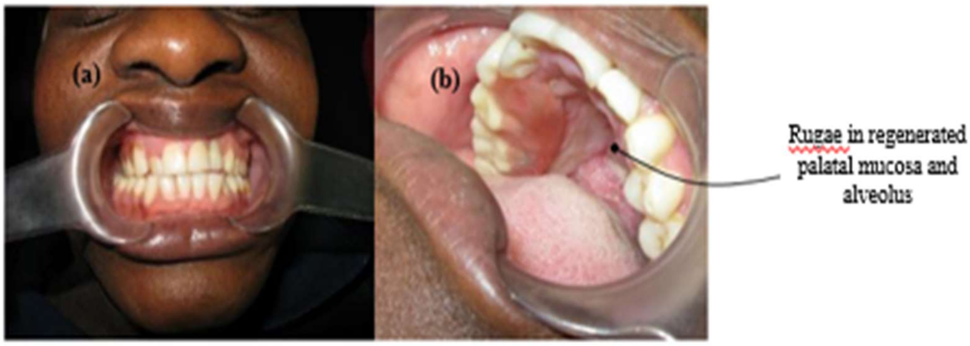

Figure 6.27: (a) The patient with temporary hybrid bridge. (b) A palatal view of the same bridge supported by healthy bone and soft tissue.

6.4.19.1 Pre- and postoperative radiographs

Figure 6.28: (a) The pre-distraction maxillectomy defect. (b) The post-distraction anatomy with the maxillectomy defect successfully obturated by new bone. Note the curvilinear shape of the neo-alveolus.

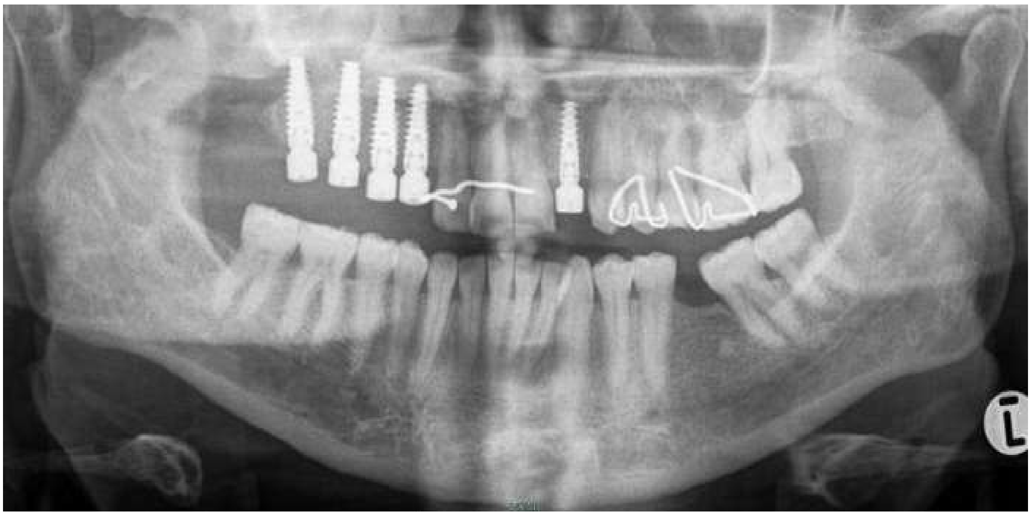

Figure 6.29: Orthopantomogram showing the healthy regenerate housing the 4 dental implants before prosthodontic rehabilitation. Note additional dental implant in #22 area.

6.5 Discussion: Engineering observations made during installation of V1 distractor

(Comments by Mr J. Boonzaier (MSc.) and Assoc. Prof. G. Vicatos (PhD, Pr. Eng)

1. During surgical installation, the device underwent many adjustments in order to perfect the geometry of the rail and cradle and to designate secure fixation screw locations. These adjustments disturbed and sometimes damaged the plastic track, which was worsened by the protocol's demand for forward and reverse movement of the locomotive during installation, and raised further concerns about the reliability of the track in delivering the necessary distraction force.
2. There were minor geometric discrepancies between the pre-operative cranial models and the real situation, particularly the surface contours of the frontal maxilla. These were attributed to poor resolution of the original CT scan, which caused certain small details of the maxilla contours to be absent. In addition, the cranial models reproduce only the bony anatomy and give no indication of the surrounding soft tissue, especially the biotype of the attached gingiva. As a result, the device required more extensive intra-operative customisation than had been expected. The first draft design did not cater for repetitive attachment and removal of the trajectory rail for 'fine tuning', having expected only minor adjustments to be made intra-operatively. Repetitive adjustment of the rail curvature disturbed the bone anchorage screws and compromised the rigidity of the installation.
3. During the installation procedure, it was necessary to place metallic spacers between the trajectory rail and the anterior part of the maxilla (Figure 6.20(b)). These spacers accommodated the thickness of the soft tissues of the gingiva, and provided space for the locomotive to move freely without injuring the soft tissues.

6.5.1 Discussion of V1 clinical performance

The V1 prototype facilitated the repair of the clinical defect (Figure 6.24), and the experience during treatment provided valuable feedback on the design and insight into how it might be improved. Specifically, it provided a more refined understanding of the surgical protocol and the distraction force, and it highlighted the need for improved ease-of-installation and removal and improved reliability of the traction mechanism.

Reviewing the performance of the V1 prototype, the following shortcomings of the first clinical case were highlighted:

- From a surgeon`s perspective, it was found that the transport disc mesh cradle was too rigid for easy shaping during installation.
- The locomotive was not sufficiently stable on the rail after customisation. In particular, the locomotive could rotate excessively about the axis of the rail; this was because of the oval, rather than rectangular, cross-section of the LDPE tube.
- The wired **confluence** joint was easily customisable, and it was evident that there would be sufficient access for removal post treatment. However, the author felt that it was a crude solution which required further development. The author requested that a bolted or screwed fixation arrangement be developed.
- The void formed between the plastic tube and trajectory rail was a hygiene and infection concern.
- The self-cutting traction mechanism presented several intrinsic shortcomings. Fundamentally, the deformation and flow characteristics of the LDPE track material were inappropriate, given the magnitude of the expected loads. The strength provided by the plastic track was found to be inconsistent, and was affected by irregularities in the trajectory and the inherent play between the locomotive and rail. It was observed that the depths of the grooves cut by the worm-screw varied unpredictably, whilst some segments of the worm-screw perforated the plastic tube entirely.
- An aspect of device functionality that was not properly considered when designing the V1 distractor was the need to move the locomotive repeatedly over the same section of rail both forwards and backwards. As this was not foreseen in the design phase, it was not investigated during bench-testing, where it might have been discovered earlier. This deficiency alone rendered the plastic cutting concept inappropriate.
- Therefore, future versions of the device should utilise a rigid mechanism, rather than the plastic track used in the V1 device, to generate the distraction force. This arrangement would ensure accuracy of distraction, predictable behaviour of the device and reliable force delivery.
- During the installation surgery, anchorage screws used to secure the anterior end of the rail to the maxilla were repeatedly inserted and removed in order to adjust the trajectory rail and

transport disc attachment cradle. This compromised the integrity of the bone-screw anchorage and it was suggested that future versions should allow repeated attachment and removal of the trajectory rail without disturbing anchorage screws. This would ensure that the anchorage screws would be inserted only once during installation and removed only after treatment had been completed.

- The use of spacers, as described in the clinical observations, was cumbersome and introduced small, loose components, adding significantly to installation time.
- More information was required on the magnitude of the distraction force. The forces found in the clinical environment appeared to be greater than expected, leading to failure of the traction mechanism. While at this stage these forces could not be quantified, *in vivo* there was noticeably more resistance to distraction than had been encountered in pre-clinical laboratory testing (see subsection 6.4.7), which evaluated the device based on data from the literature. It was assumed that mandibular distraction force data found in the literature was a suitable bench-mark.
- The **confluence** of the rail and support plates at the rear of the mouth was secured using stainless steel surgical wire. This solution accommodated substantial freedom of alignment of the buttress plates and was sufficiently strong. However, the author requested that in the next iteration of the device, the **confluence** connection should make use of a nut-and-bolt arrangement instead.

CHAPTER 7. DEVELOPMENT OF THE VERSION 2 DISTRACTOR

7.1 Introduction

7.1.1 Version 2 prototype: Worm-rack mechanism

The pitfalls experienced during the first attempt at curvilinear transport distraction provided much food for thought. It was decided that a metallic device would be more reliable and robust. Based upon the invaluable experience provided by the V1 distractor, the second phase of development began with a critique of how the problem had been defined and a revision of the design requirements. In response to the *in vivo* failure of the V1 prototype, the priority of the V2 design phase was to develop a more robust traction mechanism that would provide a greater distraction force and improved stability.

7.1.2 Planning for distraction

The clinical defect to be obturated by means of CTDO is shown below in Figure 7.1.

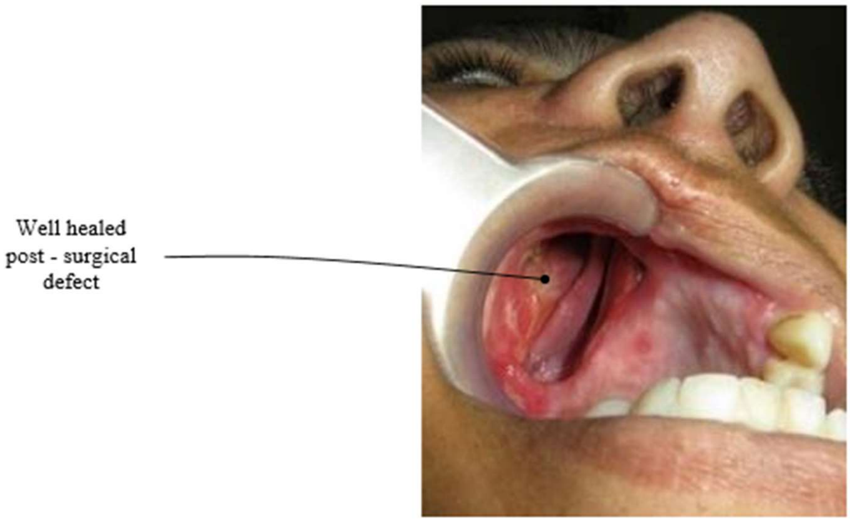

Figure 7.1: The post-surgical defect (Brown III b) of the patient before 2 teeth (#23 and #24) were to be extracted to create sufficient bone bulk to form the future transport disc.

7.2 Version 2 protoype: Worm-rack mechanism

In collaboration with engineers Assoc. Prof. George Vicatos (PhD, PrEng) and Mr James Boonzaier (MSc), the following improvements were made:

7.2.1 V2: Major design refinements

The V2 distractor retained the basic format of the V1 version, comprising distinct rail and locomotive components. The zygomatic and palatal support plates were also retained, having performed suitably in the first case – supporting the posterior end of an otherwise cantilevered trajectory rail. The major design modifications were as follows:

- A metallic worm-rack traction mechanism replaced the plastic self-cutting mechanism. This necessitated a purpose-built metallic trajectory rail with a preformed toothed rack for engagement of the worm-screw (Figures 7.2 and 7.3).
- The locomotive profile and mesh cradle were refined to improve patient comfort and customisability.
- The wired **confluence** used in the V1 device to link the posterior buttress plates was replaced with a bolted connection.

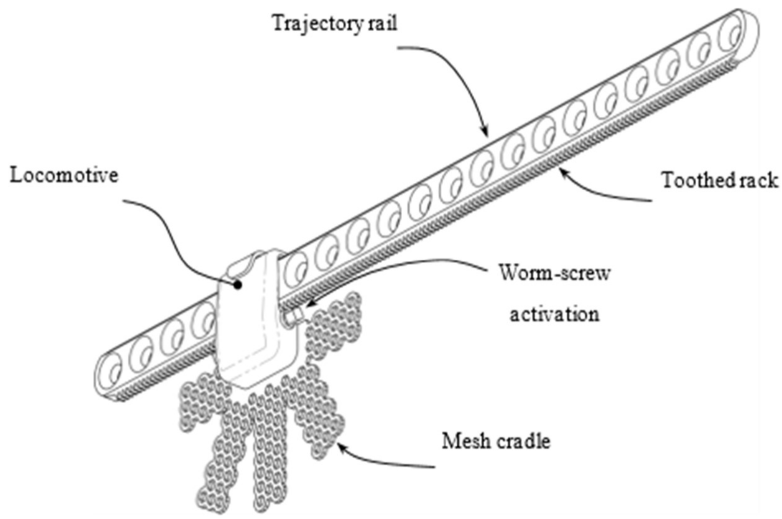

Figure 7.2: The labelled V2 distractor with toothed rail.

7.2.2 Worm-rack traction mechanism

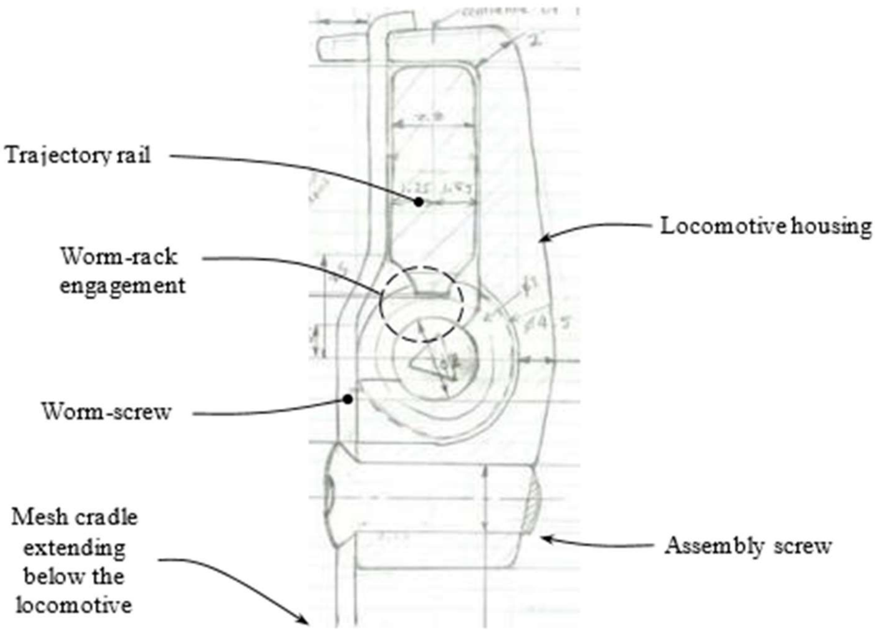

Figure 7.3: The end-view of the V2 locomotive, illustrating the traction mechanism, assembly screws and the outer profile (sketch by Mr James Boonzaier).

The plastic traction mechanism was replaced with the metal-on-metal worm-rack traction mechanism described in concept in subsection 6.3.3.1.This mechanism is self-locking, provides a large gear ratio and can easily be scaled according to the application.

Owing to the sliding engagement between the worm-screw and rack components, high friction and wear are characteristics of the mechanism, making it inappropriate for most drive applications. However, the mechanical requirements of the CTDO application are relatively undemanding:

- The applied loads are relatively small.
- Energy consumption is irrelevant.
- The device operates at very low speeds.
- The working life of the device involves less than 100 revolutions of the worm-screw.

- Friction, efficiency and wear of the mechanism are therefore insignificant issues.

In worm-rack mechanisms, to compensate for the thread angle, the worm-screw is usually orientated with its axis at an angle to that of the rack equal to the thread angle, such that more thread surface is in parallel contact between the worm and rack teeth. However, this adds to the bulk of the device and complexity of manufacturing, and complicates access to the worm activation heads. As the CTDO application involves low speeds and relatively small loads, there were no clear benefits to justify these clear disadvantages. The design therefore utilised a much simplified worm-screw arrangement, orientating the worm-screw with its axis parallel to that of the trajectory rail. Ultimately, physical testing has shown that this arrangement performs adequately in practice.

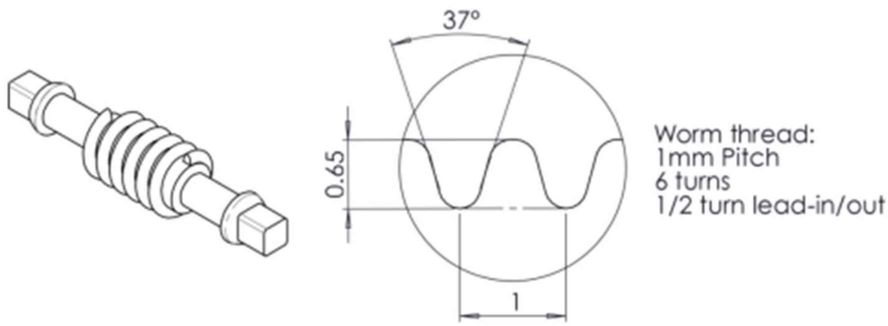

Figure 7.4: The worm-screw and detail of the worm-screw thread (sketch by Mr James Boonzaier).

The V2 locomotive and worm-screw are illustrated in Figures 7.4 and 7.5, respectively. The 1 mm pitch used in the V1 distractor was retained in the V2 device. The worm-screw thread height of 0.65 mm provided 0.6 mm of engagement with the corresponding toothed rack, with 0.05 mm of clearance.

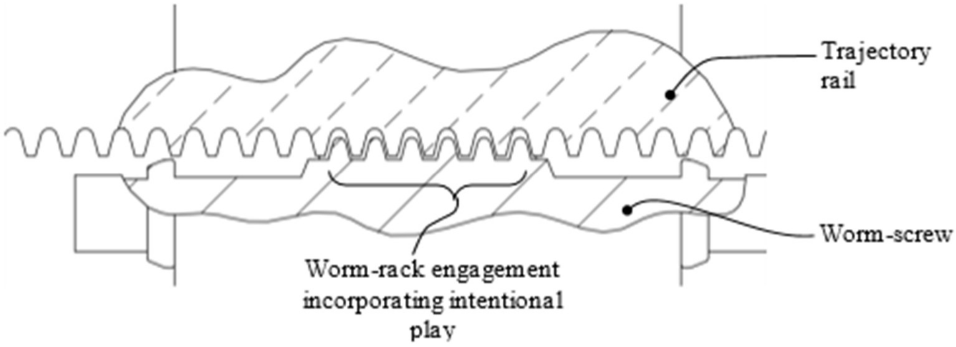

Figure 7.5: Detail of the V2 traction mechanism, illustrating play (sketch by Mr James Boonzaier).

It was both necessary and intentional to incorporate axial play into the worm-rack engagement (Figure 7.5) to compensate for distortion of the rack feature when the trajectory rail is bent to shape (the pitch of the toothed rack would become wider on the outside of the bend and narrower on the inside). The effects of curvature on the rack teeth were quantified mathematically and it was found that, for the minimum expected bend radius of 25 mm, 0.3 mm of play compensated adequately for distortion of the rack teeth.

As this type of worm-rack mechanism is not widely used elsewhere, no technical information was found to guide the design of the tooth profiles of the worm or rack. In lieu of such technical information, the design of the traction mechanism was based on engineering basics, making use of computer-aided design tools to model and analyse the mechanism. The manufactured V2 traction mechanism performed satisfactorily in bench-testing (subsection 7.2.4).

7.2.3 Trajectory rail with toothed rack

The metallic worm-rack traction mechanism incorporated a toothed rack in the trajectory rail component (Figure 7.6 below). While the V1 case had provided some insight into the requirements of the trajectory rail, the strength and deflection criteria were not yet fully understood. To overcome this uncertainty, the strength and rigidity of the trajectory rail were substantially overdesigned, but were based on the dimensions of the Biomet™ mandibular reconstruction plate, which had provided adequate rigidity in the V1 clinical case.

The layout of the anchorage holes in the V2 trajectory rail copied those of the Biomet™ mandibular reconstruction plate. Before manufacturing the final trajectory rail unit, a dummy trajectory rail was manufactured in brass to test the capabilities of the traction mechanism. The final V2 trajectory rail was manufactured from biocompatible medical-grade titanium alloy. As the trajectory rail was to be submerged in soft tissues for the duration of treatment, the use of a biocompatible material was necessary.

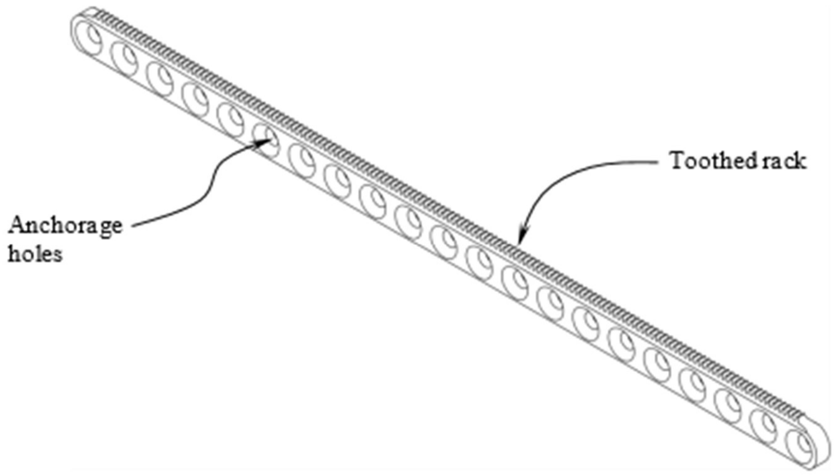

Figure 7.6: The V2 trajectory rail with serial anchorage holes and integral toothed rack.

7.2.3.1 Locomotive refinements

The locomotive, which stabilises and propels the bone transport disc, underwent minor ergonomic refinements in the second stage of development. These refinements, directed by observations made during clinical evaluation of the V1 distractor, included the following:

- The outer profile of the locomotive was improved, introducing smooth contours and removing sharp edges.

- The stability of the locomotive on the trajectory rail was improved by refining the design of the guide channel tab, which constrains the locomotive to the trajectory rail.
- The 0.8 mm thick mesh cradle of the V1 device was found to be too rigid for easy shaping. This was reduced to 0.5 mm in the V2 device, using stainless steel 316 alloy.
- The number of assembly screws was reduced to 2, greatly simplifying manufacture and assembly and further reducing the size of the locomotive.

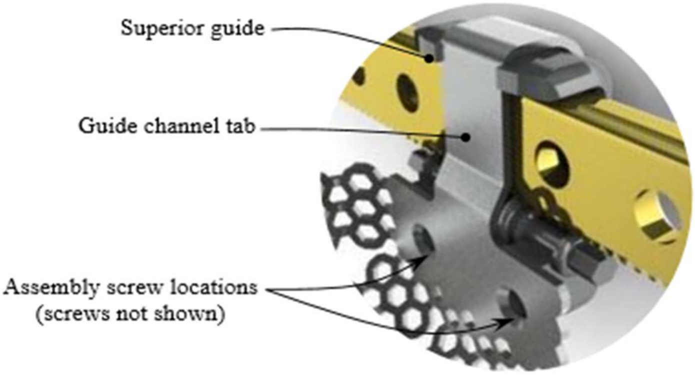

Figure 7.7: Detail of the V2 locomotive guide channel.

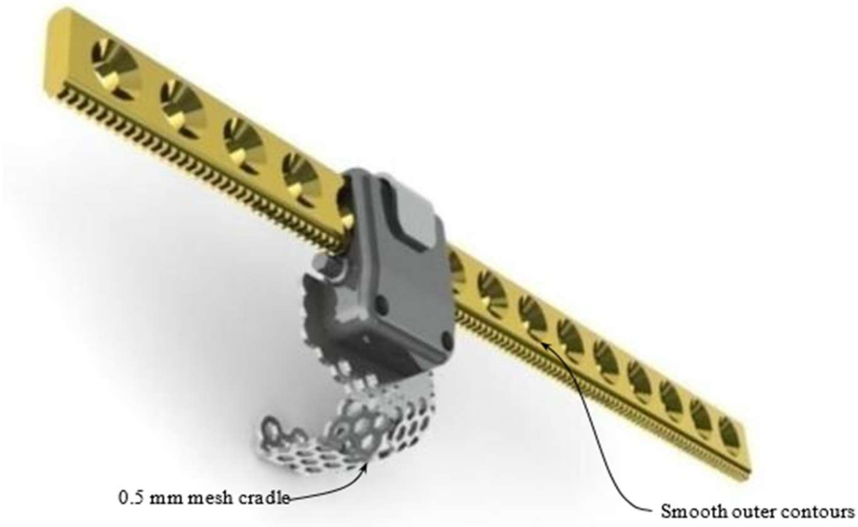

Figure 7.8: V2 locomotive refinements.

7.2.3.2 Laboratory testing

Following the failure of the V1 distractor during clinical treatment, the V2 device was subjected to more rigorous testing to ensure its reliability in the clinical stage of usage.For the sake of brevity and compactness, full details of these tests are not presented here, but similar tests are described in detail in subsection 8.4.1. which describes testing of the most recent device version.

7.2.3.3 Test distraction on worst-case trajectory

The second prototype underwent a full bench test distraction along a worst-case trajectory (25 mm radius of curvature) under a load of 40 N. The device showed no signs of jamming and the worm rotated smoothly. The displacement produced by the device was measured using a vernier caliper and, on average, it was found that 1 rotation produced 1 mm of distraction with negligible error, thus providing sufficiently accurate control.

7.2.3.4 Load test with maximum expected loads on linear vector

A straight distraction of 30 mm was carried out under the design load of 100 N, as specified in the specification (subsection 4.8). This load incorporated a safety factor of 1.5 over the maximum expected distraction load of 66 N. The 66 N distraction load was based on more recent studies in mandibular distraction [252] elicited subsequent to the V1 clinical case.

To investigate the strength of the worm-rack interface in isolation, the device was subjected to a static axial load of 200 N continuously for one hour, but without any active distraction. The device performed adequately under all the tested load conditions, generating no concerns about the strength, stability, distraction accuracy or reliability of the worm-rack traction mechanism. The results of laboratory testing were thus accepted by the engineers and the author as satisfactory justification for progression to *in vivo* testing.

7.2.4 V2: Clinical evaluation

The second clinical case involved a defect of approximately 80 mm extending from the tuberosity region in the right posterior maxilla to the left anterior maxilla. The defect extended beyond the midline, eliminating more than 70% of the alveolar ridge, hard palate and much of the nasal floor (Figure 7.9). This defect compromised the ability of the patient to speak and to eat comfortably, and severely affected facial aesthetics and symmetry.

The severity of the defect required a CTDO trajectory encompassing an arc of approximately 100°, with a length of 80 mm. It was uncertain how the regenerate would respond to this extreme extent of distraction, and there were concerns as to whether the newly formed bone would conform to the trajectory rail. It was expected that, as the transport disc progressed along the arc, the tension in the regenerate would cause the new alveolar ridge to straighten, forming a chord between the initial fracture and the location of the locomotive. This undesirable outcome was termed the 'rubber band effect'.

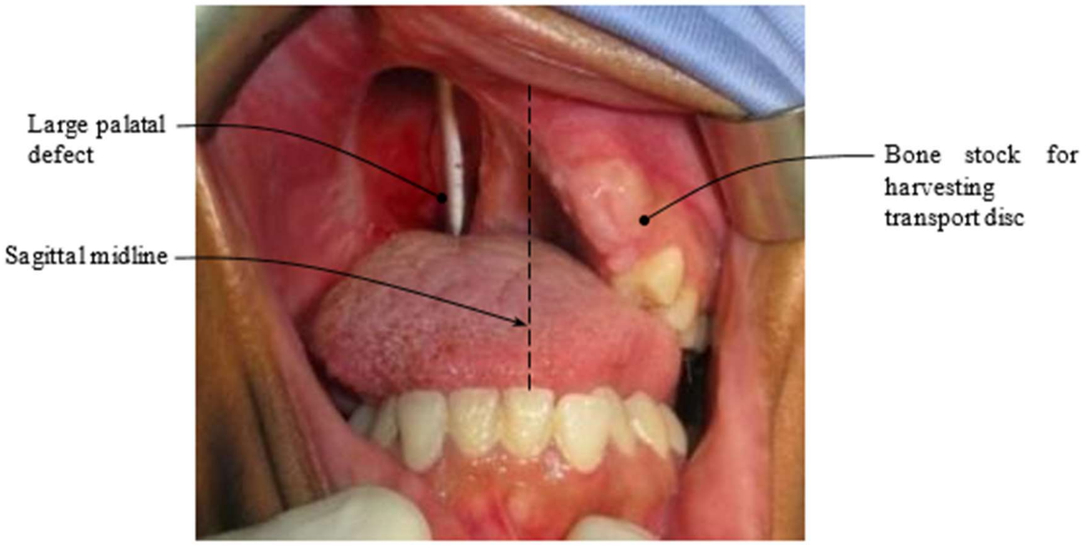

Figure 7.9: The surgical defect before repair.

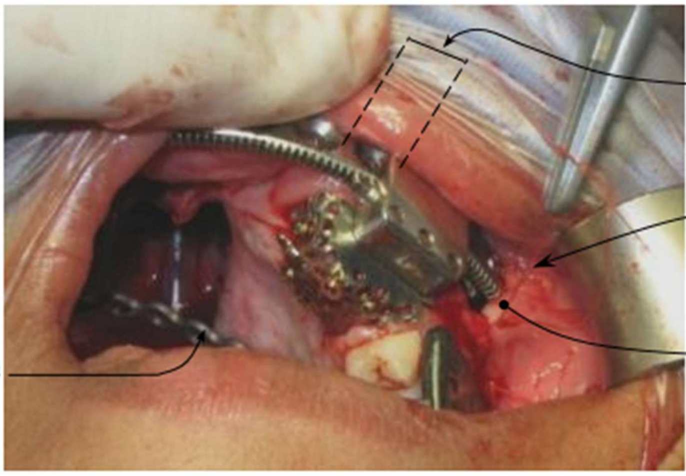

Figure 7.10: Installed V2 distractor.

Surgical installation of the V2 prototype took 3½ hours, equal in duration to that of the V1. The following problems were encountered (Figure 7.10):

- The maxillectomy defect eliminated the entire right side of the maxilla, leaving only a small segment of the left maxilla intact, posterior to the left canine. Access to this area was hindered by the proximity of the cheek, restricting the angle at which anchorage holes could be drilled and anchorage screws deployed.
- The spacing of the anchorage holes in the trajectory rail prescribed and restricted the anchorage screw spacing to precisely 7.5 mm. This lack of flexibility made it impossible to accommodate all of the desired anchorage screws amongst the dental roots.
- As was the case in the V1 installation, spacers were used to offset the trajectory rail from the maxilla in order to (1) correct the distraction trajectory, (2) compensate for irregularities in the surface contours of the maxilla, and (3) accommodate the thickness of the gingiva so that the locomotive could bypass the gingiva without injury. Placement of these spacers was cumbersome and they obstructed drilling, prolonging the procedure by approximately 30 minutes.
- As was the case with the V1 device installation, there were geometric discrepancies between the pre-operatively shaped rail and the actual anatomy. The device therefore required time-

consuming intra-operative customisation. This issue was partly attributed to discrepancies in the cranial model, owing to inadequate resolution of the original CT scan.

- At the request of the author, a nut-and-bolt arrangement was used to secure the confluence. However, this was found to be impractical during both installation and removal of the device, owing to the limited access to the confluence with the necessary tools.
- To load the locomotive, the trajectory rail had to be removed entirely, including the anchorage screws, and subsequently re-installed. This was repeated while shaping the mesh cradle, further compromising the integrity of the maxillary anchorage screws.
- The author found that the mesh cradle was too rigid for *in situ* shaping, despite refinements made to the V2 device in this regard (see subsection 6.3.3.1.).
- The locomotive, trajectory rail and buttress plates were pre-assembled outside the oral cavity once customisation was finalised (Figure 7.11). Thus, no difficulties were encountered in assembly of the bolted confluence.
- In the late stages of treatment, the unused trajectory rail anchorage holes were invaded by soft tissue, which became painful. In future versions, these holes should be reduced in size, plugged or eliminated entirely.
- As in the V1 case, the screws securing the bone transport disc to the mesh cradle worked loose and their orientation shifted under long-term loading.

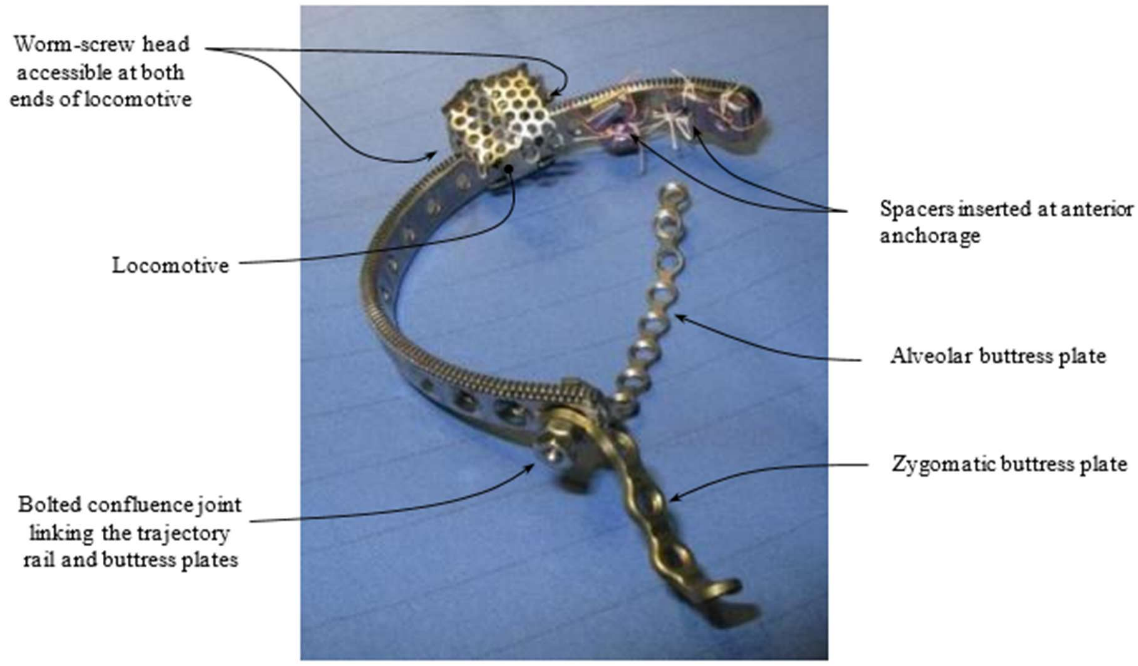

Figure 7.11: The customised device, ready for final installation.

After approximately 40 mm of distraction, the regenerate began to form a straight chord between the initial osteotomy and the locomotive, rather than the desired circular arc. Though attempts were made to preserve the curvature of the regenerate using an acrylic moulding device, this merely resulted in the regenerate thinning out at the points of contact with the retainer. This behaviour suggested the need for an alternative protocol in order to effectively treat such large, curved defects.

Removal of the V2 prototype exhibited the same difficulties as the V1*:*

- In its final position, the locomotive was confined by the surrounding muscle and soft tissue. As such, the screw securing the bone transport disc to the cradle could not be accessed with the appropriate screwdriver. To remove the device, these screws were unscrewed using a surgical forceps or their heads were ground off with a surgical drill.
- The bolted confluence joint was significantly more difficult to dismantle than the wired version used in the V1 case. Access to the nut and bolt was especially hindered by soft-

tissue invasion and trismus of the surrounding muscles, which restricted separation of the jaws.

Despite the ergonomic problems mentioned above, the V2 distractor successfully performed distraction of the bone transport disc along the entire 80 mm trajectory, with no concerns about the strength or reliability of the traction mechanism. The worm-rack mechanism produced accurate distraction in both the forward and reverse directions, and the device demonstrated a satisfactory self-locking action throughout the distraction procedure.

7.2.4.1 Discussion of V2 clinical performance

The V2 device stably propelled the transport disc along the required 80 mm trajectory. The author reported no difficulty in accessing the worm-screw for daily activation, though it was noted that the resistance to rotation of the worm-screw increased noticeably as distraction progressed. This aligned with reports in the literature that the callus stretching force increases with time. Nonetheless, having observed the V2 distractor in practice, the following ergonomic shortcomings of the device were highlighted, directing further enhancements.

7.2.4.2 The anterior anchorage

Of particular note in the V2 clinical case were difficulties associated with repeated installation and removal of the trajectory rail during the initial surgical procedure. The process of repeatedly removing and re-attaching the trajectory rail not only prolonged the installation procedure, but also compromised the integrity of the bone anchorage screws. Loosening of these screws probably contributed to pain reported in their vicinity.

While the use of spacers at the anterior anchorage provided the correct spatial orientation and fixation of the trajectory rail, manipulation of these spacers was cumbersome and time-consuming and undesirably introduced small, loose components into the oral cavity. A priority for further refinement was to develop a simple and robust installation interface to overcome these difficulties without adding complexity to the design.

7.2.4.3 Confluence joint

During removal of the device, disassembly of the bolted confluence joint was problematic and time-consuming. By the end of treatment, the posterior end of the trajectory rail had become largely obscured by the bony regenerate and the encroaching soft tissue. Further hampered by the effects of trismus, access to the nut-and-bolt arrangement (Figure 7.11) with the necessary tools was significantly restricted. In retrospect, it was found that the wired confluence (as used in the V1 case) provided a more ergonomic and satisfactory solution.

7.2.4.4 Spacing of the maxillary anchorage screws

The layout of the maxillary anchorage screws was restricted to the set spacing of the anchorage holes in the trajectory rail (Figure 7.10). To ensure that the dental roots can be suitably avoided, it was recommended that future versions of the device offer more flexibility in the layout of the anchorage screws.

7.3 Reflections on the second phase of development

The V2 prototype introduced a rigid mechanical traction mechanism to address the reliability issues encountered in the V1 case. In laboratory tests, the revised device supported the design load of 100 N (safety factor = 1.5), and successfully navigated the minimum bend radius of 25 mm. This was reinforced by the clinical success of the device – performing a curvilinear distraction of 80 mm. Ultimately, the V2 device demonstrated the feasibility of an entirely intra-oral maxillary CTDO device that can be installed, activated and removed with no damage to the facial skin.

7.3.1 Installation of distraction apparatus

As before, a 3-D stereolithographically generated model was used to pre-plan the position and shape for the V2 distractor. Figure 7.12 (a) shows the extensive surgical defect to be closed by means of transport distraction. This very large surgical defect showed alveolar and palatal bone loss of the maxilla (Brown III b) and presented an exceptional challenge to close an 80 mm surgical defect.

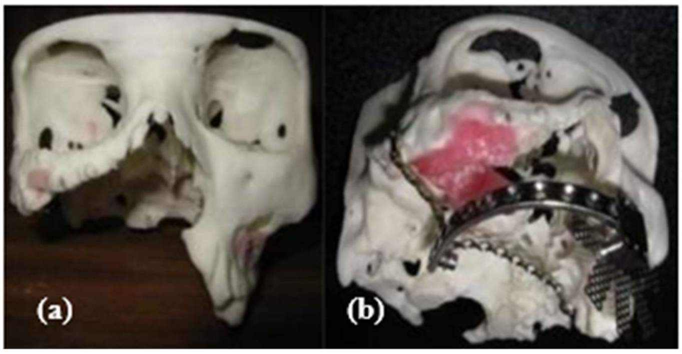

Figure 7.12: (a) The extensive maxillectomy defect. (b) The pre-bending of the distraction apparatus on a 3-D model of the patient.

The trajectory rail is prebent and adapted to the 3-D model and the stabilising plates are screwed to the rail and model.The confluence of the rail and stabilising plates is secured by means of a nut and bolt method (Figure 7.13).

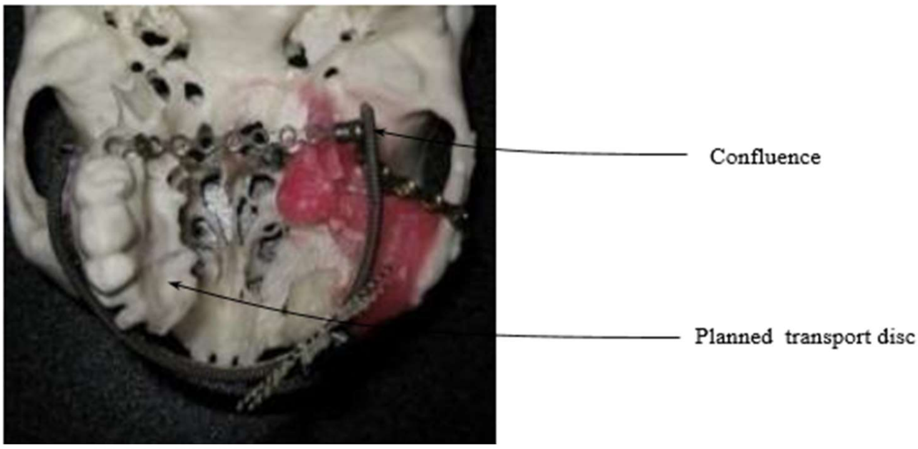

Figure 7.13: The confluence (seen from below) preventing a cantilever effect of the distal end of the trajectory rail and the planned transport disc position.

7.3.2 Surgical installation of distraction apparatus

The left zygomatic buttress was exposed via a circumvestibular incision. The anatomy of the remaining roots of the teeth were carefully studied to avoid inadvertent contact during installation of the rail. The planned transport disc was surgically exposed (Figure 7.14).

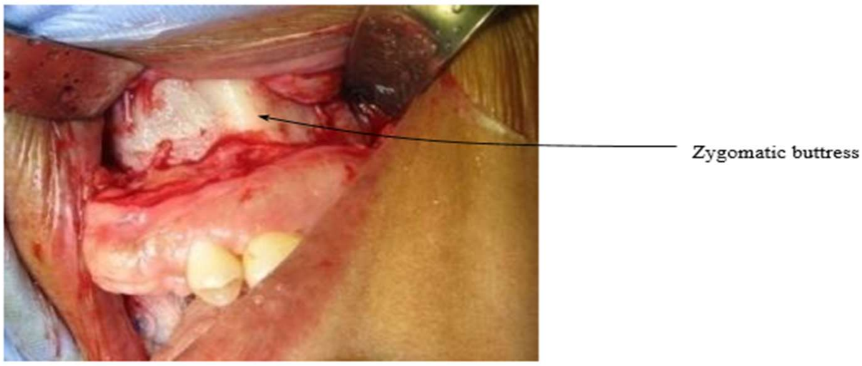

Figure 7.14: Surgical exposure for the planned transport disc.

The locomotive and basket were applied to the bone to check for spatial orientation (Figure 7.15(a)). Also, the trajectory rail was applied to the bone to check for accuracy of curvature (Figure 7.15 (b)). Once the curvature was found to be satisfactory, the trajectory rail was fixed and secured in position using 2.3 mm titanium screws (Biomet™).

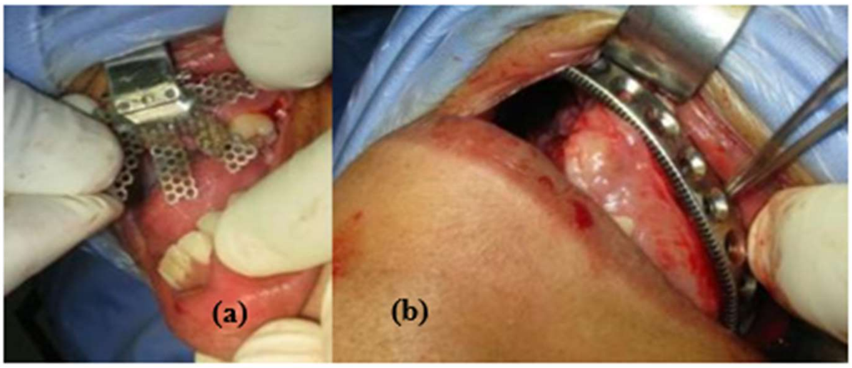

Figure 7.15: (a) The adaptation of the basket to the planned transport disc. (b) The adaptation of the trajectory rail to the maxilla.

The rail was supported proximally by means of a trans-palatal plate secured at the confluence to the zygomatic buttress plate. Use was made of a nut-and-bolt system to create rigidity of contact (Figure 7.16).

Figure 7.16: The confluence secured by a nut and bolt and stabilised by the various buttress plates.

The trajectory rail was secured by the stabilising plates and accepted as parallel to the occlusal plane before the transport disc could be prepared for osteotomy. The locomotive and mesh cradle in position is seen below in Figure 7.17.

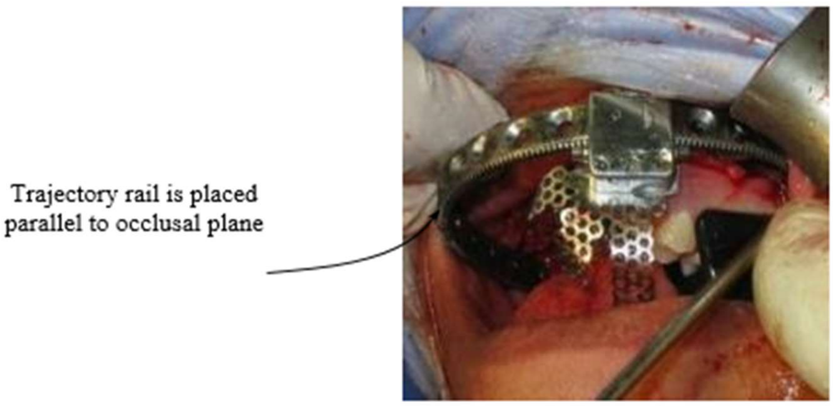

Figure 7.17: The locomotive and mesh cradle in position.

Once the transport disc had been created by means of an osteotomy, the cradle basket of the locomotive was attached by means of 1.5 mm screws (7 mm length); (Biomet^{TM}).

The locomotive is shown below in Figure 7.18(a) with the trajectory rail submerged under the cheek mucosa while the confluence of the rail was secured by the trans-palatal plate, as seen in Figure 7.18(b).

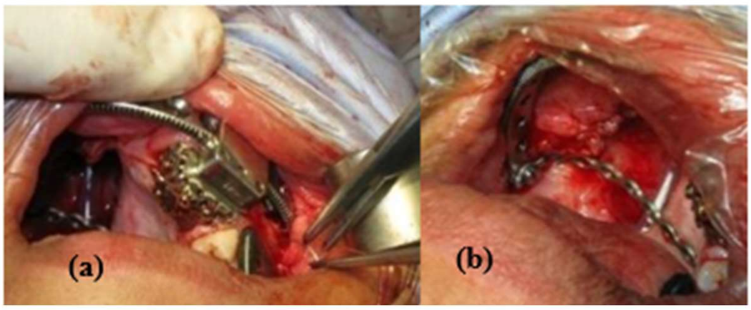

Figure 7.18: (a) The locomotive *in situ* (b) The secured confluence with trans-palatal plate (Alveolar buttress plate)

Once the confluence and buttress plates were accepted as being secure and the transport disc was checked for stability, further 1 mm diameter titanium screws (7 mm length); (Biomet^{TM}) were placed palatally. The completed assembly is seen below in Figure 7.19.

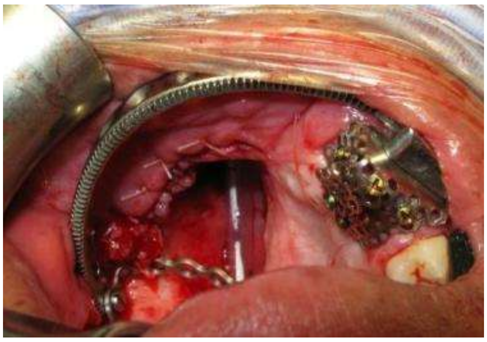

Figure 7.19: The complete distraction apparatus assembled and well secured in the patient.

The distraction equipment was tested by turning the screwdriver in the direction for anterior propulsion. Thereafter, the transport disc was returned to its original position.

7.3.3 Postoperative course

The patient was fed via nasogastric tube for the initial period of distraction (Figure 7.20). The initial stage of transport distraction was very promising, with healthy neo-alveolar bone being formed at a rate of 1 mm per day. However, as soon as the curvature of the maxilla was negotiated, an unexpected complication occurred.

Figure 7.20: The nasogastric feeding tube is seen in the right nostril and the early neo-alveolar bone is shown.

7.3.4 Complication of distraction

It was most disconcerting to note that, as the distraction process progressed, the regenerate, which at first was very thick and healthy, began straightening out as seen, in a 'rubber band effect'. In order to 'mould' the callus, as reported abundantly in the literature, a Palacos™ (Biomet) (acrylic) stent was made in an attempt to 'mould' the regenerate (Figure 7.21).

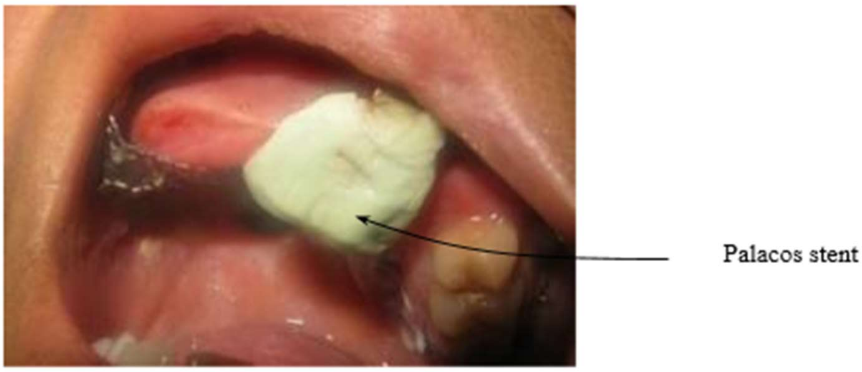

Figure 7.21: 'Moulding' of the regenerate with the Palacos stent.

Unfortunately, the palacos was not uniform in its structure, and it was decided to make a properly designed acrylic splint based upon pre-resection stone models taken previously (Figure 7.22(a)).

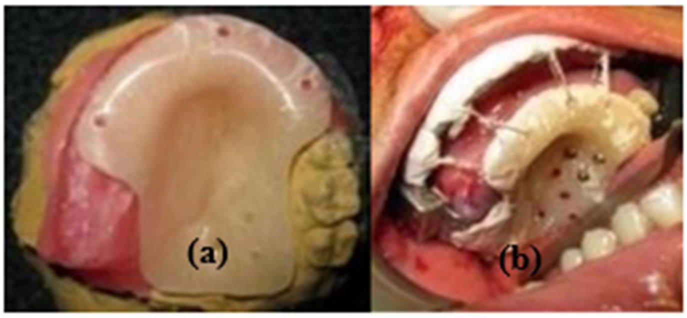

Figure 7.22: (a) The splint on a stone model. (b) The fixation of the splint to rail and palate.

7.3.5 Fabrication of acrylic splint

The acrylic splint made on a stone model was fabricated to assist the regenerate in accepting a curvature. This splint was wired to the trajectory rail and fixed to the remaining hard palate with titanium screws (Figure 7.22(b)). Distraction was concluded at the placement of the splint. A total of 90 mm of distraction was achieved in 60 days at rate of 1.5 mm per day and a rhythm of 0.75 mm twice a day.

7.3.6 Removal of distractor

Four months after cessation of the distraction process, the distraction apparatus was removed. While the production of good, healthy regenerate was not forthcoming as was expected from the initial distraction, the outcome was still satisfactory in the sense that sufficient soft tissue was produced by the process of transport distraction (Figure 7.23 (a)). Unfortunately, the soft tissue became ischaemic in areas during the moulding process. In this instance, as before, a tongue flap was used to close existing oro-nasal openings and defective areas of mucosa. A clinical comparison is seen in Figure 7.23(a) after and before CTDO (Figure 7.23 (b)).

Figure 7.23: (a) The successful closure of the very large surgical defect. (b) The surgical defect before closure with CTDO.

7.3.7 Radiological appearance of new bone

The new bone that was created compared very well with the parent bone in spite of the shortcomings and setbacks during this distraction process. Dental implants could still be placed to enhance function and aesthetics, and was subsequently carried out. Below (Figure 7.24) is a post-distraction CT scan showing the bone density in Hounsfield units for comparison.

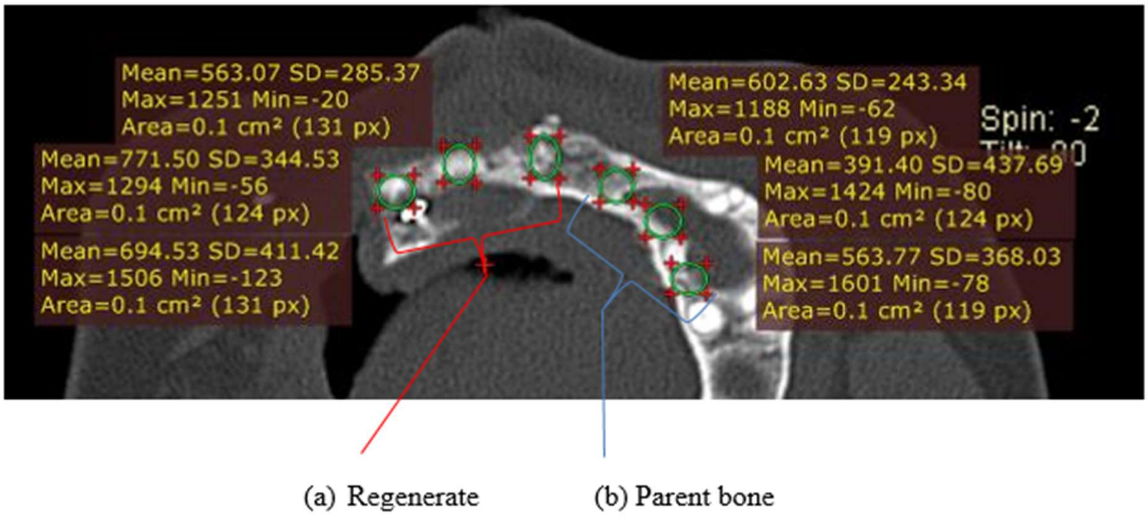

Figure 7.24: A CT scan of the maxilla showing the bone density of the regenerate (a) and parent bone (b) with regions of interest expressed in Hounsfield units (HU).

7.3.8 Placement of dental implants

After a period of consolidation of almost a year, four Closefit Adin dental implants™ (Adin Dental Implant Systems, Johannesburg, South Africa) were successfully placed into the new bone. The implants integrated well without problems. Again, trephine biopsies of the regenerate and parent bone were taken at the time of implant placement (Figure 7.25).

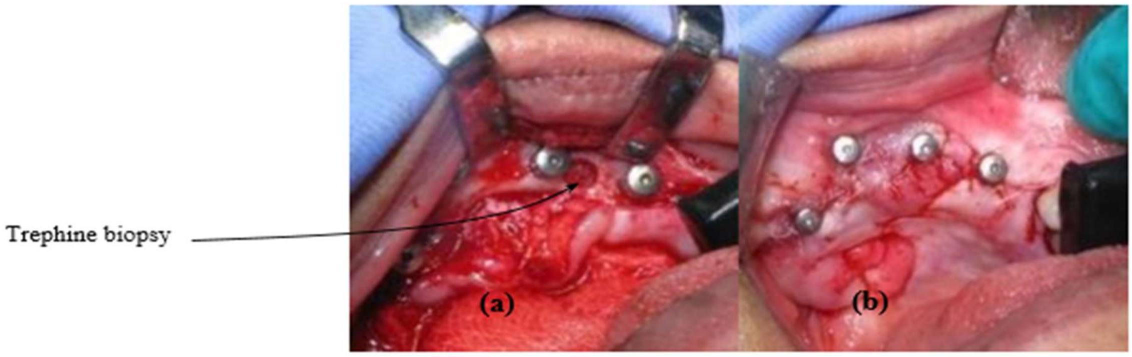

Figure 7.25: (a) The trephine biopsy done at the same time of dental implant placement. (b) The successful placement of four dental implants with healing abutments.

7.3.9 Prosthetic rehabilitation

The implants were allowed to osseo-integrate for about four months. A prosthodontist fabricated a bar-over-denture system which is shown in Figure 7.26(a) below. The patient was extremely happy with the way in which the partial upper denture integrated with her existing teeth and also the excellent support that the bar and over-denture system gave to her facial musculature. The quality of life of this patient has been greatly improved, as illustrated by her delighted smile (Figure 7.26(b)).

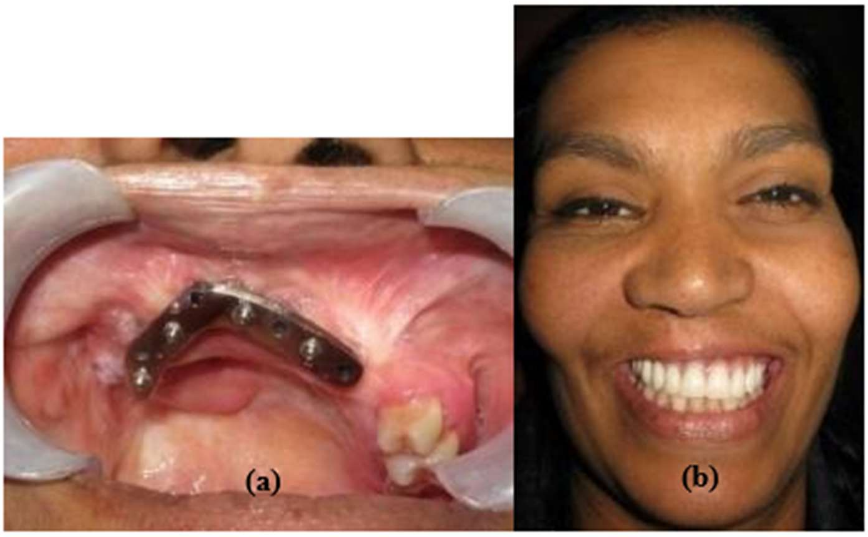

Figure 7.26: (a) The solid bar supported by four well integrated dental implants.(b) The highly satisfied patient (consent obtained).

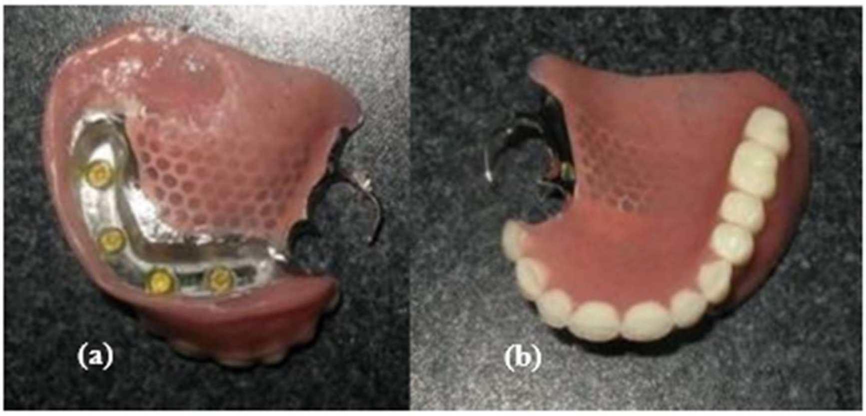

Figure 7.27: (a) The precision of attachments on top of the bar system. (b) The metal reinforced denture system.

Figure 7.28: (a) The intraoral situation with a very well-fitting upper denture in good dental occlusion with the lower teeth.(b) The natural way that the upper denture blends with the existing dentition.

The prosthodontic detail of the reconstruction is illustrated above in Figures 7.27 and 7.28 respectively. In spite of the intial setbacks, a surprisingly pleasing result has been achieved.

CHAPTER 8. LATEST VERSION CONCEPTUALISATION – THE V3 DISTRACTOR

The observations made on the V1 and V2 distractors culminated in an improved design for a functional distraction device that could be used for repairing major curvilinear defects, employing the concept of CTDO. The V3 distractor (Figure 8.1) is easy to customise and to install. It is also perfectly comfortable for the patient and satisfies all the conditions of the product requirement specification in section 4.8.

The V3 device makes use of the same worm-rack traction principle as was utilised in the V2 predecessor. However, it introduces new ergonomic improvements in its ease of installation so that the various shortcomings experienced in the previous clinical cases described in subsections 6.5.1 and 7.2.4. are avoided.

The most critical aspect of CTDO relates to the installation procedure, whereby the outcome of the treatment is influenced by the stability and integrity of the bone anchorage. Also, patient comfort, as well as the vector of the distraction, will determine the aesthetic and functional quality of the result. An overview of the device and its components is provided in section 8.1 where a description of its functionality and capabilities can be found as well as an explanation of the main design decisions. The latter is followed by a numerical justification of the critical dimensions in section 8.2.

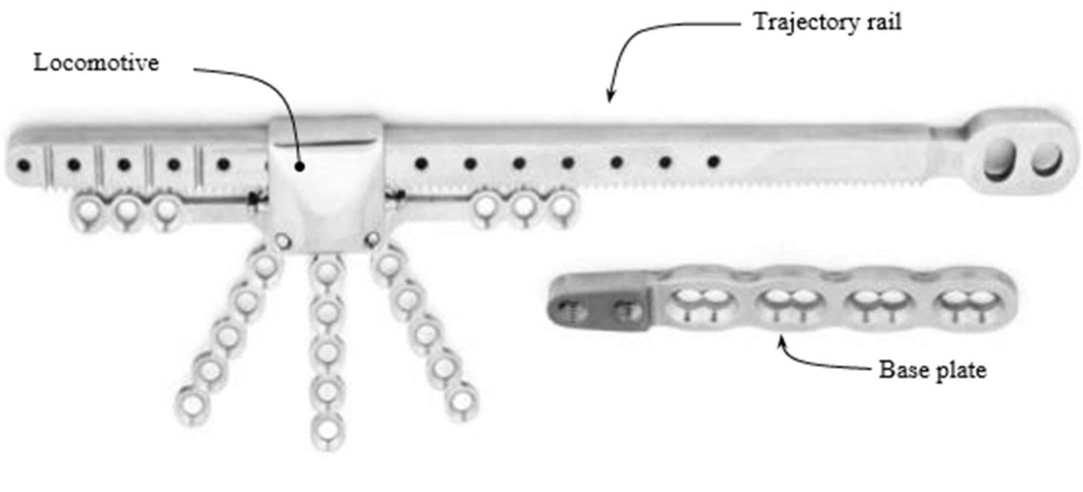

Figure 8.1: Manufactured final V3 prototype before customisation.

8.1 Description of the V3 distractor hardware

The V3 distractor comprises three main components: the base plate, trajectory rail and locomotive (Figure 8.2). The function and structure of each component is described below.

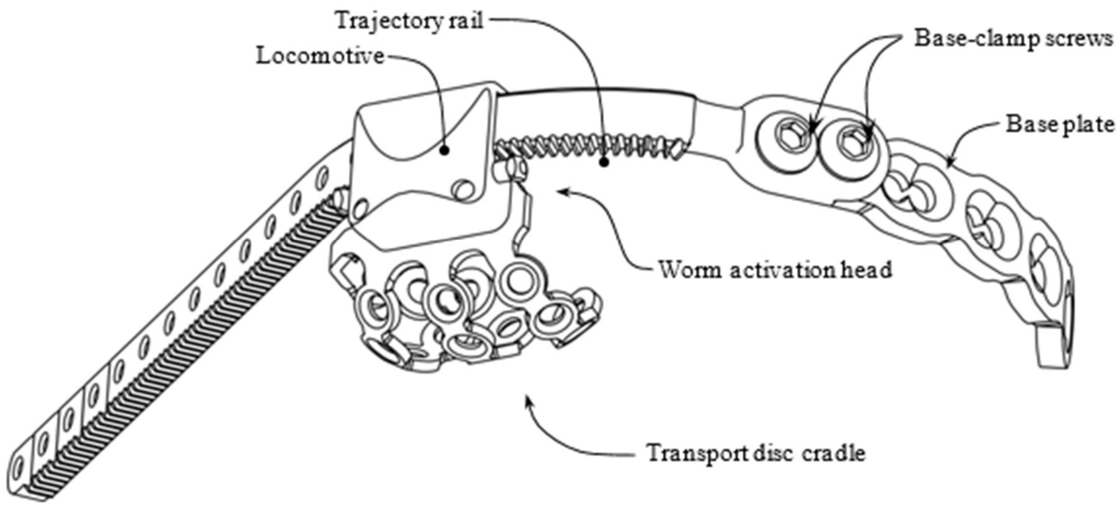

Figure 8.2: Labelled diagram of the CTDO device after customisation, ready for installation.

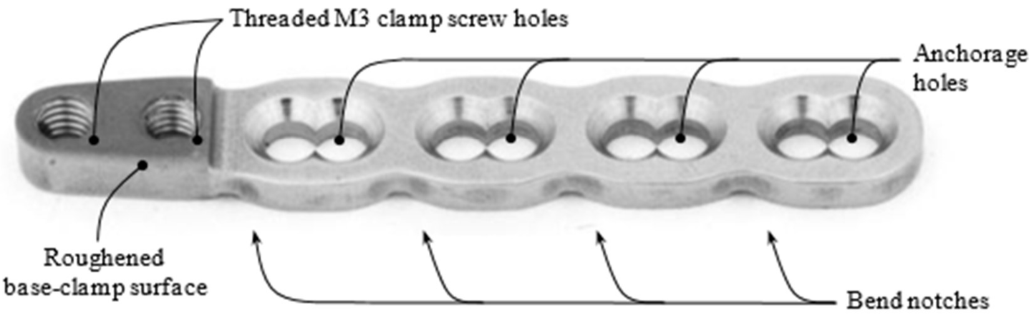

Figure 8.3: Manufactured baseplate, with two threaded clamp screw holes to the left and four pairs of anchorage holes to the right.

8.1.1 Base plate

The base plate (Figure 8.3) was developed because of the need to repeatedly attach and remove the trajectory rail during the procedure of surgical installation. In order not to disturb the bone anchorage through the repeated insertion and unscrewing of intra-osseous screws (which eventually lose their grip), a once-off, firm installation of the base plate would lend a rigid support to the trajectory rail.

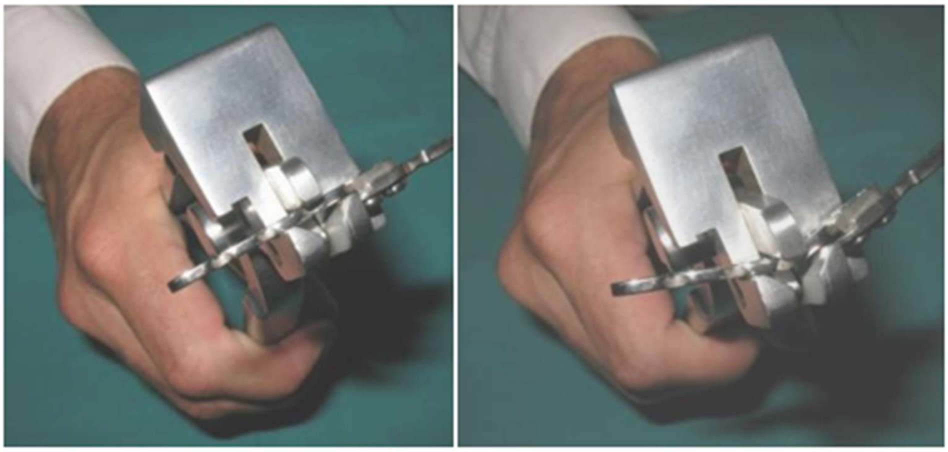

Figure 8.4: Pre-operative bending of the base plate to fit maxillary contour using the Biomet^{TM} plate bender.

The base plate is primarily a 2 mm thick titanium strip, divided into four segments by distinct bend notches (Figure 8.3). The plate form can be approximated and applied to the surface contours of the maxilla (Figures 8.4 and 8.5) and trimmed to the appropriate length. Bending of the plate is concentrated at the notches, thereby minimising undesirable distortion of the intermediate anchorage holes. The tools required for bending and trimming (e.g., the plate bender seen in Figure 8.4) are usually found in most maxillofacial surgical tool sets.

8.1.1.1 Layout of the base plate anchorage holes

To obviate the issues raised in subsection 7.2.4.4., the arrangement of the base plate anchorage holes was made to accommodate up to 4 anchorage screws, but also with enough placement options to avoid damage to the roots of the teeth in the maxilla.

The length, or pitch, of each of the segments in the base plate emulates the approximate spacing of the anterior teeth in adults (7.5 mm).[6] Thus, the base plate can be fashioned and positioned in such a way that the centre of each segment is more or less located between the roots of the teeth where there is adequate bone material to receive the anchorage screws.

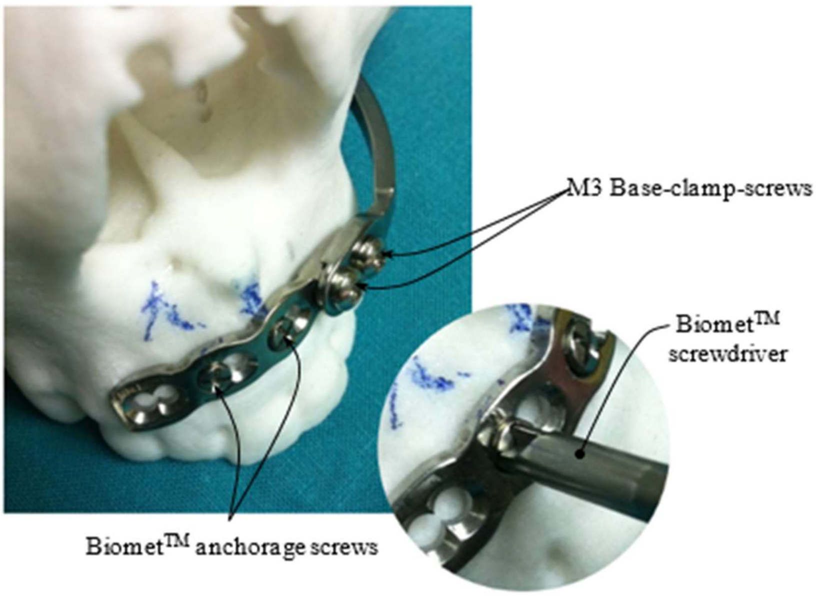

Figure 8.5: Base plate anchorage to maxilla using 6 mm – 10 mm long mono-cortical anchorage screws.

As shown in Figure 8.3, each segment of the base plate is perforated by a symmetrical pair of anchorage holes. The holes within each anchorage section are placed 2.4 mm apart so that the installer has two options to angle the anchorage screws at a pitch of 7.5 mm to avoid damage to dental roots.

[6]Tooth spacing based on measurements of 3 life-size adult stereo-lithographic cranial models and case studies of existing plating systems.

Each pair of anchorage holes is designed to accept only a single screw. This prevents the placement of screws less than 5 mm apart, as the placing of two screws in such proximity or closer might endanger the integrity of the bone. The base plate can accommodate up to 4 anchorage screws of up to 2.4 mm in diameter, each of which can be inserted at an angle of up to 15° to the anchorage hole axis.

8.1.1.2 Detachability of the trajectory rail

Once the baseplate is anchored to the bone, it facilitates numerous placements and removals without compromising the retention and stability of the device (subsection 7.2.4.1). **The latter feature represents a vital improvement to the apparatus.**

As shown in Figure 8.3, the segment at the end of the base plate has two M3 threaded holes; it is referred to as the 'base-clamp segment'. These holes are used to attach and re-attach the trajectory rail once the base plate has been suitably anchored (Figure 8.3). The base clamp segment is 3 mm thick, which provides sufficient length for the M3 clamp screws and prevents distortion of the base clamp section during customisation of the base plate. Coarse sandblasting was used to roughen the opposing clamping surfaces of the baseplate and trajectory rail (Figures 8.3 and 8.6) to increase the friction between the clamped surfaces. Further explanation of the base clamp interface is provided in subsection 8.1.2.

8.1.2 Trajectory rail

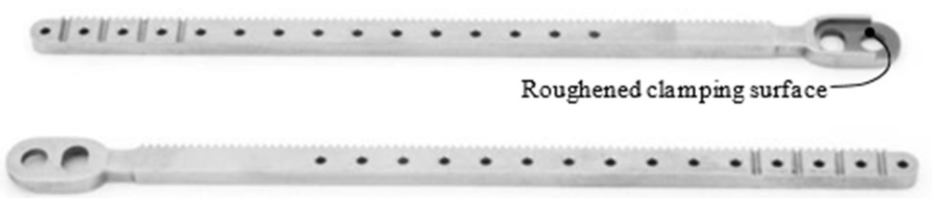

Figure 8.6: Front and rear views of the trajectory rail.

The trajectory rail (Figure 8.6) is a 2.5 mm x 4 mm rectangular titanium bar with a toothed rack on the inferior rim. By using the plate-bending tools found in standard maxillofacial tool sets, the rail can be bent and trimmed to the desired curvature and length (Figure 8.8) to produce the planned distraction path. The device accommodates a minimum bend radius of 25 mm, as prescribed in the PRS (section 4.8).

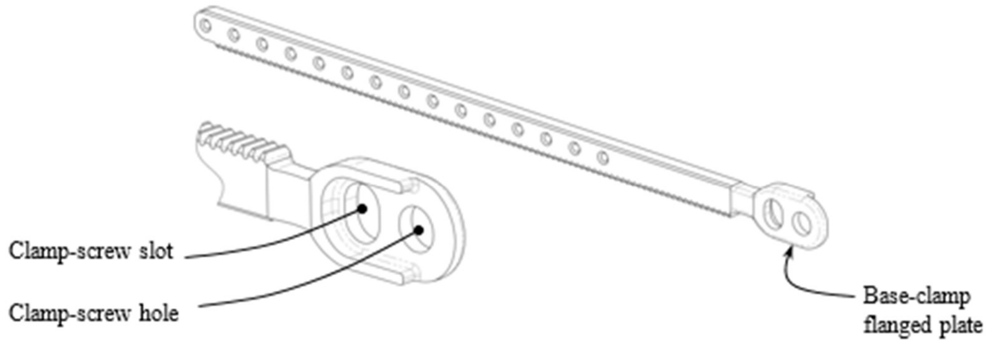

Figure 8.7: Rail and detail of flanged plate.

At one end, the trajectory track culminates in a flanged plate with two perforations (Figure 8.7). These holes match the clamp-screw arrangement in the base plate (as described in section 8.1.1 and illustrated in Figures 8.3 and 8.5). This feature allows the trajectory rail to be repeatedly attached and released, and permits the *in situ* adjustment of the exit vector, which is the angle (or direction) at which the trajectory track departs from the base clamp. **This is a useful feature for correcting the distraction plane or the cant of the occlusal plane of the rail during placement, and is referred to as the exit vector.**

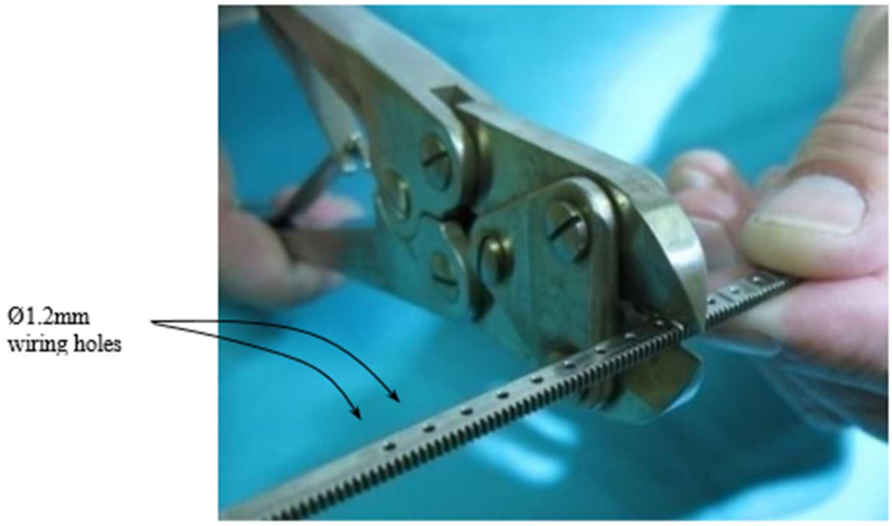

Figure 8.8: Pre-operative planning – trimming of the trajectory rail.

The exit vector is adjustable in the following three modes:

1. The base clamp permits adjustment of the trajectory rail over a range of 10° (+5° to -5°) in the vertical/coronal plane (Figures 8.9, 8.10 and 8.11).
2. By bending and twisting the trajectory track at the neck of the clamp flange, the exit vector can be adjusted in two dimensions:
   i. It can be turned sharply to set the exit vector direction within the distraction plane[7] (Figure 8.12(a)).
   ii. It can be twisted to adjust the tilt of the distraction plane (Figure 8.12(b)).

The geometry of the distraction trajectory can be adjusted intra-operatively by the installer with three different modes of adjustment, and as the trajectory rail can be detached and reattached, this does not disturb the anchorage to the bone.

The trajectory rail is perforated with a series of 1.2 mm diameter holes along its length, spaced 5 mm apart (Figure 8.8). The primary purpose of these holes is to allow attachment of the rail

[7] The **distraction plane** is a plane parallel to the occlusal plane, at a level specified by the installer.

to the buttress plates at the position of the **confluence** (section 8.1.4), but they also provide additional wiring points or locations to place sutures, should the installer so require.

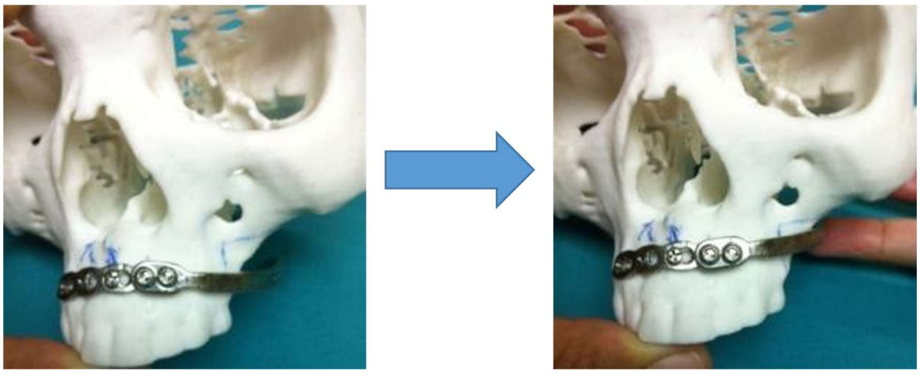

Figure 8.9: Illustration of base-clamp angle adjustment on cranial model.

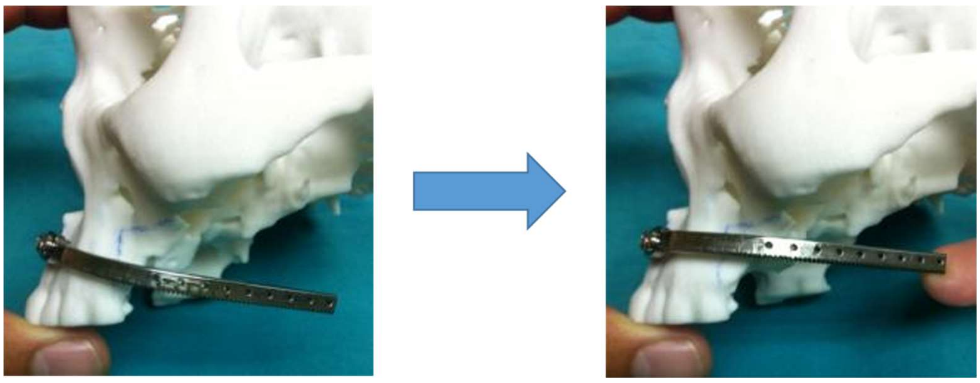

Figure 8.10: Illustration of base-clamp angle adjustment on cranial model.

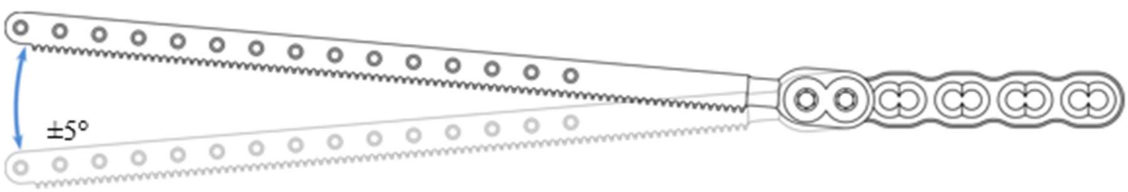

Figure 8.11: Vertical alignment of the exit vector.

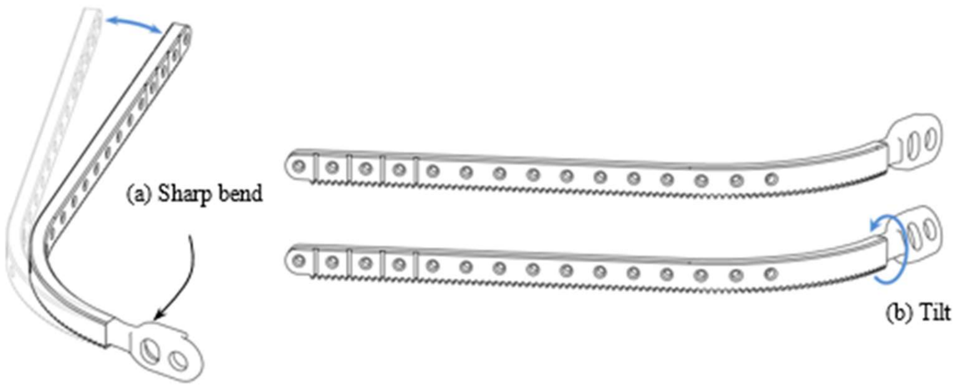

Figure 8.12: Adjustment of the exit vector and distraction plane tilt.

8.1.3 Locomotive

The locomotive is attached to the bone transport disc and stabilises, supports and propels the transport disc along the distraction path described by the trajectory rail. It consists of three components: a titanium housing, a titanium cradle plate, and a stainless steel worm-screw. These are secured by two M2 Torx-screws threaded into the housing (Figure 8.13).

The cradle plate (Figure 8.13) has five extension strips that radiate outwards from its centre. These strips can be bent and trimmed by the installer to form a cradle that envelops the bone transport disc as shown in Figure 8.14. A series of countersunk holes in each strip allow the placement of monocortical bone screws of up to 2 mm diameter. The bone screws secure the bone transport disc to the cradle from various directions, holding it securely in place in three axes. Figure 8.14 shows the carrier disc cradle *in vivo*.

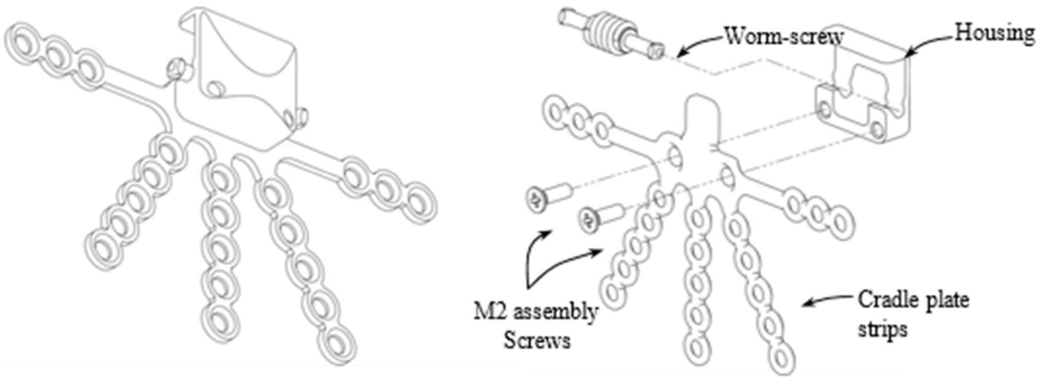

Figure 8.13: Labelled exploded locomotive assembly.

As shown in Figure 8.14, the 1.75 mm screw-heads are readily accessible to the installer because they protrude from both ends of the locomotive. A standard Biomet™ distraction screwdriver can be applied to the worm-screw head. The design of the worm-screw head permits axial misalignment between the screwdriver and the worm-screw of up to 15° in all directions (Figure 8.15), thus eliminating undesirable bending stresses on the worm-screw, and improving accessibility during installation and activation.

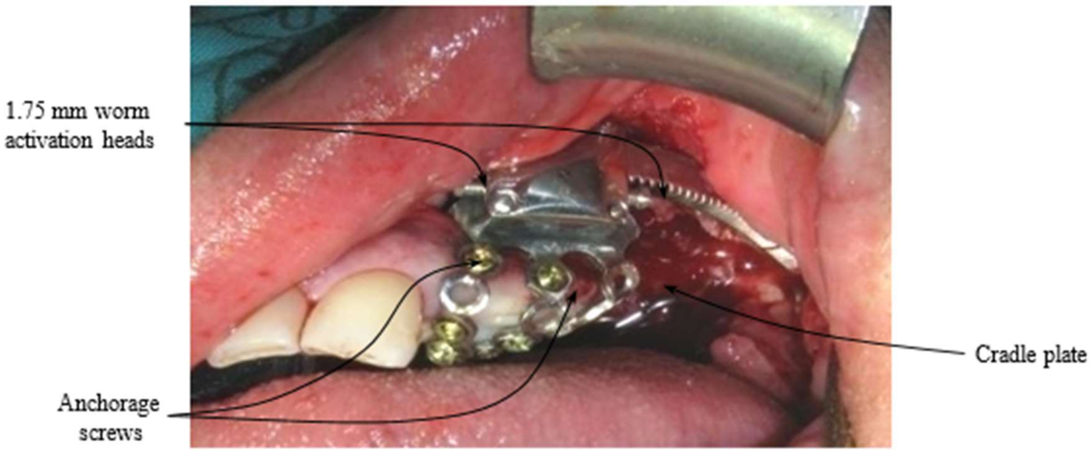

Figure 8.14: Locomotive *in vivo* – bone transport disc secured to cradle using anchorage screws.

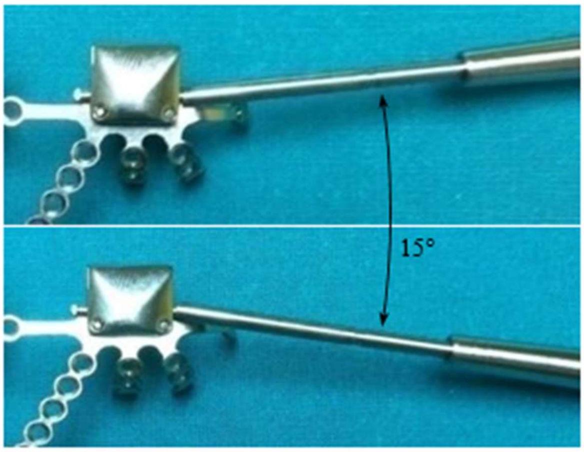

Figure 8.15: Axial misalignment permitted between the distraction screwdriver and the worm-screw.

As the V3 distractor is an intraoral device, its activation is also achieved through an intraoral approach (section 4.4). As was the case in the V1 and V2 clinical cases, intraoral activation of the device was found to be straightforward and efficient, without the need for any peripheral extension devices to assist access to the distraction device. Nevertheless, there may be instances where the device cannot be activated directly by the distraction screwdriver without causing discomfort to the patient. In anticipation of such cases, the device was made compatible with various commercially available extensions. A significant design refinement between the V2 and V3 distractors was the reduction in size and thickness of the locomotive, resulting from the more compact trajectory rail and design of the locomotive assembly. The overall dimensions of the V3 locomotive were reduced to 61% (height), 86% (length) and 86% (depth) of the V2 prototype dimensions (Figure 8.16). Overall, the V3 locomotive had a volume that was 49% of the V2 prototype, though both versions employ the same traction mechanism. As per recommendations in the literature, the outer surface of the locomotive was contoured and polished to a matt-like finish to reduce soft tissue abrasion and thereby improve patient comfort, while reducing glare during surgery.

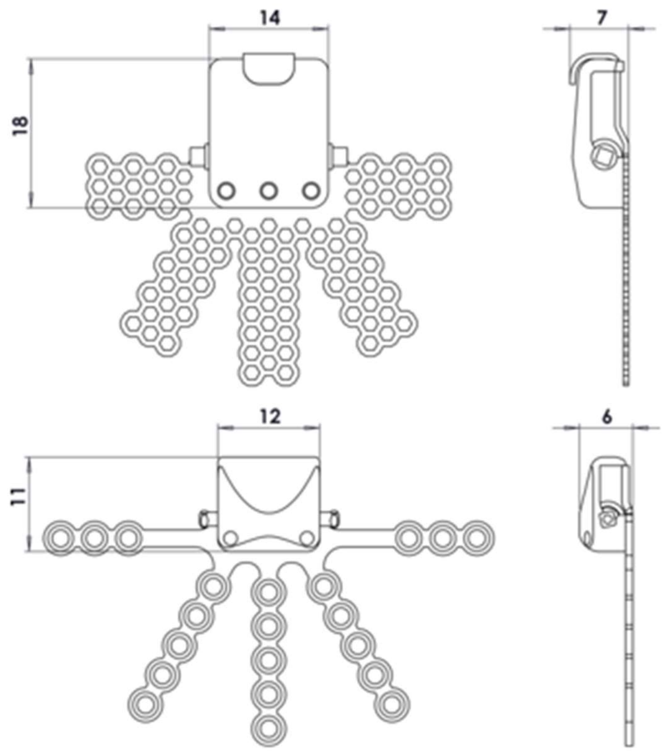

Figure 8.16: Size reduction of the locomotive between the V2 (top) and V3 (bottom) prototypes.

8.1.4 Buttress plates and confluence

Figure 8.17 shows the fully assembled V3 device pre-installed on a 3-D cranial model during the preoperative planning stage. As seen in the previous V1 and V2 devices, the V3 distractor also utilises buttress plates to stabilise the posterior aspect of the trajectory rail. As mentioned before, the point at which the buttress plates meet the trajectory track is known as the confluence. The author required a means of securing the confluence junction that was sufficiently rigid, yet easy to assemble and dismantle. Even though the use of plain wire at the confluence joint was considered to be more than sufficient for three-dimensional stability, the need for a more aesthetic alternative became an ongoing concern. Throughout the development of the V1, V2 and V3 devices, various alternative concepts were developed in consultation with the surgical and engineering teams. However, in spite of the different options, a wired confluence offered the following benefits:

- proven ease of implementation and removal, as experienced in the V1 clinical case

- allows secure connection of the trajectory rail and buttress plates
- provides a more cost-effective solution than sophisticated alternatives
- can easily be implemented using existing surgical tools
- involves no small or loose metal parts.

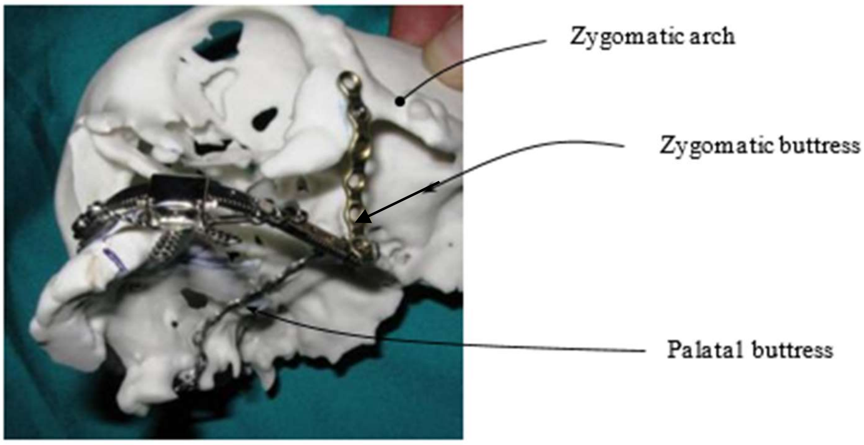

Figure 8.17: Pre-operative planning – fully customised device installed on the cranial model, with zygomatic and palatal buttresses and wired confluence.

8.2 Quantitative design

The development of the V3 distractor, as discussed at the beginning of Chapter 8, was mainly qualitative in approach, because essential requirements pertained primarily to patient comfort, user interface, and similar ergonomic factors. Nevertheless, some calculations were carried out to confirm the strength of critical features. However, these calculations could only be as accurate as the relevant design parameters.

As CTDO performed in the maxilla has no precedent anywhere in the world, many relevant aspects of this procedure were not yet clarified. Consequently, many of the mechanical requirements of the V3 device were similarly unclear. Hence, a fair number of the design calculations were not based upon accurately known parameters; instead, it was ensured that the strength, rigidity and size capabilities of the device were within reasonable parameters.

The current section discusses the quantitative aspects of the design.

8.2.1 Rail deflection owing to intraoral loads

As the quality of the new bone created using CTDO is critical, it is of fundamental importance that the device remains as sturdy and stable as possible and adheres to the principles of micromotion described in subsection 4.2.4.

As discussed in Chapter 3, the formation of the healing callus requires a highly stable mechanical environment to form the desired type of bone. During the period of latency, it is imperative that the callus remains stable before the commencement of active distraction. Sun *et al*. in 2007 specified that micromotion of up to 0.3 mm is tolerable.[266] Once the callus formation stage has been concluded, and the distraction process commences, only then does the stability of the bony fragments become less critical. This is the case for two reasons:

1. Once formed, buffering against micromotion is afforded by the cartilaginous healing callus which stabilises the fracture surfaces.
2. After the period of latency, the bone transport disc is distracted at a rate of 1 mm to 1.5 mm per day, and the relatively minor contribution of micromotion becomes irrelevant.

The effects of various tongue forces on the stability of the healing environment were investigated. However, the relatively large forces exerted by the lower jaw were not relevant. Considering their necessarily small size, no intraoral TDDO devices, nor their anchorage to the surrounding bone, could realistically withstand normal chewing forces. For this reason, the treatment protocol specifies mainly liquid food and encourages mastication to take place away from the distraction apparatus.

8.2.1.1 Trajectory rail deflection models

In a practical sense, the anterior base plate and the posterior zygomatic and the alveolar buttress plates provide three points of fixation, which constrain and stabilise the trajectory rail in the desired distraction plane.

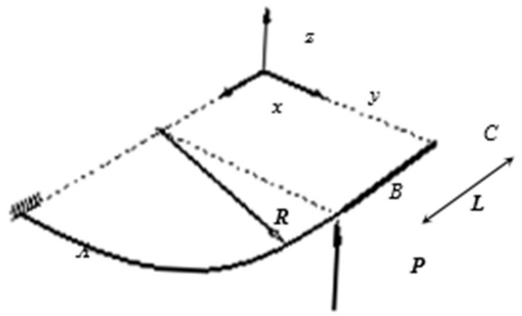

Figure 8.18: Diagram of bending model of trajectory rail for a vertical load. [264]

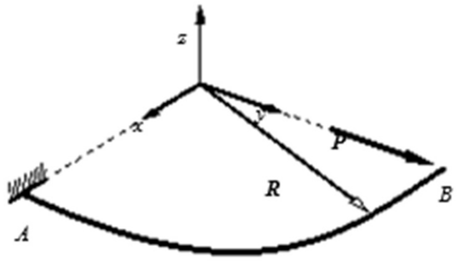

Figure 8.19: Diagram of lateral deflection model of trajectory rail for a lateral load. [264]

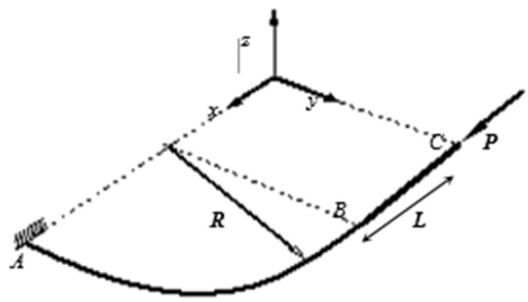

Figure 8.20: Diagram of bending model of trajectory rail for a tangential distraction load. [264]

However, the stabilising contribution of the posterior buttress plates could not be theoretically established. Given the uncertainty of the practical environment, any attempts to do so would be misguided. Therefore, when investigating the deflection characteristics of the trajectory rail, the contribution of the posterior anchorage was neglected, conservatively modelling the trajectory track as a cantilevered beam that is supported only by the anterior base plate (Figures 8.18-8.20) and the zygomatic buttress plate.

It was found that even if the contribution of the palatal buttress plates is neglected, the stability of the trajectory rail remains adequate.[264] (This stability has also been clinically demonstrated operationally by the author.)

Based on the configurations illustrated in Figures 8.18 – 8.20, Castigliano's second theorem[265] modelled the trajectory rail as a cantilevered curved beam, subjected to two types of loads:

1. Forces exerted by the tongue

Interestingly, the forces exerted by the tongue were only those in the lateral and vertical direction which act upon the posterior segment of the trajectory rail (Figures 8.18 and 8.19). Trawitzki *et al.* (2011) present an average maximum vertical tongue force of 12 N in adults of 18 – 32 years of age.[256] A separate study by Dworkin *et al.* in 1980,[258] gives an average maximum lateral tongue force of 16 N (Figure 8.21), based on a study of tongue force in healthy subjects.

2. Forces owing to callus stretching

Regarding the strength of the device, it was therefore of paramount interest to the author and engineers what the callus stretching force would demand (Figure 8.20). Regarding the trajectory rail deflection, it was expected that the maximum of the callus stretching force would be approximately 66 N acting on the rear end of the rail.

The cross-sectional dimensions of the trajectory track (2.5 mm x 4 mm) were guided by the ergonomic requirements of the device and the availability of materials. The Castigliano deflection calculations were applied to assess whether this design was adequate. The results were found to be affirmative [264].

There was only one reference in the literature that was considered to elucidate the tolerable limits of micromotion. This study by Sun *et al.* in 2007 presented that micromotion as high as 0.3 mm demonstrated no adverse effects on the success of distraction osteogenesis treatment.[266]

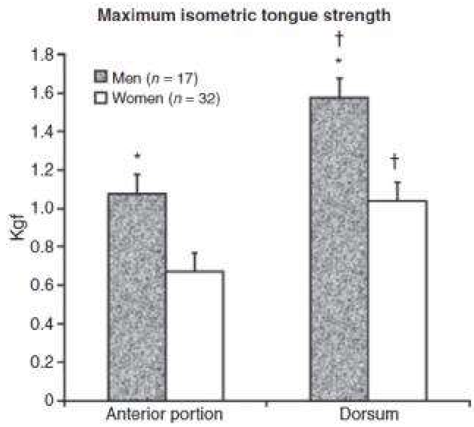

Figure 8.21: Vertical tongue force in young adults. Of interest was the force exerted by the anterior tip segment of the tongue.[255]

Note: It must be emphasised that all mathematical calculations, design drawings and manufacturing procedures were carried out by Mr James Boonzaier.[264]

8.3 Testing of the V3 prototype

All laboratory tests were carried out by Mr James Boonzaier at the Department of Mechanical Engineering, UCT, as part of his MSc dissertation.[264]

The performance of the V3 device was evaluated in two stages:

1. Laboratory testing to assess whether the traction mechanism and other critical features met the requirements of the Product Requirement Specification in section 4.8.
2. The subsequent clinical implementation provided an opportunity to observe and evaluate the ergonomic performance aspects of the device.

8.4 Laboratory testing

Guided by the PRS, the aims of laboratory testing were to assess whether:

1. The device as a whole could achieve CTDO along the 25 mm minimum radius trajectory, against the design load of 100 N.
2. The worm-rack interface could safely withstand the design load of 100 N.
3. The worm-screw could withstand torque corresponding to a 100 N distraction force.
4. The base clamp joint could withstand the effects of a 12 -16 N vertical tongue force.
5. The self-locking action of the worm screw was satisfactory.

8.4.1 Distraction force capabilities

8.4.1.1 Results – linear trajectory with a longitudinal load

The device successfully produced the required maximum distraction load of 100 N. The maximum activation torque measured was 18.56 N.cm in the dry case and 8.82 N.cm in the wetted case, both of which fall within the 20 N.cm limit specified in the PRS (section 4.8). The dry test provided a measure of the absolute worst case, but for all practical purposes, the 8.82 N.cm reading was more relevant. The relationship between activation torque and distraction load was found to be exponential over the tested range. The device performed consistently, and the graphical results were closely approximated by an exponential trendline, as shown in Figures 8.22 and 8.23. These graphs illustrate the maximum, minimum and mean activation torque required to generate distraction forces up to 100 N.

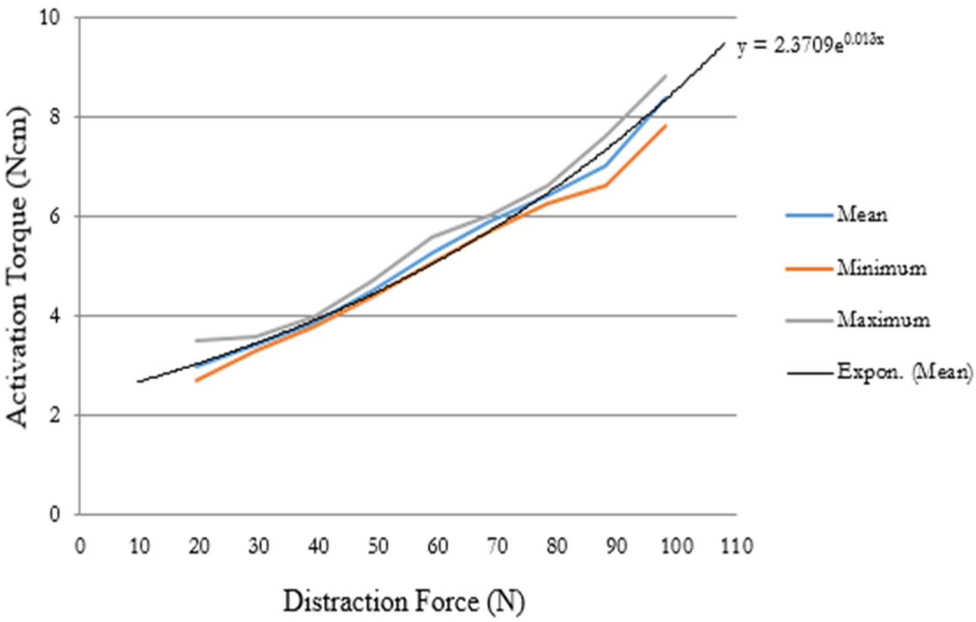

Figure 8.22: Activation torque v. distraction force on a straight trajectory, wetted with a detergent solution.

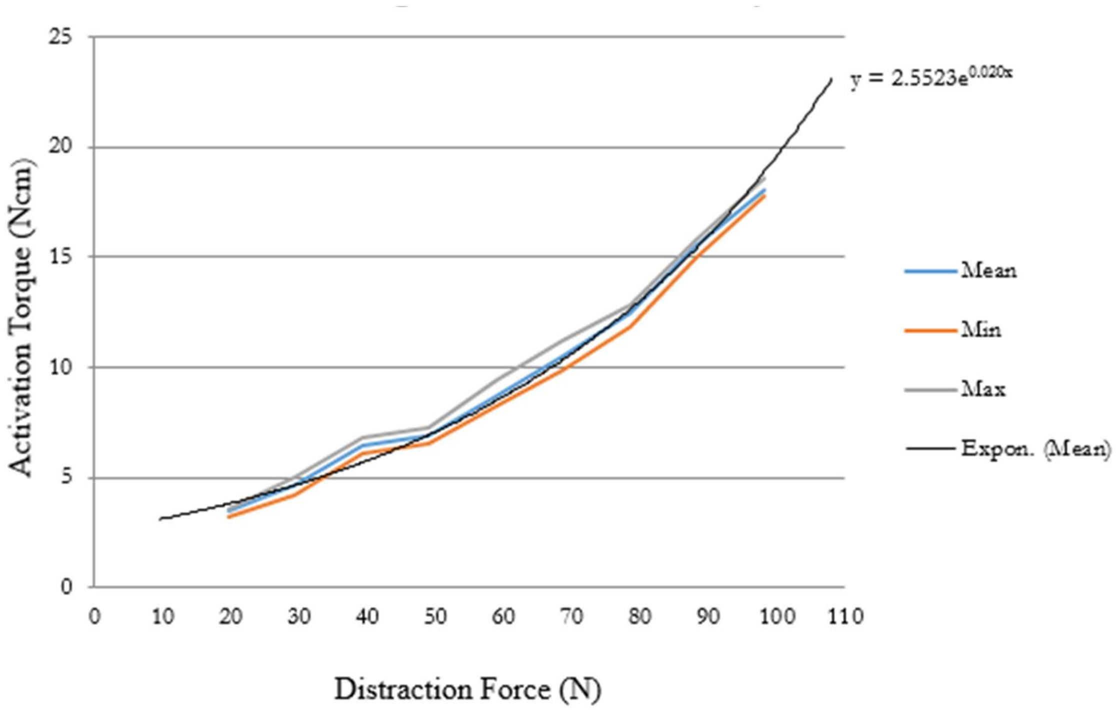

Figure 8.23: Activation torque v. distraction force on a straight trajectory, dry.

8.4.1.2 Tipping moment: Linear trajectory with an offset load

In the clinical situation, the callus stretching force acts at a distance of up to 10 mm from the worm-rack engagement, which generates a net tipping moment on the locomotive. To investigate these effects, the procedure described in subsection 8.4.1.1 was repeated under wet conditions, with the load acting on the locomotive over a moment arm of 4 mm and 10 mm, measured from the worm-rack (Figure 8.25). For each load, the device was activated by one full rotation in four quarter-turn increments. The highly sensitive torque-measuring screwdriver is shown in Figure 8.24 below.

Figure 8.24: BMS MS050S electronic torque screwdriver.

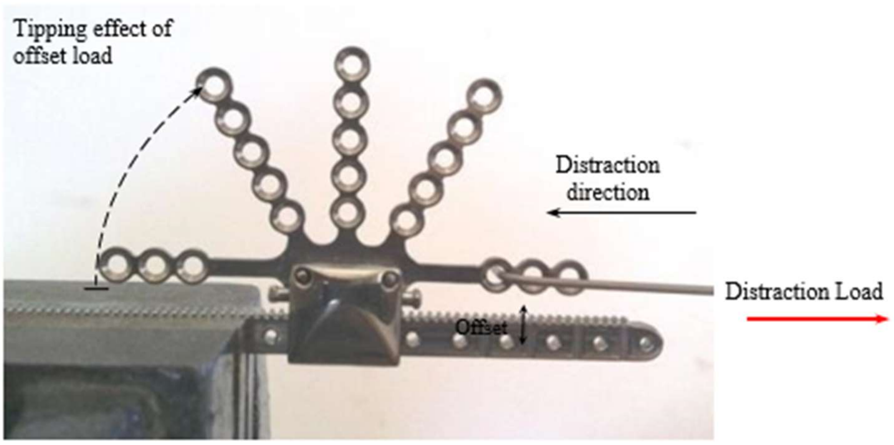

Figure 8.25: Locomotive testing with 4 mm offset load, indicating the tipping effect.

Each of the trendline functions presented above is based on an entirely independent data set. The similarity of the coefficients demonstrated the consistent behaviour of the device for a given set of loading conditions. For example, in the case of the 10 mm offset load, the base coefficients were 2.097 and 2.133 and the exponent factors were identically 0.017 and 0.017 in two independent tests. The proximity of the maximum and minimum curves in Figures 8.26 and 8.27 demonstrates the consistent behaviour of the device. The laboratory results in testing the worm and rack engagement are shown below when an offset distraction force is applied on the carousel.

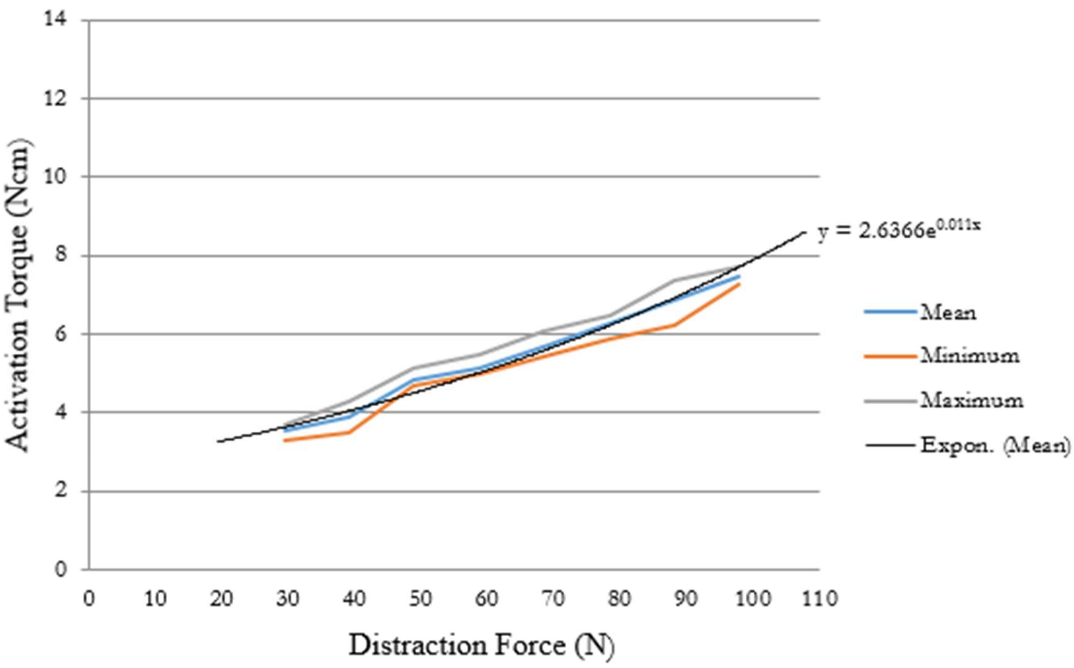

Figure 8.26: Activation torque v. distraction force on a straight trajectory with a 4 mm offset load, wetted with a detergent solution.

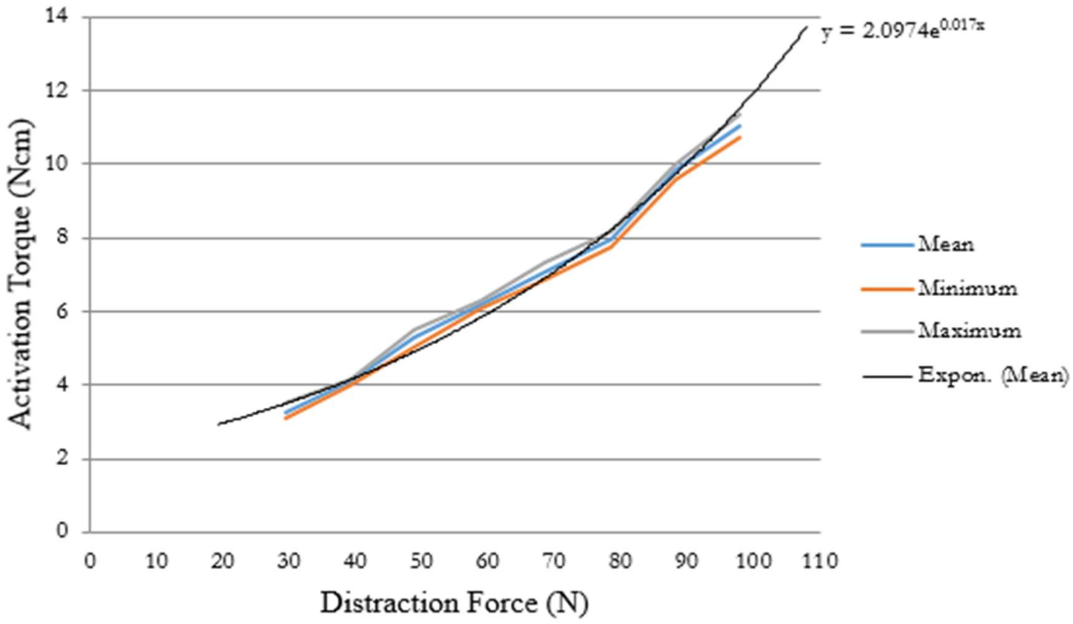

Figure 8.27: Activation torque v. distraction force on a straight trajectory with a 10 mm offset load, wetted with a detergent solution.

8.4.1.3 Curvilinear distraction under load

To assess the reliability of the device before progressing to clinical implementation, a simulated distraction was conducted on a curvilinear trajectory with the device subjected to incrementally increasing distraction loads up to 100 N. A test rig was constructed whereby the locomotive could be loaded approximately tangentially with the desired force (Figure 8.28). Mass pieces provided the weight and a spring scale provided a reading of the applied force.

The curved trajectory rail mimicked the worst expected case, with a bend radius of 25 mm. The curvilinear laboratory test results in testing the worm and track engagement, are shown below.

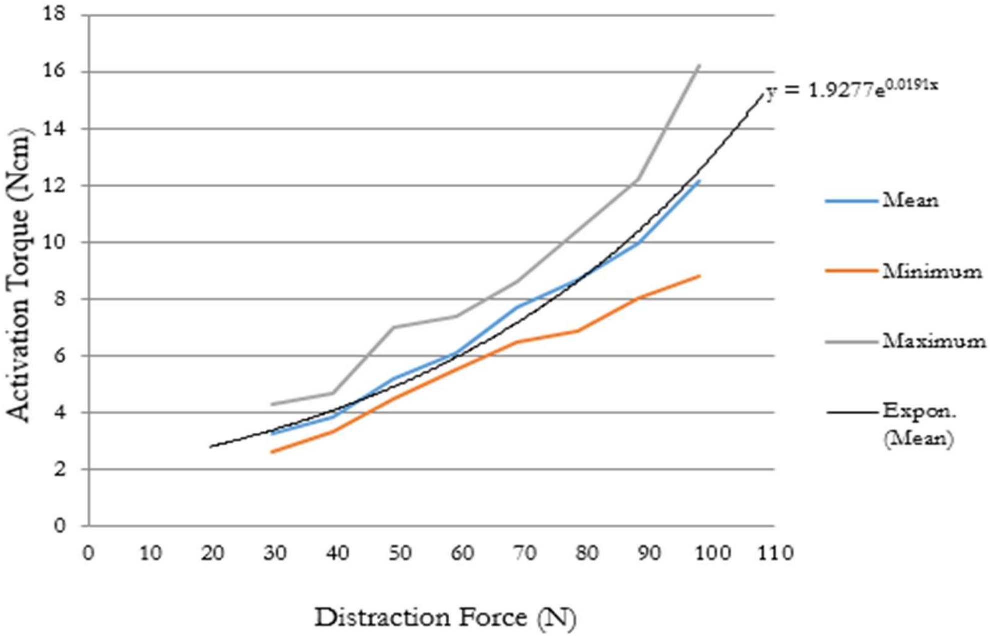

Figure 8.28: Activation torque v. distraction force with an offset load on a curved trajectory, wetted with a detergent solution.

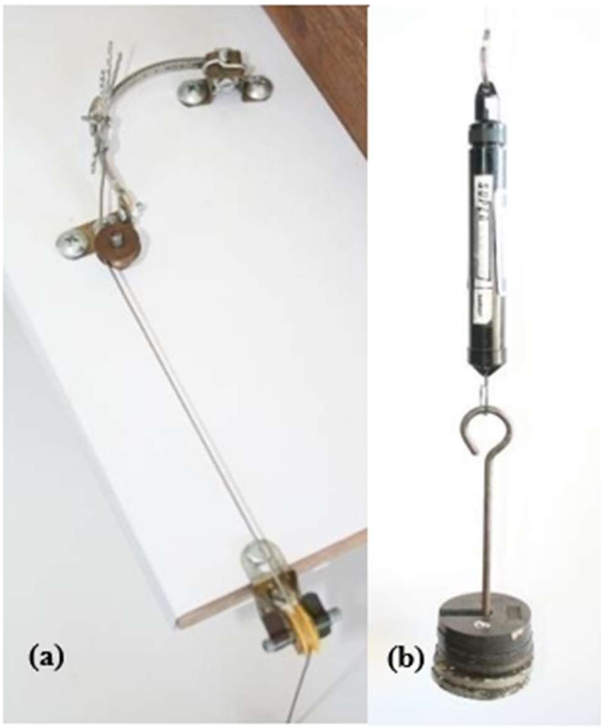

Figure 8.29: (a) The test rig for simulated curvilinear distraction. (b) The spring balance and mass piece connected to the cable in (a).

As discussed in subsection 8.4.1.2, comparing the coefficients in each equation gave an indication of how consistently the device behaved for a given set of operating conditions (Figure 8.29). Of all of the tests, the steepest gradient between activation torque and distraction force was observed in the curvilinear distraction test. Figure 8.30 compares the torque v. distraction force relationship.

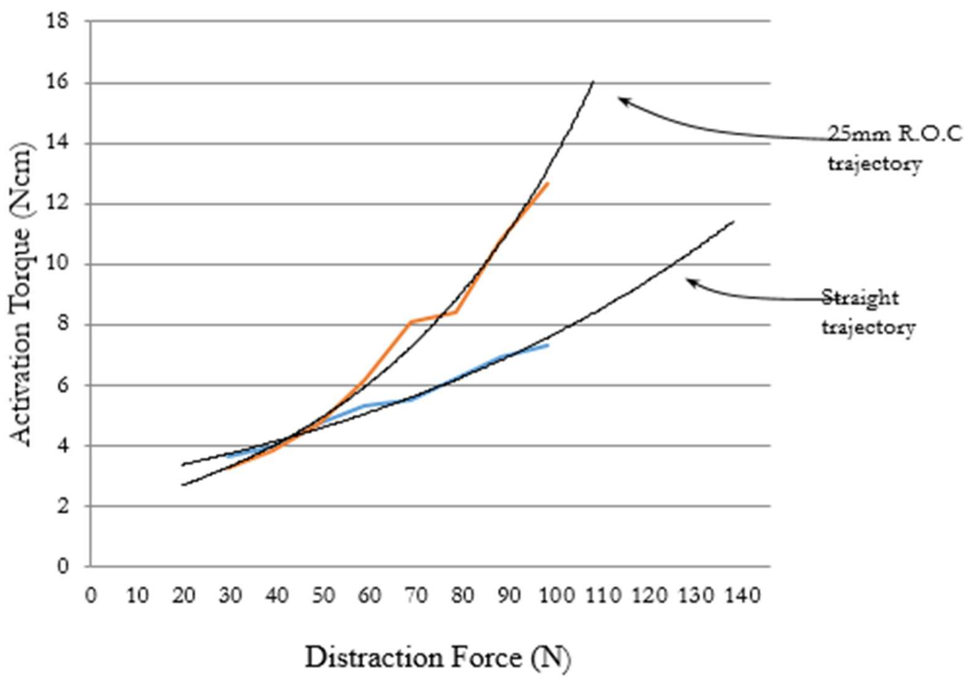

Figure 8.30: Activation torque v. distraction force with a 4 mm offset load on a curved v. straight trajectory, both wetted with a water-detergent solution. ROC refers to radius of a curve.

8.4.2 Ultimate strength testing of critical features

Features of the device with critical strength requirements were tested to establish their capabilities and the relevant safety factors. Each feature was submitted to incrementally increasing loads, either until failure occurred or until the specified upper limit was reached.

Testing assessed the following critical features:

- **Axial loading capabilities of the worm-rack mechanism**. The worm-rack traction device was subjected to an axial load up to a maximum of 200 N.

- **Torque-carrying capabilities of the worm-screw.** The worm-screw was subjected to torsional load up to 50 N.cm.
- **Tightening torque of the base clamp Torx screws**. A 2 N.m tightening torque was specified for the base clamp screws, based on laboratory slippage tests.

8.4.3 Results of laboratory testing

The purpose of laboratory testing was to assess whether the device could perform its function in the most extreme conceivable conditions, and to determine its ultimate strength capabilities. The conclusions of testing are presented below, arranged according to the aims outlined in section 8.4.

1. The V3 device navigated the minimum radius trajectory under a load of 100 N.

The apparatus performed successfully on both a straight path and the minimum 25 mm bend radius, in both cases subjected to loads up to 100 N.

2. The worm-rack interface withstood a load of 200 N – double the maximum expected distraction force of 100 N.

3. The worm-screw provides a safety factor of 2.18 over the maximum expected activation torque.

The maximum conceivable activation torque, determined by practical testing, was 16.2 N.cm. Strength testing of the worm-screw revealed a torque-carrying capacity of 35 N.cm, thus providing a safety factor of 2.18.

4. The base clamp joint withstood the effects of the maximum tongue force.

The base clamp joint sustained a moment of 2.47 N.m, providing a safety factor of 2.1 over the maximum foreseeable load of 1.2 N.m. In a separate test, the base clamp screws sustained a tightening torque of 4 N.m without failure, which is double the specified tightening torque of 2 N.m. Thus, a large margin of over-tightening can be accommodated.

5. The self-locking action of the worm-rack mechanism

The device exhibited retraction of less than 0.3 mm under extreme test conditions. These conditions mimicked disturbance by the tongue and the fluctuating distraction load. Given that distraction rates of 0.5 to 1.5 mm per day lead to the successful formation of bone, the 0.3 mm of retraction exhibited by the device was deemed acceptable.

8.5 Discussion: V3 clinical performance

The following observations were made during the third and fourth clinical cases, which employed the V3 distractor:

1. **The functionality of the base plate-trajectory rail interface was a highly beneficial development.**

By enabling the author to attach and detach the trajectory rail repeatedly, without disturbing the anchorage to the maxilla, the base clamp feature improved the efficiency of the installation procedure.

2. **Ease of deployment of the base clamp screws requires improvement.**

While the broad functionality of the base plate was found to be beneficial, the surgeon encountered difficulty with the base clamp screws. The screws were difficult to align with their respective threaded holes in the base plate. It was suggested that the design of these screws be refined with an unthreaded lead-in to aid alignment, and that tools are developed to improve the grip on the screw head for more controlled placement.

3. **Shaping of the cradle plate remained complicated.**

The cradle plate supports and secures the mobile bone transport disc. The V3 distractor employed a 0.8 mm thick titanium cradle plate. The surgical protocol requires that the cradle plate is formed so that it envelops the bone transport disc, to ensure that it is adequately supported. The author found that, within the V3 format, the cradle plate was excessively hard to bend. Also, work hardening of the material produced visible cracks in the cradle plate and led to breakage of one plate. The latter was partly attributed to the need for less than 1 mm bend radii on a relatively thick plate (0.8 mm).

The author suggested that the formability of the V2 cradle plate (0.5 mm stainless steel) was preferred.

4. **Repetitive removal of the trajectory rail to adjust the cradle plate geometry was time-consuming and awkward.**

To accurately shape the locomotive cradle plate, it was necessary to remove it from the mouth entirely. The V3 distractor facilitated this with the detachable base clamp feature. However, for the reasons mentioned in point 2 above, placement of the base clamp screws was awkward. It is suggested that, in future versions, the cradle plate should be designed to be detachable from the locomotive so that it can be quickly and efficiently removed and re-attached *in situ*.

5. Patients reported only minor discomfort.

Feedback from patients treated with the V3 distractor indicated that the device was unobtrusive. The most notable sources of irritation were the accumulation of food in the cradle plate and the palpability of the alveolar buttress plate in the roof of the mouth.

6. Clinical measurements of activation torque suggested only minor resistance from the healing callus at a distraction rate of between 1 mm and 1.5 mm per day.

The distraction activation torque was measured clinically using an electronic torque meter (subsection 8.4.1.1 and Figure 8.24). These *in vivo* measurements were consistently less than 4 N.cm.

Consulting laboratory data in the graphs from Figures 8.23 to 8.30, a 4 N.cm activation torque corresponds to a distraction force of approximately 40 N. This is well within the 100 N loading capabilities of the V3 device, as described in subsection 8.4.1.

8.6 First installation of V3 distraction device

The premaxillary region was degloved via a circumvestibular incision, and the zygomatic buttress was exposed in the second quadrant at the surgical defect. The roots of the anterior teeth were identified and the pre-shaped bone plate was approximated to the exposed bone (Figure 8.31).

Figure 8.31: Exposed bone and roots of the teeth in the anterior maxilla.

The base plate and trajectory rail were pre-assembled and placed so that the trajectory track was parallel to the occlusal plane. Once this was confirmed, the bone screws were placed into the base place, only once, so that the retention of the base plate was not degraded from repetitive placement and replacement of the intra-osseous screws (Figure 8.32).

Figure 8.32: Attachment of the base plate and trajectory rail.

The base plate remained *in situ*, and the trajectory rail could be removed and replaced at liberty to facilitate further development of the transfer disc, ensuring that the plane of the trajectory rail must always remains parallel to the occlusal plane (Figure 8.33).

Figure 8.33: Trajectory of the locomotive on the pre-bent trajectory rail.

Once the trajectory track had been removed, the locomotive was loaded onto the rail and tested for accuracy of movement and traction (Figure 8.34).

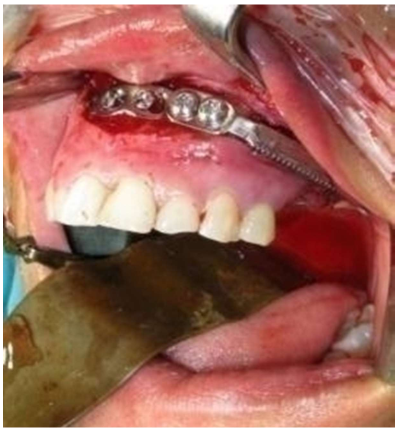

Figure 8.34: The trajectory rail placed parallel to the occlusal plane.

The horizontal and vertical osteotomies of the alveolar bone were carried out, always preserving the palatal mucosa (Figure 8.35 (a)). Once the transport disc had been mobilised, the basket of the locomotive could be attached to the transport disc. The finger extensions of the cradle were bent to accommodate the shape of the carrier disc (Figure 8.35 (b)).

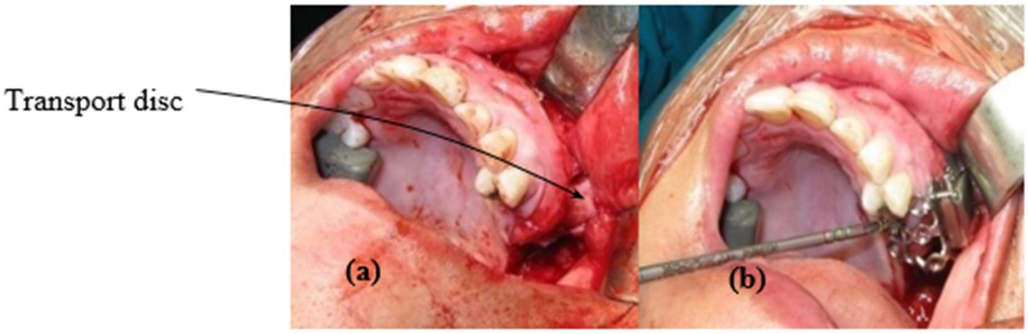

Figure 8.35: (a) The transport disc. (b) Attachment of the basket.

The 1.0 mm screws were placed at angles to each other. In this way, the transport disc was secured in all directions, ensuring the stability of the transport disk being constant during the process of distraction (Figures 8.36 and 8.37).

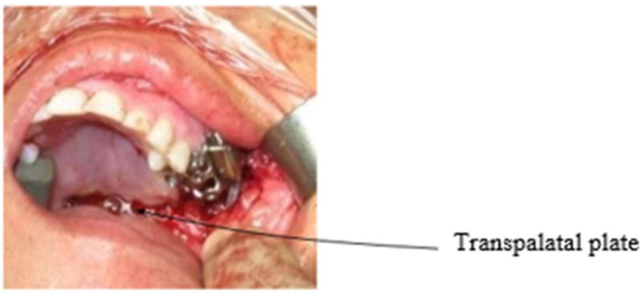

Figure 8.36: The 1.0mm screws securing the basket to the transport disc, and also the trans-palatal plate providing stability to the confluence.

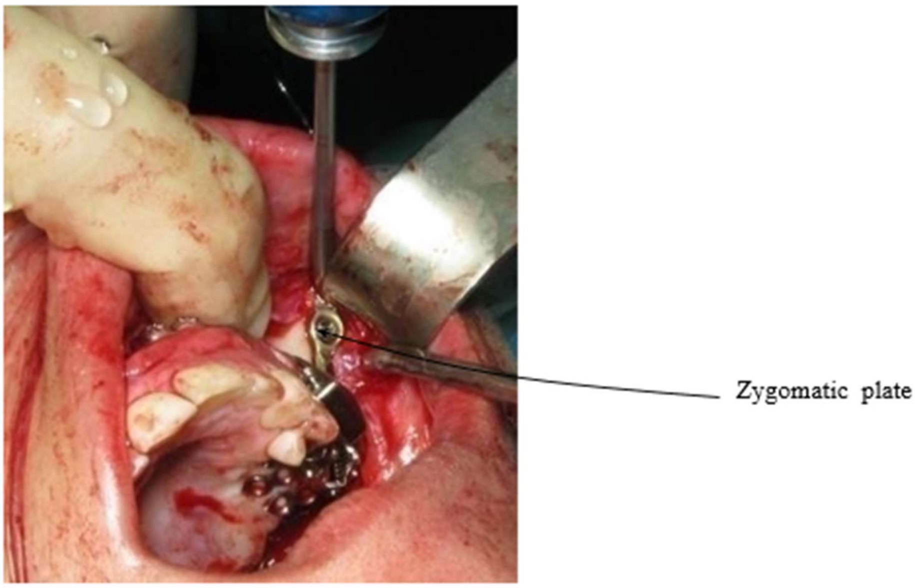

Figure 8.37: The zygomatic plate giving support to the posterior aspect of the trajectory rail (the confluence).

After confirmation of the stability and of the distraction device placement, the locomotive was activated using a screwdriver and the amount of distraction tested for only a few millimetres in a forward and backward direction. Once the author was satisfied with the installation, the retention plate was covered as far as possible under the labial mucosa (Figure 8.38).

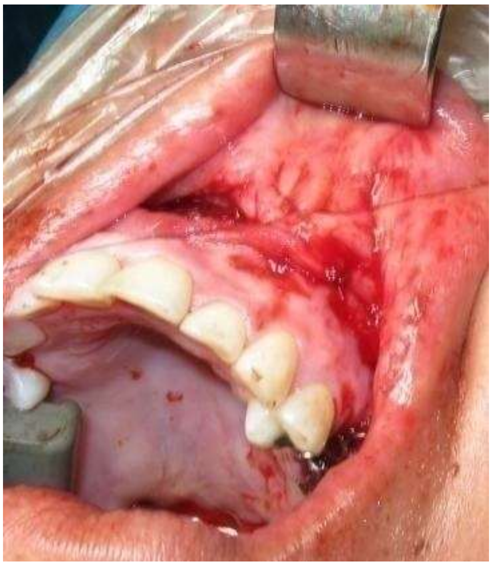

Figure 8.38: The retention plate is covered by labial mucosa as far as possible.

8.6.1 Distraction phase

After a latency period of 5 days, distraction was carried out at a rate of 1 mm per day at a rhythm of 0.5 mm twice daily. Distraction was continued for an uninterrupted period of 20 days and deemed to be sufficient if a complete seal was created at the posterior site of the surgical defect. Transport distraction was then terminated after the 20-day period (Figure 8.39).

Figure 8.39: The end of the distraction phase and the beginning of the consolidation phase (reflected image).

8.6.2 Consolidation period

The duration of the period for consolidation to take place was 12 weeks. During this time, the distraction device was left *in situ* and no callus-enhancing supplements, or other modalities of callus manipulation, were administered. After completion of the consolidation phase, the patient was returned to the operating room where the distraction appliance was surgically removed (Figure 8.40). Dental implants were placed into the newly regenerated bone (Figure 8.40).There was no need for an inter-positional bone graft as union between the neo-alveolus and zygomatic bone was present clinically. After the successful placement of two Adin^{TM} dental implants, the patient had two crowns fitted to rehabilitate the lost occlusal units.

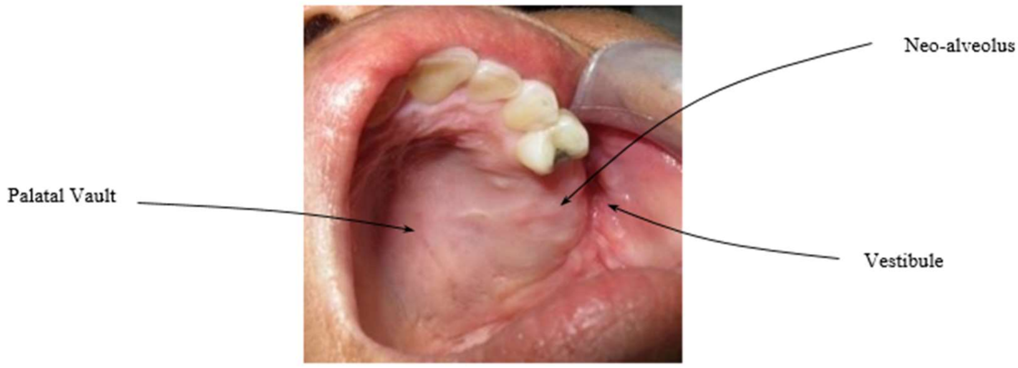

Figure 8.40: The beautifully recreated palatal vault, maxillary alveolus and vestibule.

8.6.3 Radiograph of implants in maxilla

A postoperative orthopantomogram shows the two dental implants successfully placed into the regenerate in the posterior maxilla (Figure 8.41).The radiograph also confirms the complete closure of the hard palate.

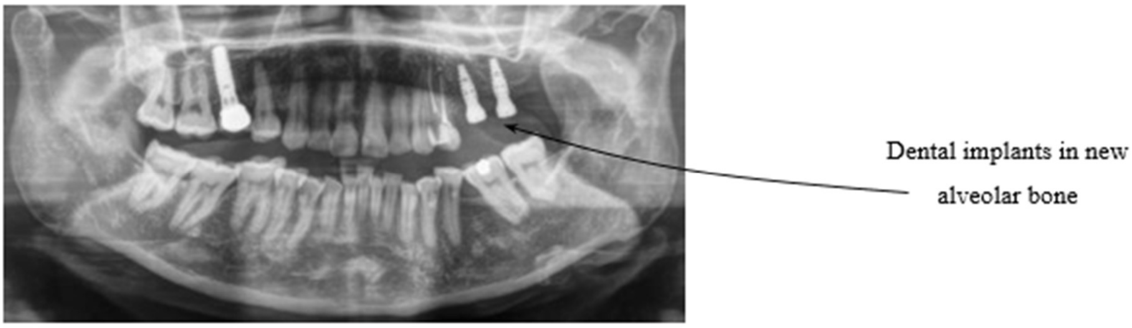

Figure 8.41: A postoperative radiograph indicating dental implants in healthy bone.

8.6.3.1 Density of new bone in maxilla

It was interesting to note that a postoperative CT scan (just before placement of dental implants) showed that the regions of interest (ROI) of the new bone compared favourably with that of the parent bone, as regards bone density (Figure 8.42).

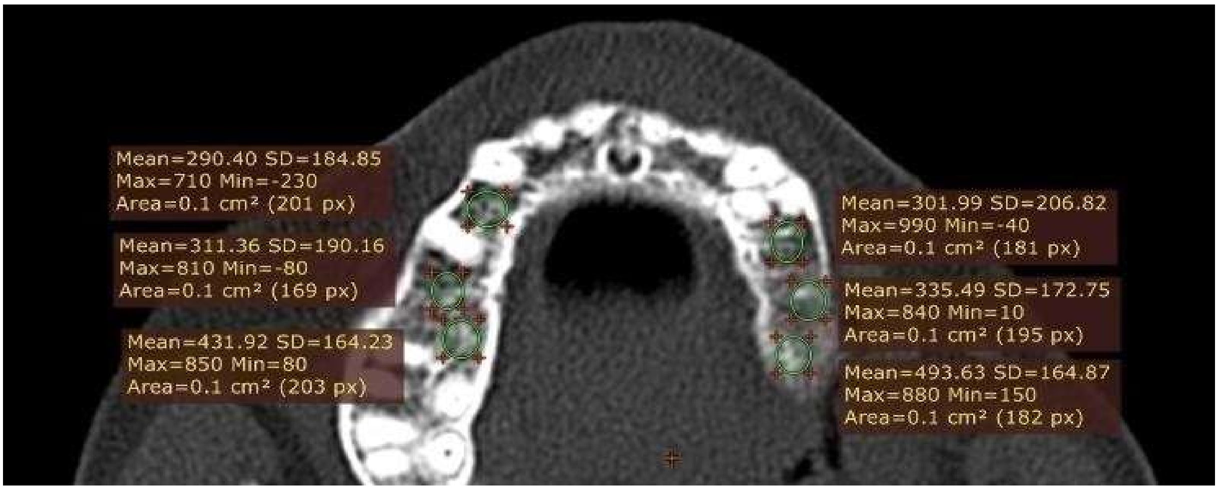

Figure 8.42: Post distraction CT scan shows regenerate v. parent bone expressed in Hounsfield units.

8.6.4 Complete rehabilitation

After a period of osseointegration of the dental implants, two crowns were placed onto the Adin dental implants. Figure 8.43 below shows the radiological appearance of the implants and bone.

Figure 8.43: The postoperative orthopantomogram of the rehabilitated dental occlusion.

The method of CTDO has successfully rehabilitated the patient (Figure 8.44).While the process may be staged and hence time consuming, it carries far less morbidity and cost to the patient, and at the same time delivers optimal function and aesthetics.

Figure 8.44: (a) The implant-supported ceramic crowns in the second quadrant (b) The highly satisfied patient (consent obtained).

8.7 Second installation of V3 distraction device

8.7.1 Treatment planning for distraction of left maxilla

A 3-D stereolithographic model (Figure 8.45) was made from a CT scan of the patient's maxilla. The distraction device was pre-bent to facilitate placement during the operational installation phase.

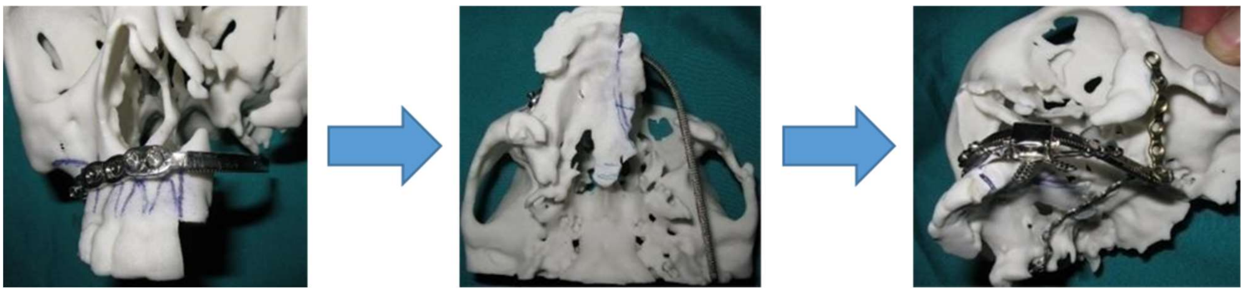

Figure 8.45: The various stages of pre-bending the distraction apparatus.

8.7.2 Installation of V3 distraction device

Before the distraction process, teeth #12 and #13 were removed and a period of healing of about 12 weeks was allowed for bone stock to be developed. Once the bone had matured, the CTDO process was intiated.

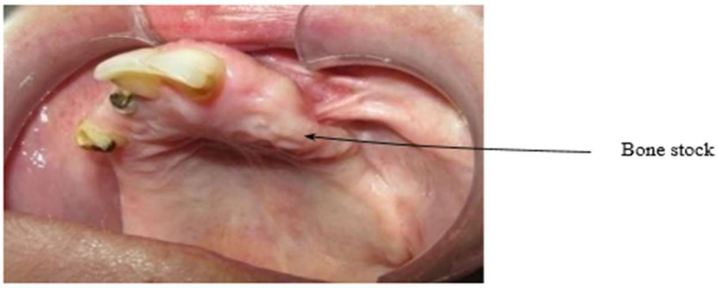

Figure 8.46: Pre-operative situation post healing after teeth #12 and #13 were removed to create bone stock.

The premaxillary region was degloved via a circumvestibular incision, and the zygomatic buttress was exposed in the second quadrant at the surgical defect (Figure 8.47).The roots of the anterior teeth were identified, and the pre-shaped bone plate was approximated to the exposed bone (Figure 8.46). Tooth #12 was extracted owing to caries.

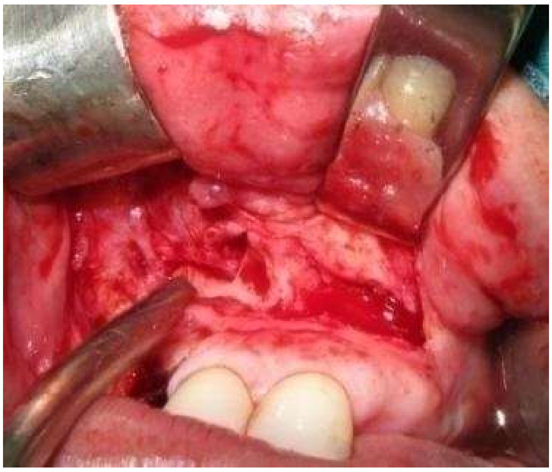

Figure 8.47: The exposed bone and roots of the anterior maxilla.

The base plate and trajectory rail were pre-assembled and placed so that the trajectory track was parallel to the occlusal plane (Figure 8.48(b)). Once this was confirmed, the intra-osseous screws were placed only once and finally into the base plate, so that retention of the base plate was not degraded from repetitive placement and replacement of the screws (Figure 8.48(a)).

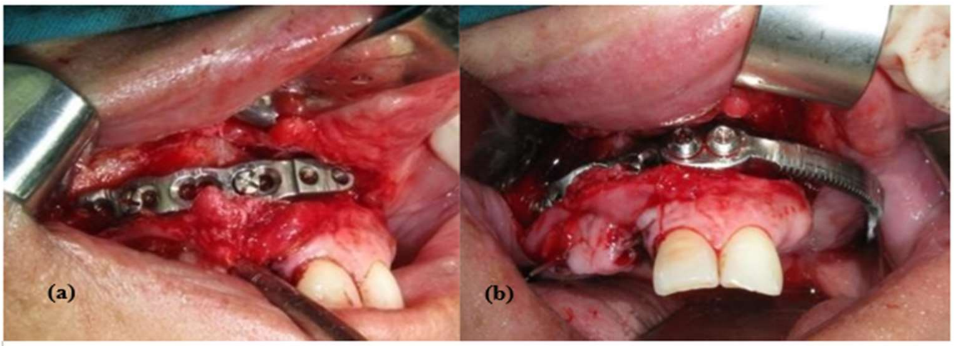

Figure 8.48: (a) Attachment of the base plate. (b) Attachment of the trajectory rail.

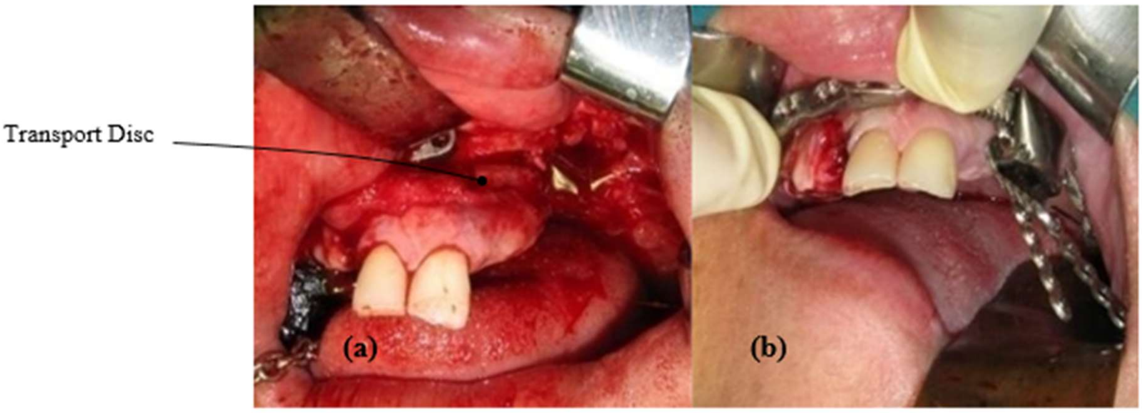

Figure 8.49: (a) Transport disc completed. (b) Adaptation of the basket.

Once the trajectory rail had been removed, the locomotive was loaded onto the rail and tested for accuracy of movement and traction. The horizontal and vertical osteotomies of the alveolar bone were carried out, always preserving the palatal mucosa (Figure 8.49(a)).Once the transport disc had been mobilised, the basket of the locomotive was attached to the carrier disc. The fingers of the cradle were bent to accommodate the shape of the carrier disc (Figure 8.49(b)).

The zygomatic and trans-palatal plate was used to secure the trajectory rail at the confluence. Soft tissue closure of the base plate was carried out, and the track was covered by soft tissue where access was not needed.

8.7.3 Commencement of distraction

After a five-day latency period, distraction was commenced at a rhythm of 0.5 mm twice per day at a rate of 1 mm daily. A total of 24 mm of regenerate was created (Figure 8.50(a) and (b)). Distraction was continued for an uninterrupted period of 20 days and deemed to be sufficient on creation of a complete seal at the site of the surgical defect. Transport distraction was then terminated after the 24-day period. A small tongue flap was used to close the small palatal defect.

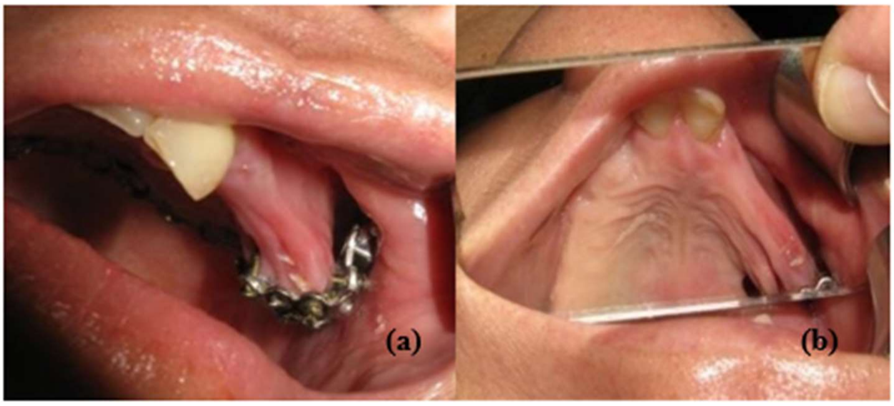

Figure 8.50: (a) Alveolar view of the regenerate. (b) Palatal view of the regenerate.

8.7.4 Consolidation period

The duration of the period for consolidation was 12 weeks. During this time, the distraction devices were left *in situ* and no callus-enhancing supplements, or other modalities of callus manipulation, were administered. After completion of the consolidation phase, the patient was returned to the operating room where the distraction appliance was surgically removed, and dental implants were placed into the newly re-regenerated bone. There was no need for an inter-positional bone graft.

Figure 8.51: Post-distraction CT scan shows regenerate v. parent bone expressed in Hounsfield units.

8.7.5 Bone density of regenerate

A postoperative CT scan performed just before placement of dental implants showed that the regions of interest (ROIs) of the new bone, though less dense than that of the parent bone in terms of bone density, were still adequate for placement of dental implants (Figure 8.51) above.

8.7.6 Complete rehabilitation

After successful placement of two Adin™ dental implants, the patient had a bar and overdenture system placed to stabilise her upper denture (Figure 8.52).

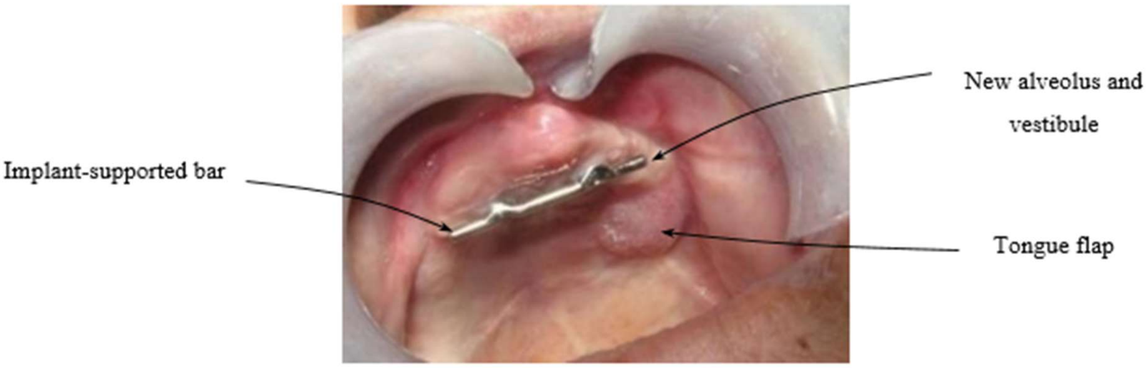

Figure 8.52: Intraoral bar supported by two dental implants. Note also the new alveolar bone with a vestibule and tongue flap closure.

It is interesting to note that this bar overdenture system was more than sufficient to stabilise a full upper denture that also gives support to the cheeks and the infraorbital region. Figure 8.53 below shows the bar and overdenture system *ex vivo*. Figure 8.54(a) shows the highly satisfied patient wearing the implant-supported denture (Figure 8.54(b)).

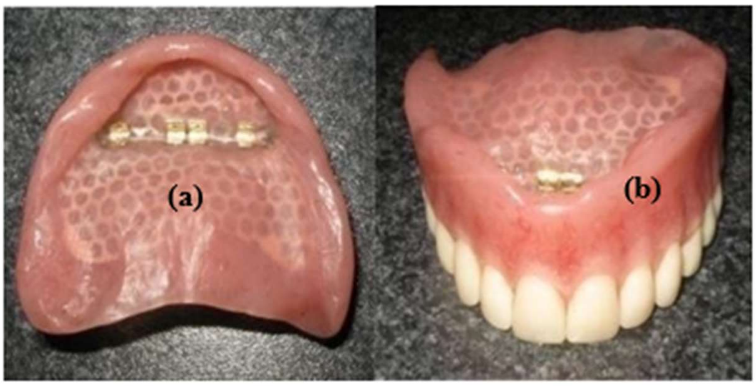

Figure 8.53: The denture with the precision attachments in (a) and (b)

Figure 8.54: (a) The highly satisfied patient. (b) The implant-supported denture.

CHAPTER 9. DEVELOPMENT OF THE V4 TANDEM DISTRACTOR

9.1 Introduction

9.1.1 The challenge of distracting along a curvature

Based upon previous experience, crossing the midline of a curvature will result in a 'rubber band' effect. In the ensuing case, one can see that only four teeth are left in the second quadrant, i.e. teeth #24, #25, #26 and #27. Hence the extraction of two critical teeth (to create a transport disc) will severely compromise the distraction process. Also, it was shown in case reports #2 and #4 that excessive tension on the regenerate will tend to extract the retention screws from the distraction basket.

9.1.2 Contingency plan

Given the above constraints, a 'tandem' distractor was developed, so that distraction could be incrementally carried out without sacrificing any of the existing teeth. The transport disc has to be large enough to undergo a second osteotomy at a later stage to continue the distraction process. This idea led to a modification of the V3 distractor as shown in Figures 9.1–9.3 below. The locomotive would 'pull' 2 vertical plates joined and attached to a tooth crown and its periapical bone respectively. Once the desired distance is attained, the cross bars are drilled apart, and the locomotive continues with the distal plate and second transport disc.

Figure 9.1: The V3 distractor fully assembled, as seen from the buccal aspect.

Figure 9.2: The V3 distractor with separate components.

Figure 9.3: The V3 distractor fully assembled as seen from the lingual/palatal aspect.

9.1.3 Planning for distraction

A 3-D stereolithographic model was used where the roots of the teeth were identified and marked so that the retention plate could be bent according to the bone and tooth root morphology. Figure 9.4 shows the adaptation of the distraction apparatus to bypass the roots of the teeth. It must be emphasised that this exercise proved to be quite difficult, given the fact that there were only four teeth to work with to produce an adequate transport disc. Hence it was decided that only two transosseous screws be used to secure the base plate.

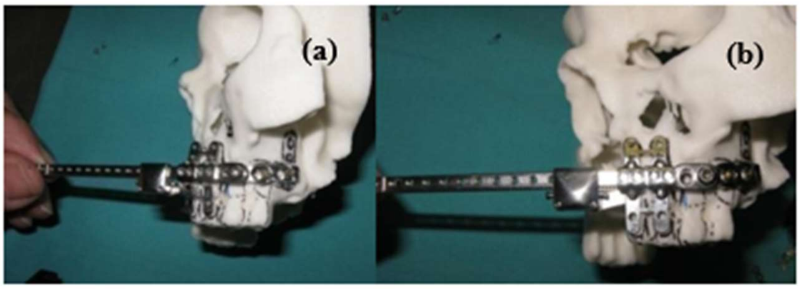

Figure 9.4: (a) Adaptation of the retention plate to the roots of the teeth.
(b) Fixation of the device to the model.

After a mirror image of the model was made, the defect was closed by cementing the dental segment of the model into it so that a symmetrical arch shape was achieved. Initially, a malleable lead plate was used to create the correct contour, as this allows easy bending of the rigid trajectory rail in the laboratory. This method is shown in Figure 9.5.

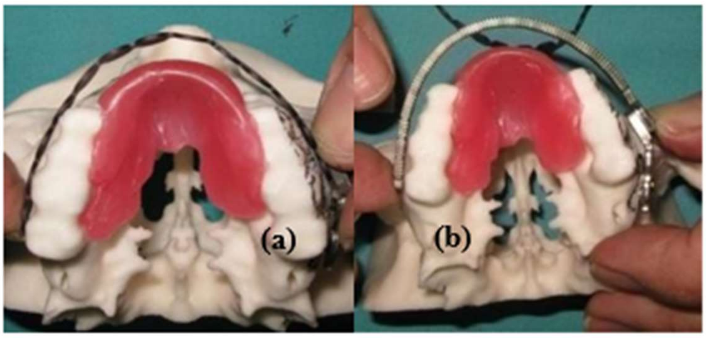

Figure 9.5: (a) Prebending of the lead template on the model to facilitate the rail curvature . (b) Trajectory rail after use of the template.

9.1.4 Installation of distraction apparatus

A general anaesthetic was administered to the patient. A circumvestibular incision was made in the second quadrant to expose the maxillary alveolus and buttress. The anatomy of the remaining roots of the teeth was carefully studied to avoid inadvertent contact during installation of the base plate. The exposed bone for the transport disc is shown in Figure 9.6.

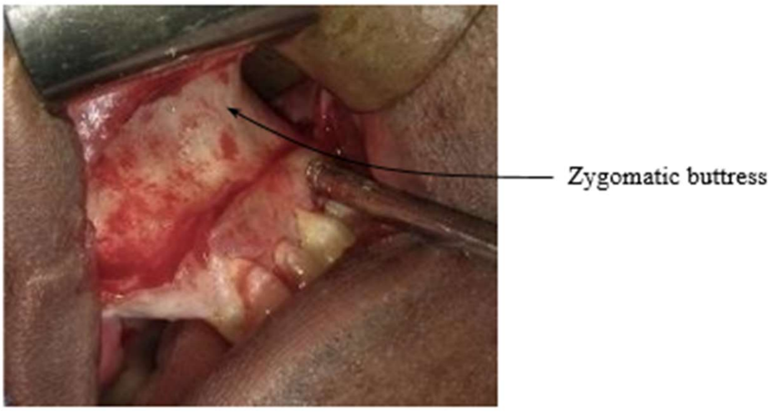

Figure 9.6: The exposed zygomatic buttress and bone for the transport disc.

The base plate was adapted to the bone in the planned area, ensuring that the trajectory rail was parallel to the occlusal plane. The base clamp allowed a 5° exit vector, as described in subsection 8.1.2 and shown below in Figure 9.7.

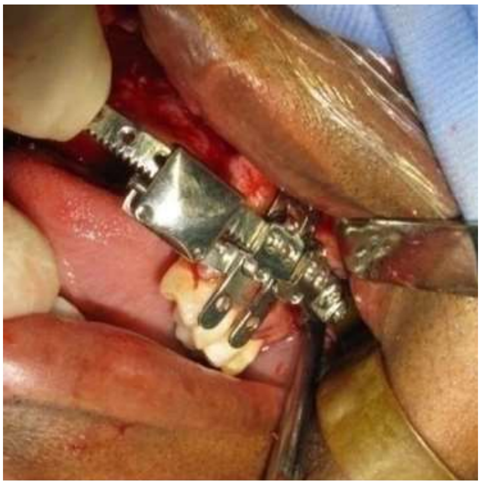

Figure 9.7: Adaptation of the trajectory rail to the dental occlusal plane.

A temporary wire ligature was placed around tooth #25 to assist in the application of the locomotive and the transport disc plates to the bone and teeth. Figure 9.8 below shows the accurate adaptation of the device to the underlying bone and teeth.

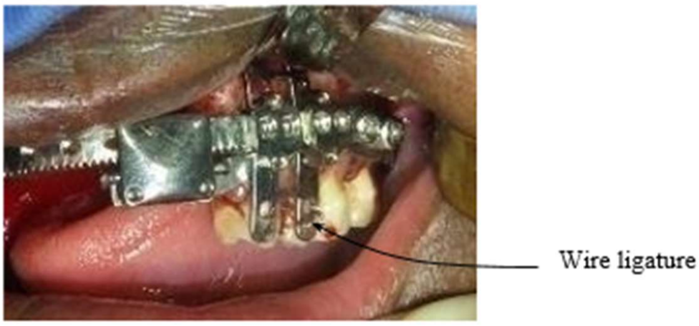

Figure 9.8: Use of a temporary wire ligature around tooth #25 to facilitate adaptation of the locomotive and transport disc plates to the bone and teeth.

After confirming the position of the vertical plates and the wire ligature, the trajectory rail was secured at the confluence end to the zygomatic bone by means of the zygomatic buttress plate (Figure 9.9(a)). The heavy screws securing the base plate to the parent bone are shown in Figure 9.9(b).

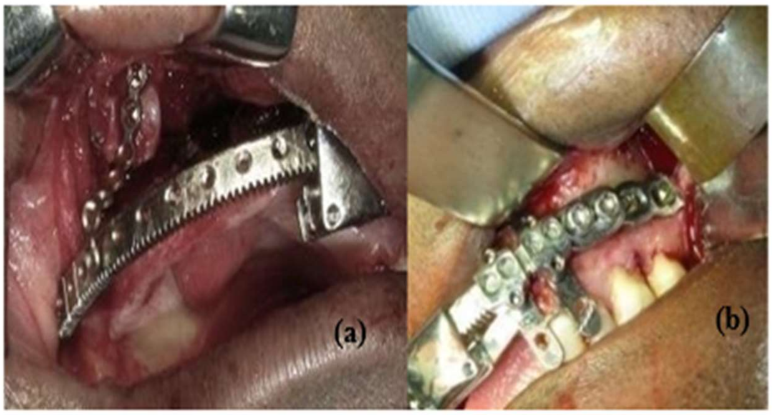

Figure 9.9: (a) The trajectory rail secured to the zygomatic buttress. (b) The fixation plate secured in a good position.

Once the device had been temporarily secured to the teeth and the base plate had been securely installed, the transport disc anatomy was planned (Figure 9.10).

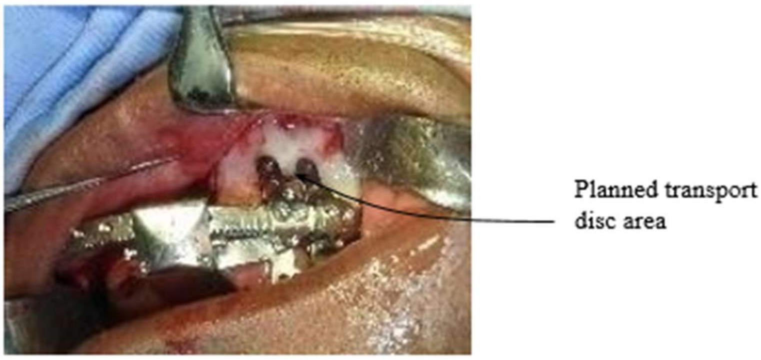

Figure 9.10: Adaptation of the vertical plates to the bone for transport disc creation.

Once the stability and three-dimensional spatial position of the device was accepted, the trajectory rail was reversed by unscrewing the two screws at the base clamp. After removal of the trajectory track, the base plate and exposed bone were visualised for planning of the transport disc (Figure 9.11).

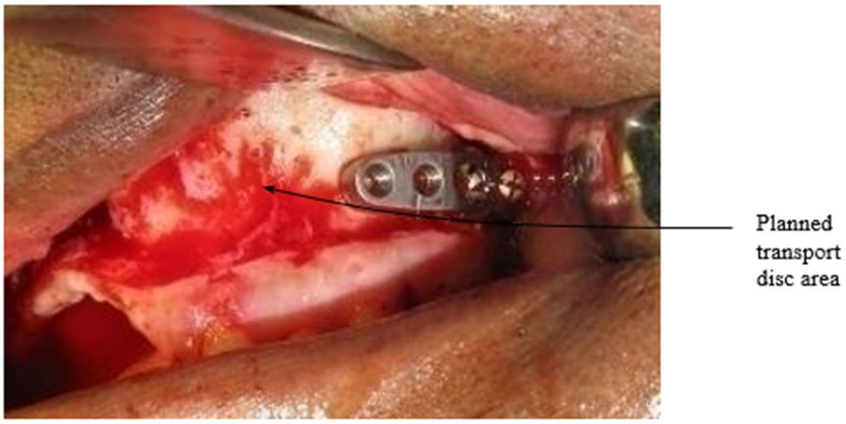

Figure 9.11: Area where the transport disc will be created and the base plate correctly placed.

The crowns of the premolar teeth were subsequently prepared for bonding to the vertical plates of the transport disc (Figure 9.12). The surrounding environment was isolated from the premolar teeth using dry gauze to provide a desiccated environment. The crowns of teeth #24 and #25 were treated with an acid etch gel and bonding agent. The bonding agent was cured with ultra-violet light.

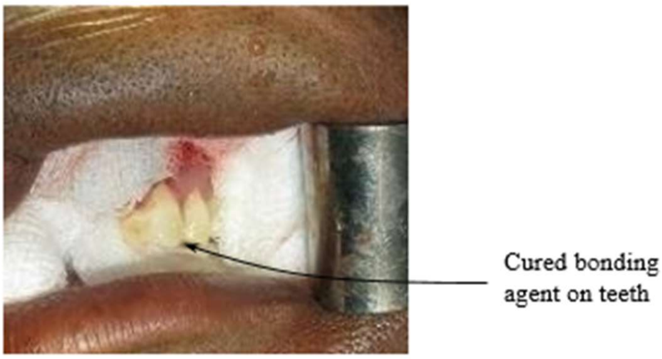

Figure 9.12: Etching procedure to the premolar teeth.

Once the teeth had been etched, and the bonding liquid cured, the horizontal and vertical osteotomies for the combined transport disc were carried out. Figure 9.13 below shows the transport disc osteotomies.

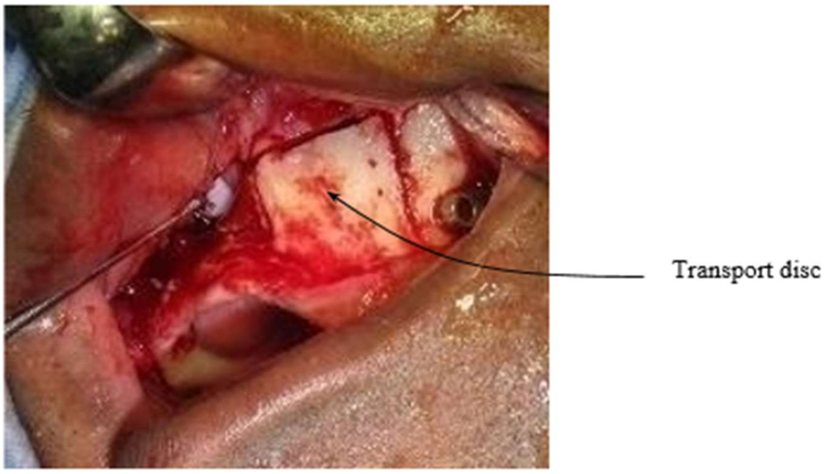

Figure 9.13: The horizontal and vertical osteotomies for creation of the transport disc.

The transport disc was then mobilised by using osteotomes in a gentle fashion so that the palatal mucosa remained undamaged (Figure 9.14). Once the mobility of the transport disc was found to be satisfactory, the appliance could be re-attached to the original position as planned.

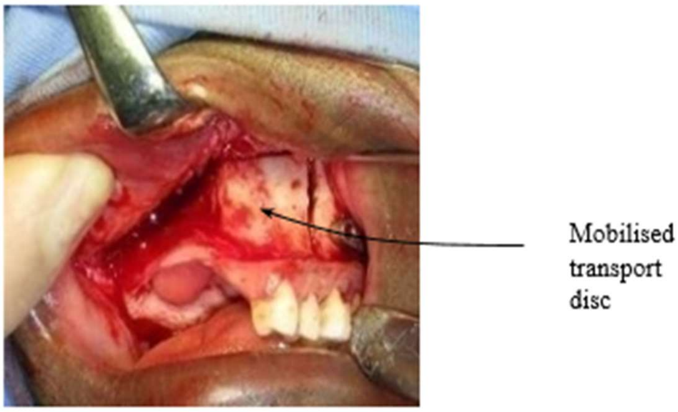

Figure 9.14: Mobilisation of the transport disc.

The assembled trajectory rail and locomotive were subsequently re-attached to the base clamp, and the two vertical plates secured to the teeth and bone respectively (Figure 9.15). Two transosseous screws were used to fix the vertical plates to the bone of the transport disc. At the lower end of the vertical plate, anchorage was achieved by employing circumcoronal wire ligatures individually to the teeth and cementing these with glass ionomer cement.

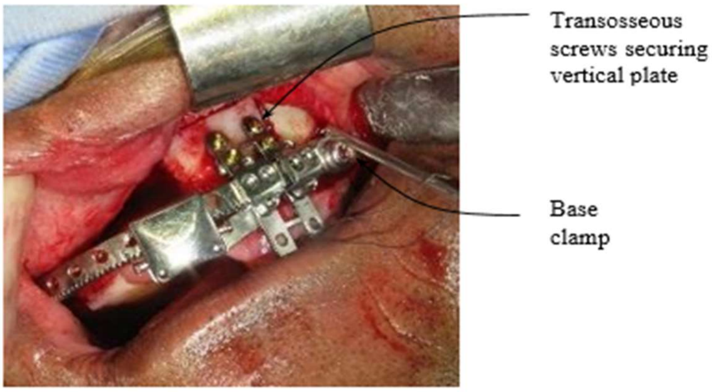

Figure 9.15: Completed assembly of the transport device to the transport disc.

Figure 9.16 below shows the cured glass ionomer cement applied to the teeth to ensure that the wire was well secured and could not slide off the crown of the tooth. Visible in the same figure is the 0.14 ligature stainless steel wire that was used to secure the inferior aspect of the vertical plate and interosseous bone screw affixed into the alveolar bone. The latter anchorage combination ensured that the transport disc had a highly stable torquing action by being secured at both ends.

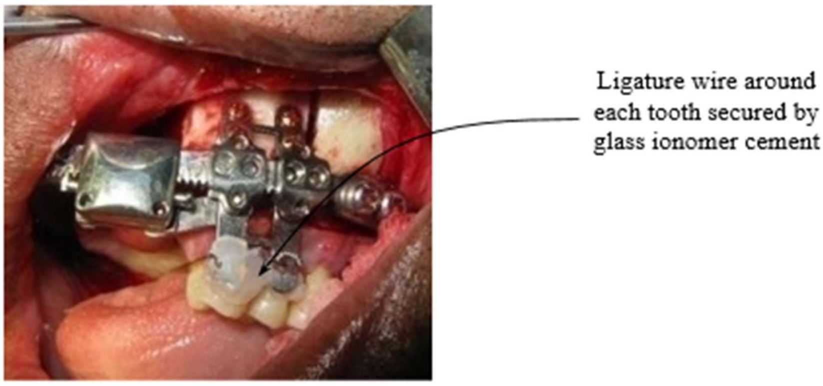

Figure 9.16: The hybrid situation with the transport disc (composed of teeth and bone) well secured above by transosseous screws and below by wire and cement.

The transport disc mechanism was tested by advancing the worm screw using a Biomet screw-driver (Figure 9.18). After a few millimetres of advancement, the transport disc was reversed to its original position for the latency period. To facilitate unimpeded movement of the locomotive and the transport disc, in cases where the palatal mucosa were not deficient, it was advisable to create a surgical defect so that the transport disc could advance into this defect unhindered. Figure 9.17 below shows the surgical defect that was made to facilitate advancement of the transport disc.

Figure 9.17: The surgical defect created to facilitate transport distraction.

Figure 9.18: Testing of the transport disc mechanism with widening of the vertical osteotomy gap.

During the latency phase, the surgical defect usually presented a problem as far as eating was concerned. By placing periodontal dressing (Coepak^{TM}) into the defect at the time of surgery, this patented opening was closed temporarily (Figure 9.19). The periodontal dressing was removed incrementally as the transport disc was moved along the trajectory rail.

Figure 9.19: Periodontal dressing applied to the trajectory rail to close the surgical defect**.**

9.1.5 Postoperative course

After a latency period of 5 days, distraction was commenced at a rate of 1 mm per day and a rhythm of 0.5 mm twice daily. Incremental removal of small amounts of the periodontal dressing was carried out to allow forward movement of the locomotive (Figure 9.20).

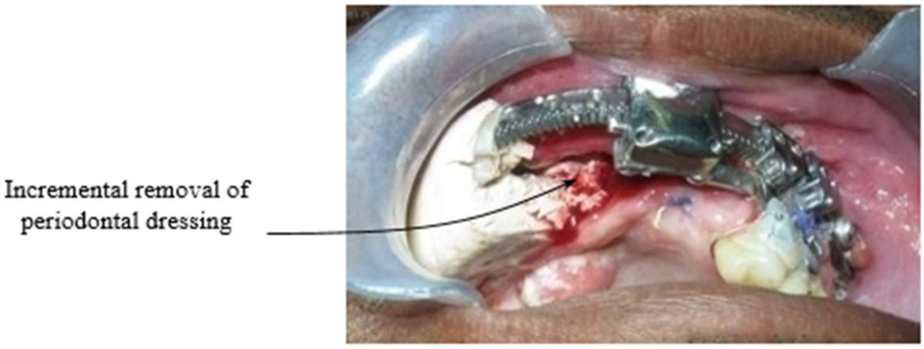

Figure 9.20: Removal of some periodontal dressing to facilitate transport.

Transport distraction was carried out for an uninterrupted period. Figures 9.21(a) and (b) show how the interdental gap widened from 5 mm to 9 mm respectively. It was also most interesting to note that this new regenerate provided minimal resistance to the force required for distraction and was easily accomplished by the V3 distraction device.

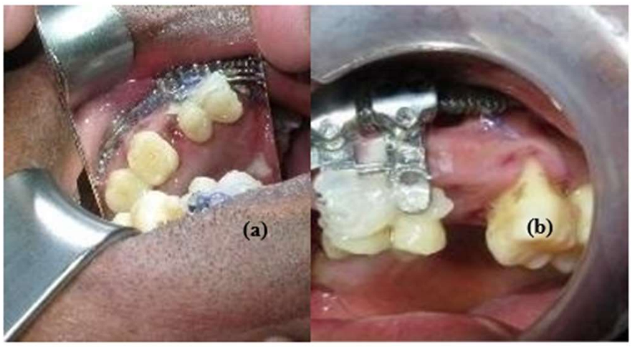

Figure 9.21: The distraction gap after five days (a) and after nine days (b).

It must also be noted that both premolar teeth were part of the same transport disc, implying that teeth #24 and #25 moved as a unit for the first phase of the transport distraction process. These teeth would be separated later with the surrounding bone once the first phase of distraction had been concluded.

9.1.6 Cessation of first phase of distraction

After 30 days of distraction, at a rate of 1 mm per day, the first phase was stopped. Figure 9.22 below shows the healthy new maxilla. This immature bone was allowed to consolidate for 10 weeks.

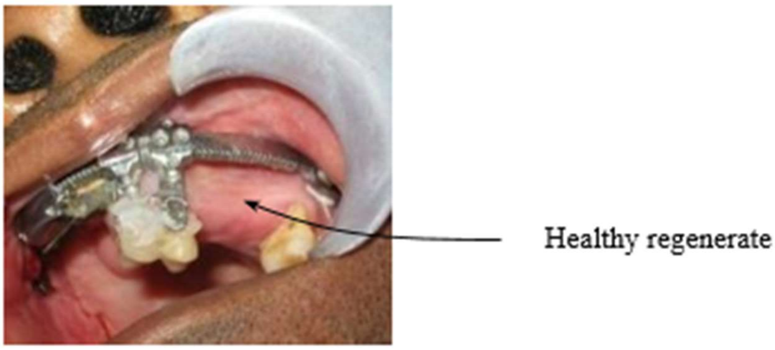

Figure 9.22: The thick, healthy regenerate.

9.1.6.1 Bone density of first phase regenerate

A CT scan of the maxilla taken three months after the first phase of distraction showed that the new bone compared favourably with the parent bone when examining the regions of interest (ROIs) measured in Hounsfield units (HU). In Figure 9.23, it can be seen that the mean figures of the regenerate bone in the left column compare favourably with those on the right side (parent bone).

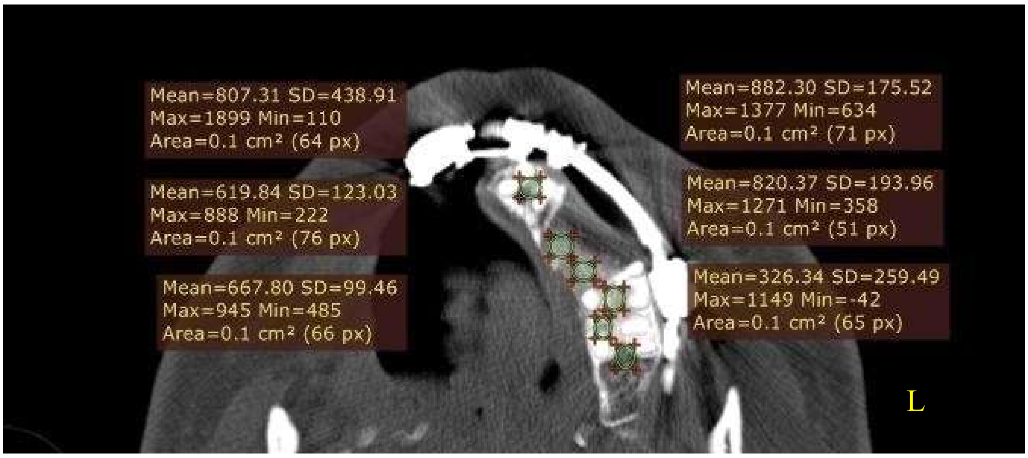

Figure 9.23: The first phase post distraction at three months with regenerate (left column) v. parent bone (right column) and ROIs expressed in HU.

9.1.7 Second phase of distraction

After the consolidation period of six months, the patient was ready to undergo the second phase of distraction, under general anaesthesia. It is important to note that the second phase of distraction could only be undertaken once sufficient consolidation had taken place in the soft osteoid which constituted the regenerate bone. At operation, the soft tissue was elevated and the transport disc was exposed (Figure 9.24).

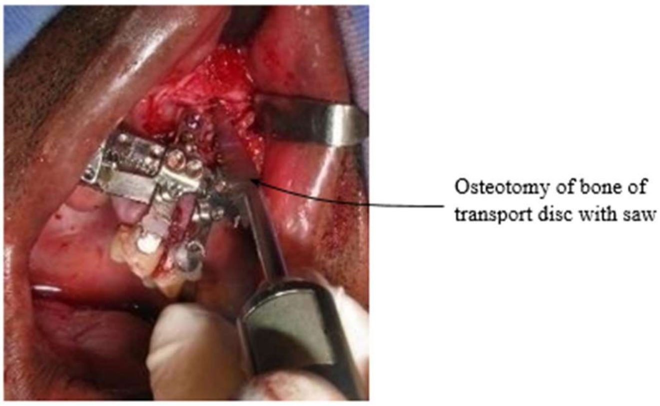

Figure 9.24: The transport disc being osteotomised by a reciprocating saw.

A reciprocating saw was used at the bone interface and a new osteotomy was performed in a vertical fashion between the teeth, using a fine osteotome. The second transport disc was mobilised from its predecessor and ready to be transported by the locomotive.

Once the transport disc had been osteotomised at the apical aspect, a fine osteotome was used to separate the teeth in the interdental space at the coronal aspect. This was done with great care so as not to tear the overlying mucosa around the crowns of the teeth. Figure 9.25 illustrates the method of osteotomising the interdental space.

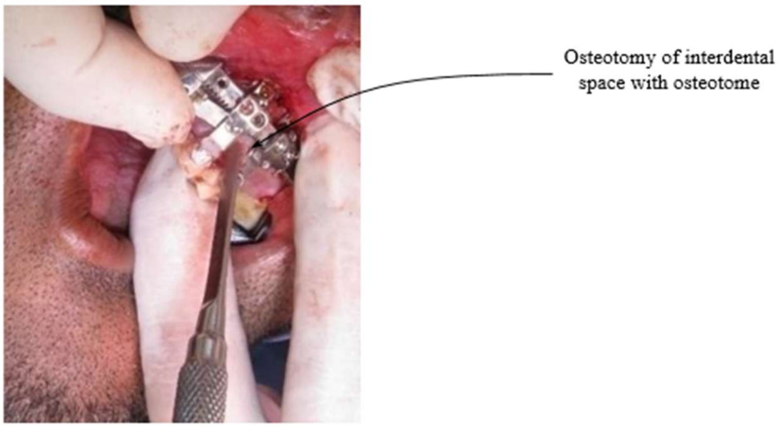

Figure 9.25: The use of a fine osteotome in the interdental space.

Once mobility was achieved, the second transport disc was tested in the forward and reverse directions. A wire ligature was used to secure the first transport disc with the adjoining regenerate to the trajectory rail in order to prevent shrinkage or relapse of the first phase regenerate. In Figure 9.26, the wire ligature can be seen passing through one of the holes in the trajectory rail. The transport disc for the second phase, which was attached to the locomotive, was ready to be transported away from the first phase transport disc.

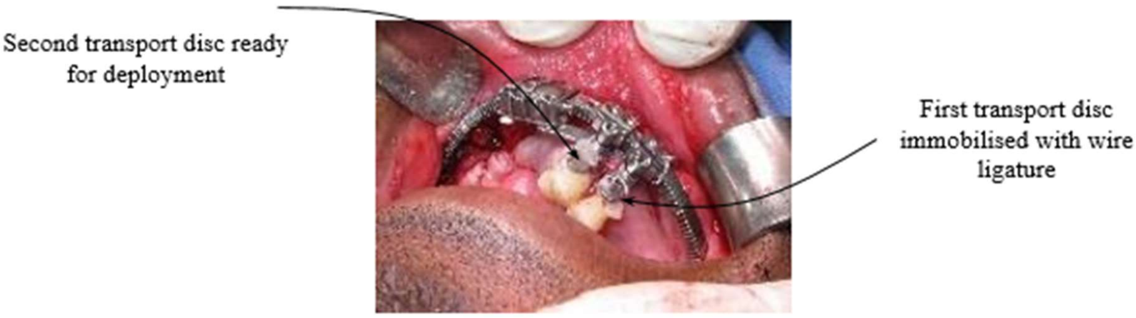

Figure 9.26: The first transport disc wired to the hole in the trajectory rail to ensure stability. The second transport disc is ready for activation.

After waiting for a latency period of another four days, the second phase of distraction was commenced and continued for a further three weeks at a rate of 1 mm per day and a rhythm of 0.5 mm twice daily. It was again interesting to note that there was very little resistance to the force required to execute the distraction process. The only hindrance to the distraction process was the mechanical placement of the confluence plates. It turned out that the position of the zygomatic buttress plate was attached too far anteriorly, hence making the trajectory rail too short for the transport of the locomotive on it. The amount of new regenerate bone and soft tissue was sufficient for the placement of dental implants.

9.1.8 Removal of distractor and placement of dental implants

After a further consolidation period of six months, the patient returned to operating theatre for the final phase of the distraction process. Figure 9.27 below shows the healthy and thick regenerate which was achieved through the process of CTDO. **It must be noted that this was the first recorded attempt of bone having been successfully transported along a curvilinear plane in the maxilla using the method described above**. Also of note was the position of the vertical plates that were attached to the teeth and to the trajectory rail. The wires and the screws in the bone were removed so that the trajectory rail could be detached.

Figure 9.27: The regenerated curvilinear bone supported by the trajectory rail.

9.1.8.1 Bone density of second phase regenerate

It is interesting to note from the CT scan of the maxilla (Figure 9.28) showing the three-month and six-month state of the new bone expressed in terms of HU, that the second phase of regenerate compared favourably with the first phase of regenerate which in turn compared favourably with the parent bone. Owing to the favourable density of the bone that was newly created, it was highly feasible to consider the placing of dental implants.

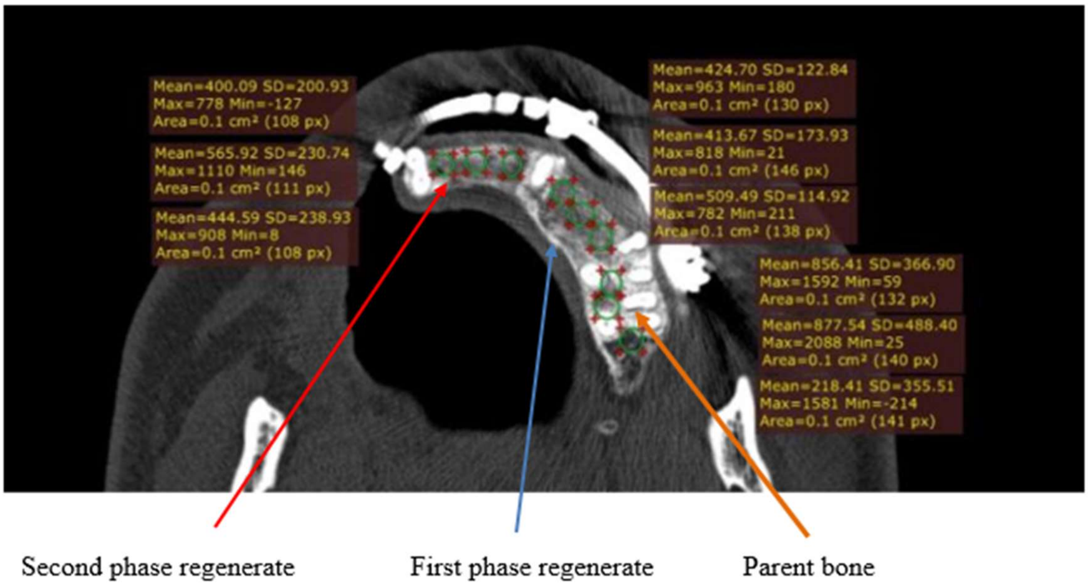

Figure 9.28: The post-distraction situation at six months with the regenerate v. parent bone and ROIs expressed in HU.

9.1.9 Final phase: Surgical exposure of regenerate and placement of dental implants

For the last time, the patient was returned to the operating theatre and a general anaesthetic was administered. In Figure 9.29(a), the new maxilla can be seen after removal of the distraction device. The two premolar teeth were extracted very carefully so that the sockets of the teeth could be preserved for the placement of dental implants. In Figure 9.29(b), regenerated bone can be seen with the preserved sockets of the premolar teeth. The very favourable thickness of the regenerated bone is evident. The quality of this bone in terms of thickness, as well as depth, made it most suitable for the placement of dental implants and their subsequent long-term stability.

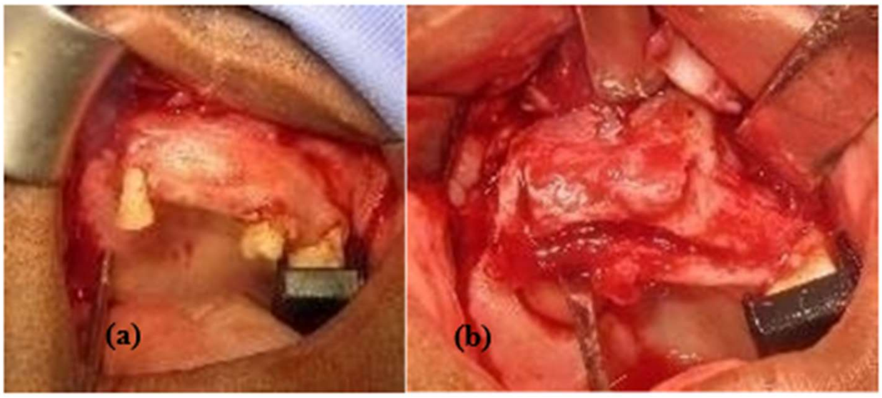

Figure 9.29: (a). The favourable curvilinear shape of the new maxilla. (b) The thick and deep new regenerated maxillary bone and healthy dental sockets

A clear acrylic splint was fabricated by a prosthodontist who used the assistance of a cone beam CT scan. This splint fitted accurately during the placement of dental implants into the new maxilla. The availability of this thick regenerate made it possible to place six Adin^{TM} Closefit dental implants with excellent primary stability into the new maxilla. Figure 9.30 shows the acrylic splint *in situ* (a) and the placement of the dental implants (b).

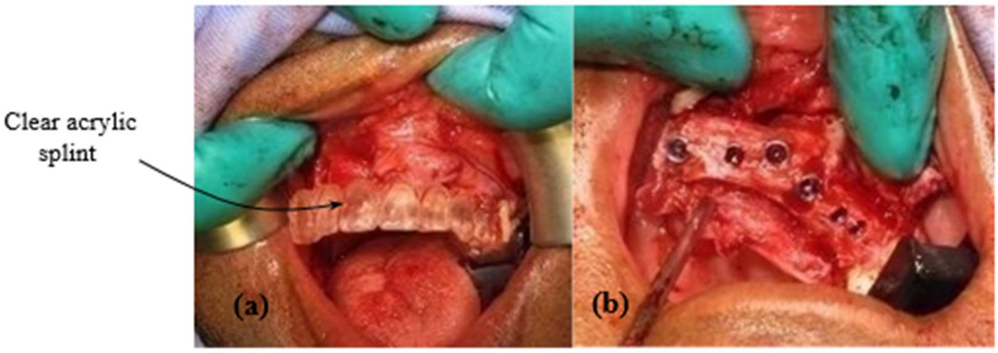

Figure 9.30: (a) The clear acrylic splint. (b) The six dental implants well placed in the maxilla.

The dental implants were well placed with healing abutments. Bone scrapings were taken from the areas of excess tissue and placed into the sockets around the dental implants to accelerate osseointegration. While there was good union between the regenerate and the parent malar corpus, a small mandibular bone graft was interposed between the neo-maxilla and the malar corpus for extra support (Figure 9.31).

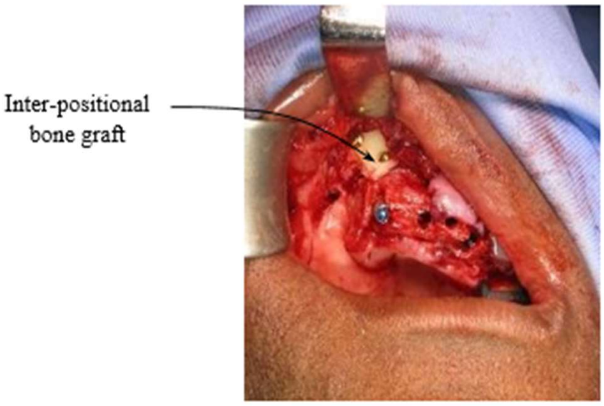

Figure 9.31: The small inter-positional bone graft to augment the union between the neo-maxilla and the corpus malar.

During the process of dental implant placement, a trephine biopsy of the regenerated bone as well as the parent bone was taken for histological comparison. In Figure 9.32(a) below, the trephine can be seen. The completed state of the dental implants and their healing abutments can be seen in Figure 9.32(b).

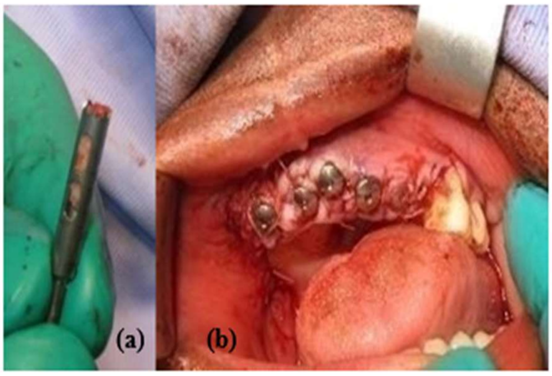

Figure 9.32: (a) The trephine with bone biopsy. (b) The final position of the six Adin™ dental implants with their healing abutments.

9.1.10 Final complication

Sufficient torque was measured while placing the implants so that it was readily feasible for an immediate temporary bridge to be constructed. The patient was due to return after a few days for its placement. Tragically, however, he was killed in a road traffic accident. The loss of this amiable and co-operative patient is deeply felt by the author, and his contribution to the greater good is greatly appreciated.

9.2 Development of the V5 distractor

9.2.1 Introduction

It must be noted that in the previous case (case report 5), the locomotive was not attached to the vertical plates which were screwed into the transport disc. In fact,there was a metal plate joining the two entities. This resulted in the creation of wasted space which meant less regenerate could be formed along the trajectory rail. This problem was solved by placing the locomotive directly onto the distractor plates, which is a design improvement for case number 6.

9.3 Planning for the V5 distractor

A 3-D stereolithographic model was fabricated from the CT scan. In Figure 9.33(a), the 3-D model and the anatomical outlines of the teeth in the bone are illustrated. In Figure 9.33(b), the adaptation of the base plate to the model, to plan the position of the transosseous screws, can be seen. A 'tandem' distractor would be placed to distract between the teeth in distinct phases, as was carried out in the previous case (case report 5). The 2 openings per slot in the base plate allow for deviation in dental root anatomy so that transosseous screws can be placed strategically to avoid the dental roots during fixation (Figure 9.34).

Figure 9.33: (a) The roots of the teeth are clearly seen. (b) Adaptation of the device with reference to the roots of the maxillary teeth.

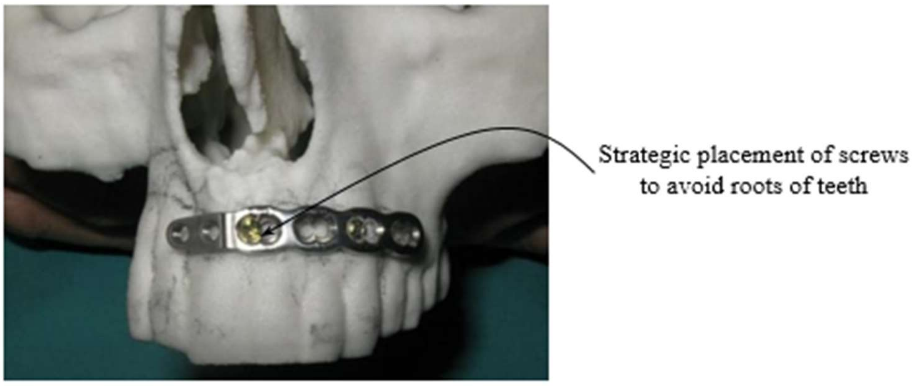

Figure 9.34: The base plate prepared for attachment to the underlying bone.

A further innovation to allow more distance to be traversed during the distraction process was achieved when the locomotive and the distraction plates were bonded together and not joined by a plate as in the previous version. Figures 9.35 and 9.36 below illustrate the modification to the V4 tandem transport distractor.

Figure 9.35: The configuration of the tandem distractor with locomotive on the trajectory rail as seen from the labial/buccal aspect.

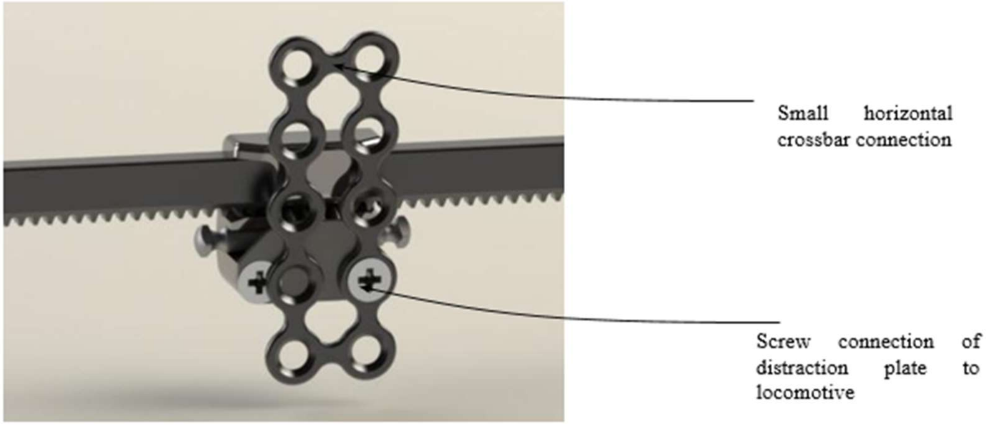

Figure 9.36: The palatal aspect of the locomotive. The vertical plates are joined to each other above and below by a thin bar. A screw fixes the vertical plates to the locomotive.

The fixing of the vertical distraction plates to the locomotive was designed so that, after the first stage of distraction, by merely sectioning the small horizontal crossbars, the locomotive can be freed to continue with the second phase of distraction (Figure 9.36). The next step in the planning was to ensure that the vertical distraction plates which are attached to the locomotive do not collide with the buttress of the malar corpus. On the model seen in Figure 9.37(b), a mark was made for the area where bone had to be removed on the inferior aspect of the corpus malar. Further on, during the installation phase, the removal of this bone by means of a

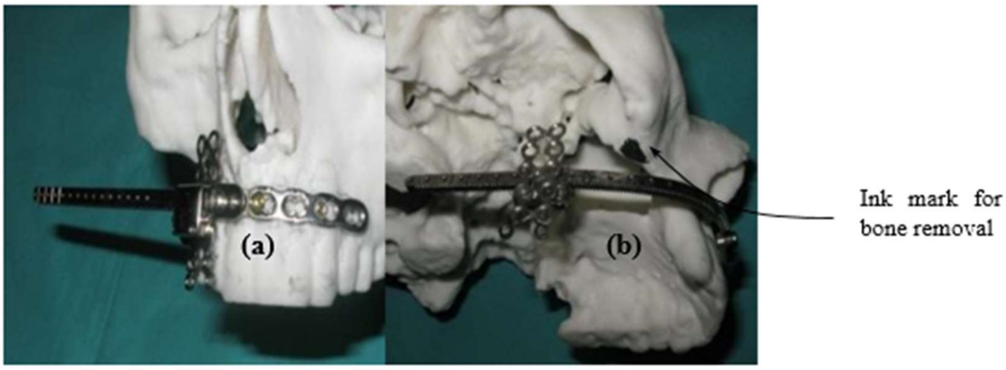

Figure 9.37: (a) The attached device and the distraction plate clearing the zygomatic buttress. (b) The proposed bone removal is marked in black ink.

reciprocating saw will be shown.

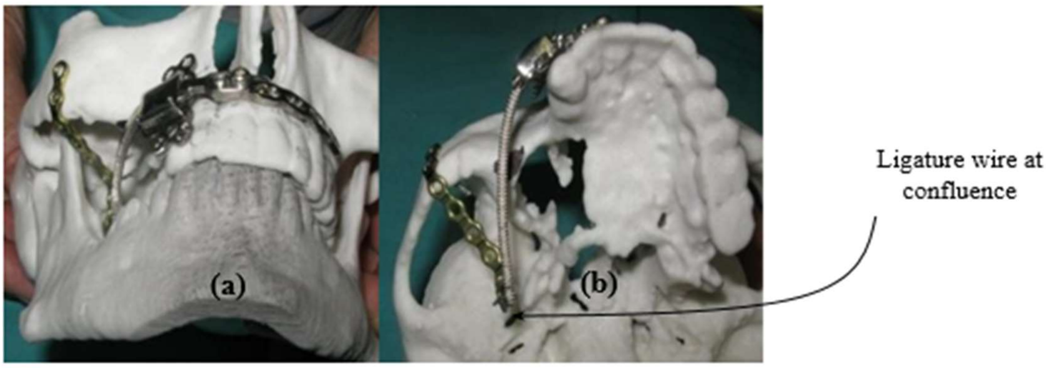

Figure 9.38: (a) The zygomatic buttress plate seen attached to the malar corpus. (b) The confluence of the trajectory rail and zygomatic buttress is secured by a wire ligature.

The adaptation of the zygomatic stabilising plate to the malar corpus and the confluence made the use of a trans-palatal plate redundant. It was found by the author that the base plate and the zygomatic buttress plate were more than sufficient for retention and stability of the complete apparatus (Figure 9.38).

9.3.1 Installation of the distraction apparatus

A general anaesthetic was administered to the patient. The anterior maxillary bone was exposed via a circumvestibular incision (Figure 9.39(a)). The base plate was secured to the pre-maxillary bone, taking into account the position of the roots of the teeth. The insertion of wide 2.5 mm diameter titanium screws (Biomet^{TM}) ensured good stability of the baseplate (Figure 9.39(b)).

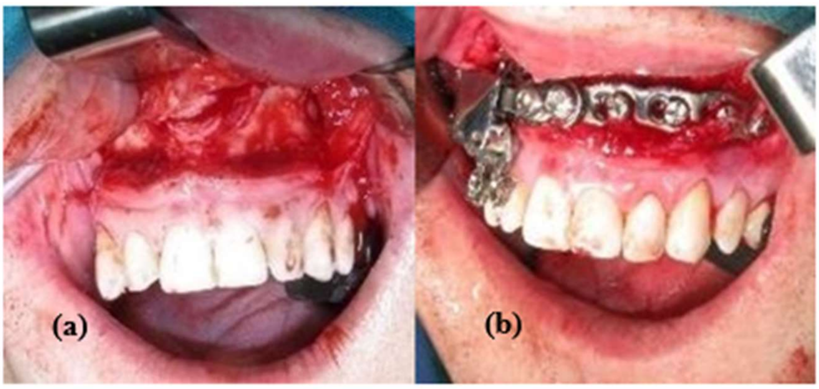

Figure 9.39: (a) The exposed premaxilla. (b) Fixation of the baseplate.

It was very important to ensure that the trajectory plate remained parallel to the occlusal plane, and that the position of the locomotive and the vertical distraction plates coincided precisely with the teeth below which make up the tandem distraction transport disc. In Figure 9.40 below, it can be appreciated that the position of the locomotive with the distraction plates has been accurately opposed to the respective crowns of the underlying teeth. Bone screws secured the vertical distraction plate to the alveolar bone superiorly.

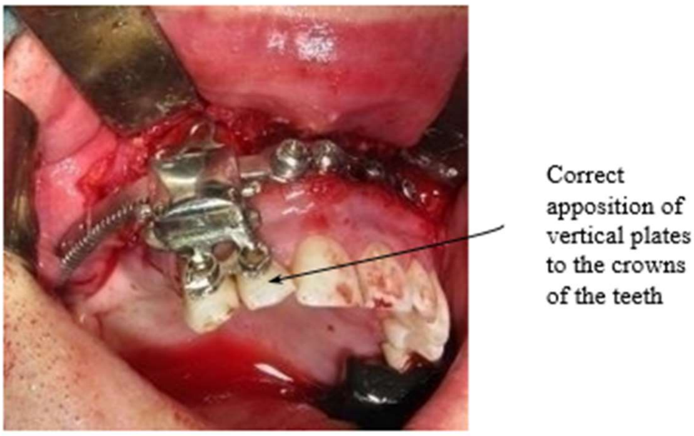

Figure 9.40: The correct placement of the locomotive and distraction plates in relation to teeth #13 and #12.

Figure 9.41: Planned removal of bone from the zygomatic buttress.

The next stage in the installation of the distraction device was to ensure that sufficient bone was removed from the zygomatic complex to allow freedom of movement of the transport disc. In Figure 9.41 above, the planned removal of bone from the zygomatic buttress to facilitate unhindered movement of the transport disc is carried out.

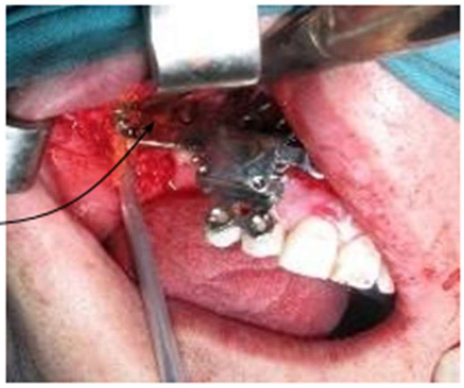

Figure 9.42: The buccal soft tissue was removed to facilitate clearance and freedom of translation for the transport disc.

It was also necessary that the trajectory rail be kept clear from any soft tissue, namely cheek muscle or buccal mucosa, to allow free access to and mobility of the locomotive and transport disc. The clearance of buccal tissue is shown in Figure 9.42.

The crowns of the anterior teeth were prepared for bonding to the vertical plates of the transport disc. The surrounding environment was cordoned off from the anterior teeth by means of dry gauze to provide a desiccated environment. The crowns of teeth #12 and #13 were treated with acid etch gel and bonding agent. The bonding agent was cured with ultraviolet (UV) light (Figure 9.43).

Figure 9.43: The acid etched teeth, with bonding agent, cured by UV light.

Once the bonding agent had been applied in a satisfactory manner, the transport disc was created by horizontal and vertical osteotomies in the bone (using a reciprocating saw and osteotomes) (Figure 9.44). During the transport disc formation, care was taken to protect the soft tissues of the palate.

The base plate was covered by buccal mucosa as far as possible, being careful not to obstruct access to the activation screw on the locomotive (Figure 9.45).

Figure 9.44: The transport disc created by a reciprocating saw and osteotome.

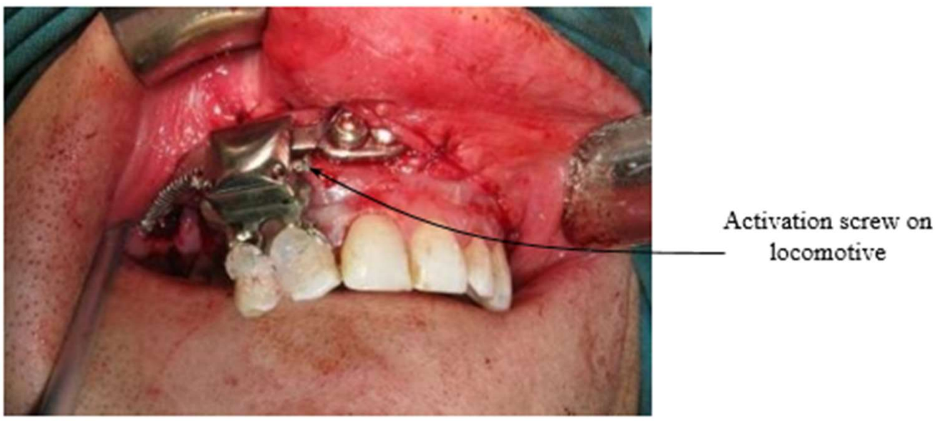

Figure 9.45: The locomotive firmly attached to the crowns of the teeth inferiorly and to the bone superiorly by two transosseous screws.

As the locomotive could be removed and replaced repeatedly, the advantage of the two-part system was greatly appreciated by the author. Figure 9.45 shows the distraction plates cemented to the crowns of the teeth with glass ionomer cement. The base plate was submerged under the soft tissue of the upper lip using 3-0 Vicryl™ (Ethicon). The exposed trajectory rail is also evident in Figure 9.45.

9.3.2 Commencement of distraction

After a latency period of 5 days, distraction was commenced. Distraction was carried out at a rate of 1 mm per day and a rhythm of 0.5 mm twice daily. After 20 days, the first phase of distraction was terminated. As shown in Figure 9.46 below**, the healthy new regenerate measuring approximately 20 mm did indeed have a curvature to it.** Also, in the hard palate, **the presence of a palatal vault was visible and rugae replication was also noted in the palatal mucosa**. It was advisable to terminate the distraction at the cornerstone of the maxilla so that a nicely blended curvature could be arrived at.

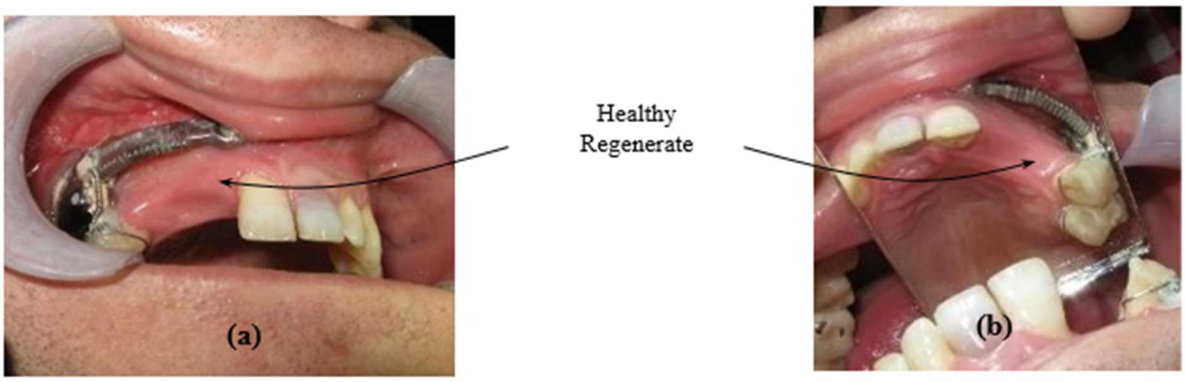

Figure 9.46: (a) Healthy regenerate. (b) Palatal vault with rugae created from this regenerate.

The above images show excellent reproduction of regenerate with anatomical replication of parent alveolar and palatal bone. This proved to be the ideal in optimising function and aesthetics. The immature bone was allowed to consolidate for 10 weeks.

9.3.3 Second phase of distraction

After the consolidation period of 6 months, the patient was now ready to undergo the second phase of distraction. It is important to note that the second phase of distraction could only be undertaken once sufficient consolidation had taken place in the soft osteoid which constituted the regenerate bone. At operation, the soft tissue was elevated and the transport disc was exposed. The metal bar between the two vertical plates of the distraction apparatus was cut using a tungsten carbide burr (SS White^{TM} #702). The metal bar superiorly at the base interface was also cut using a tungsten carbide burr (Figure 9.47).

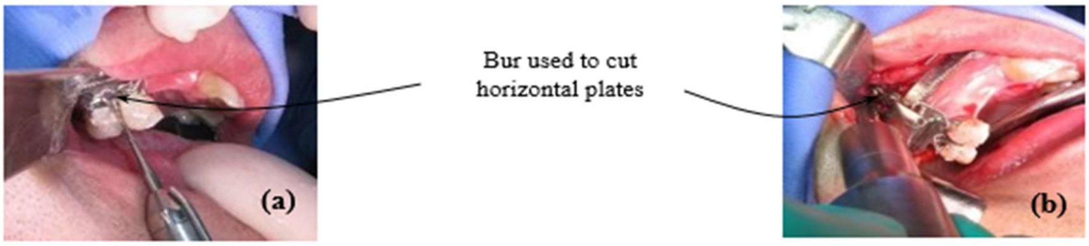

Figure 9.47: (a) The separation of the transport disc by cutting the crossbar between the vertical plates inferiorly. (b) The cutting of the crossbar superiorly, thus allowing the locomotive to advance freely to continue the distraction process.

A reciprocating saw was used at the bone interface and a new osteotomy was performed in a vertical fashion between the teeth by using a fine osteotome (Figure 9.48). The fine osteotome was then used to separate the two teeth with their surrounding bone (Figure 9.49).

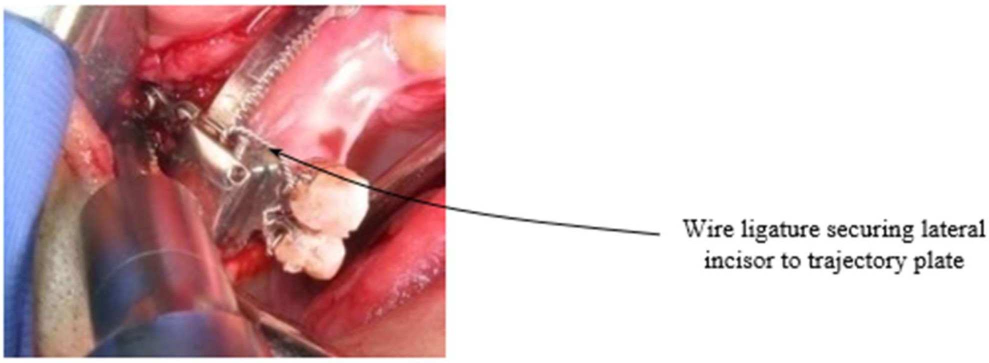

Figure 9.48: A reciprocating saw was used to create an osteotomy for the second transport disc. A wire ligature was used to secure the lateral incisor to the rail. The bone was also secured superiorly by means of the vertical distraction plate.

Figure 9.49 : Use of a fine osteotome to separate the coronal interseptal bone.

After tooth #22 was secured to the trajectory rail, the mobile segment (transport disc) and the locomotive were tested for unhindered movement and then returned to their original position for the latency period.

9.3.4 Second phase of distraction

After a latency period of 5 days, the locomotive was activated at a rate of 1 mm per day and a rhythm of 0.5 mm twice daily. It was interesting to note, once more, that there was very little resistance to the force required to execute the distraction process. An acrylic spacer was wired to the abutment teeth to maintain the space and create stability (Figure 9.50). The latter also showed the recreated palatal vault with rugae and a 'tuberosity' appearance. A further 18 mm was added to the maxilla which amounted to a total distraction of 38 mm. The amount of new regenerate bone and soft tissue was ample and sufficient for the placement of dental implants.

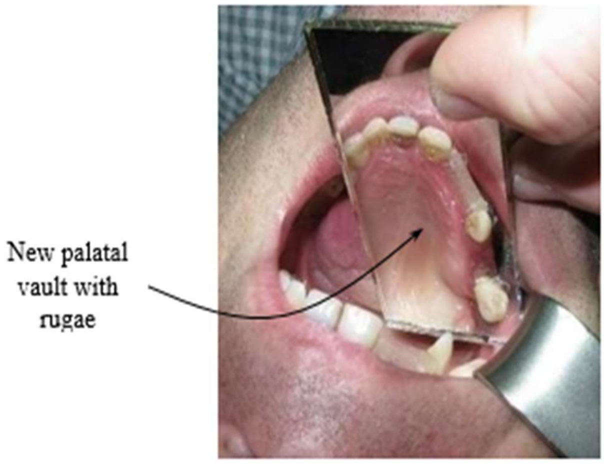

Figure 9.50: The second part of the distraction process. The shape of the bone is very anatomical, with a palatal vault and a 'tuberosity' appearance.

Figure 9.51 below shows the secured acrylic spacer in position and the healing regenerate. It must be noted that this method of **tandem distraction** indeed creates new bone on a **curvilinear trajectory. The 'rubber band' effect is obviated by dividing the regenerate into several segments**. The concept of growing bone along a curvature (CTDO) was successfully demonstrated in the previous two case reports (reports 5 and 6).

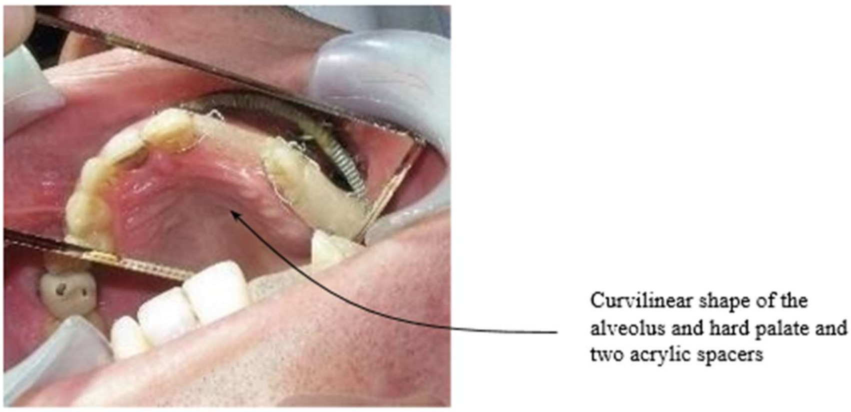

Figure 9.51: The superlatively recreated palatal vault with rugae in the palate. Note also the depth of the palatal vault and the creation of a vestibule. The two acrylic interdental spacers are wired to the abutment teeth.

Another interesting aspect learnt from this particular distraction case was that, as the teeth moved in a proximal direction during the second distraction phase, there was a problem of premature occlusion between the teeth of the maxilla and mandible. This problem was obviated by requesting the prosthodontist to manufacture a lower hemi-bite splint. When the patient wore the splint, as seen in Figure 9.52, the new maxilla with teeth were outside the traumatic occlusion. It was highly significant that the abutment teeth between the areas of bone regenerate did not have any axial or non-axial forces imposed upon them. If this had been the case, healing of the osteoid around these teeth would have been compromised.

Figure 9.52: The jaws in occlusion; the insertion of a lower bite plate helped to protect the regenerate and abutment teeth from the traumatic occlusal forces.

9.3.4.1 Bone density of second-phase regenerate

It is interesting to note from the CT scan of the maxilla the three-month state of the new bone expressed in HU. The bone density of the new regenerate at three months compared favourably with the bone density of the ROIs seen within the parent bone. Figure 9.53 below shows the favourable comparison on the CT scan.

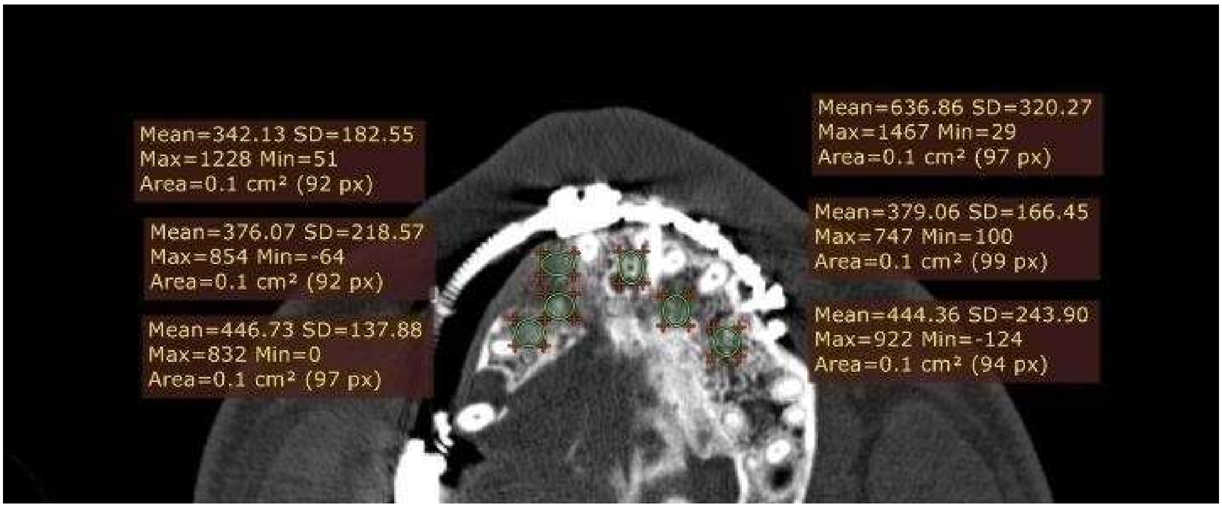

Figure 9.53: The first phase post distraction at three months with regenerate (left column) v. parent bone (right column) and ROIs expressed in HU.

9.3.5 Final phase: Surgical exposure of regenerate and placement of dental implants

For the final stage, the patient was returned to the operating theatre and a general anaesthetic was administered. In Figure 9.54(a) below, the new maxilla can be seen before removal of the distraction apparatus. The trajectory rail and the rest of the distraction device were removed. The incisor and canine teeth were extracted very carefully so that the sockets of the teeth could be preserved for the placement of dental implants. In Figure 9.54(b), the regenerated bone can be seen as well as the preserved sockets of the anterior teeth. Note the very favourable thickness of the regenerated bone. The quality of this bone made it conducive to the placement of dental implants, and the dental sockets were also favourable for dental implant placement.

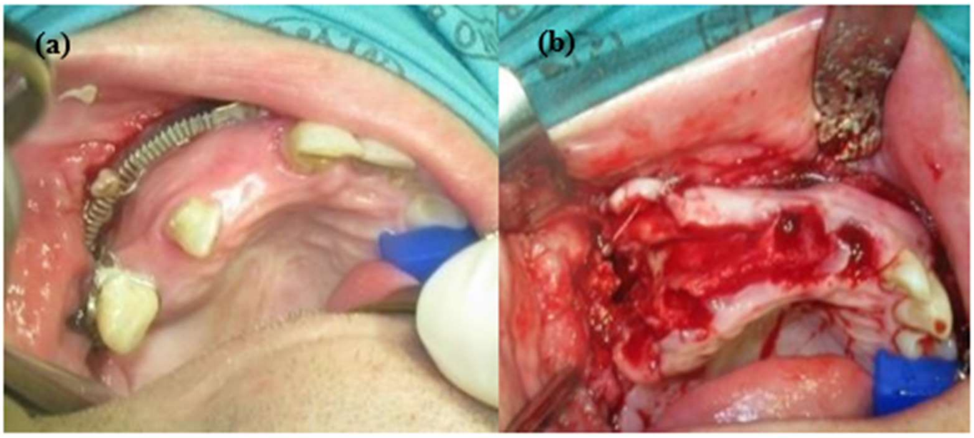

Figure 9.54: (a) The favourable curvilinear shape of the new maxilla. (b) The thick and deep new regenerated maxillary bone and healthy dental sockets.

A clear acrylic splint was fabricated by a prosthodontist using a cone beam CT scan of the maxilla. The splint fitted accurately during the placement of dental implants into the new maxilla. The availability of this thick regenerate made it possible to place six Adin^{TM} Closefit dental implants with very good primary stability into the new maxilla. Figure 9.55(a) shows the acrylic splint *in situ* and Figure 9.55(b) shows placement of the four dental implants.

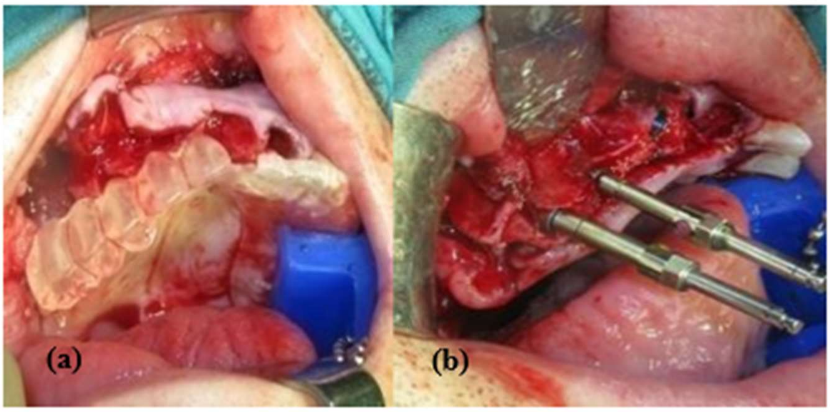

Figure 9.55: (a) The acrylic splint for implant placement. (b) Placement of the four dental implants.

As can be seen in Figure 9.56 below, the dental implants were well placed with healing abutments. Bone scrapings were taken from the areas of excess tissue and placed into the sockets around the dental implants to accelerate osseo-integration. There was good bony union between the regenerate and the malar corpus, and hence no interpositional bone grafting was required in this case.

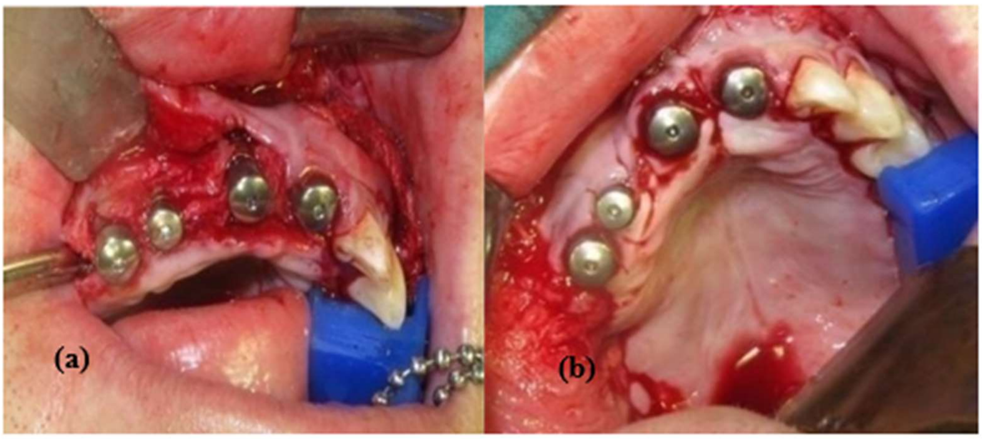

Figure 9.56: The placement of four Adin™ Closefit implants with healing abutments. (b) Primary closure of soft tissue around the dental implants.

During the process of dental implant placement, a trephine biopsy of the regenerated bone as well as the parent bone was taken for histological comparison. There was sufficient torque at implant placement for an immediate temporary bridge to be constructed. In Figure 9.57 below, the aesthetically constructed temporary bridge is seen. The temporary bridge is supported by four Adin™ dental implants. A permanent bridge will follow within 6 months after this placement.

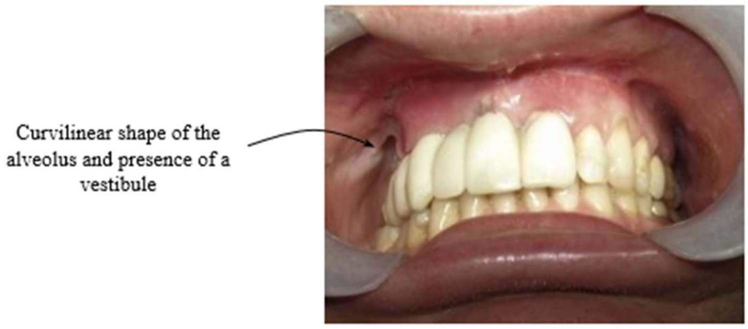

Figure 9.57: The aesthetically constructed temporary bridge *in situ.*

The use of CTDO has created not only new alveolar bone, but also recreated the palatal vault, as well as the alveolar depth with the juxtaposed vestibule and cheek muscle. In Figure 9.58(a) below is the highly pleased patient with a temporary bridge. Figure 9.58(b) shows a palatal perpective of the same bridge. The shape, depth and anatomical accuracy of the regenerated maxilla is evident.

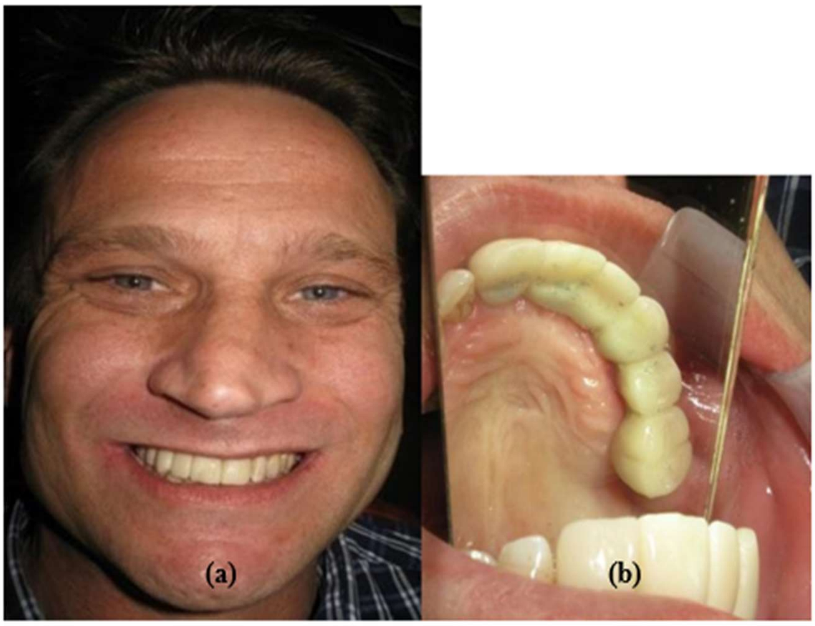

Figure 9.58: (a) The highly pleased patient with a most aesthetic and functional temporary bridge *in situ.* (b) The very pleasing anatomical recreation of the hard palate, alveolus and vestibule (mirror view); (consent obtained).

CHAPTER 10. RESULTS: CLINICAL COMPARISON OF REGENERATE TO PARENT (CONTROL) BONE

10.1 Width of bone

Clinical measurements of the depth of the alveolar vestibule at three different exact points juxtaposed, namely A, B and C respectively. The width of the alveolar bone was computed based on the measurements made from study models. Impressions were taken from all the patients and cast in stone casts. The stone models were then used to calculate the width and depth of the soft tissue and bone in the maxilla in the lateral incisor, first premolar and first molar regions. The designation of an area is based on a region of interest not dissimilar to that seen on the CT scans, save for the fact that these clinical measurements are finite points or entities.

It is interesting to note that there was no statistical difference between the clinical measurements of the new bone (regenerate) and the control (parent) bone (Figure10.1). It follows that the anatomical shape and thickness of the new bone compares very favourably to that of the parent bone.

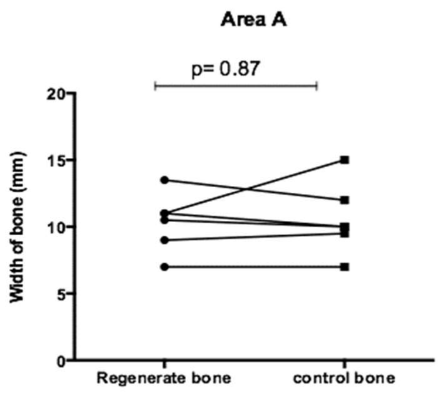

Figure 10.1: A comparison between the regenerate and parent (control) bone for Area A

Again, it can be noted, in the results illustrated in Figure 10.2, that the regenerate bone is almost identical to the parent (control) bone. As the *p*-value is approximately 1, it indicates clearly that there is no significant difference between the two types of bone morphology. When one looks at the results of area C below as shown in Figure 10.3, the same results as seen in Figure 10.2 appear.

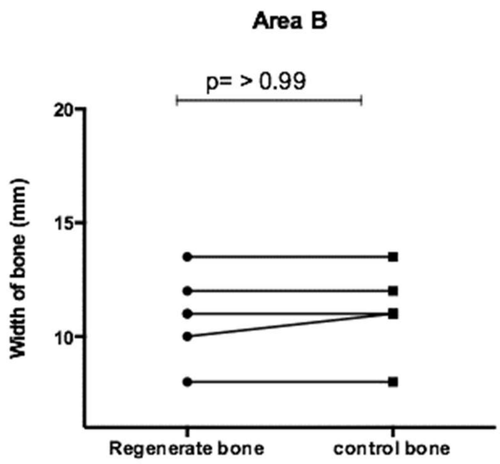

Figure 10.2: A comparison between the regenerate and parent (control) bone for Area B

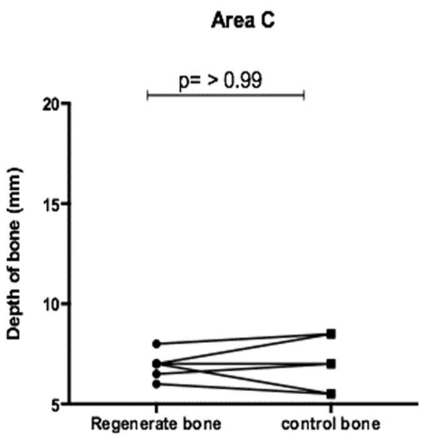

Figure 10.3: A comparison between the regenerate and parent (control) bone for Area C

10.2 Comparison of the new bone with fibula (control) bone

It is interesting to note in Figure 10.4 that the width dimension of the new bone or regenerate compares very favourably with that of the fibula bone. In the different areas of interest, there was no statistical difference between the readings of the new bone as compared with those of the fibula bone.

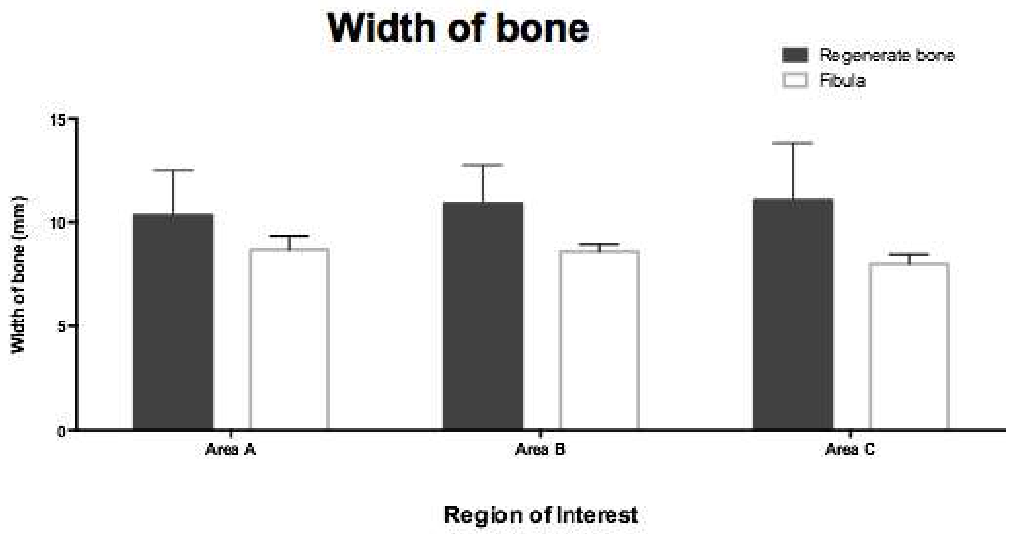

Figure 10.4: The comparison of the width of the new bone to fibula bone

10.2.1 Depth of bone: Regenerate v. parent bone

Clinical measurements of the depth of the alveolar vestibule at three different exact points juxtaposed namely A, B and C respectively, were made. Similar measurements were taken on study models to measure the depth of the vestibule from the crest of the alveolar bone to the labial or buccal sulcus. It can be seen in Figure 10.5 below, that there is no significant difference between the alveolar depth of the regenerate as compared to the parent bone. It follows that the new bone has almost the same height as the parent bone and therefore creates a deep vestibule between the cheek and the alveolar bone.

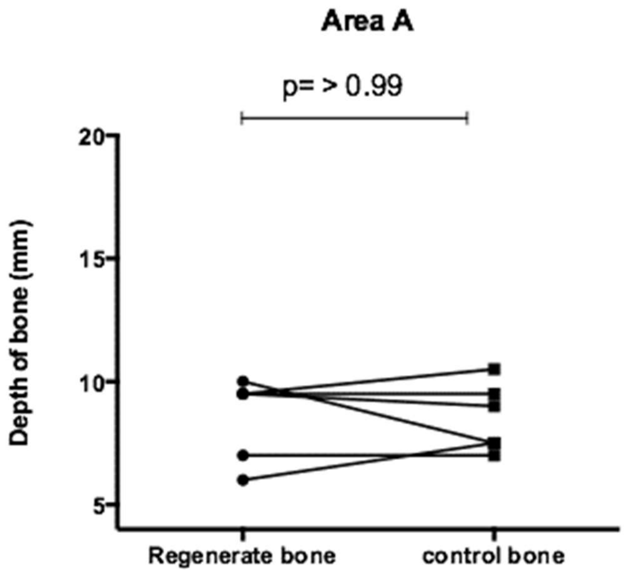

Figure 10.5: A comparison in depth between the regenerate and parent (control) bone for Area A.

In area B relating to the comparison in bone depth, it can be seen that there is a marginal difference between the regenerate bone and the control (parent) bone. This comparison can be seen in Figure 10.6 below.

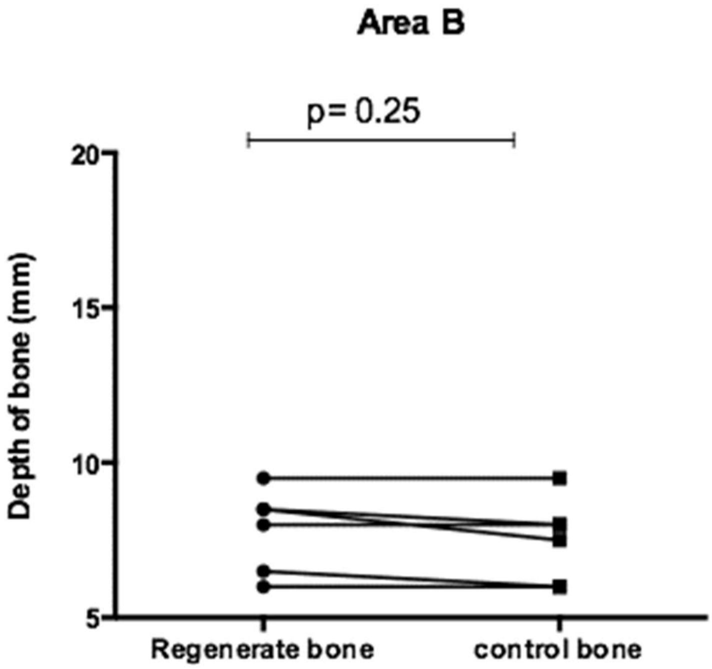

Figure 10.6: A comparison in depth between the regenerate and parent (control) bone for Area B

However, in area C where $p \geq 0.99$, there is almost no significant difference between the regenerate bone and the control or parent bone (Figure 10.7). Therefore if all three areas, namely A, B and C, are computed as an average, the difference between the regenerate or new bone compared with the control or parent bone is clinically insignificant. This means that they are almost identical.

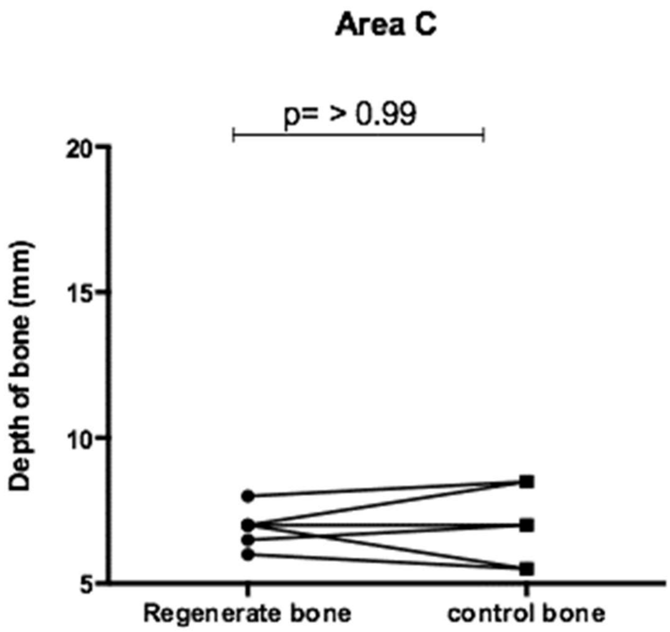

Figure 10.7: A comparison in depth between the regenerate and parent (control) bone for Area C

10.2.2 Depth of bone: Regenerate v. fibula

When comparing the depth of the alveolar bone formed in the area of the regenerate or new bone to that of the fibula bone, it can be seen that in the three regions of interest, the following readings occur (Figure 10.8). In area A, the depth of the sulcus for the fibula is approximately half that of the new bone. In area B, the depth of the sulcus for the fibula is less than half of that produced by the new bone (regenerate). In area C, the depth of the sulcus for the fibula is almost one-third that of the alveolar bone created by the regenerate. The comparison between the fibula sulcus depth and the new alveolar bone shows quite clearly that the vestibule produced by the new alveolar bone is superior to that generated by the fibula bone.

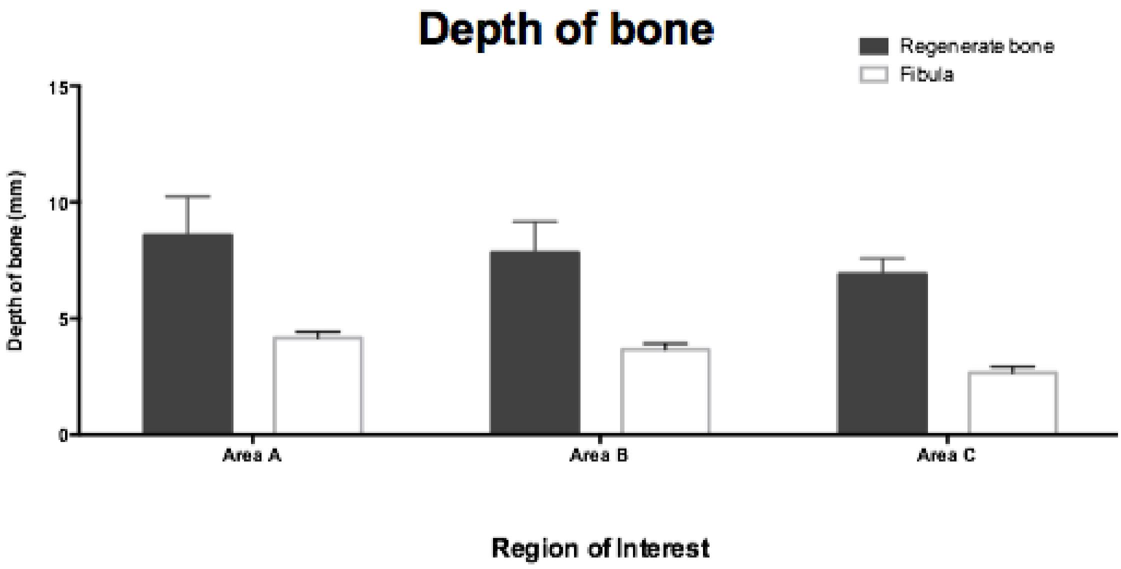

Figure 10.8: Depth of bone: Regenerate v. fibula.

10.3 Radiological comparison of regenerate to parent bone

The regenerate was analysed regarding ROIs within an area of 10 square mm (0.1 square cm). Three areas of interest, namely, A, B and C, were chosen equidistant to the mirror image of the regenerate vs. the parent bone. A like-for-like comparison was made of each area of interest. The bone density was expressed in HU.

10.3.1 Region of interest Area A at three months

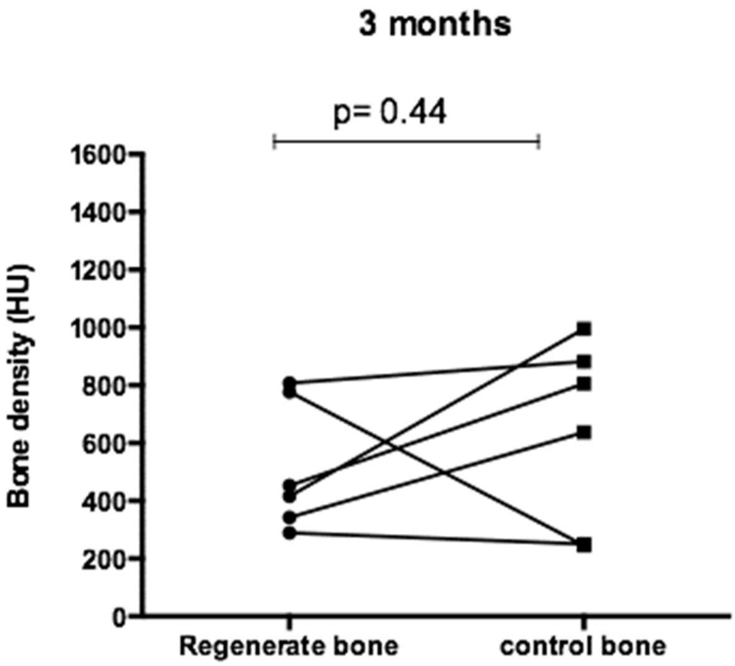

Figure 10.9: The comparison in bone density between the regenerate and the control (parent) bone expressed in Hounsfield units.

In area A, a comparison between the new bone and the control or parent bone after three months shows that there is no statistical difference in bone density between the new bone and the parent or control bone (Figure 10.9). The latter result is indeed a highly positive sign and gives an indication of the suitability of the new bone for the placement of dental implants.

10.3.2 Region of interest Area A at six months

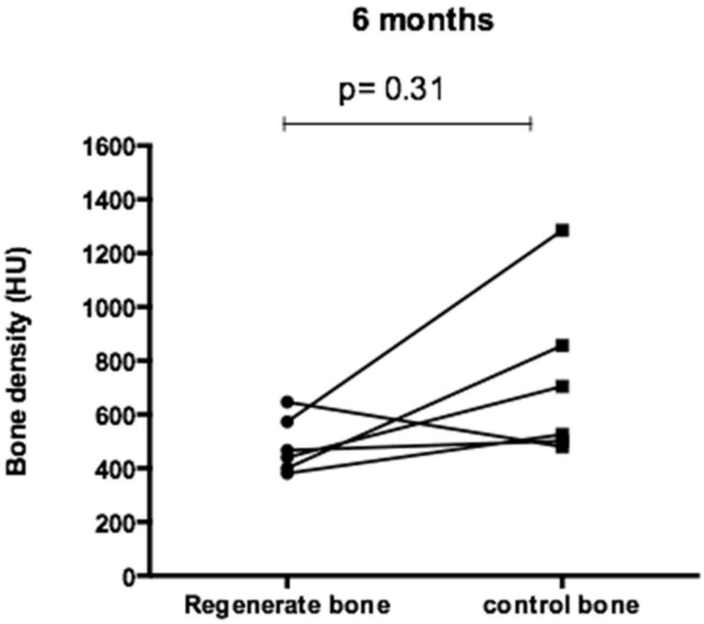

Figure 10.10: The comparison in bone density between the regenerate and the control (parent) bone expressed in Hounsfield units.

In Figure 10.10 above, it can be seen that the parent bone or control bone is slightly superior in bone density to the new bone or regenerate. However, regarding statistical significance, there is no statistical relevance in their difference, which means that the bone densities compare most favourably.

10.3.3 Region of interest Area A at nine months

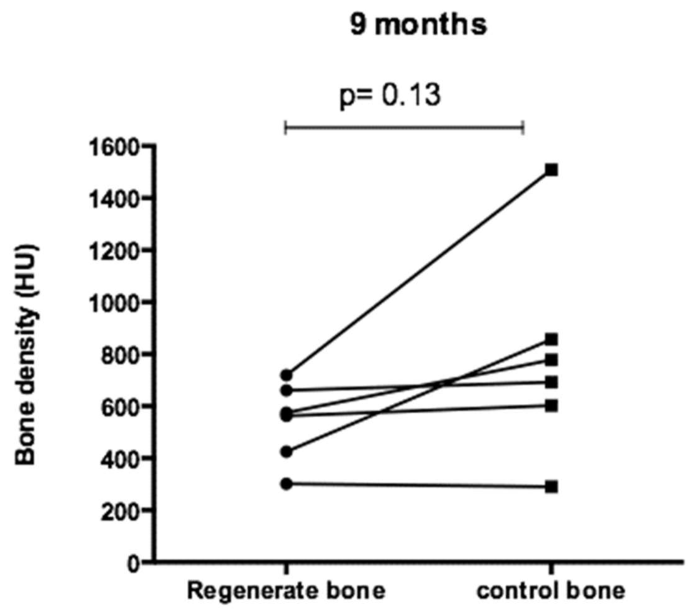

Figure 10.11: The comparison in bone density between the regenerate and the control (parent) bone expressed in Hounsfield units.

Again, in area A, after a period of nine months, a comparison between the new bone and the control or parent bone shows that there is no statistical difference in bone density between the new bone and the parent or control bone (Figure 10.11).

10.3.4 Region of interest Area B at three months

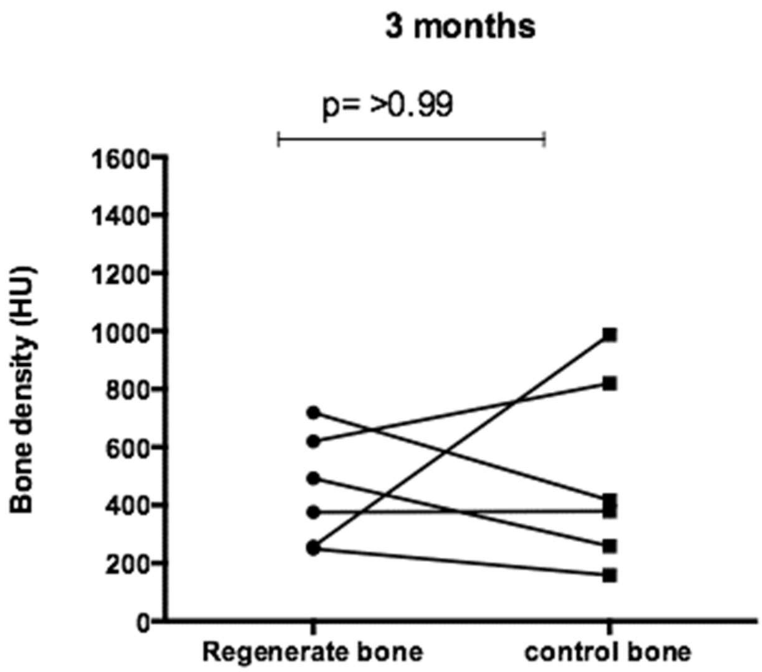

Figure 10.12: The comparison in bone density between the regenerate and the control (parent) bone expressed in Hounsfield units.

In Figure 10.12 above, it can be seen that the parent bone or control bone is slightly superior in bone density to the new bone or regenerate. However, regarding statistical significance, there is no statistical relevance in their difference, which means that the bone densities compare very favourably.

10.3.5 Region of interest Area B at six months

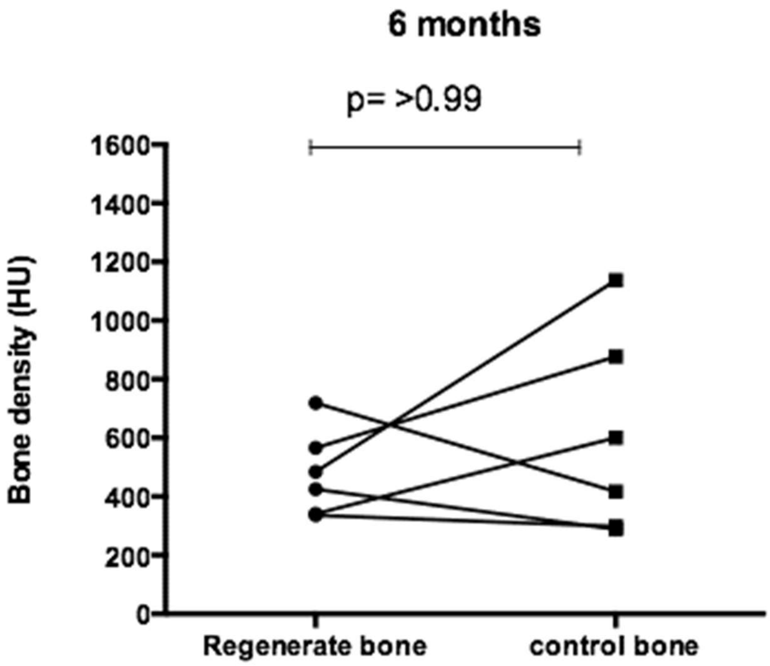

Figure 10.13: The comparison in bone density between the regenerate and the control (parent) bone expressed in Hounsfield units.

Again, in area B, after a period of six months, a comparison between the new bone and the control or parent bone shows that there is no statistical difference in bone density between the new bone and the parent or control bone (Figure 10.13).

10.3.6 Region of interest Area B at nine months

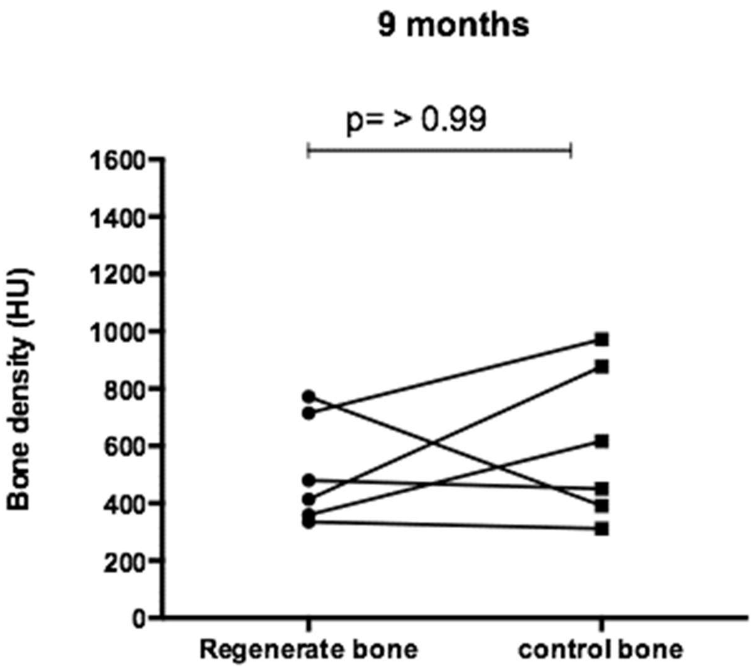

Figure 10.14: The comparison in bone density between the regenerate and the control (parent) bone expressed in Hounsfield units.

In area B, after a period of nine months, a comparison between the new bone and the control or parent bone shows that there is no statistical difference in bone density between the new bone and the parent or control bone (Figure 10.14).

10.3.7 Region of Interest Area C at three months

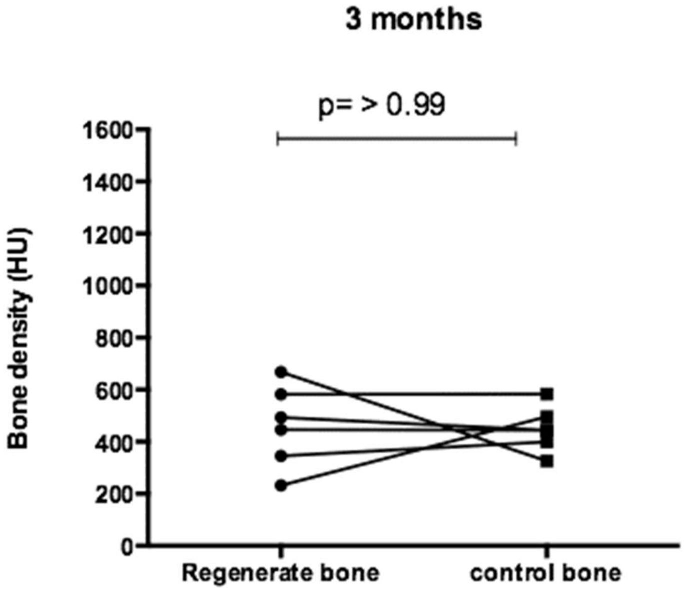

Figure 10.15: The comparison in bone density between the regenerate and the control (parent) bone expressed in Hounsfield units

In area C, after three months, a comparison between the new bone and the control or parent bone shows that there is no statistical difference in bone density between the new bone and the parent or control bone (Figure 10.15).

10.3.8 Region of Interest Area C at six months

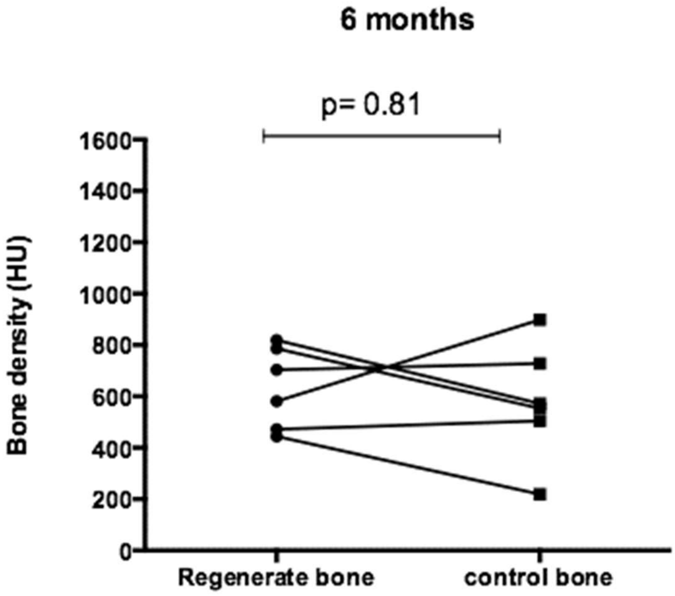

Figure 10.16: The comparison in bone density between the regenerate and the control (parent) bone expressed in Hounsfield units.

In Figure 10.16 above it can be seen that the parent bone or control bone is slightly superior in bone density to the new bone or regenerate. However, regarding statistical significance, there is no statistical relevance in their difference, which means that the bone densities compare most favourably.

10.3.9 Region of Interest Area C at nine months

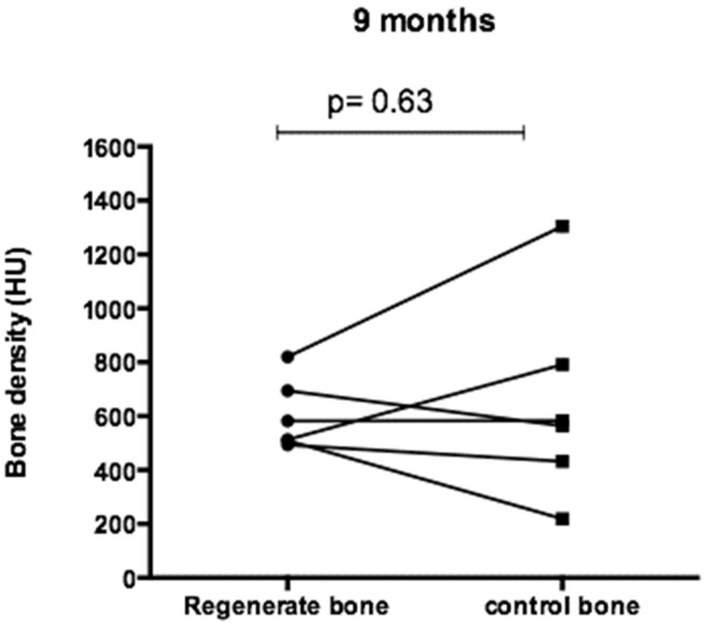

Figure 10.17: The comparison in bone density between the regenerate and the control (parent) bone expressed in Hounsfield units.

In Figure 10.17 above, it can be seen that the parent bone or control bone is slightly superior in bone density to the new bone or regenerate. However, regarding statistical significance, there is no statistical relevance in their difference, which means that the bone densities compare most favourably.

10.4 Radiological comparison of regenerate to fibula bone

A comparison was made between the regenerate and the 'gold standard' of revascularised free fibula bone (RFFF). It can be noted that there was no statistical difference between the new bone (regenerate) and the fibula bone at three months (Figure 10.18).

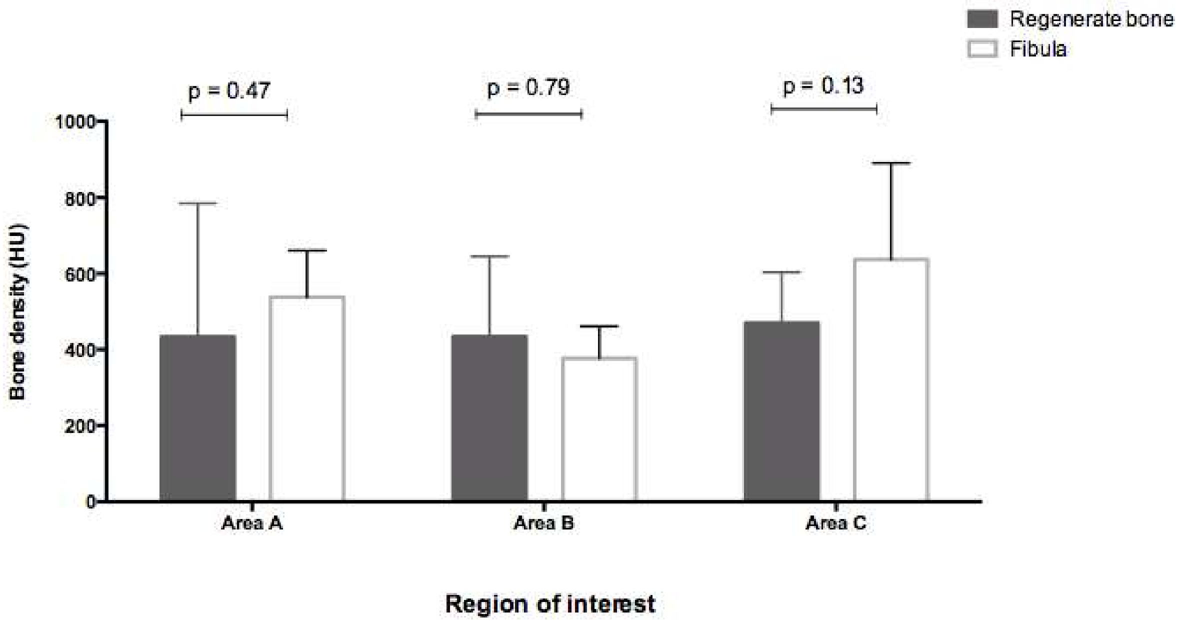

Figure 10.18: Three regions of interest, namely A, B and C, are compared with fibula bone in juxtaposed positions at a three-month interval respectively.

10.5 Statistical analysis

10.5.1 Comparison of Hounsfield region of interest over a 9-month period.

- The Wilcoxon matched-pairs signed rank test was used to compare median bone density in the regenerate bone, with the control or parent bone.
- The Wilcoxon test is a matched *t*-test. In this analysis, we compare the regenerate bone with control bone within each patient, i.e. a matched sample.
- The results showed no significant difference between the regenerate bone and control bones ($p>0.05$, see figures on graphs). The latter indicates that the test procedure or regenerate bone is as good as the control or parent bone.

10.5.2 Comparison of regenerate bone method with fibula bone method

- The Mann-Whitney test was used to compare the median bone density in the regenerate bones of test participants compared with matched controls using the fibula method.
- The Mann-Whitney test is an unpaired *t*-test and was used because in this analysis we were comparing bone density across different patients.
- The results show no significant difference in the bone density of the regenerate bone vs. the fibula. The former may indicate that the new method is as good as the current gold standard procedure (RFFF).

10.6 Quality of life comparisons before and after distraction

A questionnaire was developed by the University of Washington (UW-QOL) (Appendix III) and given to the participant to fill in before the first surgery and 6 months after completion of last distraction. The detailed survey was adjusted for obturator patients and internalised most parts of the Obturator Functioning Scale described below by Kornblith and co-workers (1996)[102] and employed in a study by Riaz and Warriach in 2010.[103] The UW-QOL was first described by Hassan and Weymuller in 1993.[104]. The current version (4) consists of 13 questions: disease specific items such as pain, appearance, activity, recreation, swallowing, chewing, speech, shoulder problem, taste, saliva, mood, and anxiety. Each patient is scored from 0 (worst) to 100 (best) using a Likert-type scale giving a maximum summary score of 1200.[267]

Quality of life questionnaire graph (Figure 10.19)

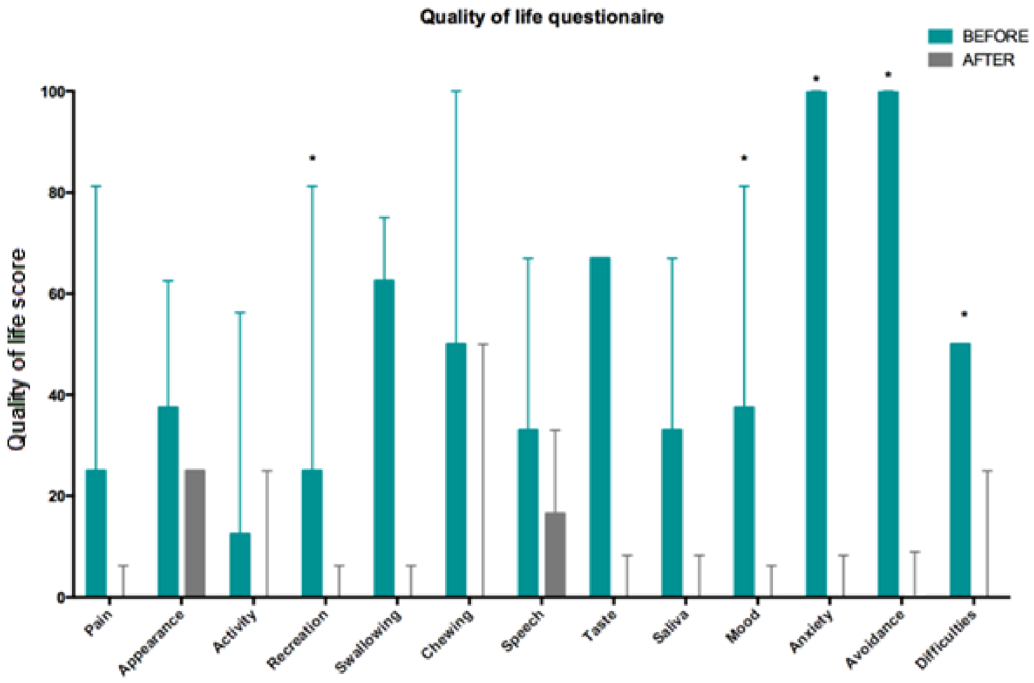

Figure 10.19: Before and after 6 months comparison in Quality of Life

- The Wilcoxon matched-pairs signed rank test was used to compare median quality of life score of the patient's pre- and post-operation.
- The Wilcoxon test is a 'matched *t*-test'. In this analysis, we are comparing the patient's quality of life pre- and post-operation. i.e. within each patient i.e. this is a matched sample.
- The results indicated:

1. A significant increase in the patient's ability to participant in recreational activities (p=0.03) post surgery.
2. A marked improvement in the patient's mood post surgery (p=0.03) post surgery.
3. A significant decrease in anxiety, avoidance and difficulties (p=0.03, p=0.03 and p=0.03 respectively) post surgery.
4. Additionally, when comparing the accumulative quality of life score, pre- and post-surgery, **there is a significant improvement on the quality of life (***$p < 0.0001$)**. This data is not shown graphically.

10.7 Histological investigation

Trephine bone biopsies (2-3 mm diameter and 10 mm depth) were carried out by the primary investigator in the designated areas of the Test and Control regions of interest at the time of the removal of the distraction apparatus. The specimens were analysed by Professor J.J. Hille, an oral pathologist at the University of the Western Cape. The specimens were decalcified in 2.5% formic acid solution for 3 days. Decalcified specimens were processed and embedded in paraffin wax. Axial sections of 6 micrometres in thickness were cut horizontally with a microtome and stained with haematoxylin and eosin and also Masson-Trichrome for light microscopic examination. The latter stain, under polarised light, is very effective for displaying lamellar bone. The trephine bone biopsies took place at the same time as the placement of the dental implants. The dental implants were placed into the same osteotomy sites as the trephine biopsy locations.

10.7.1 Patient #1

The distraction tissue core contains regular slender and parallel, anastomosing cancellous trabeculae which are less thick than the cancellous trabeculae in the control tissue. The morphology of the new cancellous bone is typical of new bone resulting from distraction osteogenesis. The new trabeculae have undergone lamellar remodelling with very early signs of Haversian differentiation. Little cortical bone is present. The intervening delicate fibrovascular stroma in the distraction specimen does not contain fibro-adipose tissue. The cancellous bone lamellae in the control tissue core are less regular in shape and thickness as a result of ongoing bone remodelling. The stroma of the control specimen is more fibro-adipose in nature and contains little bone marrow elements (Figure 10.20). **The quality of the distraction bone appears comparable to, if not better than, that of the control sample.**

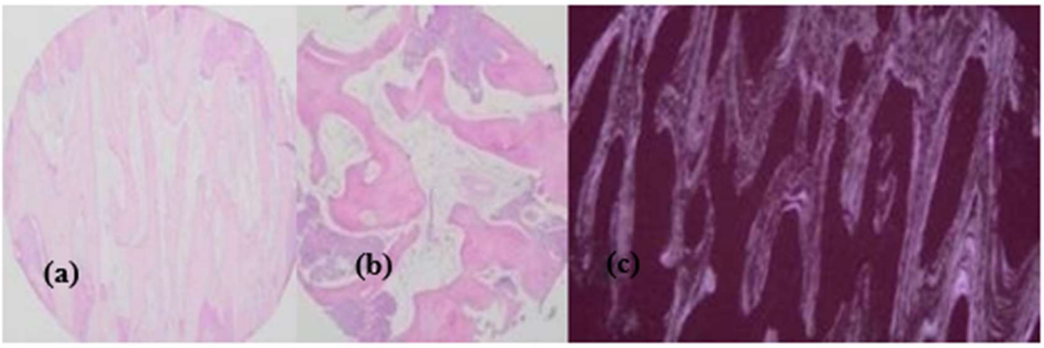

Figure 10.20: (a) is the test specimen; (b) is H&E control; and (c) is M/T control (polarised light).

10.7.2 Patient #2

The distraction tissue core shows thick new cellular cancellous bone in scanty immature fibro-cellular stroma without bone marrow elements. The volume is denser, and the thickness of the new cancellous bone is greater than that of the control cancellous bone; it has already undergone complete lamellar remodelling with Haversian differentiation (Figures 10.21 and 10.22). **The quality of the distraction bone appears as good as that of the control sample, if not superior.**

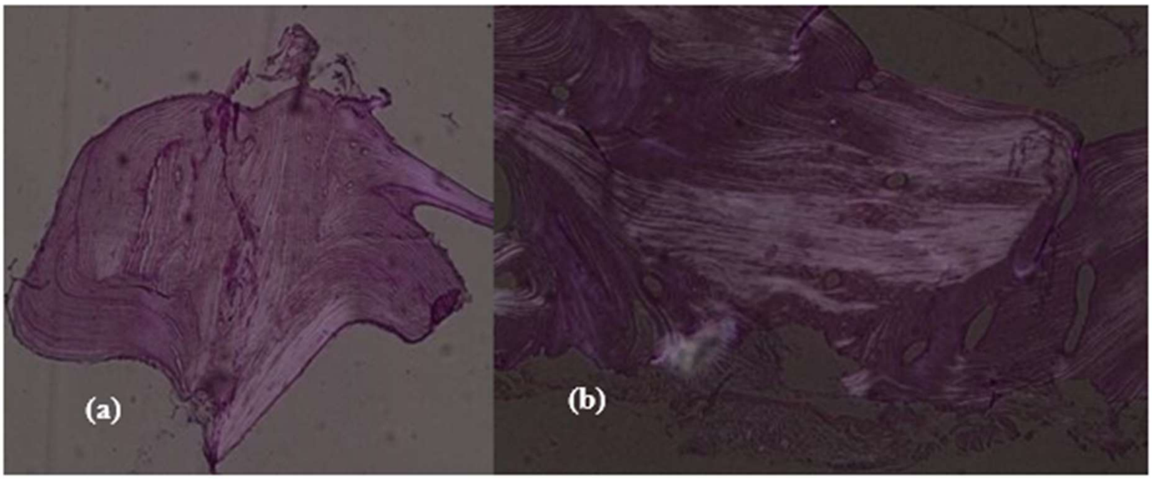

Figure 10.21: (a) The distraction core. (b) The control. Both are in M/T stain (polarised light).

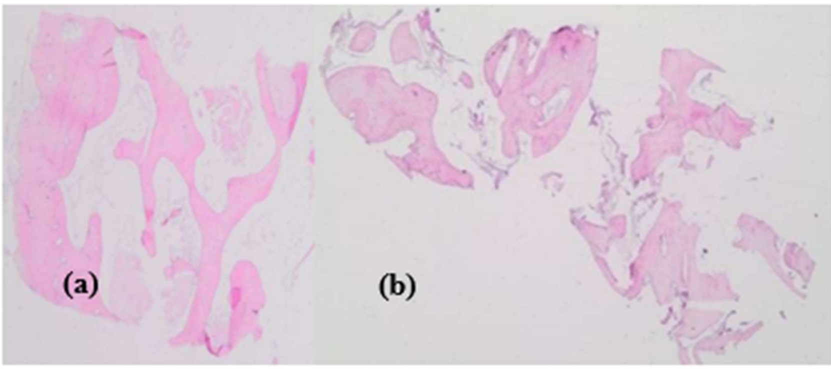

Figure 10.22: (a) The distraction core. (b) The control. Both are in H&E stain.

10.7.3 Patient #3

The distraction tissue core contains abundant, well formed, slender, anastomosing cancellous trabeculae which are less thick than the cancellous trabeculae in the control tissue. The cancellous trabeculae blend well with the surrounding new cortical bone. Both the new cancellous and cortical bone are nicely cellular and have undergone lamellar remodelling with Haversian differentiation in the cortical bone. The intervening stroma is of a delicate fibrovascular nature and contains no adipose tissue or bone marrow elements. The stroma of the control specimen is more fibro-adipose and includes bone marrow elements (Figures 10.23 and 10.24).

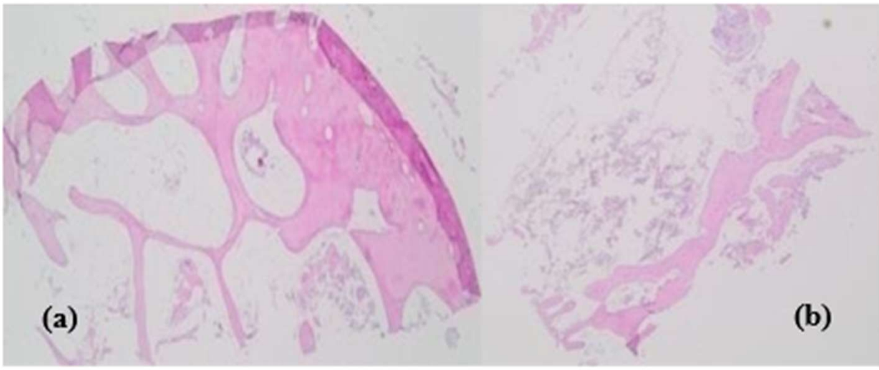

Figure 10.23: (a) The distraction core. (b) The control. Both are in H&E stain.

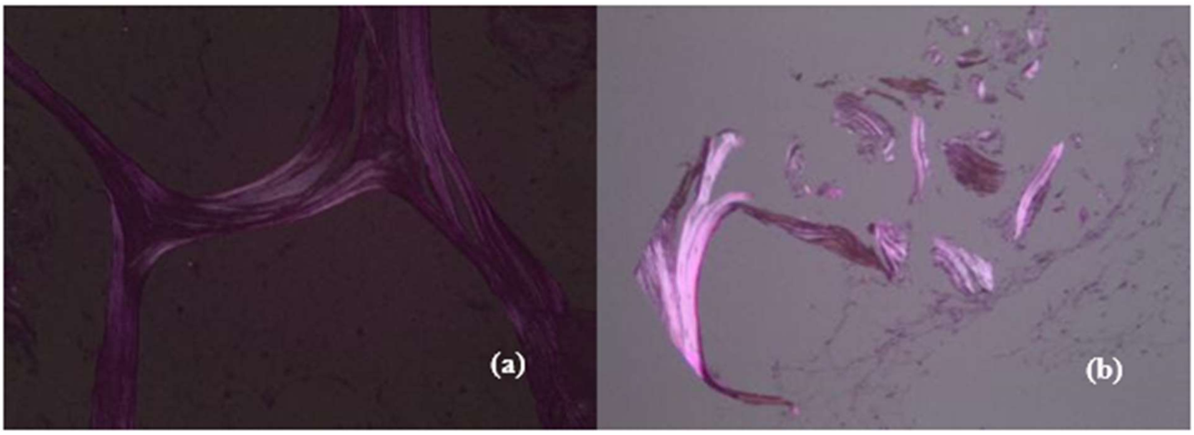

Figure 10.24: (a) The distraction core. (b) The control. Both are in M/T stain (polarised light).

10.7.4 Patient #4

The distraction tissue core contains well developed, cellular cortical bone (flanked by fibrous tissue) accompanied by a few trabeculae and islands of cellular cancellous new bone in a delicate fibrovascular stroma without bone marrow elements. Both the cortical and cancellous bone have undergone lamellar remodelling. The control tissue core consists mainly of cortical bone and fibro-vascular and adipose tissue; the latter contains little bone marrow elements (Figures 10.25 and 10.26). **The quality of the distraction bone appears as good as that of the control sample.**

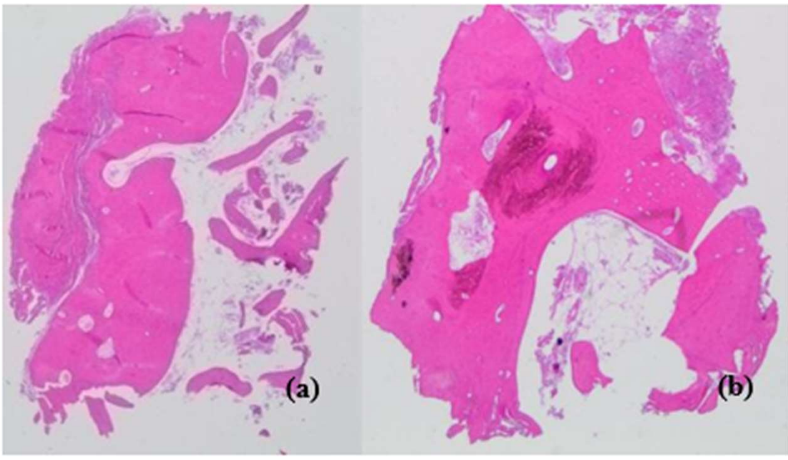

Figure 10.25: (a) The distraction core. (b) The control. Both are in H&E stain.

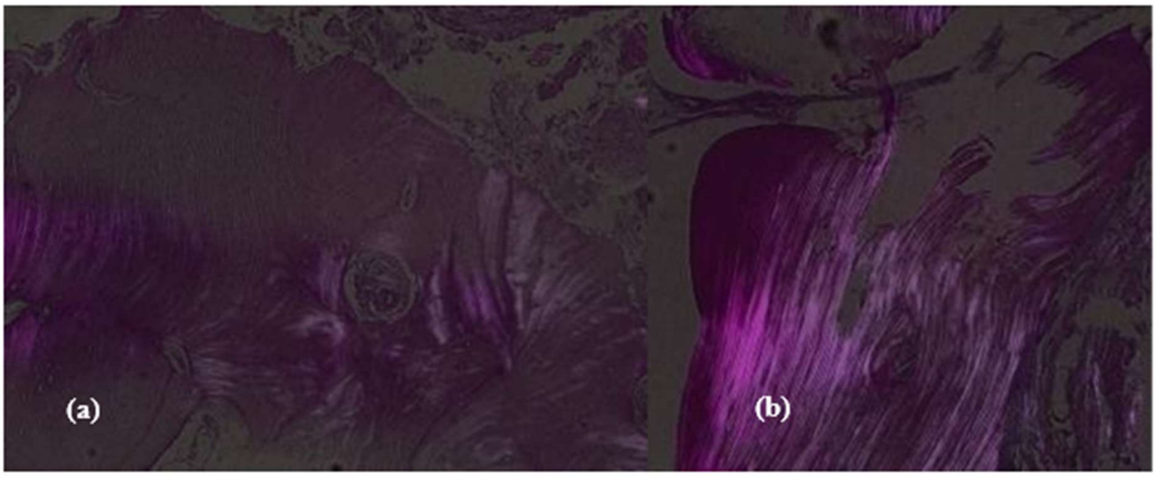

Figure 10.26: (a) The distraction core. (b) The control. Both are in M/T stain (polarised light).

10.7.5 Patient #5

The distraction tissue core contains abundant, regular slender and parallel, anastomosing cancellous trabeculae which are less thick than the cancellous trabeculae in the control tissue. The morphology of the new cancellous bone is typical of that of new bone resulting from distraction osteogenesis. The new trabeculae have undergone lamellar remodelling with early signs of Haversian differentiation and blend with the new cortical bone. The intervening delicate fibrovascular stroma in the distraction specimen contain small bone marrow elements. The stroma in the control sample is more fibro-adipose in nature and also includes small bone marrow elements (Figures 10.27 and 10.28).**The quality and strength of the distraction bone appears to be better than that of the control sample.**

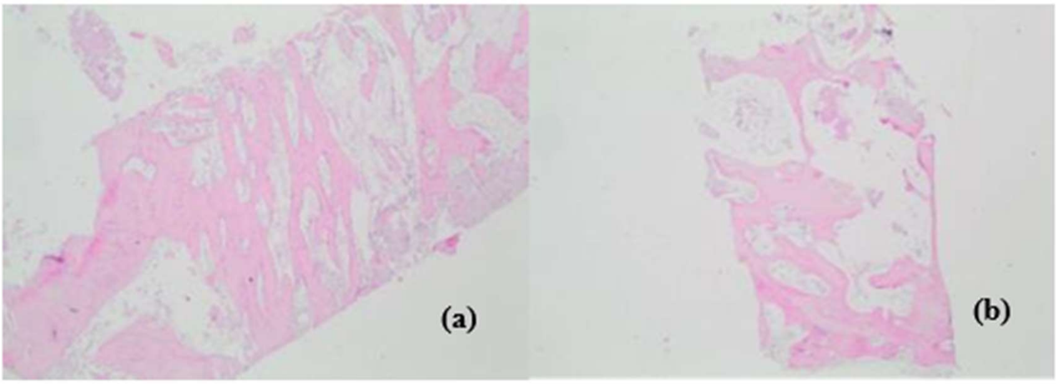

Figure 10.27: (a) The distraction core. (b) The control. Both are in H&E stain.

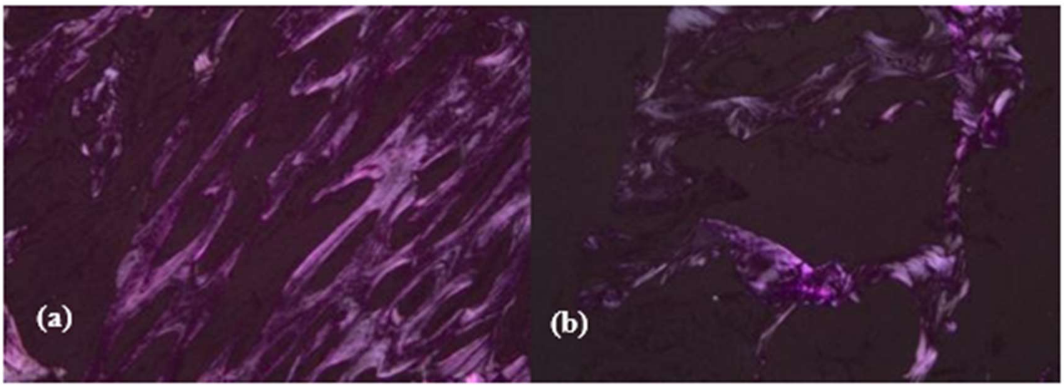

Figure 10.28: (a) The distraction core. (b) The control. Both are in M/T stain (polarised light).

10.7.6 Patient #6

The distraction tissue core shows abundant, thick new cellular cancellous bone in a maturing fibro-cellular stroma without bone marrow elements. The volume is far more copious, and the **new cancellous bone is much thicker than the control cancellous bone;** it has already undergone complete lamellar remodelling with advanced Haversian differentiation and merges with the new cortical bone. The nature of intervening stroma in the control specimen is more fibro-adipose with scant bone marrow and neurovascular elements (Figures 10.29 and 10.30).

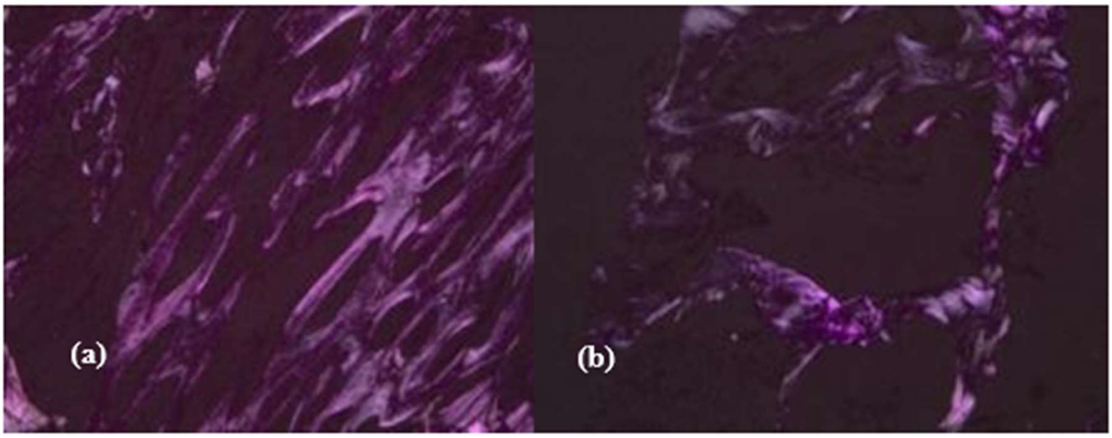

Figure 10.29: (a) The distraction core. (b) The control. Both are in M/T stain (polarised light).

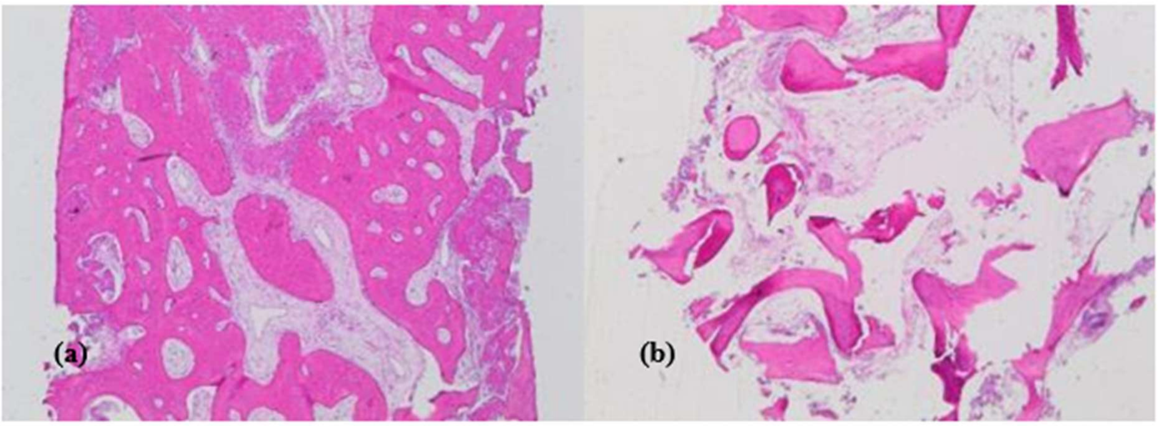

Figure 10.30: (a) The distraction core. (b) The control. Both are in H&E stain.

CHAPTER 11. DISCUSSION

11.1 Introduction

There were two arms to the development of the present project. Firstly, there was the development of the mechanical structures required to design, develop and produce the necessary components to manufacture the transport distraction apparatus. In this regard, there were three prototypes, with two additional modifications to the third prototype.

Secondly, there was the clinical aspect of the study relating to the biological responses to the application of the distraction apparatus to produce new bone and soft tissue along the lines of curvilinear transport distraction osteogenesis. In the discussion below, the first arm relating to the mechanical development of the distraction apparatus is discussed, followed by the clinical application thereof in the second arm.

11.1.1 Mechanical aspects of distractor development

11.1.1.1 Installation of the V1 distractor

The development of the V1 distractor has been extensively described in section 6.4. In retrospect, it was a somewhat primitive method of designing and manufacturing a transport distraction apparatus. Nevertheless, this design took place about four years ago when there was nothing else available as an alternative option. During surgical installation of the device, many adjustments had to be made to the rail, which was quite bulky and cumbersome, to comply with the three-dimensional anatomy of the maxillary bone. What made matters more difficult was the need to continually adjust and reinstall the trajectory rail to arrive at a satisfactory adaptation to the bony maxilla.

In spite of the availability of three-dimensional craniofacial and/or stereolithographic models, there was still a considerable discrepancy between the model and the actual bony anatomy of the patient. As a result, the device required further extensive intraoperative customisation than had been expected. The repetitive adjustment of the curvature of the trajectory rail led to the removal and subsequent replacement of the bone anchorage screws. The screws began to lose their grip and stability because the holes in the bone were deforming. This problem resulted in loss of stability of the trajectory rail when re-using the same screw holes.

The use of metallic spacers to accommodate the lack of contiguity between the bony contours and the trajectory rail also added to the difficulties with installation of the apparatus.

11.1.1.2 Clinical performance of the V1 distractor

The V1 prototype had a LDPE sheath around the trajectory rail, and the locomotive was intended to propel itself in a forward direction by using a worm-rack mechanism whereby the worm itself cut its corresponding gear form into the plastic covering material. Several problems arose in this particular setup for the distractor, which are listed below:

- The mesh cradle that was made to house the transport disc was much too rigid which made bending in three dimensions quite difficult.
- There was instability of the locomotive when attached to the rail after customisation. The locomotive could easily rotate about the axis of the rail, which was because of the oval, and not rectangular, cross-section of the LDPE tube.
- The wired confluence was easily customisable, and it was evident that there would be sufficient access for removal when the treatment was concluded. Even though the wired confluence appeared to be quite crude in its appearance, it turned out to be the easiest solution in the end. Nevertheless, at the time, the author felt that a bolt and screw fixation would be better suited for the apparatus.
- The self-cutting traction mechanism became problematic because of the obvious reasons. At first, the strength provided by the plastic track was found to be acceptable. But as more and more grooves were cut during the travel of the locomotive, the depth of the grooves was not consistent and the temperature of the tissues in the oral cavity further worsened the integrity of the plastic tubing. It was therefore just a matter of time before the worm cutting mechanism ground to a halt. In addition, at the outset of testing the locomotive, the forward and reverse action of the self-cutting worm further degraded the apparatus. It was therefore not unexpected that after transport distraction of 26 mm, the locomotive began cutting upon itself without providing further tractive force. At this point, the locomotive required

assistance to continue along its path. In addition, it was not known to the team what sort of distraction force was required to further the creation of regenerate along the path or trajectory.

- However, it was clear that in order for further distraction to take place, an auxiliary distractor would have to be attached to the existing locomotive. This was duly carried out by using titanium plates, screws and wires, and led to a further distraction of 13 mm over the ensuing 9 days.
- While the outcome of this CTDO was deemed to be successful, and produced good-quality bone and soft tissue, it was clear that further improvements were necessary and that further research would have to be carried out to determine the correct magnitude of the distraction force. It was also clear that the forces required in the clinical environment to propel the locomotive were much greater than expected, leading to inevitable failure of the traction mechanism. This led to further pre-clinical laboratory testing (see subsection 6.4.7) which evaluated the device, based on data found in the literature. It was assumed that a suitable benchmark for maxillary distraction would be to use the figures produced during mandibular distraction osteogenesis.

In spite of the mechanical failure and inadequacy of the V1 prototype, the clinical outcome was still more than satisfactory and led to the patient being the first recipient of three dental implants supporting a temporary bridge. There was also a well-formed palatal vault and healthy alveolar regenerate with a deep vestibular anatomical outline.

11.1.1.3 Installation of the V2 distractor

Major design refinements were made to the V2 distractor as far as the locomotive and the trajectory rail were concerned. A metal worm-rack traction mechanism replaced the plastic self-cutting mechanism. The profile of the locomotive and the mesh cradle were refined to improve patient comfort and customisability. The wired confluence was replaced with a bolt and nut connection. All these improvements led to a more **robust** distraction apparatus which was bench tested in a laboratory and found to be more than adequate to perform CTDO. In fact, the worm-rack traction mechanism was found to be stable even at forces of up to 200 N. Further detail on the ergonomics of the apparatus has already been described in subsections 7.2.1 and 7.2.2

A further improvement was to provide sufficient play in the pitch of the teeth on the rack of the trajectory rail so as to allow a bending radius of 25 millimetres. This was necessary to provide 0.3 mm play so that the locomotive could track around a gentle curvature without 'derailing'. As this type of worm-like mechanism was not widely used elsewhere, there was no technical information available to provide a guide to the design of the tooth profiles of the worm or the rack. The design, therefore, of the traction mechanism was based on engineering basics, making use of computer-aided design tools to model and analyse the mechanism. As stated before, the manufactured V2 traction mechanism performed satisfactorily in bench testing (subsection 7.2.4).

The V2 device was subjected to rigorous testing to ensure its reliability in the clinical situation. The details are described in subsection 8.4.1.

The second clinical case involved a maxillectomy defect of approximately 80 mm where about 70% of the alveolar ridge, hard palate and much of the nasal floor was resected (Brown III d). The robust V2 distraction device was designed to easily manage the distraction forces required to transport the disc for the required distance of about 80 mm.

As shown in Figure 7.20, the early formation of a neo-alveolus was most encouraging until the locomotive had to negotiate a curvature. This was followed by a most disturbing 'rubber band' effect which is further elaborated on below (subsection 11.1.1.6).

11.1.1.4 Technical issues during installation

- As only three teeth were left (post extraction of 2 teeth for bone stock formation) in the second quadrant, namely #25, #26 and #27, there was not much bone available for support of the trajectory rail.
- The spacing of the anchorage holes in the trajectory rail prescribed and restricted the anchorage screw spacing to precisely 7.5 mm. This lack of flexibility made it impossible to accommodate all the desired anchorage screws between the dental roots.

- There were geometric discrepancies between the preoperatively shaped rail and the actual bony anatomy. This caused a time-consuming customisation process during the operation.
- As was the case in the V1 installation, spacers again had to be used to offset the trajectory rail from the maxilla. The placement of these spacers was cumbersome, and they obstructed the drilling process and placement.
- The nut and bolt arrangement used to secure the confluence was found to be impractical during installation owing to limited clinical access to the confluence region.
- When the locomotive was re-attached to the trajectory rail, the latter had to be removed in its entirety, including the anchorage screws, and subsequently re-installed. In addition, the mesh cradle was found to be too rigid for shaping *in situ*, despite the further refinements made (see subsection 6.3.3.1).
- Once customisation had been finalised, the locomotive, trajectory rail and buttress plates were pre-assembled outside the oral cavity.
- Most importantly, the repeated installation and removal of the trajectory rail resulted in the loss of integrity of the anchorage screws.
- The screws securing the bone transport disc to the mesh cradle also had a tendency to loosen under long-term loading. Figure 7.11 shows the device fully assembled before final installation.

11.1.1.5 V2 clinical performance

The V2 device performed remarkably well and the locomotive propelled the transport disc along the 80 mm trajectory with ease. It was also noted that resistance to rotation of the worm screw increased progressively as the distraction process continued. The following ergonomic shortcomings of the device were highlighted, directing further enhancements:

- Owing to repeated removal and re-attaching of the trajectory rail, this action compromised the integrity of the anchorage screws. Micro-movement of the trajectory rail could have contibuted pain and discomfort to the patient.
- The use of spacers to offset anatomical defects to correct the spatial orientation and fixation of the trajectory rail was a cumbersome and time-consuming exercise. This issue created a priority for further refinement during installation.

- During removal of the device, the disassembly of the bolted confluence joint was found to be awkward and time-consuming. Hence it was found that the simple wired confluence provided just as good an ergonomic and satisfactory solution.
- The spacing of the maxillary anchorage screws was restricted to the set spacing available on the trajectory rail (Figure 7.10). It was concluded that a different approach had to be more flexible to deal with the position of the dental roots when applying the trajectory rail or baseplate.

In summary: the V2 prototype introduced a rigid mechanical traction mechanism which was superior to and more reliable than the V1 prototype. The V2 was able to deal with torque ratios in excess of 100 N (with a safety factor of 1.5) and successfully navigate the minimum bend radius of 25 mm. The success of this device in performing a curvilinear distraction of 80 mm demonstrated its feasibility for use during intraoral CTDO.

11.1.1.6 The 'rubber band' effect

After the initial phase of distraction with the V2 device, the early neo-alveolar bone which was formed at a rate of 1.5 mm per day appeared to be thick and healthy. The problem arose when the curvature of the premaxilla was to be negotiated by the locomotive. It subsequently transpired that when the locomotive reached the opposite side of the curvature in the premaxilla, the regenerate straightened out into almost a straight line across the premaxillary region (cf. the experience by Neelankandan *et al*. in 2012, shown in Figure 11.1 below[68]). This phenomenon was found to be most disturbing and the author timeously constructed a Palacos (acrylic) stent in order to mould the regenerate as shown in Figure 7.21. Unfortunately, the desired effect was not achieved because the regenerate behaved like a tube of toothpaste being bent in the centre. What one in fact sees is that the regenerate, which is soft and malleable, displays a tendency to bulge out towards the ends of the tube. It was therefore decided to construct a properly designed acrylic splint based on pre-resection stone models taken previously (Figure 7.22(a)). This splint was wired to the trajectory rail and fixed to the remaining hard palate by means of titanium screws as shown in Figure 7.22(b). The process of transport distraction was hence concluded at the placement of the splint, and a total of 90 mm of distracted tissue was achieved in a period of 60 days.

Figure 11.1: The ‘rubber band’ effect of the premaxilla (after Neelankandan 2012).[68]

The splint was left *in situ* throughout the consolidation process, and it was rather disappointing to find that the shape of the premaxilla was not as aesthetic as might have been hoped for. Nevertheless, there was sufficient bone and soft tissue for support of dental implants with a bar overdenture system.

From this experience, it was deduced that it was not possible to mould the regenerate in a **horizontal plane** and still expect uniformity in the anatomical shape of the alveolar bone and the hard palate. In the literature, the only type of moulding of the regenerate documented relates to the axial plane which runs parallel to the distraction vector. This type of moulding can also be referred to as **angular moulding** and usually is performed at the angle of the mandible after forward distraction of the lower jaw. It was well documented by Luchs *et al.* in 2002 who performed this procedure in canine mandibles with much success.[268] Aizenbud and co-workers in 2009 carried out curvilinear mandibular distraction along the sagittal plane of the mandible with much success in 40 patients.[269] The floating bone concept was also described by Bodo Hofmeister in 2001[270] as well as Kunz *et al.* in 2005.[271]

Peacock *et al.* in 2014 showed the results of curvilinear distraction osteogenesis using continuous distraction in Yucatán guinea pics. Again, this type of distraction was carried out in a sagittal plane. Therefore it was a rather mythical notion to expect distracted regenerate to follow the shape of a curvature.[272]

11.1.1.7 Installation of the V3 distractor

The V3 distractor was a major improvement and allowed easy installation and repeated removal of the trajectory rail during the period of installation. This distractor consisted mainly of two components: the first is a very robust base plate which is usually installed only once and does not have to be removed again. The trajectory rail can be repeatedly attached onto this base plate, and detached, until the operator is happy with the final installation.

The V3 distractor was laboratory tested to verify the critical strength requirements and establish their capabilities and the relevant safety factors. Testing included the following:

- The axial loading capabilities of the worm-rack mechanism. This mechanism was subjected to an axial load up to a maximum of 200 N.
- The torque-carrying capabilities of the worm screw. The worm screw was subjected to a torsional load of up to 50 N.cm.
- The tightening torque of the base clamp Torx screws. It was found that a tightening torque of 2 N.m was specified for the base clamp screws based on laboratory slippage tests.

The purpose of the laboratory testing was to ensure that the device could perform its function under the most extreme conditions and also to determine its ultimate strength capabilities. It turned out that the V3 device navigated the minimum radius trajectory under a load of 100 N. Not only did the apparatus perform successfully on a straight path, but it also performed just at as well on a bend radius of a minimum of 25 mm while subjected to loads of up to 100 N. Further testing provided the following data:

- The worm-rack interface withstood a load of 200 N – double the maximum expected distraction load of 100 N.
- The worm screw provided a safety factor of 2.18 over the maximum expected activation torque. The maximum conceivable activation torque, determined by practical testing, was

16.2 N.cm. The strength testing of the worm screw revealed a torque-carrying capacity of 35 N.cm, thus providing a safety factor of 2.18.

- The base clamp joint sustained a moment of 2.47 N.m thus providing a safety factor of 2.1 over the maximum foreseeable load of 1.2 N.m. In a separate test, the base clamp screws sustained a tightening torque of 4 N.m which was double the specified tightening torque of 2 N.m. Therefore a large margin of over-tightening could be accommodated.
- The self-locking action of the worm-rack mechanism limited retraction of the locomotive to tolerable levels.The device exhibited retraction of less than 0.3 mm under extreme test conditions.These conditions mimicked disturbance by the tongue and the fluctuating distraction load. Given that the distraction rates would amount to 0.5 mm – 1.5 mm per day, this led to the successful formation of bone, and the 0.3 mm of detraction exhibited by the device did not affect bone formation.

11.1.1.8 Clinical performance of the V3 distractor

The V3 distractor performed with great success in the third and fourth clinical cases. The following improvements were recorded:

- A highly beneficial development was the ability to attach and detach the trajectory rail repeatedly without disturbing the anchorage to the maxilla. This was effected by the base clamp feature which meant that the base clamp was installed only once and thereby its rigidity was not affected again.
- It was found that the Torx screws were still difficult to align into their respective threaded holes in the base plate. It was then decided that the design of these screws be refined with a non-threaded lead-in to aid alignment, and that tools would be developed to improve the grip of the screw head for more controlled placement.
- The cradle plate was still found to be too cumbersome to bend, even though the thickness of the titanium fingers was reduced to 0.8 mm. Also, the problem of work hardening of the material produced visible cracks in the cradle plate and led to breakage of one plate. It was decided to reduce the thickness of the stainless steel cradle plate to 0.5 mm.

- Repeated removal of the trajectory rail to adjust the cradle plate geometry was indeed time-consuming and awkward. It was decided that the cradle plate be removable so that it could be quickly and efficiently re-attached *in situ.*
- Report-back from the two patients treated with the V3 distractor indicated that the device was well tolerated. The most notable sources of pain and irritation were the result of accumulation of food in the cradle plate and also the palpability of the alveolar buttress plate in the roof of the mouth. It was subsequently found that this trans-palatal plate was not necessary.
- The clinical measurements of the activation torque suggested only minor resistance from the regenerate at a distraction rate of between 1 mm and 1.5 mm per day. This distraction activation torque was measured clinically using an electronic torque meter as discussed in subsection 8.4.1.1 and illustrated in Figure 8.24. These *in vivo* measurements were consistently below 4 N.cm.
- When comparing the laboratory data in the graphs in Figures 8.23 and 8.30, the activation torque of 4 N.cm corresponds to a distraction force of approximately 40 N. This fell well within the 100 N loading capabilities of the V3 device as described in subsection 8.4.1.

In summary, it was found that the V3 distractor constituted a valuable improvement in the concept of transport distraction and proved to be a real winner in transporting a prefabricated transport disc along a curvilinear plane. However, one negative observation of this concept was the extrusion of retention screws from the cradle/basket owing to the tension exerted by the regenerate onto the cradle. Even though this did not amount to any clinical reduction in regenerate formation, it was nevertheless an issue, with screws working loose and falling out.

11.1.1.9 Installation of the V4 distractor

As shown in the literature by Neelankandan *et al.* in 2012, it is not possible to grow bone on a curvilinear trajectory in a horizontal plane.[68] The regenerate will follow the shortest distance between two points, hence creating a straight line, which is known as the ‘rubber band’ effect. To overcome this problem of how to create a curvature, the author decided to perform multifocal distraction using a method of creating a second transport disc from the first one. It was fortuitous that, in our fifth clinical case, there was insufficient maxillary bone and soft tissue for the creation of bone stock as was done previously in the study. In fact, this patient had only four teeth remaining in the second quadrant, namely #24, #25, #26 and #27.

In view of the above constraints, the author decided to design a tandem distractor so that distraction could be carried out without sacrificing any of the existing teeth. This is referred to as hybrid distraction, where the tooth and the surrounding alveolar bone are transported as a single unit. It was therefore designed that a second osteotomy could be performed at a later stage to continue the distraction process after a consolidation period of three months had been allowed to take place. Subsequently the V3 distractor was modified as shown in Figures 9.2 and 9.3 where the locomotive would 'pull' two vertical plates that were joined to each other by a thin horizontal plate. The idea was to separate the vertical plates at a later stage by cutting through the horizontal plate with a burr.

The outcome of this tandem distraction was highly successful and, indeed, a curvature of the premaxillary bone was achieved. The only disadvantage experienced was that the vertical plates were pulled by the locomotive. This meant that almost 10 mm of wasted space existed between the locomotive and the vertical distraction plates. In a practical sense, it amounted to insufficient horizontal transport distraction being carried out because the locomotive abutted the stabilisation plates found at the proximal end of the trajectory rail.

However, the quality of the newly created bone was found to be more than satisfactory, and the teeth that were transported were extracted and dental implants were placed into their respective sockets. The results of the bone that was produced are shown in Figures 9.27 and 9.29.

While the V4 distractor exceeded our expectations, a further modification was designed to maximise the amount of translation that this tandem distractor could produce.

11.1.1.10 Installation of the V5 distractor

The performance of the V4 distractor was highly reliable, and the proof of concept of multifocal distraction (tandem) was established to be the way forward for the creation of bone and soft tissue along a curvilinear trajectory. As stated above, the only setback of the V4 distractor was its inability to maximise the distance along the trajectory rail for the production of new bone. A further modification was made whereby the locomotive was placed directly onto the vertical plates which were attached to the teeth and bone, and hence an additional 10 mm – 12 mm could be added to the distraction distance for the locomotive to acquire. The adaptation of the locomotive onto the vertical plates is seen in Figures 9.35 and 9.36. In Figure 9.36 it can also be seen that the small horizontal crossbar connections can easily be cut using a tungsten carbide burr for the second stage of distraction to take place.

Another advantage of having a 3-D stereolithographic model was to plan the trajectory from beginning to end. In our last case, it could be seen that the malar corpus would obstruct the free passage of the locomotive and the vertical plates. This was easily corrected during surgery and a free passage for the locomotive was obtained.

It was also found, as in the previous case, that the transpalatal buttress plate was no longer adding to the stability of the confluence. This meant less inconvenience to the patient and, at the same time, the same amount of stability was provided by the zygomatic buttress plate.

To summarise the design of the V5 distractor, it was concluded that this design was simple yet highly effective and also sufficiently slender to be comfortable for the patient during the distraction period.

Installation of the V5 distractor was fairly straightforward, and distraction in the first phase was usually carried out to the greatest part of the curvature that needed to be negotiated. Another interesting aspect to this form of distraction, as compared with distracting in a linear direction over a prolonged distance, was that when short distances were distracted, there was much less resistance encountered to the force of distraction, which made it much easier for the patient to tolerate. In other words, it was more convenient to divide a segment into two or three sub-units and distract with ease and comfort rather than distracting one long segment of regenerate.

In addition, the singular advantage of distracting in a multifocal manner was that the collagen could remain in its original state rather than being subjected to the ‘rubber band’ effect. It has been shown again in case number 6, as was done in case number 5, that curvilinear distraction could be successfully effected by means of multifocal hybrid distraction.

The superlative bone and soft tissue illustrated in Figure 9.46 not only shows the healthy regenerate but also the replication of the palatal rugae.

The vertical osteotomy that was performed to initiate the second phase of distraction was fairly simple and required minor surgical intervention. Again, it was found that the ease of distraction was most encouraging and that the desired distance to complete the transport distraction could be achieved. One interesting point was that the transport of the teeth resulted in the creation of premature contacts with the mandibular occlusion. This phenomenon needed to be avoided at all cost and, to mitigate damage to the developing segments, a sectional removal acrylic bite appliance was made (Figure 9.52). Another interesting tip was to place an acrylic spacer between the teeth so as to prevent relapse of the new segments of the bone (Figure 9.51).

After a further consolidation period of three months, the teeth were extracted and dental implants were placed into the newly created bone and dental sockets. A temporary bridge was placed, to be followed by a permanent bridge after a period of 6 months.

In the present study, and especially in cases 5 and 6, the production of curvilinear bone and soft tissue along a horizontal plane has been clearly demonstrated. The quantity and the quality of the newly created bone and soft tissue has been shown in Chapter 10. From a clinical perspective, the new alveolar bone achieved all the goals that were set out from the beginning, namely the correct width, height to create a physiological vestibule and palatal vault shape, and depth to re-establish the shape of the hard palate as well as the integrity to place dental implants in the aesthetic zone. This clinical picture is well demonstrated in Figures 9.56 – 9.58.

The method of CTDO as described above surpasses all forms of bone grafting in the post-maxillectomy domain.The results are superior to non-vascularised bone grafting and also the RFFF (except in bone density, where RFFF is superior). In spite of the latter, the HU produced by CTDO was sufficient for dental implant placement after 3 months. Besides also providing hermetic closure of the oro-sinonasal cavities, the method of CTDO also maximises function and aesthetics.

11.1.2 Clinical aspects and interpretation of the results

11.1.2.1 Bone width

The width of the alveolar bone was computed based on the measurements taken from the study models. In the postoperative phase, clinical impressions of the soft tissue and bone were taken from all the patients and these were cast into stone models. There were three areas of interest, namely A, B and C respectively. These areas of interest were not dissimilar to those chosen on the CT scans, save for the fact that these clinical measurements were finite points. In Figure 10.1, where the regenerate was compared to the control (being the parent bone), it was interesting to note that the anatomical shape and thickness of the new bone compared very favourably to that of the control (parent) bone. With $p=0.87$ in relation to area A, this meant that there was no statistical difference between the clinical measurements of the new bone and those of the control. In area B, shown in Figure 10.2, where $p\geq 0.99$, it again appeared that there was no significant difference between the two types of bone morphology. In area C, as seen in Figure 10.3, where $p\geq 0.99$, again there was no statistical difference between the regenerate and the control bone. When comparing all three areas of interest, namely A, B and C collectively, it is clearly noted that the newly formed bone is clinically as good as the control bone, and these findings corroborate those found in an animal study by Peter Costantino in 1993.[61] **It can therefore be stated unequivocally and with confidence that CTDO is an effective and successful method of regenerating new bone and soft tissue in post-maxillectomy defects.**

11.1.2.2 Comparison of the new bone with fibula (control) bone

In Figure 10.4 it can be seen that the width of the new bone compared most favourably with that of the fibula bone. In the areas A, B and C, there was no statistical difference between the new bone and the fibula bone. While it is well known clinically that the fibula bone has a thickness of about 10 mm, this provides sufficient width for the placement of dental implants. However, the results shown in Figure 10.4 indicate that the regenerate was equally as favourable for the placement of dental implants in terms of its width.

11.1.2.3 Depth of bone: Regenerate v. parent bone

The clinical measurements of the depth of the alveolar vestibule were taken at three different points as described above. Again, the use of study models assisted in measuring the height of the vestibule from the crest of the alveolar bone to the depth of the labial or buccal sulcus. In area A as shown in Figure 10.5, there was no significant difference between the alveolar depth of the regenerate as compared with the parent bone. It follows therefore that the new bone had almost the same height as the parent bone and therefore created a deep vestibule between the cheek and the alveolar bone ($p \geq 0.99$). In area B, there was a marginal difference between the regenerate and the control bone as shown in Figure 10.6. In this case, $p=0.25$. The latter indicates that there was no significant difference between the regenerate and the parent bone in terms of sulcular depth in area B.

In area C, $p \geq 0.99$, again indicating almost no significant difference between the regenerate and the control bone (Figure 10.7). When all three areas, namely A, B and C, are taken as an average, then there was no statistical significance between the control and the parent bone. This indicated that the new bone was almost identical statistically to that of the parent bone in terms of vestibular depth.

11.1.2.4 Depth of bone: Regenerate v. fibula

In Figure 10.8, the following observations were made. In area A, the depth of the vestibular sulcus for the fibula was approximately 50% of that of the new bone. In area B, the depth of the sulcus was less than 50% of that produced by the new bone or regenerate. In area C, the depth of the sulcus for the fibula was less than 50% of that of the alveolar bone created by the regenerate. When the average of the three areas, namely A, B and C, was calculated, it was found that the new alveolar bone had a vestibular depth **almost double** that created by the fibula bone. This was indeed a **highly significant clinical** finding as it determined the functional and aesthetic value of the new alveolar bone. It was therefore highly significant that the process of CTDO was found to be **vastly superior** to that of fibula bone reconstruction in the maxilla.

This finding was also clinically shown in a study by Futran & Mendez in 2006.[273] The clinical picture of a patient is shown in Figure 11.2(c).

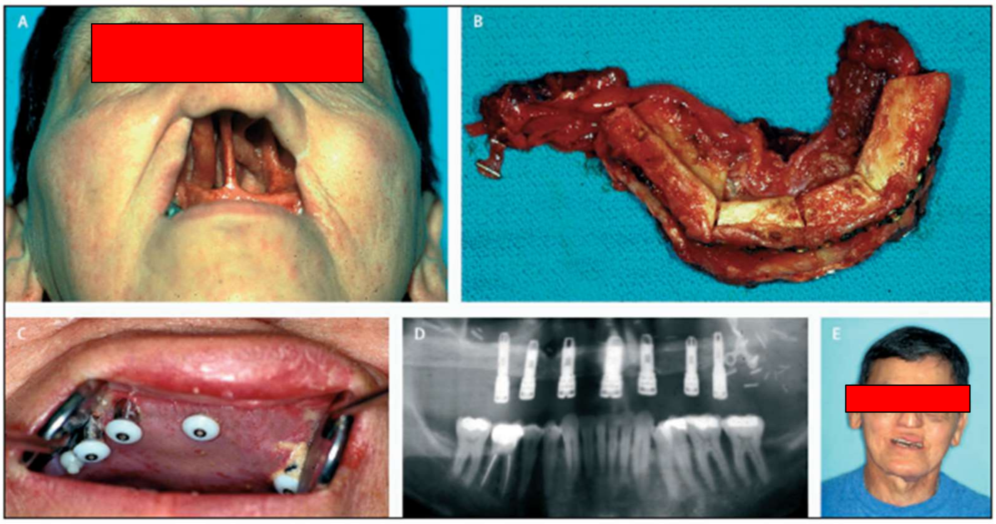

Figure 11.2: In (c) it can be seen that the musculocutaneous flap is unable to create a palatal vault as there is a lack of bony support for this to happen. After Futran and Mendez 2006. [271]

11.1.2.5 Radiological comparison of regenerate with parent bone

The regenerate was analysed according to regions of interest (ROIs) within an area of 10 mm^2 or 0.1 cm^2. Three areas of interest, namely A, B and C, were chosen equidistant to the mirror image of the regenerate versus the parent bone. A like-for-like comparison was made for each area of interest respectively, and the bone density was expressed in Hounsfield units (HU).

11.1.2.5.1 Analysis of area A

After a period of three months, a comparison made between the new bone and the parent bone in area A showed that there was no statistical difference in the **bone density** between the new bone and that of the parent bone (Figure 10.9). This result indicated that the suitability of the new bone for the placement of dental implants was indeed highly favourable; and with $p=0.44$, this new bone was as good as the parent bone in terms of its radiological appearance.

After a period of six months for area A, the comparison between the regenerate and the control bone changed. In Figure 10.10, it can be seen that the parent bone was slightly superior in bone density to the new bone or regenerate ($p=0.31$). The finding of a lesser bone density for the regenerate could well have been related to the physiological activity of bone remodelling. However, there was still no statistical relevance in their difference, which meant that the bone densities compared most favourably.

After a period of nine months for area A, comparison between the new bone and the parent bone again showed that there was no statistical significance between the new bone and the parent bone. In Figure 10.11, it can be seen that the new bone compared highly favourably to the control bone ($p=0.13$).

In summary, it can be stated that the new bone was radiologically equal to that of the parent bone and that the feasibility for placement of dental implants was already a reality at the interval of three months post distraction.

11.1.2.5.2 Analysis of area B

After a period of three months, it was found (Figure 10.12) that the parent bone was slightly superior in bone density to the new bone or regenerate ($p\geq0.99$) However, there was no statistical difference between the two densities, which indicated that the regenerate compared favourably to the parent bone.

After a period of six months, comparison between the new bone and the parent bone in area B again showed no statistical difference in bone density between the new bone and the control (Figure 10.13). In this case, $p\geq0.99$ which again indicates that the bone densities were virtually the same.

After nine months for area B, a comparison between the new bone and the control bone again showed that there was no statistical difference in bone density between the new bone and the control bone (Figure 10.14). Again it was shown ($p \geq 0.99$) that the radiological appearance after nine months was highly favourable between the new bone and the control bone.

In summary, as shown above for area A, the new bone was radiologically most acceptable and compared favourably to control bone.

11.1.2.5.3 Analysis of area C

After a period of three months, a comparison between the new bone and the parent bone in area C showed no statistical difference in bone density between the two types of bone (Figure 10.15). In this particular case, $p \geq 0.99$, which again expressed the lack of significant difference between the new bone and the parent bone.

After a period of six months for area C, it was found that the parent bone was slightly superior in bone density to the new bone. However, there was still no statistical difference between the two types of bone which meant that the bone densities compared most favourably. The p value was 0.81, and the results are seen in Figure 10.16.

After a period of nine months for area C, again it can be seen that the parent bone was slightly superior in bone density to the new bone. However, as there was no statistical difference between the two bone densities, it can be stated that the regenerate compared favourably to the control bone regarding bone density, with $p=0.63$.
In summary, it can be seen that areas B and C might well have been slightly superior in bone density at six months and nine months respectively for the parent bone. However, from a statistical perspective, this difference was of no relevance.

11.1.2.6 Radiological comparison of the regenerate with fibula bone

As shown in Figure 10.18, the three regions of interest, namely A, B and C, were compared with similar areas in the fibula at an interval of three months postoperatively. The p value for area A was 0.47, for area B was 0.79, and for area C was 0.13 respectively. It was therefore noted that there was no statistical difference between the regenerate or new bone and the fibula at the time interval of three months. This finding confirms that **the new bone regenerated through the process of CTDO was as good as that of the so-called 'gold standard' for post maxillectomy reconstruction**.

11.2 Statistical analysis

When comparing Hounsfield units over a period of nine months between the regenerate and the parent bone, the Wilcoxon matched-paired signed rank test was employed to compare the median bone densities. The Wilcoxon test is a matched *t*-test and, in this analysis, a comparison was made between the regenerate and the control bone within the same patient. The latter was a matched sample and it was interesting to note that the results in all comparisons showed no significant difference between the regenerate and the control bone ($p>0.05$). The result indicated clearly that the regenerate bone was as good as the parent bone.

When comparing the regenerate bone method to that of the fibula bone, the Mann-Whitney test was used to compare the median bone density of the regenerate with matched controls using the fibula method. The Mann-Whitney test is an unpaired *t*-test and was employed because in this case a comparison was made between different patients.

The results showed no significant difference in bone density between the regenerate bone and the fibula bone. **This may well indicate that the method of CTDO is as good as the current gold standard procedure, namely revascularised free fibula flap (RFFF)**.

11.3 Quality of life

According to the questionnaire given to patients before, and six months after, surgery, the results were interpreted as follows:

There was a significant difference between the experience of pain, physical activity, recreation, swallowing, chewing, taste and saliva between the preoperative and postoperative situation. This means that the quality of life relating to mastication as well as living a normal life was much improved.

There was a significant improvement in the mood of the patient after surgery ($p=0.03$). This was also a very significant finding because patients who have defects in their mouths or wear obturators become quite depressed. In the present study, this turned out not to be the case.

There was a significant decrease in anxiety levels as well as avoidance, both of which were quite high before surgery, as well as a significant reduction in difficulties after surgery ($p=0.03$).

When comparing the accumulative quality of life score before and after surgery, as a whole there was a significant improvement in the overall quality of life. ($p<0.0001$) The latter is an indication that the surgical procedure of CTDO was indeed highly successful and very well tolerated by the patients in the study.

11.4 Histological investigation

A comparison between the new bone and the parent bone was made in all six patients. Trephine bone biopsies were taken by the primary investigator in designated areas of interest in both the test and control regions at the time of removal of the distraction apparatus.The sections were stained with haematoxylin and eosin and also with Masson trichrome staining to interpret collagen patterns under polarised light.

11.4.1 Patient number one

The quality of the distracted bone appeared **comparable if not better** than that in the control sample. A possible reason for this could be that the new bone had more uniform trabeculation than the control which was more patchy regarding trabecular formation.

11.4.2 Patient number two

The quality of the distracted bone appeared **as good as** that of the control sample, **if not stronger**. Again this was an interesting finding, which corroborates the clinical and radiological finding **that the bone was sufficiently good for dental implant placement.**

11.4.3 Patient number three

The distracted tissue contained abundant, slender anastomosed cancellous strands which were typically less thick than the cancellous typical of the control tissue. The stroma of the control specimen had more fibro-adipose tissue which is usually seen in mature bone. However, there was still a **good comparison** between the distracted and the control bone.

11.4.4 Patient number four

The quality of the distracted bone appeared **as good as** that of the control sample. In this slide (Figures 10.25(a) and (b)), it is seen that there was very well-developed cellular cortical bone which had undergone lamellar remodelling.

11.4.5 Patient number five

The quality and the strength of the distracted bone appeared to be **superior** to that in the control sample.

11.4.6 Patient number six

While the volume was much more copious, the new cancellous bone was much thicker than the control cancellous bone. The new cancellous bone had already undergone lamellar remodelling with advanced Haversian differentiation and merged with the new cortical bone. In summary, it would appear that the distracted bone had a very high quality in terms of the thickness of the trabeculae as well as the morphological distribution of the lamellar pattern. It was indeed most interesting to note that the **quality of the new bone was not only equal to but even better than that of the control bone** in the majority of the biopsies taken.

It can therefore be stated unequivocally that **CTDO can be used with confidence as a method of bone regeneration and that the morphological and anatomical structure and quality of the new bone would be as good as the parent bone from which it was generated**. There can be no doubt that this method of bone regeneration developed from the concept of distraction osteogenesis is **anatomically and physiologically the optimal way of reconstructing defects in the maxilla**. While the method of CTDO requires more patience from both the surgeon and the patient, the results finally achieved would far outweigh those found in autogenous bone grafting, whether vascularised or not.

11.5 Classification of maxillectomy defects

One of the most utilised classifications for maxillectomy defects was put forward by Brown *et al.* in 2010.[262] This classification predicts the functional and aesthetic outcome likely to result from the surgery and it relates to the method of population or reconstruction that is suitable for each maxillectomy defect. Brown described six different types of maxillectomy defects (Figure 5.1).
The Brown defect sizes were classified as follows: Brown class II (41%); Brown class III (41%); Brown class IV (18.1%). The most frequently used microvascular free flap was the radial forearm flap (45.8%) which was used mostly in Brown class II defects. The RFFF was the most common choice for Brown class III and also class IV reconstructions.

11.5.1 Advantages of RFFF

The first RFFF was described by Hidalgo *et al.* in 1989 to reconstruct a mandibular defect.[105] Subsequently, the RFFF has been demonstrated to be most reliable for the reconstruction of maxillary defects following ablation for benign or malignant tumours or osteoradionecrosis of the mandible or the maxilla.

According to Peng *et al.* in 2004, donor site morbidity was acceptable in all the treated patients, with limited postoperative pain and gait disturbances.[106] The following unique advantages make RFFF the ideal choice for maxillary reconstruction:

- long vascular pedicle
- wide diameter of the peroneal vessels
- availability of a composite flap consisting of bone, muscle tissue and skin
- relatively straightforward harvesting procedure resulting in minimal donor morbidity
- distant donor site from the head and neck region makes a two-team approach feasible
- anatomical three-dimensional shape of the fibula makes a simulation of the maxillary alveolar process possible
- high density of the fibula bone is conducive to placement of osseointegrated dental implants.[107]

The survival rates of fibula flaps in a case series by Chiapasco *et al*. (2006) was 94.9%[108] and consistent with those reported by other authors ([109-117]). Also, Mucke *et al.* in 2011 reported a successful outcome with flap transfer in 80 out of 83 patients who underwent maxillary reconstruction. In 10 out of 28 patients, with transferred bone, dental implants were placed for prosthodontic rehabilitation.

11.5.2 Disadvantages of RFFF

A significant problem of the RFFF is that skin does not do well with dental implants, owing to the hyperplasia and inflammation that leads to pain and bleeding. Also, the maximum height of the fibula bone is 14 mm and presents problems in the aesthetic zone of the mouth.[118,119] In particular, patients treated by partial resection of the maxilla have a residual dentition on the healthy side. In these cases, despite a successful reconstruction, an inappropriate step at the graft-to-residual stump level may be present.

In mandibular reconstruction, the fibula is amenable to vertical distraction to increase vestibular depth.[120, 121] However, in the maxilla, this would not be a feasible proposition owing to anatomical constraints.[59] From a functional perspective, the implants would support very high prosthetic superstructures to approximate the occlusal plane. These superstructures pose the risk of unfavourable bending moments and also implant overload. The latter may jeopardise the long-term survival of dental implants.[122, 123] Also, the aesthetic appearance of very high crowns is most undesirable.[59]

Additionally, the shape of the palatal vault is a major problem because this area lacks a hard bony support and is usually obturated by the musculocutaneous portion of the composite flap. It is quite unaesthetic in the sense that it has a flattened shape and hence no natural curvature.[124] Subsequently, its use in reconstructing the malar prominence, the infra orbital rim and the maxillary wall is limited, and is better reconstructed by means of the subscapular flap.[273]

According to Mücke *et al.* in 2011, the success in using RFFF for post-maxillectomy reconstruction is very high. He reported success in 80 out of 83 free flaps.[124] However, it appears that some of the reporting could be misleading. The very short follow-up period for the placement of dental implants casts doubt on the long-term success. Outcome research on dental implant therapy should have a follow-up of at least one year.[274]

It is accepted that outcome measures of maxillary reconstruction should include local recurrence and distance metastasis of primary disease (in the case of oncology patients), facial appearance, eyeball position, oral fluid intake and continence, speech intelligibility, and nasal functions. Also and no less important is the social activity of the patient; although 91.6% of the patients in Mücke`s study suffered from malignant disease, there is no mention of recurrence and metastasis.

Another significant concern regarding microsurgical research relates to the factors around flap failure. Various factors are implicated in the outcome of free tissue transfer.[275-277] Because of the relatively small sample size of each subgroup, the multivariate analysis could not be performed. However, univariate analysis were reported between the complications and five predictor variables, namely:

1. defect size (Brown's classification)
2. type of flap
3. number of flaps used (single or multiple)
4. reconstruction type (immediate/delayed)
5. operation time.

If this information were provided in the publication, the risk factors of the complications following free tissue transfer for the maxilla would have been elucidated.

Outcome research on maxillary reconstruction should not be mainly based on objective assessment and facial appearance. In general, patient satisfaction is in line with the improved quality of life. Herein lies the real success regarding reconstructive surgery. In the study by Mucke *et al.*, he stressed the importance of dental rehabilitation. However, it is not known why 18 patients out of 83 did not want to receive dentures but opted for lengthy and complicated reconstructive procedures. It is also unclear what type of dental rehabilitation these 18 patients received afterwards. When a study discloses only favourable results while adverse events are underreported or selectively reported, it can be considered as having ‘outcome reporting bias'.

11.5.3 Comparison between RFFF and CTDO patients in the present study

- **Clinical appearance:** It can be seen in many clinical pictures that the lack of a bony palatal vault is very unsightly when the patient opens their mouth.Also, the lack of a vault does not give good peri-implant support to the bone on the palatal aspect. When using RFFF, a myocutaneous flap substitutes for the palatal vault. While the texture of the tissue can be quite firm, it is not possible to be contoured into a three-dimensional vault. This is a major drawback of RFFF.
- **Alveolar height:** It has been shown in subsection 10.2.2, that the alveolar height which produced the depth of the sulcus was very poor in RFFF and compared unfavourably with CTDO cases.This consideration is further elaborated in the conclusion section to follow.

11.5.4 Complications associated with microvascular flap surgery

Often the complications associated with microvascular flap surgery reconstruction are underreported. However, when these complications do occur, invariably the morbidity associated with them is quite high. In a study by Triana *et al*. in 2000,[278] they treated 58 patients with partial or total maxillectomy defects resulting from oncologic surgical resection (Table 11.1). Seven patients had partial maxillectomy defects resulting from trauma. Their main outcome measures were a separation of the oral cavity from the sinonasal cavities, diet, the type of dental restoration, the type of orbital restoration, speech intelligibility and complications. The complications were reported as follows (Table 11.1):

Table 11.1 List of complications in the study by Triana *et al.* 2000.[278]

Complication	No. of Patients
Flap failure	1
Partial flap failure with loss of bone or skin	3
Return to operating room for flap salvage	5
Wound infection and dehiscence	3
Donor site hematoma	1
Neck hematoma and seroma	3
Postoperative pneumonia	3
Postoperative meningitis	1
Postoperative death (within 1 mo)	1

1. Five flaps required urgent return to the operating room on the first postoperative day: three for arterial compromise and two for Venus compromise. In both cases of venous compromise, pedicle geometry was identified. Proper vessel alignment was achieved and venous outflow restored. In the cases of arterial compromise, one patient disrupted the arterial anastomoses upon awakening from anaesthesia. This was quickly recognised, the neck reopened, the anastomoses revised and the flap was saved. In the other two cases, arterial compromise was suspected because of apparent partial loss of the skin paddle of these two flaps (one scapular and one fibula). In each of these cases, the anastomoses were evaluated and found to be patented. The partial skin loss was attributed to poor skin perforators of these two flaps. In the case of the fibula flap, the skin loss was in the area of the hard palate, the patient was returned to the operating room 10 days following the first reconstructive procedure, and a radial forearm flap was used to line the palate . There were two cases of scapular-latissimus dorsi flaps that exhibited delayed bone loss requiring operative treatment; the wound completely healed. There was one case of complete flap failure in this series that involved a scapular flap (osteocutaneous) that failed within the first postoperative week and was replaced with a latissimus dorsi flap.

2. Other complications included 1 neck haematoma, 1 donor site haematoma, and 2 neck seromas that resolved without complication after percutaneous drainage.

3. Three patients developed partial dehiscence of the palatal wound within 10 days of the reconstructive procedure. Two patients were treated with local wound care and subsequently returned to the operating room for delayed wound closure, one on postoperative day 14 and one on postoperative day 22. Both wounds healed completely, although one wound healed by secondary intention.

4. Postoperative pneumonia occurred in three patients. Two cases were resolved with intravenous antibiotic therapy. One patient developed a pneumothorax and a pulmonary abscess and died after two months in hospital.

5. One patient developed meningococcal meningitis which resolved with intravenous antibiotic therapy, but left the patient with a significant functional deficit.

11.5.5 Functional results

In the same study by Triana *et al.* in 2000, the following data were presented at six months post follow-up after the primary reconstructive procedure.[278]

All 58 patients had wound closure and successful separation between the oral and sinonasal cavities. Of the 56 patients who lived, 37 were able to partake of a regular diet, and 19 were able to eat a soft diet. Although formal speech evaluations were not performed, 56 patients were able to be understood on the telephone.

Dental rehabilitation consisted of the following: 9 patients had placement of osseointegrated implants. In 2 patients with partial palatal defects, the implants were placed in the remaining native bone, and they were able to wear an implant-borne prosthesis. In the other 7 patients, those with subtotal or total palatal defects had osseointegrated implants placed into the free bone flap, which supported an implant-borne prosthesis. Thirty patients were able to wear a conventional partial prosthesis, and 17 patients did not choose dental rehabilitation. Financial limitations were cited as the cause for Croatian patients in the study not being able to afford osseointegrated implants.

It can be seen from the above study that, while the results of microvascular reconstructive surgery are excellent when they proceed smoothly, the outcome of severe complications can be devastating when things go wrong. The associated morbidity attributed to these complications is also quite dramatic and can lead to neurological complications and even death. It is therefore mandatory, when maxillectomy reconstructive procedures are embarked upon, that these operations take place in specialised hospitals where highly skilled personnel are involved in the management of these patients.

There is no doubt that, since the introduction of microsurgical procedures in the reconstruction of moderate to severe maxillofacial defects, outcomes have improved dramatically and that, in oncology in oncological cases, this modality of treatment is unsurpassed. However, microsurgical procedures should be left as a last resort in cases of oncological reconstruction where there may be simpler and more predictable reconstructive procedures available, such as bone regeneration through the process of distraction osteogenesis. Table 11.2 below lists the outcome in function in the study by Triana *et al.* (2000).

Table 11.2: The list of functional results in the study by Triana *et al.* (2000).[278]

Functional Result	No. of Patients (%)
Closure between sinonasal and oral cavity	58 (100)
Diet (n = 56)	
Regular	37 (66)
Soft	19 (34)
Speech (n = 56)	
Ability to be understood in telephone conversation	56 (100)
Dental restoration (n = 56)	
Implant-borne prosthesis	9 (16)
Conventional partial prosthesis	30 (54)
None	17 (30)
Orbit restoration (n = 25)†	
Implant-borne prosthesis	2 (8)
Conventional orbital prosthesis	6 (24)

*Two patients died, 1 and 2 months postoperatively.

CHAPTER 12. CONCLUSIONS

12.1 The burden of maxillectomy defects

Maxillary defects caused by trauma or tumour resection in the head and neck region can be devastating to the patient from a cosmetic and functional perspective. The reconstruction of maxillary defects presents a significant challenge to both the surgeon and the prosthodontist. The aesthetic needs that have to be taken into account comprise the restoration of the mid-facial contour; for this, there needs to be proper anatomical restoration of the bony contours of the cheekbone or malar, the orbital rim, the zygomatic buttress, and the alveolar arch of the maxilla in addition to the very important vault of the hard palate.The latter plays a pivotal role in aesthetics, swallowing and speech as well as support for the velopharyngeal valve. The functional aspects relating to this reconstruction concern mainly occlusal forces, and the functions of mastication, articulation and phonation as well as deglutition or swallowing. When defects of the oral cavity are small and inconspicuous, the placement of an obturator usually fulfils the needs of such patients. However, when defects are large and deforming, these obturators do not function with hermetic closure and sealing and can be a huge inconvenience to the patient, compounded by the fact that they do not perform optimally during speech, swallowing and mastication. Patients who are obliged to use obturator prostheses often become frustrated in having to deal with removable devices, and most of them wish to have some permanent closure of the maxillectomy defect.

12.2 Principles of reconstruction

The basic principles of reconstruction revolve around the rebuilding of anatomical structures using tissue as similar as possible to that which was resected. While it is not always possible to replace surgical defects with the exact issue that was removed, functional rehabilitation revolves around soft tissue support and hard tissue anatomical reconstitution. For a surgeon to reconstitute the tissue that was lost and enact rehabilitation, the following principles have to be adhered to:

1. creation of a well-healed wound or surgical defect

2. hermetic closure between the oral and sinonasal cavities

3. reconstruction of the zygomatic and maxillary buttresses

4. restoration of a functional occlusion, masticating ability, phonation and deglutition

5. reconstitution of midfacial contours.[273, 278]

Several options are available for reconstructing defects of the midface. These involve the use of local flaps, in combination with non-vascularised bone grafting, and are usually sufficient to deal with the reconstruction of small and suitable defects. However, in the case of large resections of the midface, the extensive size of the defects and the possible compromisation of blood supply as well as the use of adjuvant radiation therapy call for the use of microvascular free flaps, usually with an adequate soft tissue paddle in order to achieve proper soft tissue function and aesthetic closure. While there are many modalities of free flap transfer, the most popular one for maxillary closure to date has been the RFFF. In a study by Brown *et al.* in 2010, it can be seen that from the various modalities attempted to close maxillary defects, that the RFFF is still the most popular method of post maxillectomy reconstruction.[262]

12.3 The purpose of the present study

While the modality of treatment often referred to as the RFFF has been popularised to the extent where it is known as the current 'gold standard', in this discussion I demonstrate that the RFFF does not fully comply with all the requirements to be regarded as the international 'gold standard' and is in fact rather 'substandard' in certain aspects. In the present study, the newly created bone and soft tissue referred to as the regenerate was compared not only with its parent bone, but also with the RFFF reconstruction procedure.

12.3.1 Composite RFFF

12.3.1.1 Soft tissue biotype around implants

The composite RFFF is usually accompanied by a skin paddle to obturate the hard palate and also provide soft tissue cover for the bone of the fibula. One of the main problems in having skin around dental implants is the resultant hyperplasia and inflammation that leads to pain and bleeding. This is often followed by peri-implantitis with subsequent bone loss around the implants.[118] A solution to this problem is free palatal grafting from the vault of the hard palate. When this procedure was done by Chiapasco and co-workers in 2006, it was shown that implant survival in RFFF cases was as high as 98.6% after 7 years.[108] However, in the absence of sufficient hard palate mucosa as a donor site, which often occurs in RFFF cases, the donor site would either be very small or impractical for use. This shortcoming makes a very strong case for using CTDO, which the author has effectively demonstrated in the present study; **where there is abundant regeneration of keratinised palatal mucosa, as well as the underlying supporting palatal shelf.** However, it must be noted that the use of CTDO is dependent on a residual fragment of maxilla comprising at least 4 teeth in alveolar bone. This situation is fortunately more commonly seen than in total maxillectomies, where the RFFF is the only solution.

12.3.1.2 Aesthetic appearance

The creation of a vestibule is problematic in the case of RFFF reconstruction owing to the anatomical composition of the skin paddle, it being muscle, fat and skin. This tissue has a tendency to fibrose and contract and therefore a shallow, if not non-existent, vestibule often results. As a consequence, the upper lip line (and high smile line) as well as cheek function is affected negatively because of the lack of sulcular depth, which the muscles of facial expression use to animate during function. In the experience of the author, subsequent vestibuloplasties have proved to be unsuccessful in mitigating this problem (Figure 12.1 below).

A further unsightly problem is the pendulant palatal closure which is provided by the soft skin paddle that lacks bony architectural support. In fact, **there is no palatal vault**, and hence the speech and swallowing functions are defective. Also, patients are not confident to laugh aloud for fear of exposing this unsightly palate (Figure 11.2).

In the case of CTDO, the recreation of the hard palate is naturally formed by the process of osseo-distraction. This is indeed a **great advantage over the RFFF** and, moreover, the recreation of a vestibule allows optimisation of function and aethetics (Figure 9.58).

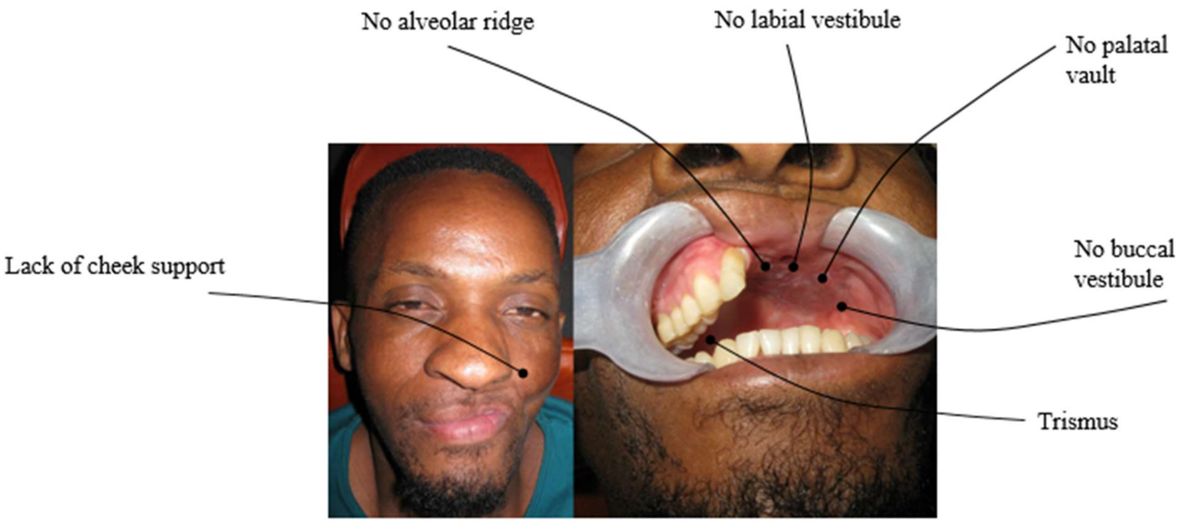

Figure 12.1: An unsatisfactory result of RFFF reconstruction post maxillectomy for the treatment of a malignant salivary neoplasm. The lack of alveolar bone and vestibular obliteration is evident. In this case, the placement of dental implants was unsuccessful.

The 'mythological' nature of creating bone in a curvilinear plane on a horizontal level has been shown not to exist. However, to finally attain this quest, the V5 distractor, using the concept of tetrafocal distraction, has given rise to the curvilinear movement of collagen and bone, in a staged manner, over a protracted period of distraction. The idea of tandem distraction periods, allowing for consolidation and subsequent ongoing distraction, has also proven to be successful in creating a curvature within the regenerate.

The seminal work done in the mandible by Alan Herford in 2004[279] and Daniel Spagnoli in 2006[280] unfortunately cannot lay claim to true curvilinear contours, as it has been shown by Neelakandan and Bhargava in 2012[68] that distracted bone moves only in a linear direction (Figure 11.1).

Hence, the present study has shown, for the first time, the methodology required to achieve true curvilinear trajection and contour integrity.

In a study by Wang *et al*. in 2016, it can be seen how trifocal transport distraction was employed in a linear fashion to overcome the problem of a curvature at the symphysis of the mandible (Figure 12.2).[281]

Figure 12.2: Linear trifocal transport distraction to reconstruct the symphysis of the mandible. After Wang *et al*. 2016.[279]

12.3.2 The clinical outcomes

In all the categories of bone and soft tissue regeneration, namely in respect of width, depth, density and radiological presentation, there was **no statistical difference** between the bone created by the CTDO procedure and the parent bone which was used as a control. Histologically, of interest, the **CTDO-generated bone appeared superior** to the parent bone. These results reinforce the notion that the new bone created can function and appear as good as the bone that it replaces, mainly in the area of implantology.

The statistical and clinical comparisons made to the RFFF technique show that **CTDO is superior** in mainly the **anatomical and aesthetic areas** and as good as the RFFF in the **dental**

implant domain. It is to be understood that the bone density of fibula bone, owing to its physiological function before harvest, will be superior to maxillary bone. However, the fibula remodels with time to the new function and stresses of the maxillary bone.This is the only area of superiority where the bone density is naturally better, but does not represent any advantage as the HU figures of the regenerate have been proven to be sufficient for dental implant placement.

12.3.3 Commercial implications

The cost of providing RFFF services to patients requires highly technical and sophisticated medical infrastructure. In South Africa, there are presently only a few centres providing the medical facility, and the personel and funds required to provide the service are under severe financial strain. In addition, the back-up support required to manage complications is also quite costly. Hence, this type of surgery is high-end and demands not only perfection but also attention to detail.

In comparison with CTDO, there is much less cost involved, the technical expertise can be taught to surgeons of average skill, and the technique is straightforward yet very effective, with maximum yield. More importantly, the technology can be exported to third-world countries with internet back-up. Pre-planning of cases with CT scans and stereolithographic model support can be done in Cape Town and exported anywhere in the world with accompanying installation instructions. Also, internet webinars can assist surgeons in carrying out the protocols and follow-up procedures. The quality of life of post maxillectomy patients no longer needs to be poor.

12.3.4 Recommendation for future research

The one area of concern for CTDO is the oncological patient who is planned to undergo chemo-irradiation. Some aspects of this topic has already been discussed in subsection 1.4.3. While there have been reports of limited success in performing distraction osteogenesis in the mandibles of irradiated patients,[78, 282] further studies will need to be undertaken to evaluate the prospect of using this modality of bone regeneration in chemo-irradiated patients.

12.3.5 Origin of the concept of CTDO

In 2007, the author presented an oral paper at the 18th International Conference of the International Association of Oral and Maxillofacial Surgeons in Bangalore, India.[283] At this meeting, the author showed successful closure of a 40 mm maxillary defect, using the concept of transport distraction osteogenesis from one fixed point to another. The author placed four dental implants into the regenerate and immediately placed a four-unit fixed bridge onto the implants using a guided implant system. This was indeed a novel procedure and resulted in considerable interest in using distraction osteogenesis for the closure of large maxillectomy defects. The chairman of the session questioned the author on whether he had any experience in distracting bone from an anterior to a posterior direction, in other words, creating new bone in an area where there was no surrounding bony support. The author responded that he would investigate this possibility, i.e. a successful method to regenerate bone into a three-dimensional open space – and that event was the catalyst for initiating the present project.

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CHAPTER 14. APPENDICES

14.1 APPENDIX I

Ethics approval from the Faculty of Health Sciences

UNIVERSITY OF CAPE TOWN

Faculty of Health Sciences
Faculty of Health Sciences Research Ethics Committee
Room E52-24 Groote Schuur Hospital Old Main Building
Observatory 7925
Telephone [021] 406 6338 • **Facsimile** [021] 406 6411
e-mail: sumayah.ariefdien@uct.ac.za

28 May 2012

HREC REF: 147/2012

Dr R Hendricks
Department of Plastics & Reconstructive Surgery
J-Floor
OMB

Dear Dr Hendricks

PROJECT TITLE: EVALUATION OF THE CLINICAL OUTCOME OF CURVILINEAR TRANSPORT DISTRACTION OSTEOGENESIS AND REVASCULARISED FIBULA FREE FLAPS IN THE RECONSTRUCTION OF LARGE POST-MAXILLECTOMY DEFECTS.

Thank you for addressing the issues raised by the committee.

It is a pleasure to inform you that the Ethics Committee has **formally approved** the above mentioned study.

Approval is granted for one year till the 15 June 2013.

Please submit a progress form, using the standardised Annual Report Form (FHS016), if the study continues beyond the approval period. Please submit a Standard Closure form (FHS010)if the study is completed within the approval period.
(Forms can be found on our website:www.health.uct.ac.za/research/humanethics/forms)

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the REC. REF in all your correspondence.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, HSF HUMAN ETHICS

Federal Wide Assurance Number: FWA00001637.

sAriefdien

14.2 APPENDIX II

PARTICIPANT INFORMATION LEAFLET AND CONSENT FORM

TITLE OF THE RESEARCH PROJECT: Evaluation of the clinical outcome of curvilinear transport distraction osteogenesis and revascularised fibula free flaps in the reconstruction of large post-maxillectomy defects

REFERENCE NUMBER:

PRINCIPAL INVESTIGATOR: Dr Rushdi Hendricks

ADDRESS: Dept of Plastic and Reconstructive Surgery
Faculty of Health Sciences
University of Cape Town

CONTACT NUMBERS: 083 261 8472 and 021 671 5040

You are invited to take part in a research project. Please read the information presented here, which explains the details of this project. Please ask the staff or the doctor any questions about any part of this project that you do not understand. It is very important that you are satisfied that you understand what this research is all about and how you could be involved. Also, your participation is **entirely voluntary** and you are free to decline being part of the study. If you decline, it will not affect you negatively in any way whatsoever. You are also free to withdraw from the study at any point, even if you have agreed to take part.

This study has been approved by the Health Research Ethics Committee (HREC) at University of Cape Town. It will be conducted according to the International and South African ethical guidelines and principles for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research.

What is this research study all about?

This study relates to growing back your own bone and soft tissue that you lost in your top jaw. The method for doing this is called Transport Distraction Osteogenesis; and its aim is to close the gap in your top jaw.

This means that you will undergo surgery under full anaesthesia. The surgeon will create a break in your jaw and the small piece of bone will be attached to a mechanical device which will be fixed to your jaw. This mechanical device will move 1.5 mm per day carrying this bone, and by doing so will generate your own bone. This will continue until your jaw is closed completely. The movement of the bone is usually not painful. A screwdriver will be used to move the mechanical device twice a day.

If there is any discomfort or pain then medication will be given to you to assist you to complete the procedure.

Why have you been invited to participate?

A large part of your top jaw has been removed surgically due to some type of tumour or trauma. The hole is usually covered by an obturator which you may or may not be wearing. As you will agree an obturator is not very pleasant to wear and the purpose of this study is to rebuild your mouth by regrowing your top jaw from your existing tissue. Once this has been done, after a period of 3-6 months the mechanical device will be removed and Dental Implants will be put into your jaw. These Implants will then support ether a denture or a bridge.

While the mechanical device is in your mouth, you will not be able to use your mouth to eat and you will be fed through a naso-gastric tube, for the duration of the bone growing period.

What will your responsibilities be?

- You will have to brush your teeth and keep your mouth clean and take sips of water.
- You may choose to stay in hospital or go home.

- While the growing process is taking place the procedure may not be stopped until the desired bone growth is achieved. If the growing process stops for whatever reason, it will not be possible to grow bone again thereafter.

Will you benefit from taking part in this research?

You will certainly benefit from this procedure as you will be permanently free from wearing your obturator and the communication between your nose and mouth will be closed, so that you can eat and drink and speak with confidence. In addition, you will enjoy being able to wear a denture or fixed bridge work, depending on what you can afford.

Are there any risks involved in your taking part in this research?

There is a small risk of infection or an appliance may become loose. In this case you may need to be taken back to theatre. There is also a small risk that the growing bone may harden too soon. In this case either bone grafting will be used or the growing procedure may have to start again.

If you do not agree to take part, or if this procedure proves unsuccessful what alternatives do you have?

If you do not agree to take part or if this procedure proves unsuccessful you can either continue to wear your obturator or undergo major surgery in the form of bone grafting by pieces of bone taken from elsewhere.

Who will have access to your medical records?

All the medical information collected will be treated confidentially and be protected at all times. If it is used in a publication or thesis your identity will be kept concealed.

What will happen in the unlikely event of some form injury occurring as a direct result of your taking part in this research study?

- *Clarify issues related to insurance cover if applicable. If any pharmaceutical agents are involved will compensation be according to ABPI guidelines? (Association of British Pharmaceutical Industry compensation guidelines for research related injury which is regarded as the international gold standard). If yes, please include the details here. If no, then explain what compensation will be available and under what conditions.*

Will you be paid to take part in this study and are there any costs involved?

No, you will not be paid to take part in the study but your transport and meal costs will be covered. There will be no costs involved for you, if you do take part.

Is there anything else that you should know or do?

- You should inform your family practitioner or usual doctor that you are taking part in a research study. (*Include if applicable*)
- You should also inform your medical insurance company that you are participating in a research study. (*Include if applicable*)
- You can contact Dr R. Hendricks at tel: 0832618472 if you have any further queries or encounter any problems.
- You can contact the Health Research Ethics Committee if you have any concerns or complaints that have not been adequately addressed by your study doctor.
- You will receive a copy of this information and consent form for your own records.

Declaration by participant

By signing below, I ……………………………………………………………… agree to take part in a research study entitled *(insert title of study)*.

I declare that:

- I have read this information and consent form (or it has been read to me) and it is written in a language with which I am fluent and comfortable.
- I have had a chance to ask questions and all my questions have been adequately answered.
- I understand that taking part in this study is **voluntary** and I have not been pressurised to take part.
- I may choose to leave the study at any time and will not be penalised or prejudiced in any way.
- I may be asked to leave the study before it has finished, if the study doctor or researcher feels it is in my best interests, or if I do not follow the study plan, as agreed to.

Signed at (*place*)………………… on (*date*) …………………… 2011.

....

Signature of participant Signature of witness

Declaration by investigator

I *(name)* ……………………………………………..……… declare that:

- I explained the information in this document to ………………………………….
- I encouraged him/her to ask questions and took adequate time to answer them.
- I am satisfied that he/she adequately understands all aspects of the research, as discussed above
- I did/did not use an interpreter. (*If an interpreter is used, the interpreter must sign the declaration below.*

Signed at (*place*)..………………. on (*date*) …………..………. 2011.

....

Signature of investigator Signature of witness

Declaration by interpreter

I *(name)* ……………………………………………..……… declare that:

- I assisted the investigator (*name*) ………………………………………. to explain the information in this document to (*name of participant*)……………………………………..

……………..……………………………. using the language medium of Afrikaans/Xhosa.

- We encouraged him/her to ask questions and took adequate time to answer them.
- I conveyed a factually correct version of what was related to me.
- I am satisfied that the participant fully understands the content of this informed consent document and has had all his/her questions satisfactorily answered.

Signed at (*place*)……………………………….………. on (*date*) ………………..…..………………….

....

Signature of interpreter Signature of witness

14.3 APPENDIX III

University of Washington Quality of Life Questionnaire (UW-QOL) incorporating the Obturator Function Scale

Name:

Date:

Sociodemographic and medical characteristics of patients

Gender (Check one box: ☑)
☐ Male
☐ Female

Age in years (Check one box: ☑)
☐ 30–39
☐ 40–49
☐ 50–59
☐ 60–69
☐ 70-79
☐ 80–89

Marital status (Check one box: ☑)
☐ Single
☐ Married
☐ Divorced /Widowed

Educational status (Check one box: ☑)
☐ Not educated
☐ Basic primary school (can read and write)
☐ Secondary school level I certificate

Employment status (Check one box: ☑)
☐ Retired
☐ Not retired

This questionnaire asks about your health and quality of life **over the past seven days**. Please answer all of the questions by checking one box for each question.

1. **Pain**. (Check one box: ☑)

☐ I have no pain.

☐ There is mild pain not needing medication.

☐ I have moderate pain - requires regular medication (codeine or nonnarcotic).

☐ I have severe pain controlled only by narcotics.

☐ I have severe pain, not controlled by medication.

2. **Appearance**. (Check one box: ☑)

☐ There is no change in my appearance.

☐ The change in my appearance is minor.

☐ My appearance bothers me but I remain active.

☐ I feel significantly disfigured and limit my activities due to my appearance.

☐ I cannot be with people due to my appearance.

3. **Activity**. (Check one box: ☑)

☐ I am as active as I have ever been.

☐ There are times when I can't keep up my old pace, but not often.

☐ I am often tired and have slowed down my activities although I still get out.

☐ I don't go out because I don't have the strength.

☐ I am usually in bed or chair and don't leave home.

4. **Recreation**. (Check one box: ☑)

☐ There are no limitations to recreation at home or away from home.

☐ There are a few things I can't do but I still get out and enjoy life.

☐ There are many times when I wish I could get out more, but I'm not up to it.

☐ There are severe limitations to what I can do; mostly I stay at home and watch TV.

☐ I can't do anything enjoyable.

5. **Swallowing**. (Check one box: ☑)

☐ I can swallow as well as ever.

☐ I cannot swallow certain solid foods.

☐ I can only swallow liquid food.

☐ I cannot swallow because liquid "goes down the wrong way" and chokes me.

☐ I cannot swallow because food "goes down the wrong way" and chokes me.

6. **Chewing**. (Check one box: ☑)

☐ I can chew as well as ever.

☐ I can eat soft solids but cannot chew some foods.

☐ I cannot even chew soft solids.

7.**Speech**. (Check one box: ☑)

☐ My speech is the same as always.

☐ I have difficulty saying some words but I can be understood over the phone.

☐ Only my family and friends can understand me.

☐ I cannot be understood.

8. **Taste**. (Check one box: ☑)

☐ I can taste food normally.

☐ I can taste most foods normally.

☐ I can taste some foods.

☐ I cannot taste any foods.

9. **Saliva**. (Check one box: ☑)

☐ My saliva is of normal consistency.

☐ I have less saliva than normal, but it is enough.

☐ I have too little saliva.

☐ I have no saliva.

10. **Mood**. (Check one box: ☑)

☐ My mood is excellent and unaffected by my tumour.

☐ My mood is generally good and only occasionally affected by my tumour.

☐ I am neither in a good mood nor depressed about my tumour.

☐ I am somewhat depressed about my tumour.

☐ I am extremely depressed about my tumour.

11. **Anxiety**. (Check one box: ☑)

☐ I am not anxious about my tumour.

☐ I am a little anxious about my tumour.

☐ I am anxious about my tumour.

☐ I am very anxious about my tumour.

12. **Avoidance of family or social events** (Check one box: ☑)

☐ Not at all
☐ Sometimes

13. **Difficulties inserting and removing the obturator** (Check one box: ☑)

☐ Not at all
☐ Little
☐ Moderate
☐ Severe
☐ Very much

14.4 APPENDIX IV

Patent Documentation

science & technology
Department: Science and Technology
REPUBLIC OF SOUTH AFRICA

NIPMO
NATIONAL INTELLECTUAL PROPERTY MANAGEMENT OFFICE
An initiative of the Department of Science and Technology

The Department of Science and Technology
through the
National Intellectual Property Management Office
hereby awards

Mogamat Rushdie Hendricks

with a

CERTIFICATE OF RECOGNITION

for the contribution made in the invention of South African patent
No. 2014/03775 entitled "Transport Distraction Apparatus"

Mr Mmboneni Muofhe
Deputy Director-General: Technology Innovation
Department of Science and Technology
Date: 22/03/2016

Dr Kerry Faul
Head: NIPMO
Date: 31/03/16

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(54) **TRANSPORT DISTRACTION APPARATUS**

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(57) **ABSTRACT**

Transport distraction apparatus for performing transport distraction osteogenesis is provided which includes a track capable of being formed into a curvilinear shape with a carriage movable longitudinally along the track. The carriage has a fixation plate secured or securable to it and at least one gear for moving the carriage along the track in order to adjust its position relative to the length of the track. The track has a series of formations extending along one edge of the track and engaged by the gear which is at least partially accommodated within a space between a plane including the front face of the track and a plane including the rear face of the track. Preferably, the apparatus creates a gap between a central region of the track and a patient's bone in use. A fixation plate is also provided.

14.5 APPENDIX V

Statistical Validation

From: Dr Rushdi Hendricks[mailto:rushdi.hen@webafrica.org.za]
Sent: 19 March 2015 21:46
To: 'Henri Carrara' <henri.carrara@gmail.com>
Cc: George Vicatos <george.vicatos@uct.ac.za>
Subject: PhD study
Importance: High

Dear Henri

Greetings and welcome back.

I do need your advice, but on another matter.

This has to do with a human study for which I have been registered as a PhD student since 2012.

I need to look at means of making my sample smaller by reducing my power from 99% to 80%.In other words, I would like to reduce the number of operated cases from 10 to maybe 6 or 7 cases.

There are lots of variables or observations per patient, eg histology, QOL, radiology and clinical markers.

When can I come to you to show you the stats that was done by Rauf Sayed in 2011?.

I am available next week Monday am or can make plans around you!

Many thanks and warm regards

Rushdi

From: Henri Carrara [mailto:henri.carrara@gmail.com]
Sent: 02 April 2015 12:18 PM
To: Dr rushdi hendricks
Cc: George Vicatos
Subject: Re: PhD study

Hi Rushdie

The power calculations for such small sample sizes and with repeated measures (before and after) are very difficult and somewhat inaccurate, therefore I was suggesting that we do a pilot analysis of the actual data.

With the 4 subjects you are almost at statistical significance, see attached.... What I did for interest was to simply replicate subject 4's data so that we "pretend" we have 5 subjects - and then we have statistical significance.

Hope this makes sense.

Kind regards
Henri