OUTCOMES OF IMPLANT BASED PROSTHETIC ORAL REHABILITATION OF HEAD AND NECK ONCOLOGY PATIENTS

by

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Abstract (200 words)

Aims: To conduct a systematic review on dental implant survival in autogenous bone grafts and flaps in head and neck (H&N) oncology patients.

Thereafter, to retrospectively report a service evaluation on implant- and prosthetic- outcomes of implant based oral rehabilitation in H&N oncology patients in a regional centre.

Method: For the systematic review, various databases were searched (01/1980-08/2017).

Retrospective analysis of implant- and prosthetic- outcomes of 167 patients treated within service from 2012-2017 was also undertaken, applying Kaplan-Meier survival curves and Cox proportional-hazards models.

Results: For the systematic review, 20 articles were reviewed, reporting on 1905 implants. Implant survival varied from 54-100%.

The service evaluation revealed implant survival estimates of 95.7% [95%CI 94.3-97.2%] at 3-years and 95.5% [95%CI 93.9-97.0%] at 5-years. Higher implant failure rates were shown in autogenous bone grafts/flaps in comparison to native bone (p=<0.001).

Fixed implant prostheses had a higher 5-year survival and 5-year complication-free survival, with fewer complications compared to removable implant prostheses.

Conclusion: The systematic review revealed implant survival in autogenous bone grafts in H&N oncology patients to be promising. The service evaluation supported the use of dental implants in the rehabilitation of H&N cancer patients, whilst demonstrating the risk of prosthetic failure and complications.

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CHAPTER 1: INTRODUCTION

1. Introduction

1.1 Introduction

Patients with Head and Neck (H&N) cancer often undergo ablative surgery, radiotherapy and chemotherapy [Chan et al., 1997]. Both surgical and non-surgical interventions can lead to several significant complications including facial deformity, loss of hard and soft tissue, reduced saliva flow, impaired speech, swallowing, and impaired mastication [Barrowman et al., 2011]. This can result in functional disabilities and aesthetic deformities with defects usually requiring tissue grafting procedures with vascularized or non-vascularized flaps for oral reconstruction [Curi et al., 2018].

Oral and dental rehabilitation has conventionally required removable prostheses to obturate defects, to replace missing tissue structures and to restore function and aesthetics [Pace-Blazan & Rogers., 2012]. However, conventional removable prostheses are often poorly tolerated, are difficult for the patient to maintain and frequently fail to fully achieve the intended functional improvement [Curi et al., 2018].

The use of dental implants has been proposed to enable secure anchorage for prostheses, reduce loading on vulnerable tissues and provide a better functional and cosmetic solution [Harrison et al., 2003]. The use of implants to retain prostheses as part of oral and dental rehabilitation of H&N cancer patients is becoming an increasingly common treatment approach. [Schoen et al., 2004], [Müller et al., 2004], [Reintsema et al.,1998]

1.2 Head & neck cancer overview

1.2.1 Head & neck cancer

H&N cancer refers to a group of biologically diverse cancers involve start in the upper aerodigestive tract (UAT) and include the oral cavity, nasal cavity, pharynx and larynx. Other UAT sites include the salivary glands, sinuses and middle ear. Cancers can also originate in the nerves and bones; however, these are much rarer [NICE, 2004].

The majority of these cancers arise from the surface layers of the UAT with around 90% of all H&N cancers being squamous cell carcinomas (SCC). [Jemal et al., 2007], [Boyle & Levin, 2008]

1.2.2 Incidence

The global annual incidence of H&N cancers is estimated to be more than 550,000 cases with around 300,000 deaths each year. [Jemal et al., 2011] Within the UK, H&N cancer is the 8th most common cancer. It accounts for 3% of all newly diagnosed cancers with around 11,700 patients being diagnosed annually. The incidence of H&N cancer is rising steeply with a 31% increase in incidence since the 1990's. Males are more commonly effected with a male to female ratio of around 2:1; however, this disparity is rapidly reducing with rates in females having increased by two-fifths (40%) and in males by just over a fifth (22%), since the 1990's. The incidence of H&N cancer in the UK is highest amongst those aged between 70 to 74 years old. [Cancer Research UK, 2019]

1.2.3 Risk factors

H&N cancers are strongly associated with certain environmental, lifestyle and genetic risks. Well established lifestyle risk factors include tobacco (smoking and smokeless products such as betel quid) and alcohol intake. They account for 75% of H&N cancer cases and have a synergistic effect when combined. [Mehanna et al., 2010] Exposure to viruses such as the human papilloma virus (HPV-16, -18) and Epstein Barr virus (EBV) are linked with oropharyngeal [Gillison & Lowy, 2004] and nasopharyngeal cancer respectively [Mehanna et al., 2010], with HPV related oropharyngeal cancer showing increasing prevalence, particularly within western society [Mehanna et al., 2013].

Patients with premalignant lesions such as leukoplakia and erythroplakia, oral lichen planus and proliferative verrucous leukoplakia, and those with inherited conditions including Fanconi anaemia, ataxia telangiectasia, Bloom's syndrome and Li–Fraumeni syndrome have been shown to be at an increased risk of developing H&N cancer. Acquired immunodeficiency as a result of poor nutrition, advanced age, immunosuppressive therapy after transplant or acquired immunodeficiency syndrome (AIDS) are also at greater risk of developing H&N cancer. [Shaw & Beasley, 2016]

1.2.4 Teams involved in H&N cancer care

Within the UK NHS services, H&N cancer care is provided in regional cancer centres with multidisciplinary care teams (MDTs). These H&N cancer MDTs are comprised of a well-established group of experts with a specialist interest in the diagnosis, treatment and management of people with H&N cancer and take overall

responsibility for the assessment, treatment planning and management of H&N cancer patients throughout the course of their disease and rehabilitation. [NICE, 2004]

The core members of a H&N cancer MDT include; surgeons, clinical oncologists, restorative dentists, pathologists, radiologists, clinical nurse specialists (CNSs), speech and language therapists (SALT), senior nursing staff from the H&N ward, palliative care specialists, dietitians, team secretary, data manager and the MDT coordinator. Other individuals or teams from a variety of specialties may be brought in to assist this process as and when their expertise is required with these individuals/teams, being termed extended members. [NICE, 2004]

1.2.5 Diagnosis and staging

Diagnosis and staging of H&N cancer normally entails clinical examination and biopsy of the potential cancer site. Once a malignancy has been confirmed, further investigations including radiographic imagery such as computerized tomography (CT) and Magnetic resonance imaging (MRI) may be under taken to assist in the radiographic staging of the disease. [SIGN, 2006] H&N tumors are staged using the UICC: TNM classification of malignant tumors (Union for International Cancer Control: Tumor, Node, Metastasis classification). This classification system is used worldwide and is employed to describe the anatomical extent of the disease, based on an assessment of the extent of the primary tumour, the absence or presence and extent of regional lymph node metastasis and the absence or presence of distant metastasis [Roland et al., 2016].

1.2.6 Treatment modalities

The overall aim of H&N cancer treatment is to remove the malignant cells and maximise the chances of patient survival, whilst minimising the resulting damage to form and function of the H&N structures. Treatment of the primary tumour may involve surgical resection with or without reconstruction and/or radiotherapy with or without chemotherapy. Adjuvant radiotherapy or chemoradiotherapy may be required following surgical resection. [RD-UK, 2016] Chemotherapy alone is rarely used with a curative therapeutic intent but is often used to enhance the effects of radiotherapy (chemoradiotheraphy). [NICE, 2004]

Surgical resection, wherein the tumour is completely removed with uninvolved resection margins, is challenging and can involve sacrificing critical structures. The resection site can either be closed primarily, left as they are, surgically reconstructed with a variety of soft and/or hard tissue flaps or prosthodontically reconstructed [Kanazawa et al., 2011].

In some cases, curative treatment may not be possible. In such cases treatment may be offered with a palliative intent to improve or prolong the individual patients life.

1.2.7 Consequences of H&N cancer treatment on oral health

Treatments for H&N cancer result in modification of the patient's oral environment which can impact on QoL and general wellbeing. Prevention or reduction of these side effects is a matter of increasing importance, especially due to the improvement in H&N cancer survival rates. [RD-UK, 2016], [Laverty et al., 2017]

Treatment can result in adverse short- and long-term oral, facial

and dental complications. Surgical tumour resection can produce alterations to normal anatomy which adversely affect function and appearance. Radiotherapy causes unavoidable radiation damage to normal tissues surrounding the tumour, affecting the function of these tissues both in the short- and long-term. Chemotherapy causes acute mucosal and haematological toxicity, with the former being potentiated if chemotherapy is delivered concurrently with radiotherapy. [RD-UK, 2016], [Butterworth et al., 2016]

1.3 Prosthodontic rehabilitation of H&N cancer

1.3.1 Aims of treatment and delivery of care

The primary objective of oral prosthodontic rehabilitation is to preserve and restore function, aesthetics, oral competence, swallowing, speech, mastication and the patient's ability to interact effectively within society and maintain psychological well-being [Cawood & Stoelinga., 2006]. In general, the prosthodontic rehabilitation of H&N cancer patients is challenging and brings with it increased work-load and technical complexity [Keller et al., 1988], [Okay et al., 2001], [Laverty et al., 2017] in comparison with non-oncology patients [Keller et al., 1988], [Laverty et al., 2017]. As such, many of these patients have complex needs that cannot be adequately met by primary care dental services. Within the NHS services, the delivery of dental care is co-ordinated by Consultants in Restorative Dentistry who are core members of the H&N cancer MDT and have experience in maxillofacial prosthetics and implantology. These consultants also co-ordinate the dental care of patients after treatment by liaison with primary care dental practitioners. [NICE, 2004], [Butterworth et al., 2016]

1.3.2 Oral prosthodontic rehabilitation of H&N cancer patients

Oral prosthodontic rehabilitation has radically changed over the past 20 years. Defects created as a result of surgical ablation were typically managed with removable prostheses. [Fierz et al., 2013], [Laverty et al., 2017] Over the past decade there has been a clear shift towards surgical reconstruction of the defect site to close communications between facial compartments and utilization of dental implants to retain prostheses. Dental implants began to be used in oral rehabilitation in H&N cancer patients in the mid-1980s with promising long-term observations being first reported by the late 1980s. These revealed that rehabilitation with implants could be successful with improved outcomes in comparison with conventional tissue-supported prostheses. [Klein et al., 2009], [Fierz et al., 2013], [Laverty et al., 2017] Conventional removable prostheses are often poorly tolerated, are difficult for the patient to maintain and can fail to meet their intended function such as swallowing and chewing. The key deficiencies include poor adaption and stabilisation of the prosthesis due to altered post-surgical anatomy, low salivary flow and a lack of emotional resilience of the patient rendering it difficult, if not impossible, to prosthodontically rehabilitate these patients, even with the use of reconstructive surgery. [Sclaroff et al., 1994], [Watzinger et al., 1996], [Mericske-Stern et al., 1999], [Smolka et al., 2008], [Laverty et al., 2017] A UK study identified that the number of individuals who underwent surgical reconstruction for H&N cancer had increased from 38% to 91% and the use of dental implants had also increased from 43% to 93% from 1995 to 2009 [Alani et al., 2009]. This shift has also been widely reported in the literature in most developed countries. [Müller et al., 2004], [Schoen et al., 2004], [Reintsema et al., 1998], [Smolka et al., 2008]

In comparison with removable prosthodontic reconstructions, implant based oral rehabilitation has been shown to be more effective, achieving a high clinical success with good patient satisfaction. [Nelson et al., 2007], [Júlia Real-Osuna et al., 2012], [Weischer et al., 1999], [Laverty et al., 2017] Implants strategically placed are now proven to be a therapeutic option to compensate – at least in part – for both hard and soft tissue defects. This change in practice has coincided with a decrease in the need for traditional prosthetic obturator provision. [Brown et al., 2006], [Adell et al., 2008], [Laverty et al., 2017] Despite this shift in practice, reconstructive surgery and placement of dental implants may not be appropriate for all patients, such as those patients with significant medical co-morbidities, those lacking suitable donor sites or patients that do not want to embark on this often lengthy treatment pathway. Conventional prosthetic rehabilitation can therefore still be more appropriate and should be appreciated and considered when treatment planning. [Smolka et al., 2008], [Laverty et al., 2017] Dental implant-based rehabilitation is certainly more expensive and time consuming, and it can take several years to complete the definitive treatment. It also requires specialist practitioners that are trained in carrying out the surgical and prosthodontic elements. With this increasing complexity it is essential that treatment is provided as part of an MDT approach. [Dingman et al., 2008], [Laverty et al., 2017]

1.4 Implants in H&N cancer patients

1.4.1 Definitions of implant survival and success

Within the literature there are a variety of definitions for implant survival and implant success. A generally accepted consensus for the definition of implant survival is an implant fixture that is still physically in situ and has not be lost or removed [ten Bruggenkate et al., 1990], [Misch et al., 2008]. This, however, does not give any indication of the status of the implant such as whether peri-implant tissue is healthy, whether the patient is free from pain or even if the implant is restored with a prosthesis.

Implant success is used to describe the implant within ideal clinical conditions. A commonly accepted criteria for the assessment of implant success was proposed by Albrektsson et al, [Albrektsson et al., 1986]. Since then a variety of authors [Smith & Zarb., 1989], [Albrektsson & Zarb., 1998], [Misch et al., 2008], [Annibali et al., 2009] have tried to define implant success using various subjective and objective measures such as implant survival rates, prosthetic restoration, radiographic peri-implant bone loss, and peri-implant soft tissue health. [Papaspyridakos et al., 2012] Despite these developments, there is a clear lack of consensus on what specifically defines implant survival and success. As such, these terms are commonly used interchangeably with a lack of consistency within the literature. This makes it challenging to interpret and compare the results of studies reporting on implant survival and success.

1.4.2 Overview of implant survival and success in H&N cancer patients

A number of studies have investigated the survival of dental implants in H&N cancer patients. In the main it would appear that implant survival is high (over 80%), however the vast majority of evidence available to guide clinicians is formed from retrospective studies using low patient numbers with limited follow up. [Shaw et al., 2005], [Yerit et al., 2006], [Hessling et al., 2015], [Ch'ng et el., 2016] This is however, understandable as the service provided to this patient group does not lend itself to well-designed highly controlled trials. [Weischer & Mohr, 1999], [Granstrom et al., 1999], [Goto et al., 2002], [Shaw et al., 2005], [Ch'ng et al., 2016]

In the main however, it would appear that implant survival rates in H&N cancer patients are lower in comparison to the general population [Pjetursson et al., 2014]. There is also limited evidence to suggest that treatment modalities for H&N cancer treatment may impact upon implant survival such as radiotherapy, hyperbaric oxygen, chemotherapy, bone type and timing of implant surgery [Weischer & Mohr, 1999], [Granstrom et al., 1999], [Goto et al., 2002], [Shaw et al., 2005], [Ch'ng et al., 2016].

1.4.3 Dental implant provision in NHS services

The provision of dental implants within the NHS is guided by a document compiled jointly by the Royal College of Surgeons of England and Restorative Dentistry-UK. [Dabar et al., 2019] This guidance document outlines which patient groups may be considered for access and funding to dental implant provision within NHS services.

This includes patient groups such as those that have undergone ablative surgery for H&N cancer, patients with developmental conditions of teeth, including deformed and/or missing teeth, patients who have experienced dental trauma, and in patients with severe denture intolerance. [Dabar et al., 2019]

1.5 Prosthodontic rehabilitation of H&N cancer patients

1.5.1 Definition of prosthetic survival and success

There is a lack of consensus within the literature on what defines prosthetic survival and success. The literature is limited on reporting and defining such outcomes. This is particularly true for literature reporting on implant-based prosthesis with outcomes of these studies mainly focused on implant rather than prosthodontic based outcomes. Where prosthodontic based outcomes are reported within the literature there is commonly an inability to distinguish between different types of prosthetic reconstruction, leading to challenges in interpreting such outcomes. [Pjetursson et al., 2012].

This was highlighted in a systematic review by Papaspyridakos et al., which reported that the parameters given for prosthetic survival and success were inconsistent and varied. Despite this, the authors attempted to define prosthetic survival and success as follows:

- Survival was defined as a prosthesis remaining in-situ with or without modification for the entire observation period.
- Success was defined as a prosthesis being free of all complications over the entire observation period.

These definitions, however, were only used to describe fixed prostheses and not removable prostheses, as the latter were not included within the review. [Papaspyridakos et al., 2012]

As such, there is currently a lack of clarity on what defines prosthetic survival and success within the literature.

1.5.2 Overview of prosthetic survival and success in H&N cancer patients

There are a limited number of studies reporting on implant based prosthodontic outcomes in H&N cancer patients. Those that do are predominantly aimed at reporting on implant rather than prosthetic based outcomes. [Ali et al., 2018], [Linsen et al., 2012], [Kovacs, 2000] The lack of consensus on what defines prosthetic survival and success also renders a comparison of such studies difficult.

1.6 Aims & Objectives of study

1.6.1 Rationale for study

Despite implant based prosthodontic treatment being shown to be a predictable treatment modality within the general population [Pjeterssuon et al., 2012], [Moraschini et al., 2015], the evidence base within H&N cancer patients is limited by the availability (or lack thereof) of large, well-constructed studies in the literature. [Ch'ng et al., 2016] As stated, the vast majority of the evidence available to guide clinicians is universally formed from retrospective studies with low patient numbers

and limited follow up. With the increasing use of dental implants in the oral rehabilitation of H&N cancer patients [Alani et al., 2009], an improved evidence base is required to help inform clinical decision making.

1.6.2 Aims & Objectives

The following aims and objectives are proposed:

1. To evaluate the survival of dental implants placed into autogenous bone grafts in H&N oncology patients within the literature by conducting a systematic review.

2. Retrospectively report a service evaluation on implant and prosthetic based outcomes of implant based oral rehabilitation in H&N oncology patients in a regional centre in the West Midlands (Birmingham Dental Hospital and University Hospital Birmingham). Specifically, reporting on:

   i. Implant survival rates and co-variance that may affect implant survival in this patient cohort and report on surgical complications experienced during the process of surgical implant placement.

   ii. Complications encountered during the process of prosthetic restoration of the dental implants and where possible the effect of these on the process of rehabilitation in this patient cohort, including the impact on implant success.

   iii. The complications and maintenance requirements of implants and implant retained prosthesis after delivery and furthermore the peri-implant soft tissue health in this patient cohort.

1.7 Published aspects of thesis

The following book chapter has been published:

- Laverty DP, Addison O, Elledge R, Parmar S. (2017) 'Oral Prosthodontic Rehabilitation of Head and Neck Cancer Patients', in Kuriakose MA (ed) Contemporary Oral Oncology Rehabilitation and Supportive Care. 1st edn. Switzerland: Springer, pp. 35-104.

The following chapters have been published in peer review journals:

- Chapter 2: Systematic Review: Survival of dental implants placed in autogenous bone grafts and bone flaps in head and neck oncology patients, [Laverty et al., 2018].
- Chapter 3: Service Evaluation of Outcomes of Implants placed for the Oral Rehabilitation of Head and Neck Oncology patients in a large regional cohort, [Laverty et al., 2019].

CHAPTER 2:

SYSTEMATIC REVIEW: SURVIVAL OF DENTAL IMPLANTS PLACED IN AUTOGENOUS BONE GRAFTS AND BONE FLAPS IN HEAD AND NECK ONCOLOGY PATIENTS

2. Systematic Review: Survival of dental implants placed in autogenous bone grafts and bone flaps in head and neck oncology patients

This chapter is based on a publication that arose from this thesis. Systematic Review: Survival of dental implants placed in autogenous bone grafts and bone flaps in head and neck oncology patients, [Laverty et al., 2018].

2.1 Rationale

As outlined in Chapter 1, the use of implants to retain prostheses as part of oral and dental rehabilitation of head and neck (H&N) cancer patients is becoming an increasingly common treatment approach [Reintsema et al., 1998], [Schoen et al., 2004] [Muller et al., 2004], A number of benefits advocating implant anchorage over conventionally secured prostheses have been proposed [Chan et al., 1997] but importantly include a significant improvement in the reported Quality of Life (QoL) of patients [Marx & Morales, 1998]. However, dental implants can only be placed if there is sufficient bone to encase the implant so that a direct interface between the implant surface and bone can be achieved. Frequently following resective surgery, insufficient bone volume remains and bony reconstruction of the surgical defect is required to enable successful dental implant placement [Esposito et al., 2009]. Patients are commonly reconstructed with either a non-vascularised bone graft or a composite free flap. A non-vascularised bone graft is a free piece of non-vascularised bone (or bone substitute) that is placed within the recipet tissues. A free flap is a

vascularised piece of bone (pedicle), which is being increasingly used to reconstruct tumour patients. High 'survival' and 'success' rates have been reported in the literature for dental implants placed into autogenous bone grafts in healthy patients but notably the success rates remain lower than for implants placed into healthy native bone [Lekholm et al., 1999], [Schliephake et al., 1999]. With the increasing use of complex reconstructive techniques in rehabilitation following H&N cancer and the placement of dental implants into transported bone, there is a need to appraise the highly varied evidence that is currently available in order to help inform clinical decision making.

2.2 Objectives

It is the aim of this systematic review to evaluate the survival of dental implants placed into autogenous bone grafts, in H&N oncology patients.

2.3 Methods

2.3.1 Protocol

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) for describing and summarizing the results of the review was used [Moher et al., 2002], [Moher et al., 2009].

A quality assessment of all selected full-text articles was performed using the Methodological Index for Non-Randomized Studies (MINORS) [Slim et al., 2003] assessment tool to assess the risk of bias of the included studies. The MINORS

scoring list consists of 12 items, eight apply to non-comparative studies and a further four apply to comparative studies. Items are scored as 0 (not reported), 1 (reported but inadequate) and 2 (reported and adequate) with this then totaled up to give a score with the higher scores representing a reduced risk of bias [Slim et al., 2003]. MINORS was chosen over the Cochrane collaborations' tool for assessing risk of bias for randomized controlled studies because none of the studies included were randomised control trials.

2.3.2 Eligibility criteria

Inclusion criteria

Studies that met the following criteria where included;

1.   Dental implant placement into patients with cancer of the H&N.

2.   Dental implants placed into autogenous bone grafts.

3.   Studies performed on humans.

4.   Patients over 18 years old, or if there are patients under 18 years old within the study that these patients and their data can be removed from the analysis.

5.   English language articles.

6.   Any study design reporting on at least 35 dental implants or 20 patients who have had implants placed into autogenous bone.

7.   Data related to implant number and implant survival in autogenous bone grafts that was either directly reported or can be calculated from data within the study.

Exclusion criteria

Studies were excluded if they met the following criteria;

1.   Studies that reported on craniofacial or extra-oral implants only.

2.   No reported implant survival or an inability to calculate implant number or
        survival from reported data.

3.   Studies reporting on patients under 18 years old where there was an inability
        to remove these patients and their data from the analysis.

4.   Laboratory or animal-based studies.

5.   Studies with less than 20 patients or 35 dental implants placed into
        autogenous bone grafts.

6.   Review articles.

2.3.3 Information sources

Four electronic databases were used to systematically search the available literature: (1) The National Library of Medicine (MEDLINE via Pubmed); (2) Embase, (3) Cochrane Central Register of Controlled Trials and (4) Science Direct. The searches were limited to studies involving human subjects and publication dates from January 1980 to August 2017 that satisfied the inclusion criteria.

2.3.4 Search

The following search terms were used; Population: (<[text words] dental implant OR dental implant* OR oral implant OR oral implants OR osseointegrated implants OR endosseous implant OR dental implantation <[MeSH terms/all subheadings] AND

(<[text words] head neck OR squamous cell carcinoma OR oncology OR tumour OR cancer OR malignant OR neoplasm <[MeSH terms/all subheadings] AND Intervention: free flap OR vascularized flap OR hard tissue graft OR micro vascularized flap OR micro anastomosed flap OR anastomosed flap OR native bone OR DCIA OR deep circumflex iliac artery OR radial OR scapula OR fibula OR iliac OR rib OR costochondral <[MeSH terms/all subheadings].

2.3.5 Study selection

Two reviewers Mr Dominic Laverty (DL) and Mr Robert Kelly (RK) carried out the primary search by screening independently the titles and abstracts and identifying the studies appearing to meet the inclusion criteria. Studies with insufficient information in the title and abstract to make a clear decision were identified and the full paper was reviewed. Those studies selected for evaluation of the full manuscript were carried out independently by the same reviewers who determined final inclusion. Any disagreement was resolved by discussion with a third independent reviewer Prof Owen Addison (OA). The reasons for rejecting studies at this or subsequent stages were recorded.

2.3.6 Data collection process

Two reviewers (DL and RK) independently extracted the data using a bespoke data extraction form. Any disagreement was resolved by discussion with a third reviewer (OA). Studies with missing or incomplete data were excluded and reference lists of

the selected studies were checked for cross-references to search for papers that might meet the eligibility criteria for inclusion.

2.3.7 Data items

Data was collected for; implant survival, implant success, implant failure, implant complications, surgical implant placement protocol, implant system used, clinical follow up, how the author defined success/survival, the type of autogenous bone graft, implant site, the prosthodontic rehabilitation, type of cancer and the use of radiotherapy were documented where possible.

2.3.8 Risk of bias in individual studies

A quality assessment of all selected full-text articles was performed using the Methodological Index for Non-Randomized Studies (MINORS) assessment tool [Slim et al., 2003].

2.3.9 Summary measures

The primary outcome measure was implant survival. This review will define implant survival as an implant still in situ that has not been removed or lost at the census date and thus implant failure defined as an implant that has been removed or lost and is no longer in situ.

2.3.10 Synthesis of results

The survival and success figures documented where possible are taken directly from the study; however where the study did not specifically document the survival or success of implants placed into autogenous bone as a percentage, this was calculated from the data provided (as a function of surviving or successful implants from total reported as placed), and studies that lacked data to calculate this were rejected as part of the secondary screening process.

2.4 Results

2.4.1 Study selection

Searches of Embase, the Cochrane Central Register of Controlled Trials, Science Direct and MEDLINE generated 619 articles. After duplicate articles were removed 566 unique articles remained. After initial review of the titles and abstracts, 151 articles were accepted for further consideration, and 415 were rejected. After the full text was obtained and reviewed for the 151 articles, 131 articles were rejected as they did not meet the eligibility criteria leaving 20 articles to be included in the systematic review. (Figure 2.1)

Figure 2.1: Flow chart of study selection procedure

Identification

| 619 articles identified through database searching | 0 additional articles identified through other sources |

Screening

566 articles after duplicates removed

566 articles screened → 415 articles were excluded

Eligibility

151 full-text articles assessed for eligibility → 131 full-text articles excluded.

Included

20 articles included
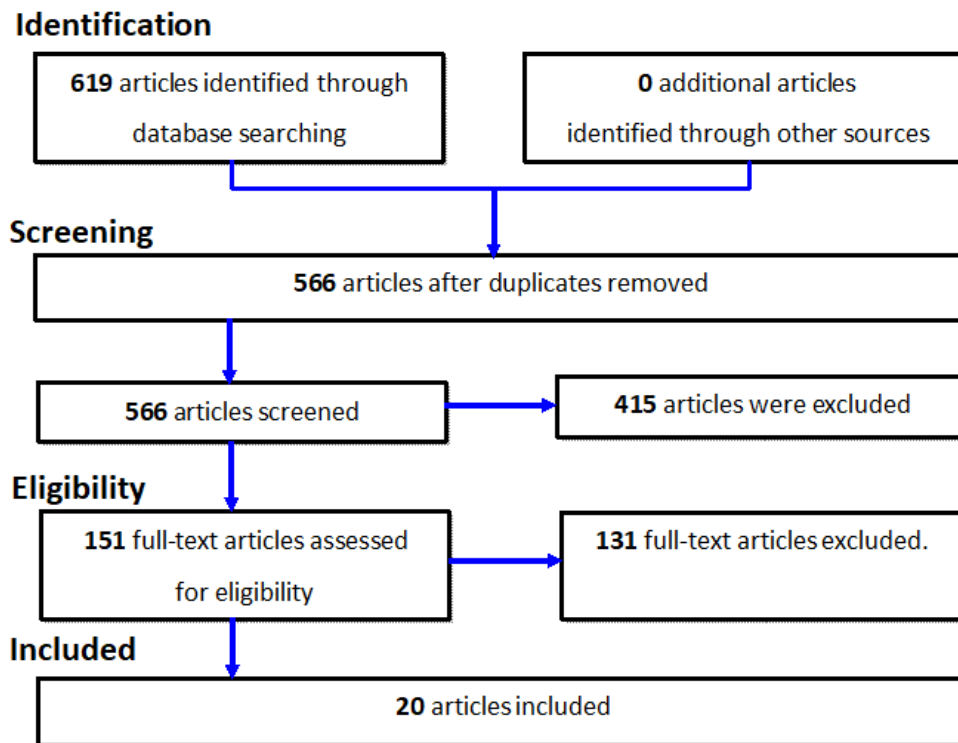
2.4.2 Study characteristics

The following data was extracted from the studies; study design, centres (single vs multiple centres), patient demographics (patient age, H&N cancer diagnosis), treatment modalities (surgery, radiotherapy, chemotherapy), donor site of autogenous bone graft, outcome measures, implant details (implant system, implant number, implant site, type of bone implant placed into (non-vascularised vs vascularised/free flap), implant placement surgical protocol implant survival/success/failure figures), implant definitions (implant survival/success/failure), type of Prosthetic rehabilitation (fixed vs removable) and any reported complications.

2.4.3 Risk of bias within studies

There were varying scores allocated to the studies using the MINORS assessment

tool, ranging from 7/16 to 13/16 representing varying degrees of bias within the

studies (Table 2.1).

Table 2.1: Study Characteristics and MINORS scores

Author & Year of Publication	Study Design	Outcome Measure	Criteria - Survival	Criteria - Success	Quality Assessment using MINORs Assessment Tool	Head and Neck Cancer Diagnosis	Patients Age Range	Follow Up Period	Implant site	Implant System	Implant Placement Protocol	Prosthodontic Rehabilitation
Studies with an average follow-up of 3 years or greater												
Watzinger, 1996	Retrospective observational	Implant survival in irradiated mandibles and Outcomes of Peri-implant bone	Not defined	N/A	7/16	SCC	Range = 41-79 Yrs	Upto 3 years	Mandible	IMZ	Primary and secondary implant placement. Secondary placement 6months after oncological reconstruction. Delayed loading of implants of at least 6 months.	Removable
Teoh, 2005	Retrospective observational	Implant Survival in the reconstructed mandible and prognostic factors.	Own - implant not removed then survived.	N/A	12/16	SCC, Osteogenic sarcoma, Benign Tumors, Mucoepidermoid Carcinoma & other Sarcomas	Mean = 42 Yr (Range = 67-80.5 Yrs)	Mean = 51.7 months (Range = 1.3-138 months)	Mandible	Nobel & Osseotite	Delayed loading of implants 6 months after placement. Fixations screws removed prior to implant placement	Fixed & Removable
Wu, 2008	Retrospective observational	Clinical outcomes of dental implants placed in fibula-free flaps for orofacial reconstruction	Own - Implants still functioning with no mobility, pain or infection, but with peri-implant bone resorption more than 2mm were classified as survived.	Albrektsson, 1986	9/16	Benign and Malignant Head and Neck Tumours	Average 47.1 Yrs	Average 47.8 months	Maxilla & Mandible	ITI & Branemark	19 patients had primary implant placement 10 patients had secondary placement after oncological reconstruction. Delayed loading of implants of at least 3months after placement.	Fixed & Removable
Fenlon, 2012	Retrospective observational	Implant Survival	Poorly defined - implant osseointegrated and in situ then survived (usefulness of implant assessed using own 4 point index)	N/A	12/16	Cancer	Unknown	At least 3 years	Unknown	Nobel Biocare, Endopore, Astra & unknown implants	95 implants were primarily placed and 50 implants had secondary placement 3months after oncological reconstruction.	Unknown
Ch'ng, 2014	Retrospective observational	Implant Survival, Assess effect of Risk Factors associated with poor healing.	N/A	Own - Implant success was defined as a painless and stable fixture without evidence of peri-implant infection or radiographic lack of osseointegration	12/16	SCC, Recurrence, Osteosarcoma, Desmoid tumour, Adenoid Cystic Carcinoma, adenocarcinoma, fibrosarcoma, Melanoma, MEC, Hemangioma-Endotheiloma	Median age = 59 Yrs	Mean = 3.1 Years	Unknown	Astra	Primary and secondary implant placement. Patients had implants placed prior to radiotherapy. Reconstruction plates and screws removed if hindering implant placement. Debulking of soft tissues and	All Removable

											vestibuolplasty also carried out as required.	
Shaw, 2005	Retrospective observational	Implant Survival and Complications and Surgical Complications	N/A	Own - Implant success was defined as remaining function, no mobility, pain or infection.	10/16	80% of patients SCC, other 20% unknown	Mean = 58 Yr (Range = 15-80 Yrs)	Mean = 3.5 years (Range = 0.3/14 years)	Maxilla & Mandible	Frialit II, IMZ, Branemark & IMTEC	Secondary implant placement 1 year after oncological reconstruction. Delayed loading of implants of 3-6 months. Debulking of soft tissue and mucosal grafts carried out as required.	Fixed & Removable
Wang, 2015	Retrospective observational	Vertical Bone Height - double barrel vs Vertical distraction Osteogenesis in Fibula Free Flaps, Implant Survival and Success	Poorly defined - implant still in situ then survived.	Albrektsson, 1986	12/16	Ameloblastoma & OKC	Range = 28-55 Yr	Mean = 42.5 months +/- 4 months	Mandible	Straumann	Secondary implant placement after oncological reconstruction. Delayed loading of implants 3-5months after placement. Distraction osteogenesis devices used as implants and restored.	All Fixed
Yerit, 2006	Retrospective observational	Implant survival in the mandible after radiotherapy and radical surgery in oral cancer patients.	N/A	Own - Implant Success when no complaints of the patient, no mobility, no peri-implant tissue inflammation and no peri-implant bone loss exceeding one-third of implant length was observed	10/16	Cancer of oral cavity (majority of the subjects having destructive oral squamous cell carcinomas stage T2–T4)	Range = 16-84.1 Yrs	Mean = 5.42 years (+/- 3.21) years	Mandible	IMZ, Frialit II & Xive	Implant insertion at various intervals with the mean at 1.41 years after reconstruction. Delayed loading of implants of at least 6 months. Gingivoplasty and vestibuloplaty procedures carried out as required.	All Removable
Linsen, 2009	Retrospective observational	Survival of implants and implant-retained prostheses in patients after ablative surgery of oral cancer with or without adjunctive radiation therapy.	N/A	Kaplan, 1958	9/16	SCC, Ameloblastoma, Adenoid Cystic Carcinoma, OKC, Carcinoma of other origins	Mean = 55.7 Yr (Range = +/- 16.25 Yrs)	Mean = 47.99 months (+/- 134.31 months)	unknown	Branemark & Straumann	Delayed implant placement with an average of 41 months after oncological treatment. Delayed loading of implants of 4.9 months (average).	Fixed & Removable
Studies with an average follow-up of less than 3 years or no average follow-up reported												
Fierz, 2013	Retrospective observational	Reports on Surgical and Prosthodontic Rehabilitation after resection for Oral oncology resection	Own - implant not removed then survived, those functioning given a 'survival rating'	N/A	9/16	SCC, Adenocarcinoma & Others tumours	Mean = 57 Yr (Range = +/- 7.2 Yrs)	Range = Less than 12 months upto 5 years	Maxilla & Mandible	Unknown	No described protocol.	Fixed & Removable

Barrowman, 2011	Retrospective observational	Audit experience of implant placement in jaws after oral cancer resection, Success of Prosthodontic Rehabilitation	Poorly defined - implant still in situ then survived	N/A	10/16	SCC, Verrucous Carcinoma, Osteosarcoma & Adenoid Cystic Carcinoma	Range = 20-76 Yr	Upto 15 years	Maxilla & Mandible	Branemark	No described protocol.	Fixed & Removable
Zou, 2013	Retrospective observational	Long-term clinical outcomes on immediate or staged Implant Placement in iliac bone for restoring defects after tumour resection.	Own - Implants provided supportive function and were stable when torque tested	Albrektsson, 1986	7/16	SCC, Ameloblastoma, OKC, Myxoma	Range = 24-61 Yr	Upto 12 years	Mandible	Nobel & Straumann	17 patients had primary implant placement 15 patients had secondary placement after oncological reconstruction. Delayed loading of implants of 5-6months. Bone condensing was performed to enhance the bone density.	Fixed & Removable
Schultes, 2002	Retrospective observational	Stability of Implants in Microvascular Free Flaps	Poorly defined - implant still in situ then survived	N/A	8/16	Alvolear Crest Carcinoma T4	Average 58.2, 53.6 Yrs	Upto 12 months	Mandible	SIS (Austria)	Implants placed 4months after radiotherapy Delayed loading of implants of 4 months	All Removable
Buddula, 2010	Retrospective observational	Implant Survival in irradiated bone	Own - Implant present in oral cavity at time of data collection then deemed to have survived.	N/A	13/16	SCC, Adenoid Cystic Carcinoma, BCC & Unknown	Mean = 60.2 Yrs	Upto 7 years	Maxilla & Mandible	Unknown	Median time from ending radiotherapy to implant placement was 3.4 years.	Unknown
Klein, 2009	Retrospective observational	Prognostic parameters for the rehabilitation of mandibular continuity defects with free autologous bone and dental implants for patients after intraoral squamous cell carcinoma	N/A	Naert, 1992	11/16	SCC	Mean = 55.7 Yrs	Not Documented	Mandible	Unknown	Implants were principally placed into the following 4 tissue conditions: non-irradiated local bone, irradiated local bone, osteoplastic in non-irradiated tissue and osteoplastic in irradiated tissue.	Unknown
Burgess, 2017	Retrospective observational	Implant survival in a variety of composite free flaps	Own - implant not removed then survived	N/A	10/16	Head & neck neoplasia	Average age at implantation was 51 years (range, 18–77 years)	At least 6months follow up	Maxilla and Mandible	Neoss, Straumann Dentsply Sirona, South Africa - Head Office implants	Primary and secondary implant placement. The mean time to implant placement from reconstruction was 19 months (range, 0–141 months) with 2 patients (7 implants) having their implants placed into the fibula 6 weeks before harvesting.	Unknown

Chiapasco, 2006	Retrospective observational	Fibula Free flap Survival, Implant Survival	Albrektsson, 1986	Albrektsson, 1986	9/16	Rabdomiosarcoma, Sarcoma, SCC, Osteosarcoma & Ameloblastoma	Range = 13-66 Yr	Range = 24-106 months	Maxilla & Mandible	Branemark, ITI & 3i	Placement using surgical guides. Secondary implant placement 3-12 months after oncological reconstruction. Implants immediately loaded in 2 patients. Delayed loading for the all other patients 3-6months after placement.	Fixed & Removable
Chiapasco, 2008	Retrospective observational	Bone Graft Success, Implant Success, Patient Satisfaction	Own - similar to Albrektsson, 1986 but authors allow greater bone loss around implants.	Albrektsson, 1986	7/16	Ameloblastoma, Ossifying fibroma, Cementoblastoma, Myxoma, SCC, Gigantocellular tumor, OKC & Rabdomyosarcoma.	Range = 17-54 Yr	Range = 48-132 months	Mandible	Straumann, Nobel biocare & Branemark	Placement using surgical guides. Secondary implant placement 4-7 months after oncological reconstruction. Delayed loading of implants 4-6months after placement.	All Fixed
Chiapasco, 2000	Retrospective observational	Bone Resorption of Bone Grafts, Behaviour of Bone around Implants, Implant Failure	Albrektsson, 1986	Albrektsson, 1986	10/16	Ewing sarcoma, Epidermoid carcinoma, Cylindroma, Desmoplastic fybroma, Chondroblastic sarcoma, Cementoblastoma, Ameloblastoma, Chondrosarcoma, Ossifying fibroma, Myxoma & Giantocellular tumour	Range = 20-58 Yr	Range = 14-34 months	Maxilla & Mandible	Branemark & ITI	Placement using surgical guides. Secondary implant placement 4-8 months after oncological reconstruction. Delayed loading of implants 4-6months after placement.	Unknown
Hessling, 2015	Retrospective observational	Implant Survival, Peri-implantitis	Poorly defined - implant still in situ then survived.	N/A	8/16	SCC & Odontogenic tumours with malignant degeneration	Range = 18-77 Yr	Range = 3-82 months	Maxilla & Mandible	Xive & Templant	No described protocol.	Fixed & Removable

2.4.4 Statistical analysis

Due to the lack of controlled studies and the heterogeneity of the studies concerning patient selection, surgical protocols, implant loading, follow up and prosthetic rehabilitation, implant survival definitions and figures, measurement protocols and inconsistency in data reporting a formal meta-analysis was deemed statistically inappropriate and was therefore not conducted. Descriptive statistics where used to interpret and present the data from these studies.

2.4.5 Results of the studies

Descriptive data extraction was carried out for the 20 studies and is summarised in Table 2.1 & 2.2. All studies were retrospective observational studies in design with the majority undertaken at single centres, however for 3 studies this was unclear [Schultes et al., 2002], [Yerit et al., 2006], [Linsen et al., 2012]. These 20 studies were published over a range of 21 years (1996 to 2017) and provide cumulative data on 1905 implants placed into autogenous bone grafts in H&N cancer patients with both benign and malignant tumours being reported. The exact patient number for this intervention within some of the studies was unclear as a result of the studies reporting on implant rather than patient number, or there was an inability to identify which population that received dental implants to identify patient numbers. 1 study [Chiapasco et al., 2006] included reported on patients under 18 years old (2 patients in total) however these patients and their data were removed from the analysis. Implants were placed into both vascularised and non-vascularised autogenous bone grafts, with a number of donor sites being reported. (Table 2.2 & 2.3) These implants

were placed in a variety of intra-oral sites with implants placed into autogenous bone grafts within the mandible in 8 studies, bi-maxillary placement in 9 studies, and in 3 studies it was not reported whether the implant fixtures were placed in the maxilla or the mandible other than that they were placed into autogenous bone grafts [Linsen et al., 2012], [Fenlon et al., 2012], [Ch'ng et al., 2016]. There were no studies included where implant fixtures were placed solely in the reconstructed maxilla.

Radiotherapy to the autogenous bone graft/implant site was reported in 16 studies. 2 studies [Wang et al., 2015], [Zou et al., 2015] reported that radiotherapy was not carried out on the study population and in 1 study [Yerit et al., 2006] bone graft sites were not irradiated. 1 study [Chiapasco et al., 2008] failed to report whether the study population received radiotherapy or not. Of 20 studies included in this systematic review, only 7 studies reported on outcomes related to implant survival in irradiated autogenous bone grafts [Teoh et al., 2005], [Barrowman et al., 2011], [Buddula et al., 2012], [Fenlon et al., 2012], [Fierz et al., 2013], [Ch'ng et al., 2016], [Burgess et al., 2017].

The surgical and implant loading protocols were reported in 17 studies with no description given in 3 studies [Barrowman et al., 2011], [Fierz et al., 2013], [Hessling et al., 2015]. The implant placement protocols were diverse with variables including; the use of surgical templates/guides, primary and/or secondary implant placement following autogenous bone grafting and immediate and/or delayed implant loading however, the majority of the studies reported on delayed implant placement following initial healing of the transported bone graft and delayed loading of the implant fixtures. 6 studies reported primary implant placement [Watzinger et al., 1996], [Wu et al., 2008], [Fenlon et al., 2012], [Zou et al., 2015], [Ch'ng et al., 2016], [Burgess et al.,

2017] and 1 study reported immediate implant loading [Chiapasco et al., 2006]. Additional procedures were also reported which included; removal of reconstruction plates and screws at the time of implant placement, bone condensing to enhance the bone density and further peri-implant surgery in the form of debulking of soft tissues, gingivoplasty / vestibuloplasty and free mucosal grafts to optimize the soft tissue conditions (Table 2.1). Prosthodontic reconstruction of the implant fixtures were reported in 15 of the studies which included fixed and removable prosthesis and is summarised in Table 2.1.

Table 2.2: Summary of Implant Survival & Implant Success in autogenous bone grafts

Author & Year of Publication	Donor site of Autogenous Bone Graft	Radiotherapy/ Chemotherapy to bone graft site	Complications	IMPLANT SURVIVAL				IMPLANT SUCCESS				
				No. of patients who had implants placed into Autogenous bone grafts (and failures)	Overall patient Implant Survival in Autogenous bone grafts	No. of Implants placed into Autogenous bone grafts (and failures)	Overall Implant Survival in Autogenous bone grafts	No. of patients who had implants placed into Autogenous bone grafts (and unsuccessful)	Overall patient Implant Success in Autogenous bone grafts	No. of Implants placed into Autogenous bone grafts (and unsuccessful)	Overall Implant Success in Autogenous bone grafts	Reasons for a lack of Implant success
Studies with an average follow-up of 3 years or greater												
Watzinger, 1996	Vascularised iliac Bone Graft and Non-Vascularised iliac & Rib Bone Graft	Yes - All patients had Chemotherapy and RDX	Marginal bone loss, periodontal pocketing, gingival index and sulcus bleeding index showed wide variation	Not Reported	N/A	52 (14)	73.1%*	Not Reported	N/A	52 (22)	57.7%*	Non-functioning implants (not prosthetically loaded)
Teoh, 2005	Vascularised Fibula Free Flap	Yes - 5 patients had chemotherapy, 1 patients had chemo/RDX (pre-implant placement), 6 patients had pre-op RDX, and 1 patient had post-op RDX.	13 patients had soft tissue hyperplasia that need debulking or skin grafting.	22 (2)	90.9%*	71 (3)	95.8%*	Not Reported	N/A	Not Reported	N/A	N/A
Wu, 2008	Fibula Free Flap	Yes - 3 pts had RDX (unsure if pre or post op)	Soft tissue hyperplasia needed surgical removal in 6 patients (17 implants).	29 (not reported)	N/A	100 (9)	91.0%	29 (not reported)	N/A	100 (14)	86.0%	Unfavourable local soft tissue and implant left as sleepers. Peri-implant bone loss greater than 2mm
Fenlon, 2012	Vascularised Free Flap - DCIA, Radial, Fibula & Rib	Yes - 35 implants had RDX	High rate of poor implant positioning in primary implant placement.	41 (10)	75.6%*	145 (18)	87.5%*	Not Reported	N/A	145 (34)	76.6%*	Implants osseointegrated but prosthetically unusable
Ch'ng, 2014	Vascularised Fibula Free Flap	Yes -66/243 patients had RDX (43 patients pre-op RDX, 23 patients post-op RDX)	ORN 7.7% of all implants (19 patients, 4 cases in vascularised fibula free flap and 15 in native bone, smoking was shown to be a significant risk factors. Also modification of peri-implant soft tissue required such as debulking of soft tissue and vestibuloplasty as required.	54 (10)	81.5%*	243 (20)	91.8%	Not Reported	N/A	Not Reported	N/A	N/A

Study	Graft Type	RDX	Complications/Notes	Implants (lost)	%	Implants (lost)	%			Implants (lost)	%	Notes
Shaw, 2005	Vascularised Composite DCIA, Fibula and Radius and Non-vascularised Bone Grafts	Yes - 47% of patients had RDX	Soft tissue overgrowth in 3 patients (5 implants). Also, surgical debulk of soft tissue reported in number of cases.	33 (12)	**63.6%***	123 (32)	**69.0%**	Not Reported	**N/A**	Not Reported	**N/A**	N/A
Wang, 2015	Vascularised Fibula Free Flap (Double barrel or Vertical Distraction Osteogenesis techniques)	NO	Implant hygiene and bleeding increased over time. 6 patients (11 implants) required soft tissue reduction however recurrence of soft tissue overgrowth occurred.	19 (0)	**100%**	51 (0)	**100%***	Not Reported	**N/A**	51 (7)	**86.3%***	Peri-implant bone loss greater than criteria (radiographic assessment)
Yerit, 2006	Vascularised and Non-Vascularised iliac Bone Graft	NO - No RDX to bone graft sites	None noted only documenting causes of implant loss	Not Reported	**N/A**	78 (13)	**54.0%**	Not Reported	**N/A**	Not Reported	**N/A**	N/A
Linsen, 2009	Avascularised iliac Bone Graft	Yes - 39 implants had RDX, 44 implants didn't have RDX	Peri-implantitis in 12 patients (31 implants).	Not Reported	**N/A**	79 (8)	**89.9%***	Not Reported	**N/A**	Not Reported	**N/A**	N/A
Studies with an average follow-up of less than 3 years or no average follow-up reported												
Fierz, 2013	Vascularised Free Flap - Fibula, radius, scapula.	Yes - 20 out of 46 implants had RDX.	Fraile patients limited treatment, and prosthetic rehabilitation was challenging.	Not Reported	**N/A**	46 (8)	**82.6%***	Not Reported	**N/A**	Not Reported	**N/A**	N/A
Barrowman, 2011	Vascularised Free flap - illiac, DCIA & fibula and Non-vascularised bone graft.	Yes - 15 implants in to irradiated vascularised free flap	Inability of patients to tolerate prosthesis. Peri-implantitis and lack of integration of some implants.	Not Reported	**N/A**	38 (5)	**86.8%***	Not Reported	**N/A**	Not Reported	**N/A**	N/A
Zou, 2013	Vascularised iliac Bone Graft	NO	Increase in plaque index over time. Prosthodontic complications overtime after prosthesis fitted also tumour recurrence.	32 (not reported)	**N/A**	110 (4)	**96.4%**	Not Reported	**N/A**	110 (9)	**91.8%**	Severe gingival hyperplasia and bone resorption in peri-implant area
Schultes, 2002	Vascularised Scapula & iliac Bone Graft	Yes - ALL patients had RDX 60 Gys.	Increased pocket depth around implants placed into non-native bone in comparison to native bone. 7 implants with pocketing greater than 5mm were all in vascularised free flaps.	38 (2)	**94.7%***	96 (2)	**97.9%***	Not Reported	**N/A**	96 (4)	**95.8%***	Implants inadequately positioned and could not be used for further prosthetic treatment
Buddula, 2010	Bone graft - Fibula, iliac & Scapula (unsure of Vascularised or Non-Vascularised)	Yes - All patients had RDX	None noted only documenting implant survival	Not Reported	**N/A**	59 (8)	**83.3%**	Not Reported	**N/A**	Not Reported	**N/A**	N/A

Study	Graft	RDX/Chemo	Complications									Notes
Klein, 2009	Avascular iliac Bone Graft	Yes - some patients had RDX	None noted only documenting implant survival	Not Reported	N/A	128 (22)	78.4%	Not Reported	N/A	Not Reported	N/A	N/A
Burgess, 2017	Vascularized bone grafts – fibula, DCIA, scapula and radial	Yes - some patients had RDX	None noted only documenting implant survival	59 (not reported)	N/A	199 (11)	93.6%	Not Reported	N/A	Not Reported	N/A	N/A
Chiapasco, 2006	Vascularised Fibula Free Flap	Yes - Some patients had RDX and Chemo - unknown number	Soft tissue overgrowth in 2 patients that required removal and palatal mucosal graft placed.	14 (1)	92.9%*	62 (1)	98.3%*	14 (2)	85.7%*	62 (5)	91.9%*	Peri-implant bone loss greater than criteria (radiographic assessment)
Chiapasco, 2008	Non-Vascularised - Calvarium or iliac bone graft	Unknown	Soft tissue grafting required around implants in 3 patients.	16 (1)	93.8%*	60 (2)	96.7%	16 (2)	87.5%*	60 (4)	93.3%	Peri-implant bone loss greater than criteria (radiographic assessment)
Chiapasco, 2000	Non-Vascularised - ilieum & fibula, and Vascularised free flap - ilieum & fibula	Yes - 3 patients had RDX (unknown if pre or post)	Soft tissue grafting required around implants in 3 patients.	18 (2)	88.9%*	72 (3)	95.8%*	18 (2)	88.9%*	72 (3)	95.8%*	N/A
Hessling, 2015	Free iliac crest, Microvascular iliac, microvascular Fibula, Microvascular Scapula, Calavarial Bone graft	Yes - Some patients had RDX and Chemo (pre- & post-op) unknown number	67% peri-implantitis due to a lack of attached gingivae.	Not Reported	N/A	93 (8)	91.4%*	Not Reported	N/A	Not Reported	N/A	N/A

Table 2.3: Implant survival in autogenous bone grafts placed in vascularised & non-vascularised bone grafts

Author & Year of Publication	Non-Vascularised Bone graft				Vascularised Bone Graft			
	No. of patients who had implants placed into Non-Vascularised Autogenous bone grafts (& Failures)	Overall Patient Implant Survival in Non-Vascularised Autogenous bone grafts	No. of Implants placed into Non-Vascularised Autogenous bone grafts (& Failures)	Overall Implant Survival in Non-Vascularised Autogenous bone grafts	No. of patients who had implants placed into Vascularized Autogenous bone grafts (& Failures)	Overall Patient Implant Survival in Vascularised Autogenous bone grafts	No. of Implants placed into Vascularised Autogenous bone grafts (& Failures)	Overall Implant Survival in Vascularised Autogenous bone grafts
Studies with an average follow-up of 3 years or greater								
Watzinger, 1996	Not Reported	**N/A**	33 (13)	**60.6%***	Not Reported	**N/A**	19 (1)	**94.7%***
Teoh, 2005	N/A	**N/A**	N/A	**N/A**	22 (2)	**90.9%***	71 (3)	**95.8%***
Wu, 2008	N/A	**N/A**	N/A	**N/A**	29 (Not Reported)	**N/A**	100 (9)	**91%**
Fenlon, 2012	N/A	**N/A**	N/A	**N/A**	41 (10)	**75.6%***	145 (18)	**87.5%***
Ch'ng, 2014	N/A	**N/A**	N/A	**N/A**	54 (10)	**81.5%***	243 (20)	**91.80%**
Shaw, 2005	2 (1)	**50%***	8 (2)	**75%***	31 (11)	**64.5%***	115 (30)	**73.9%***
Wang, 2015	N/A	**N/A**	N/A	**N/A**	19 (0)	**100%**	51 (0)	**100%***
Yerit, 2006	Not Reported	**N/A**	Not Reported	**N/A**	Not Reported	**N/A**	Not Reported	**N/A**
Linsen, 2009	Not Reported	**N/A**	79 (8)	**89.9%***	N/A	**N/A**	N/A	**N/A**
Studies with an average follow-up of less than 3 years or no average follow-up reported								
Fierz, 2013	N/A	**N/A**	N/A	**N/A**	Not Reported	**N/A**	Not Reported	**N/A**
Barrowman, 2011	Not Reported	**N/A**	6 (0)	**100%***	Not Reported	**N/A**	32 (5)	**84.4%***
Zou, 2013	N/A	**N/A**	N/A	**N/A**	32 (Not Reported)	**N/A**	110 (5)	**96.40%**
Schultes, 2002	N/A	**N/A**	N/A	**N/A**	38 (2)	**94.7%***	96 (2)	**97.9%***
Buddula, 2010	Not Reported	**N/A**	Not Reported	**N/A**	Not Reported	**N/A**	Not Reported	**N/A**
Klein, 2009	Not Reported	**N/A**	128 (22)	**82.8%***	N/A	**N/A**	N/A	**N/A**

Burgess, 2017	N/A	**N/A**	N/A	**N/A**	59 (Not Reported)	**N/A**	199 (11)	**93.60%**
Chiapasco, 2006	N/A	**N/A**	N/A	**N/A**	14 (1)	**92.9%***	62 (1)	**98.3%***
Chiapasco, 2008	16 (1)	**93.8%***	60 (2)	**96.7%***	N/A	**N/A**	N/A	**N/A**
Chiapasco, 2000	10 (1)	**90%***	41 (2)	**95.1%***	8 (1)	**87.5%***	31 (1)	**96.8%***
Hessling, 2015	Not Reported	**N/A**	62 (4)	**93.5%***	Not Reported	**N/A**	31 (4)	**87.1%***

2.4.5.1 Overall implant survival

Overall survival of implants placed into autogenous bone grafts varied markedly (both at an implant and patient level) between the included studies ranging from 100% with a mean follow up of 3.5years +/- 0.3 years in a study by Wang et al., [Wang et al., 2015], to 54% with a mean follow up 5.4 years (+/- 3.2) years by Yerit et al., [Yerit et al., 2006] (at an implant level). (Table 2.2)

11 studies compared implant survival in autogenous bone grafts to native bone within their studies. 9 of these studies [Watzinger et al., 1996], [Shaw et al., 2005], [Yerit et al., 2006], [Klein et al., 2009], [Barrowman et al., 2011], [Fenlon et al., 2012], [Hessling et al., 2015], [Ch'ng et al., 2016], [Linsen et al., 2016], reported higher implant failure rates within autogenous bone grafts in comparison to native bone. In 2 studies [Teoh et al., 2005], [Buddula et al., 2012], no significant difference was reported.

2.4.5.2 Autogenous bone graft type and implant survival

17 studies reported on the specific bone graft type (non-vascularised or vascularised) into which the implant fixtures were placed. In the remaining 3 studies [Yerit et al., 2006], [Buddula et al., 2012], [Fierz et al., 2013], there was an inability to distinguish between the bone graft types.

Of these 17 studies, 8 studies reported on implant survival in non-vascularised bone grafts and 14 studies reported on implant survival in vascularised bone grafts with 5 studies [Watzinger et al., 1996], [Chiapasco et al., 2000], [Shaw et al., 2005],

[Barrowman et al., 2011], [Hessling et al., 2015], reporting on implant survival in both non-vascularised and vascularised bone grafts (Table 2.3).

Overall implant survival appeared to be higher for those implants placed into vascularised in comparison to non-vascularised bone grafts. Of the 5 studies reporting on both vascularised and non-vascularised bone grafts 3 of these studies [Watzinger et al., 1996], [Chiapasco et al., 2000], [Barrowman et al., 2011], reported higher implant survival in vascularised bone grafts whereas the other 2 studies [Shaw et al., 2005] [Hessling et al., 2015], reported higher implant survival in non-vascularised bone grafts. Despite this, Shaw et al., reported that implants placed into 'vascularized bone grafts were superior to non-vascularized bone'. [Shaw et al., 2005]

12 studies reported on the use of more than one autogenous bone graft donor site within their study [Watzinger et al., 1996], [Chiapasco et al., 2000], [Schultes et al., 2002], [Shaw et al., 2005], [Yerit et al., 2006], [Chiapasco et al., 2008], [Barrowman et al., 2011], [Fenlon et al., 2012], [Buddula et al., 2012], [Fierz et al., 2013], [Hessling et al., 2015], & [Burgess et al., 2017]. Of these, 5 studies reported on the survival of implants within the different autogenous bone graft donor sites. 2 studies [Fenlon et al., 2012], [Burgess et al., 2017] reported no significant effect on implant survival whereas 3 studies [Chiapasco et al., 2000], [Shaw et al., 2005], [Hessling et al., 2015], reported varying implant survival rates within different autogenous bone grafts. However, only 1 study [Hessling et al., 2015] found this to be significant with higher implant failure being reported within composite fibula free flap grafts.

2.4.5.3 Radiotherapy and implant survival

7 studies reported on outcomes related to implant survival in irradiated autogenous bone grafts [Teoh et al., 2005], [Barrowman et al., 2011], [Buddula et al., 2012], [Fenlon et al., 2012], [Fierz et al., 2013], [Ch'ng et al., 2016], [Burgess et al., 2017] (Table 2.4). 1 study reported solely on irradiated patients [Buddula et al., 2012] the other 6 studies [Teoh et al., 2005], [Barrowman et al., 2011], [Fenlon et al., 2012], [Fierz et al., 2013], [Ch'ng et al., 2016], [Burgess et al., 2017] reported on both irradiated and non-irradiated patients. These 6 studies [Teoh et al., 2005], [Barrowman et al., 2011], [Fenlon et al., 2012], [Fierz et al., 2013], [Ch'ng et al., 2016], [Burgess et al., 2017] all reported higher implant failure (at an implant and a patient level (where applicable)) of implants placed into autogenous bone grafts in irradiated patients in comparison to those patients that did not receive radiotherapy (Table 2.4).

All of these studies [Teoh et al., 2005], [Barrowman et al., 2011], [Fenlon et al., 2012], [Fierz et al., 2013], [Ch'ng et al., 2016], [Burgess et al., 2017] reported on the deleterious effect of radiotherapy on implant survival in autogenous bone grafts. 2 studies [Fenlon et al., 2012], [Ch'ng et al., 2016] reported this to be statistically significant. Fenlon et al., reported a close correlation between implant survival in vascularised free composite grafts and an absence of radiotherapy using a multiple correspondence analysis (MCA). [Fenlon et al., 2012] Ch'ng et al., reported a statistically significant higher implant failure rate in irradiated fibula free flaps in comparison to non-irradiated fibula free flaps (P=0.041). [Ch'ng et al., 2016]. 2 studies [Teoh et al., 2005], [Burgess et al., 2017] reported no statistically significant

difference between radiotherapy and implant failure despite higher implant failure

rates being reported.

Table 2.4: Implant survival in autogenous bone grafts of irradiated & non-irradiated patients

Author	RDX				No RDX			
	No. of Implants placed into Autogenous bone grafts with RDX (& Failures)	Overall Implant survival of implants placed into Autogenous bone grafts with RDX	No. of patients who had implants placed into Autogenous bone grafts with RDX (& Failures)	Patient based implant survival of implant placed into Autogenous bone grafts with RDX	No. of Implants placed into Autogenous bone grafts with No RDX (& Failures)	Overall Implant survival of implants placed into Autogenous bone grafts with No RDX	No. of patients who had implants placed into Autogenous bone grafts with No RDX (& Failures)	Patient based implant survival of implant placed into Autogenous bone grafts with No RDX
Teoh, 2005	14(2)	85.7%*	4(1)	75%*	57(1)	98.2%*	22 (1)	95.4%*
Fenlon, 2012	35 (15)	57.1%*	12 (8)	33.3%*	110 (3)	97.3%*	29(2)	93.1%*
Ch'ng, 2014	66 (11)	83.3%*	Not Reported	N/A	177(9)	94.9%*	Not Reported	N/A
Fierz, 2013	20 (6)	70.0%*	Not Reported	N/A	26 (2)	92.3%*	Not Reported	N/A
Barrowman, 2011	15 (5)	66.7%*	Not Reported	N/A	23 (0)	100%*	Not Reported	N/A
Buddula, 2010	59(8)	83.30%	Not Reported	N/A	N/A	N/A	N/A	N/A
Burgess, 2017	45* (7)	84.4%*	Not Reported	N/A	154(4)	97.4%*	Not Reported	N/A

2.4.5.4 Primary & secondary implant placement and implant survival

6 studies clearly reported the use of both primary and secondary implant placement within their study [Watzinger et al., 1996], [Wu et al., 2008], [Fenlon et al., 2012], [Zou et al., 2015], [Ch'ng et al., 2016], [Burgess et al., 2017], however, only 1 study [Fenlon et al., 2012] reported on implant survival in primary and secondary implant placement within autogenous bone grafts. Fenlon et al., reported on implant survival in immediate vs delayed placement of the implant fixtures into free vascularised grafts and found that implant survival of immediately placed implants was significantly worse than for implants placed after a delay of 3 months in free vascularized grafts. [Fenlon et al., 2012]

2.4.5.5 Cancer diagnosis and implant survival

With regards to tumour type (malignant vs benign), 3 studies [Watzinger et al., 1996], [Schultes et al., 2002], [Klein et al., 2009] reported exclusively on implant survival in patients with malignant H&N tumours with varying implant survival rates being reported, whilst 1 study reported exclusively on benign H&N tumour patients with a 100% implant survival rate being reported [Wang et al., 2015] (Table 2.2). 2 studies [Fenlon, 2012], [Burgess et al., 2017] provided non-descriptive terms (cancer, head and neck neoplasia) for the type of H&N tumour of the patients within their studies and therefore differentiation between benign and malignant disease could not be made. The other 14 studies reported on both malignant and benign H&N tumours; however, the implant survival data was not reported or presented in a manner that

permitted comparison of implant survival in patients with malignant or benign H&N tumours.

2.4.5.6 Implant survival and peri-implant soft tissue

Only one study [Linsen et al., 2012] reported on the peri-implant soft tissues and implant survival in autogenous bone grafts. Linsen et al., reported higher implant failure rates for those placed into composite (bone and soft tissue) grafts in comparison to implants placed into a bone grafts with residual soft tissues. This difference however, was not found to be statistically significant ($p = 0.436$). [Linsen et al., 2012]

In the other 19 studies the effect of the peri-implant soft tissue on implant survival was not reported. However, implant success appeared to be significantly affected by the type of peri-implant soft tissues which is discussed in further detail in sections 2.4.5.7 and 2.4.5.8.

2.4.5.7 Implant survival and implant success

In 9 studies [Watzinger et al., 1996], [Chiapasco et al., 2000], [Schultes et al., 2002], [Chiapasco et al., 2006], [Chiapasco et al., 2008], [Wu et al., 2008], [Fenlon et al., 2012], [Wang et al., 2015], [Zou et al., 2015] both implant survival and implant success data were reported or provided (Table 2.2).

When comparing implant survival to implant success in 8 studies [Watzinger et al., 1996], [Schultes et al., 2002], [Chiapasco et al., 2006], [Chiapasco et al., 2008], [Wu et al., 2008], [Fenlon et al., 2012], [Wang et al., 2015], [Zou et al., 2015] implant

survival was found to be higher than implant success. In 1 study [Chiapasco et al., 2000] implant survival and success were reported as being the same.

The reasons for reduced implant success in comparison to implant survival within these 8 studies (other than implant failure/loss) was related to excessive peri-implant bone loss in 5 studies [Chiapasco et al., 2006], [Chiapasco et al., 2008], [Wu et al., 2008], [Wang et al., 2015], [Zou et al., 2015], an inability to prosthetically restore the implants in 4 studies [Watzinger et al., 1996], [Schultes et al,. 2002], [Wu et al., 2008], [Fenlon et al., 2012], and gingival hyperplasia in 1 study [Zou et al., 2015]. Six of these studies [Schultes et al., 2002], [Chiapasco et al., 2006], [Chiapasco et al., 2008], [Wu et al., 2008], [Wang et al., 2015], [Zou et al., 2015] reported that the peri-implant soft tissue profile around the implant contributed to this reduced success and most frequently occurred in composite (bone and soft tissue) free flaps (most commonly external skin) in comparison to implants placed into bone grafts with residual soft tissue around the implant fixtures.

2.4.5.8 Complications

A variety of implant-based complications were documented. Complications were often described within the study rather than being formally assessed, defined or used as outcome measures. Due to there being a lack of formal definition and variability in the documentation within the studies, the data cannot be considered sufficently robust to allow collective appraisal but are described for information purposes. Common "complications" reported in the studies included soft tissue overgrowth/hyperplasia of the peri-implant tissues [Wang et al., 2015], [Chiapasco et al., 2006], [Teoh et al., 2005], [Wu et al., 2008], [Shaw et al., 2005]; peri-implantitis

and periodontal pocketing [Barrowman et al., 2011], [Schultes et al., 2002], [Linsen et al., 2012], [Burgess et al., 2017], [Hessling et al., 2015]; the need for soft tissue debulking/modification of free flaps [Ch'ng et al., 2016], [Shaw et al., 2005] and the need for mucosal/soft tissue grafting around implants to improve the soft tissue profile [Chiapasco et al., 2008], [Teoh et al., 2005], [Chiapasco et al., 2000]. Other complications included; poor oral hygiene [Wang et al., 2015], [Zou et al., 2015]; challenging prosthodontic rehabilitation/ inability of the patient to tolerate the prosthesis provided [Barrowman et al., 2011], [Zou et al., 2015], [Fierz et al., 2013], poor implant positioning [Schultes et al., 2002], [Fenlon et al., 2012], [Watzinger et al., 1996], [Wu et al., 2008] and osteoradionecrosis [Ch'ng et al., 2016] (Table 2.2).

2.5 Discussion

2.5.1 Summary of evidence

The main findings from this systematic review did identify with the exception of a small number of studies that implant survival (at an implant level) in autogenous bone grafts was clinically promising (>85%). However, this appears to be lower than for implants placed into the native bone in H&N cancer patients. Weak evidence was identified to suggest that radiotherapy is a prognostic factor affecting implant survival in this patient cohort, however this has also been reported as having a detrimental effect on implant survival in native bone within the literature [Chambrone et al., 2013]. The type of autogenous bone graft donor site and implant survival was also reviewed within the included studies that compared varying autogenous bone graft donor sites and implant survival. There was weak evidence from these studies to suggest that

implants placed into vascularised bone grafts appear to have a higher survival rate in comparison to non-vascularised bone grafts within this review. This evidence however is unreliable, due to the clear lack of studies reporting on implant survival in non-vascularised bone grafts and thus the subsequent number of implants and patients included within this review. Implant survival did not appear to be affected by the type of H&N tumour (malignant vs. benign); however, no studies within this review directly compared or provided data to permit this comparison, and accordingly no robust conclusion can be made on this.

The implant placement protocol with regard to primary (immediate) or secondary (delayed) implant placement was also reviewed and there was limited evidence from Fenlon et al., [Fenlon et al., 2012] that implant failure is significantly worse in immediately placed implants in comparison with a delayed approach in free vascularized grafts.

Implant success was shown to be lower than implant survival and was related to peri-implant bone loss, peri-implant soft tissue hyperplasia and an inability to prosthetically restore the implants. This was most commonly related to composite (bone and soft tissue) free flaps, specifically the soft tissue component. This soft tissue component provides a less optimal soft tissue profile around the implant fixture, which could contribute to implant failure (as a result of peri-implantitis); however, well designed long-term studies are needed to fully comprehend the effect of this on implant survival.

Implant complications were also noted specific to autogenous bone grafts, including peri-implant soft tissue overgrowth/hyperplasia and the need for soft tissue debulking/modification and mucosal/soft tissue grafting around implants, which

occurred commonly in combined bone and soft tissue grafts. These findings however, are limited due to low level of evidence in the form of a small number of retrospective observational studies.

2.5.2 Limitations

This systematic review has identified that the quality of evidence to inform clinical decision making regarding the use of implants in transported bone in this patient group is currently poor. All studies included in the review were retrospective observational studies and in general reported on low patient and implant numbers and were found to have a moderate to high risk of bias.

A lack of consistency in definitions of the primary (implant related) outcome measures was observed. The outcome measures used in the studies varied and implant survival/success was not necessarily the primary outcome measure. Only 14 of the 20 studies reported the primary outcome measure to be implant survival/success. whilst the remainder reported on free flap survival, graft success and bone resorption of bone grafts as the primary outcome.

A clear deficiency in many of the studies was the imprecise and inconsistent definitions of implant survival and/or implant success, as detailed in Table 2.1. Additionally, in a number of studies the terminology 'implant success' and 'implant survival' were used interchangeably within the narrative making comparison of the studies challenging and rendering statistical analysis of the survival data inappropriate.

The reporting of implant survival data varied between studies and was presented in a variety of ways which included cumulative survival and implant survival incidence. In some cases, no attempts to estimate implant survival were made but adequate data was documented to enable its calculation (Table 2.2). Best practice would be for the reporting of cumulative survival to give context to survival over time and account for patient drop-outs which may be high in this particular patient group. Due to the variability in the methods of data reporting and their comprehensiveness, there was insufficient confidence in extracted data to report statistical findings. Notably, as all studies presented different deficiencies in data reporting or study definitions, there was no clear way to further exclude studies using these criteria.

As such, there is a clear need for a consensus on what minimum data set is required for published articles reporting on implant survival in this patient cohort to allow further investigation via systematic reviews (e.g. effect of benign vs malignant H&N tumour and implant survival). The inclusion and exclusion criteria were highly variable and in some studies the criteria were such that there was a pre-disposition to selection bias and reporting higher implant survival rates. Patient follow-up was variable and was variably reported on, but in general was insufficient. Where possible follow-up of at least 5 years is required to begin to evaluate the outcomes of implant sin this patient group. Unfortunately, information on long-term implant survival in this patient cohort is still scarce and the results of the present review should not be extrapolated beyond early implant survival. Data on peri-implant health was lacking despite peri-implantitis being a major cause of late implant failure. There was also a lack of reporting on the maintenance regimes adopted within the studies which may influence the survival and success of dental implants.

In order to understand the use of implants in autogenous bone grafts in H&N oncology patients larger, well designed prospective studies are required. There needs to be clear set definitions of implant survival and success and appropriate presentation and statistical analysis of the data so that studies can be brought together to enable meta-analysis.

CHAPTER 3:

SERVICE EVALUATION OF OUTCOMES OF IMPLANTS PLACED FOR THE ORAL REHABILITATION OF HEAD AND NECK ONCOLOGY PATIENTS IN A LARGE REGIONAL COHORT

3. Service evaluation of outcomes of implants placed for the oral rehabilitation of head and neck oncology patients in a large regional cohort

This chapter is based on a publication that arose from this thesis. Service Evaluation of Outcomes of Implants placed for the Oral Rehabilitation of Head and Neck Oncology patients in a large regional cohort, [Laverty et al., 2019].

3.1 Background

Osseointegrated dental implants as a treatment modality have been shown to offer high success and survival [Pjetursson et al., 2014]. However, the reliability, safety, and usefulness of implant placement in the H&N cancer population remains poorly defined, mainly due to the limited availability of large, well-constructed studies in the literature as reported in Chapters 1 and 2. The vast majority of evidence available, to guide clinicians is formed from case reports and case series, using low patient numbers. Furthermore, the data is universally retrospective in nature which can be understood, as the service provided to this patient group does not lend itself to well-designed highly controlled trials. With the increasing use of dental implants in the oral rehabilitation of H&N cancer patients [Alani et al., 2009] an improved evidence base is required to help inform clinical decision making. Accordingly, there is an opportunity to add to the knowledge base through a service evaluation of a large

service that has been using dental implants in conjunction with surgical reconstruction for an extended period of time.

3.2 Aims & Objectives

The aim of this service evaluation is to present implant survival rates in a large H&N cancer patient cohort, where a consistent care pathway for oral and dental rehabilitation has been operative for the past five years. The primary objective was to ascertain the standard of implant outcomes achieved by the service. The cohort includes patients where osseointegrated implants have been placed into a variety of bone types including native, native resected, autogenous non-vascularised and autogenous vascularised bone/free flaps. The secondary objective was to the report the effect of covariates associated with implant failure such as radiotherapy and chemotherapy, which are frequently eluded to as prognostic factors for implant survival, and also to report on surgical complications during implant placement documented in this specific patient group.

3.3 Methods

3.3.1 Service evaluation approach and setting

The service evaluation was performed by retrospectively examining treatment records of H&N oncology patients who were provided with an implant retained prosthesis as part of oral and dental rehabilitation. The survey sample was taken from a population of H&N oncology patients that attended the Restorative Dentistry department at Birmingham Dental Hospital (BDH), Birmingham, UK (United

Kingdom), for care following primary management of their H&N cancer, in a continuous 55-month period from November 2012 to May 2017. The H&N restorative service provided at BDH is a tertiary care service which covers a population of 5.5 million people within the West Midlands region of the UK. The service was led by a single specialist clinical lead during this period and treatment was provided at no cost to the patients. Treatments were linked with Oral and Maxillofacial surgical (OMFS) teams at BDH or at University Hospitals Birmingham (UHB), Birmingham, UK. Despite the variability in disease presentation and in its management, a consistent co-ordinated care pathway leading to oral and dental rehabilitation including MDT planning was followed. The treatment period for data collection included the care of patients who had received implant-based reconstructions within same service at an earlier date but required prosthodontic maintenance or revision. These patients were included in the analysis., subject to the completeness of the minimum data-set.

All H&N oncology patients who had completed oral rehabilitation that included the use of dental implants to retain a prosthesis, during the census period were included. Patients were excluded if the minimum data-set could not be collected. Completion of restoration of the dental implant with a definitive prosthesis was the criterion for successful oral rehabilitation in this evaluation.

Implant planning

The majority of patients were planned for implant-based rehabilitation by a specialist restorative dentist in consultation with surgical teams from BDH and UHB. In the Birmingham service, patients are only provided with implants when conventional non-implant retained prostheses are deemed inappropriate. As part of the informed

consent process, patients understood the amount of time it would take for the planning, placement and restoration of dental implants, the need for multi-stage treatment and for regular review. All treatment costs were met by the service provider. Radiographic images were taken to assist in planning and included cone beam computed tomography (CBCT) with or without reformatting for implant planning software (SIMPLANT® Computer-Guided Implant Treatment Software (Dentsply Sirona, York, PN, USA) and conventional radiographs.

Surgical implant placement technique

Implants were placed by experienced surgical and restorative dental teams accustomed to placing a variety of implant systems in this patient group. Implants were placed into the native mandible/maxilla, resected mandible/maxilla or autogenous bone grafts. Implants were placed either free hand or using a surgical implant guide. Implant placement was both primary (at the time of surgical resection/reconstruction) or secondary/delayed (after surgical resection/reconstruction) however, within this service primary implant placement was uncommon. At the time of restoring or uncovering the implants, the stability of the implants was assessed (manually). Any unstable implants were removed, not used or buried to allow a longer healing time and then potentially used at a later date. Any soft tissue modifications such as further free flap skin paddle debulking and sulcoplasty to provide a sulcus were carried out prior to oral prosthodontic reconstruction, usually at the time of implant placement.

3.3.2 Eligibility criteria

Inclusion criteria

1. Patients who had suffered with H&N cancer.

2. Patients who had completed oral rehabilitation with an implant retained intra-oral prosthesis.

3. Patients who had been followed up on at least one occasion after placement of dental implants.

Exclusion criteria

1. Patients who did not suffer with H&N cancer.

2. Patients who did not complete oral rehabilitation with an implant retained intra-oral prosthesis.

3. Patients who were not followed up after dental implant placement.

4. Patients where the minimum data-set could not be collected.

3.3.3 Variables considered in the service evaluation

The minimum data-set required for inclusion required; patient demographics (age, gender), tumour diagnosis, the oncological treatment carried out in the form of; surgery (tumour ablation, reconstruction), radiotherapy (field and timing) and/or chemotherapy (drugs). Adjunctive surgeries (implant site augmentation), location of implant placement (maxilla, mandible, native bone, resected native bone, autogenous bone grafts vascularised and non-vascularised), dental rehabilitation (fixed, removable and timing) and the implant system used.

3.4 Ethical approval

Approval for this service evaluation (following completion of the Health Research Authority assessment tool and confirmation with BCHC NHS Trust R&D) was given by Birmingham Community Healthcare NHS Foundation Trust R&D team (Birmingham, UK) (Appendix 1).

3.5 Data collection

Patients were identified from electronic patient management systems (iSoft Patient Manager (iPM) software, RiO (Servelec HSC)). The case notes of all potential patients were retrieved and reviewed at BDH. Records were comprised of a combination of paper medical records, scanned paper medical records (Iron Mountain Digital Record centre) and electronic medical records (Care Stream R4 Clinical+ Practice Management Software). In addition, the clinical notes of all patients were also reviewed at UHB where primary management of their H&N cancer was undertaken using an electronic patient record system (Clinical Portal). Data were collected from the point of implant planning up until their most recent review appointment either at BDH or UHB.

Data were extracted in an anonymised format to a Microsoft Excel template. The data collected is shown in table 3.1.

Table 3.1: Data collection

Demographics
gender; age; oncological diagnosis; TNM classification and staging

Treatment
whether the patient had surgery; radiotherapy (dose and site); chemotherapy (drug types and dosages); nature of the surgical reconstruction; type of microvascular free flap/graft used.

Implant
whether surgical guides were used at time of implant placement; types of imagery taken for implant planning; number of implants placed; date(s) of implant placement; site of the implant placement; types of bone into which the implants were placed; documented surgical complications; date(s) of implant failure; number of implant failures; the clinically defined reasons for implant failure; the number of unsuccessful implants and the clinically defined reasons for the implant(s) being unsuccessful; implant manufacturer; implant fixture dimensions.

Prosthetic Rehabilitation
Date of restoration of the implants; site of the oral rehabilitation (maxilla or mandible); the classification of the prosthesis (fixed or removable), the details of the prosthesis provided (fixed - single implant crown or bridgework, removable - the retention system used); any adjunct surgery to accommodate prosthodontic treatment; the date of prosthetic failure, the type/cause of the prosthetic failure, the date of the 1st prosthetic complication, the type/cause of all reported prosthetic complications; the type of complications that occurred during implant based prosthodontic rehabilitation and their consequences (grouped into; patient complications, clinician and laboratory complications, implant complications, peri-implant soft tissue complications and clinical prosthodontic complications).

Dates
date of the last follow up; or where appropriate; the date of death.

For the purpose of this service evaluation, implant survival was defined as an implant fixture still in situ and implant failure defined as implant fixture not in situ which had been lost or removed for whatever reason. Implant survival time was defined as the time interval from date of implant placement to the date of implant failure or last follow-up date, whichever occurred first.

3.6 Statistical analysis

Statistical analyses using Kaplan-Meier survival curves was applied to compare differences in the survival rates of groups of variables. The log-rank test method was used to evaluate for significance of differences between groups of covariates on time to failure of implants. A Cox proportional hazards model was applied to identify the covariates associated with the time to failure of implants. The statistical analysis (α=0.05) was conducted considering the patients as the unit of analysis for patient-based variables (gender, chemotherapy, radiotherapy) and with the implant as the unit of analysis for nature of the implant site. Patients that died during the observational period were included in the analysis, but their data was censored beyond the date of their last follow up appointment. Data were analysed using statistical analysis software R version 3.3.2.

3.7 Results

3.7.1 Population demographics

3.7.1.1 Patients

A total of 167 patients who had undergone implant-based oral rehabilitation from November 2012 to May 2017 were included in this service evaluation. The population comprised of 58 women (35%) and 109 men (65%) with a mean age of 63.2 years (range: 27-88 years). The 167 patients had a variety of malignant and benign H&N tumours at various sites and stagings (Tables 3.2 & 3.3).

Table 3.2: Summary of cancer type and site

Cancer Type	No. of Patients										
	Buccal	FOM	Mandible	Maxilla	Nasal	Tonsil	Skin	Tongue	Pharynx	Not specified	Total
SCC	8	14	23	24	3	19	2	27	8	0	128
Adenoid Cystic Carcinoma	0	1	1	5	0	0	0	0	0	0	7
Ameloblastoma	0	0	5	2	0	0	0	0	0	0	7
Unspecified carcinoma/tumour	0	0	1	2	0	0	0	0	1	1	5
Malignant Melanoma	0	0	1	1	0	0	0	0	0	1	3
Osteogenic sarcoma	0	0	1	2	0	0	0	0	0	0	3
Mucoepidermoid	0	0	1	1	0	0	0	0	0	0	2
Pleomorphic Adenoma	0	0	0	2	0	0	0	0	0	0	2
BCC	0	0	0	0	1	0	1	0	0	0	2
Adenocarcinoma	0	0	0	2	0	0	0	0	0	0	2
Primitive Neuroectodermal Tumour	0	0	1	0	0	0	0	0	0	0	1
Chondrosarcoma	0	0	0	1	0	0	0	0	0	0	1
Odontogenic keratinocyst	0	0	1	0	0	0	0	0	0	0	1
Lymphoma	0	0	0	0	0	0	0	1	0	0	1
Dendritic Cell Sarcoma	0	0	0	1	0	0	0	0	0	0	1
Pindburg Tumour	0	0	1	0	0	0	0	0	0	0	1
TOTAL	8	15	36	43	4	19	3	28	9	2	167

Table 3.3: Description of cancer staging and implant failures

Cancer Staging	No. of Patients	No. of Patients with Implant Failure	Patient Implant Failure (%)
I	22	1	4.5
II	20	3	15.0
III	12	2	16.7
IVA	63	12	19.0
IVB	1	0	0
IVC	1	0	0
Unknown	48	6	12.5
TOTAL	167	24	14.4

Patients (from date of implant placement to their most recent review) were followed up for a median of 38months (range: 1-142 months). 779 implants in total were placed in 167 patients. 124 patients had 583 implants placed at UHB, and 43 patients had 196 implants placed at BDH. A total of 148 patients (89%) had resective surgery and of these 92 patients had reconstructive surgery (55%) with a variety of microvascular free flaps and autogenous bone grafts as shown in Table 3.4. (Note that a single patient received both an anterolateral thigh flap (ALT) and a fibula free flap (FFF) reconstruction). During the observation period 28 patients included within this service evaluation died. As such their data was censored from any further analysis beyond the date of their last follow up appointment.

Table 3.4: Summary of surgical interventions and tissue type used for head and neck reconstruction

Surgical Intervention	No. of Patients
No Surgery[1]	19
Surgery and no Reconstruction	56
Surgery and Reconstruction with Free Flap/Autogenous bone graft	92
TOTAL	167
Reconstructive Tissue Used	**No. of Patients**
Fibula	31
Radial	30
Deep Circumflex Iliac Artery (DCIA)	11
Scapula	9
Anterolateral thigh (ALT)	7
Iliac crest (Non-Vascular)	3
Pectoralis Major	2
TOTAL	93

1. No Surgery: these patients did not received surgical intervention for their cancer but were treated by other means such as radiotherapy and chemotherapy or a combination of these treatment modalities.

(Additional note: one patient was reconstructed with both an ALT and a fibula free flap reconstruction)

3.7.1.2 Implant imaging and planning

138 patients (83%) had a CBCT scan taken and reformatted for SIMPLANT® for implant planning purposes, once planned this scan was used to construct SIMPLANT® Surgical Guides (Dentsply Sirona, York, PN, USA) for use at the time of surgical implant placement. For two patients, CBCTs were taken for implant planning (in both these cases these acquired CBCTs were not reformatted for use with SIMPLANT® planning software); 23 patients had conventional plain radiographs

taken for planning and for four patients it was unclear what radiographic imagery was employed for implant planning purposes.

3.7.1.3 Implants

A variety of implant systems were used which included; 679 Straumann (Institut Straumann, Basel, Switzerland) implants, 63 Brånemark (Nobel Biocare, Zurich, Switzerland) implants, 36 Astra Tech (Dentsply Implants, Mannheim, Germany) implants and one Oktagon (Dental Ratio, Langenfeld, Germany) implant, with a range of one to 11 implants used per patient. Of these 373 (48%) implants were placed in the maxilla and 406 (52%) implants in the mandible (Table 3.5). Ten patients had primary implant placement with 26 implants, and 157 patients had secondary/delayed placement with 753 implants. Implants were placed into either non-resected native bone, resected native bone (which has not been reconstructed), or into free flaps/autogenous bone grafts. Of the 92 patients who received reconstructive surgery with microvascular free flaps/autogenous grafted bone, 52 patients had implants placed into these reconstructed sites with 129 implants placed. In the remaining patients, 22 implants were placed into resected native bone (which had not been reconstructed) and 628 implants were placed into non-resected native bone with 323 implants into non-resected native mandible and 305 into non-resected native maxilla.

Table 3.5: Implant survival in specified bone type

Bone Type	No. of Implants	No. of implant failures	Implant Survival (%)
All Patients	779	34	95.6
Native maxilla/mandible (non-resected)	628	12	98.0
Native Mandible (non-resected)	323	7	97.8
Native Maxilla (non-resected)	305	5	98.4
Resected Mandible/Maxilla not grafted with autogenous bone	22	0	100
Native autogenous bone graft	129	22	82.9

3.7.1.4 Radiotherapy & chemotherapy

A total of 105 patients (63%) received some form of radiotherapy with or without chemotherapy. Of these, 75 patients received radiotherapy (45%), 30 patients received chemo-radiotherapy (18%) and no patients received chemotherapy in isolation (Table 3.6).

Table 3.6: Use and timing of radiotherapy, chemotherapy and implant failure

Treatment modality	No. of patients	No. of Implants	No. of Patients with failed implants	Patient level implant failure (%)	No. of implant failures	Implant level failure (%)
Radiotherapy	75	382	11	14.7	15	3.9
Pre-Operative	68	360	8	11.8	9	2.5
Post-Operative	7	22	3	42.9	6	27.3
Chemo-radiotherapy	30	143	7	23.3	11	7.7
Pre-Operative	29	138	7	24.1	11	8.0
Post-Operative	1	5	0	0	0	0
Chemotherapy	0	0	0	0	0	0
Neither	62	254	6	9.7	8	3.2
TOTAL	167	779	24	14.4	34	4.4

Due to the retrospective nature of this evaluation, the precise radiation fields could not be obtained in 30 patients and, therefore, it was not possible to estimate dosimetry to each of the implant sites. In the 75 patients where radiation fields were documented the radiation dose for therapeutic radiotherapy ranged from 50 to 70 Grays in 72 patients. Two patients received palliative radiotherapy at 30 Grays with one of these patients stopping at a 7.5 Gray dose due to radiation related complications and one patient received a higher dose of 88 Grays. A variety of adjunct chemotherapy drugs were used in 30 patients and shown in Table 3.7.

Table 3.7: The drugs and regimes of chemotherapy agents used within the

evaluated service in the management of their H&N cancer

Chemotherapy Agents	No. of Patients
Carboplatin	13
Cisplatin	10
Cetuximab	2
MAP Chemo (Methotrexate, Doxorubicin, Cisplatin)	2
R-CHOP (Rituximab, Cyclophosphoamide, Doxorubicin, Vincristine, Prednisolone)	1
TPF (Docetaxel, Cisplatin, 5-Fluorouracil)	1
Carboplatin and Paclitaxel	1
TOTAL	30

3.7.2 Pre-prosthetic surgery

In total, 19 patients required further surgery prior to oral rehabilitation. 8 patients required debulking of the soft tissue component of the microvascular free flap, ten patients required a sulcoplasty and one patient required surgery to release the tongue and improve its mobility to assist in oral rehabilitation.

3.7.3 Surgical complications during implant surgery

Surgical complications during the placement of the dental implants were noted in 24 of 167 patients (14.4% of patients). Complications have been categorized as: Treatment plan related; Anatomy related; Procedure related and Other (according to Misch et al., [Misch & Wang, 2008]) and are summarised in Table 3.8. Note that when CAD-CAM surgical implant guides (SIMPLANT® Surgical Guides (Dentsply Sirona, York, PN, USA) are referred to, these are from re-formatted CBCTs and were planned using SIMPLANT® implant planning software.

Table 3.8: Surgical complications reported during implant placement

Surgical Complications	No. of Cases
Treatment Planning Related	
During implant placement reconstruction screw hit and reconstruction screw removed to accommodate implant	2
Implant position changed during surgical procedure and implant placed free hand as implant position from surgical guide was deemed inappropriate	2
Anatomy Related	
Difficult surgical access to place implants so implants not placed	2
Implant not placed as high risk of Inferior dental nerve damage	1
CAD-CAM surgical guide made access more challenging so was not used to prepare posterior sites	1
Lack of bone volume to place implant - so an alternative site used	3
Large incisions required to attain surgical access to fit the CAD-CAM surgical guide which was deemed inappropriate and the implants were subsequently placed free hand	1
Procedure Related	
Lack of primary stability of implant so larger implant diameter used to achieve primary stability	3
Lack of primary stability of implant - implants left in situ	2
Lack of primary stability of implants - so the implant was not placed	1
Lack of primary stability of implant - so implant placed in an alternative site	1
Implant not placed due to being placed too deep	1
Other	
Inadequate fit of CAD-CAM surgical guide – either was not used or was used in to estimate the implant bed preparation site and angulation but then prepared and placed free hand.	3
CAD-CAM surgical guide needed adjusted to allow it to fit	1
TOTAL	24

3.7.4 Implant failure

3.7.4.1 Overall implant failure

34 implant failures were observed out of 779 implants placed (median follow-up of 38 months; mean follow-up of 43 months and a range: 1-142 months). A Kaplan-Meier survival curve for overall implant survival is shown in Figure 3.1. The median survival

time is not attainable since the survival rate for the overall trend is better than 0.50. Survival rate estimates at 3 years and 5 years were 95.7% [95%CI 94.3-97.2%] and 95.5% [95%CI 93.9-97.0%], respectively. Implant failure occurred in 24 of the 167 patients included (14.4% failure at a patient level). The mean age of the evaluated cohort was 63.2 years and the mean ages of patients exhibiting implant failure or no failures were similar at 62.7 and 63.3 years, respectively. Of the 58 female patients within this cohort five experienced implant failure (8.6%) whereas 19 of 109 male patients had implant(s) fail (17.4%) although this was not statistically significant (p=0.09) (Figure 3.2a).

Figure 3.1: Kaplan-Meier survival curve for overall implant failure in the patient cohort
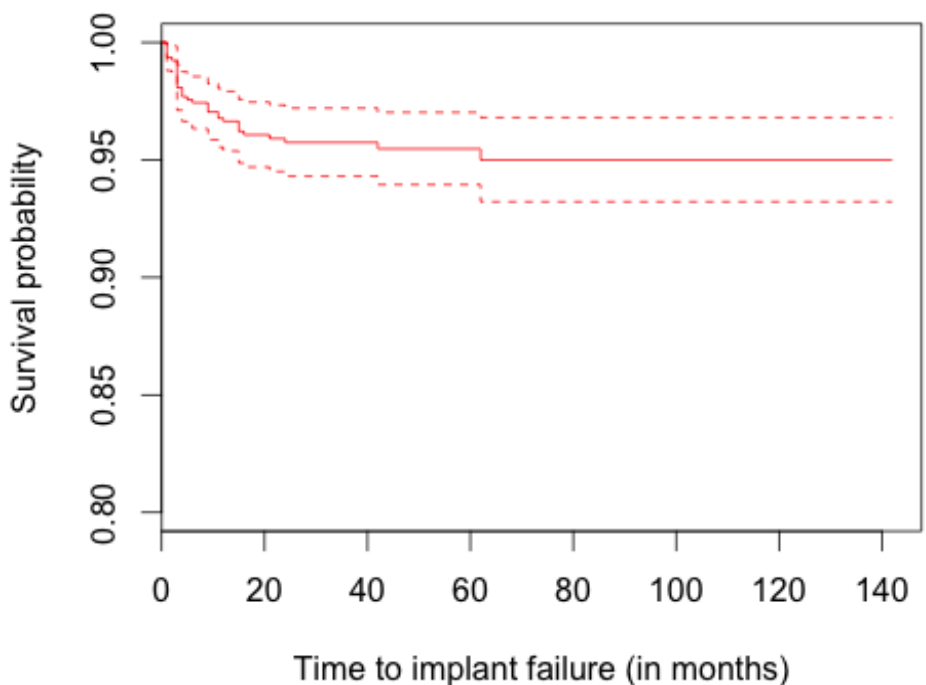
The survival rate at 3 and five years with the corresponding 95% confidence interval.

Time (in months)	No. at risk	Event[1]	Survival rate	Standard Error	95% Confidence Interval for Survival rate	
3 years (36 months)	423	32	0.957	0.00738	0.943	0.972
5 years (60 months)	215	1	0.955	0.00784	0.939	0.970

The median follow-up time (in months) and its range:

Min.	1st Qu.	Median	Mean	3rd Qu.	Max.
1.00	23.00	38.00	43.07	63.00	142.00

1. 34 implants failed in total. 32 implants had failed by year 3. 33 implants had failed by year 5. 1 implant failed after year 5.

Figure 3.2a: Kaplan-Meier survival curve comparing implant survival according to gender
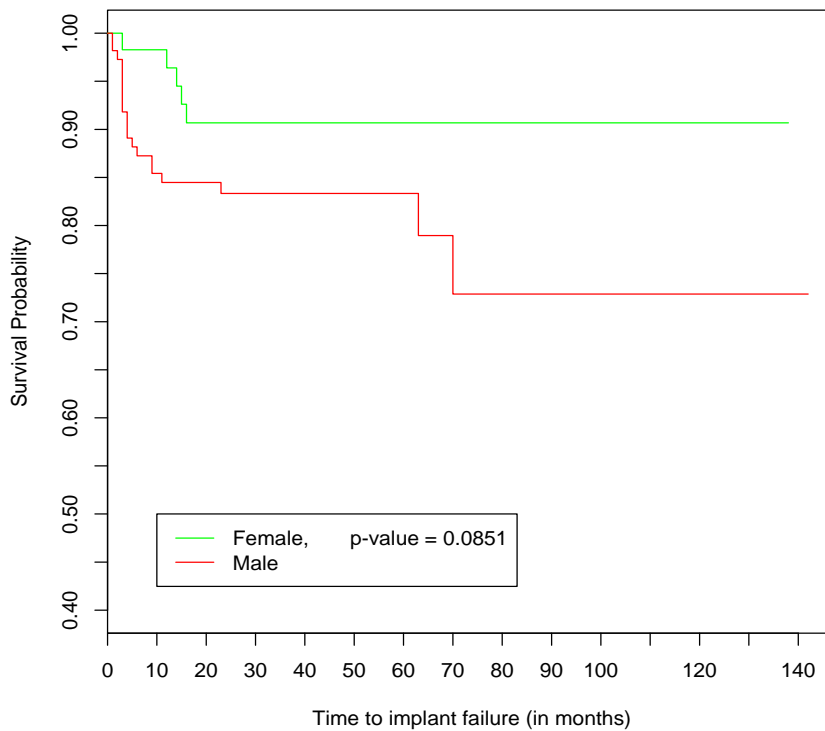
3.7.4.2 Timing

The 34 implant failures were classified by the stage of treatment at which they failed, where Stage II is the surgical uncovering of the implant fixture to allow prosthodontic restoration;

- Prior to Stage II - 3 implant failures.

- At Stage II and before prosthetic loading - 22 implant failures.

- After Prosthetic Loading - 9 implant failures.

For the 22 implants (in 17 patients) that failed due to a lack of initial osseointegration the mean and median times to failure were 140 and 97 days, respectively. The mean and median time to failure of the five implants (in four patients) that failed due to peri-

implantitis were 915 and 683 days, respectively. Of the six implants that failed due to free flap failure (in two patients), for one of these patients, failure occurred at day 16 after free flap reconstruction and primary implant placement and the other occurred at 451 days after implant placement when there was late failure (as a result of a pathological fracture due to osteoradionecrosis (ORN)). One implant (in one patient) was explanted as it was deemed to be in an unrestorable position and was causing soft tissue trauma after 366 days.

3.7.4.3 Bone type

Implant survival was high for implants placed into native bone (both resected and non-resected) (Table 3.5). Implant survival for implants placed into autogenous free flaps was 100% in scapula flaps, 83.0% in fibula free flaps (FFF), 80.0% in radial composite free flaps (RFF) and 76.0% in deep circumflex iliac artery flaps (DCIA). Implant survival in non-vascularised iliac bone graft was 80.0%. Implant survival in native bone associated with microvascular soft tissue flaps was 100% for anterolateral thigh flap (ALT). For pectoralis major flaps (PMF) no implants were placed through this soft tissue flap (Table 3.9).

Table 3.9: Type of microvascular free flap/autogenous bone graft implant placed into and implant survival

Type of Microvascular free flap/autogenous bone graft – Implant inserted into	No. of Patients	No. of Implants	No. of Implant failures	Implant Survival (%)
Scapula	5	12	0	100
Fibula	27	65	11	83.1
ALT	1	2	0	100
Radial	6	15	3	80.0
Pectoralis Major	0	0	0	-
DCIA	10	25	6	76.0
Iliac crest (Non-Vascular)	3	10	2	80
TOTAL	52	129	22	82.9

Kaplan-Meier survival curve comparing outcomes of a simplified comparison between implant failure in native and autogenous bone grafts/free flaps is shown in Figure 3.2b. A statistically significant difference in implant failure was demonstrated with increased implant loss in transported bone (autogenous bone graft/free flap sites) in comparison to implant loss in native bone ($p < 0.01$). The majority of implant loss events were recorded in the first 6 months in native bone whereas loss in autogenous bone graft site were more progressive up until 24 months.

Figure 3.2b: Kaplan-Meier survival curve comparing implant survival in native and transported bone
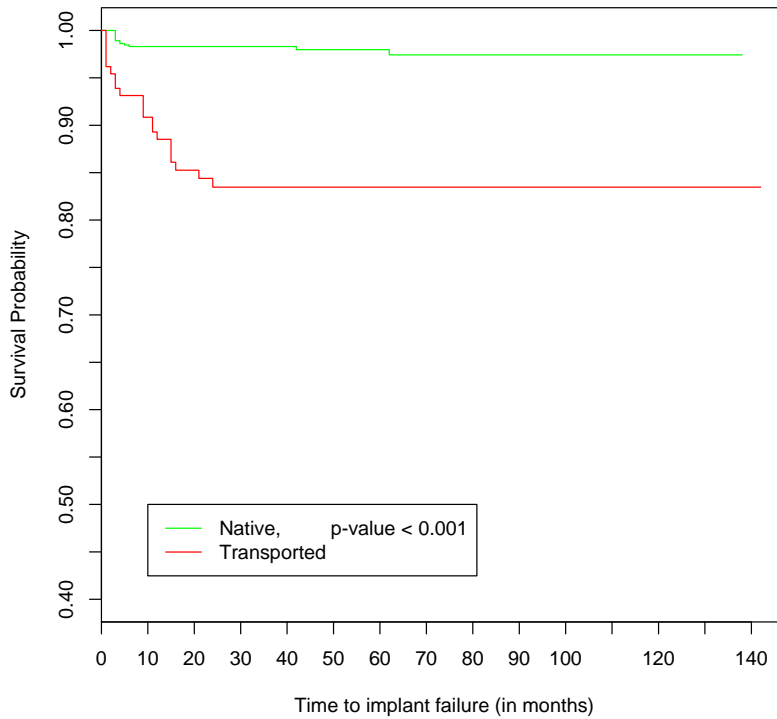
3.7.4.4 Radiotherapy & chemotherapy

In total 105 patients received some form of radiotherapy with 525 implants placed into this patient group. Of these, 18 patients experienced implant failure with 26 implants failing in total with a patient implant failure rate of 17.1% and an implant failure rate of 5.0%. There were 62 patients that received 254 implants that did not receive any radio- or chemoradiotherapy, of these 6 patients experienced implant failure with 8 implants failing in total, with a patient implant failure rate of 9.7% and an implant failure rate of 3.2%. Kaplan-Meier survival curves for radiotherapy and chemotherapy are presented in Figures 3.2c,d. Both variables were not found using the log-rank test method to have a statistically significant effect on implant survival (p=0.16 radiotherapy, p=0.17 chemotherapy).

For patients receiving a combination of chemotherapy with radiotherapy a higher implant failure rate than those patients who received radiotherapy without chemotherapy was observed. 30 patients in total received chemoradiotherapy with 143 implants being placed into this patient group. 11 implant failures occurred in 7 patients (patient implant failure of 23.3% and an implant failure of 7.7%). This is in comparison with radiotherapy were 75 patients received radiotherapy with 382 implants placed with 15 implant failures occurring in 11 patients (patient implant failure of 14.7% and an implant failure rate of 3.9%) (Table 3.6). Despite this indication, a fitted Cox PH model for implant failure considering factors radiotherapy and chemotherapy and their combination identified no significant difference. The vast majority of patients received radiotherapy and/or chemotherapy prior to implant placement (Table 3.6) and therefore it is not appropriate to discuss timing of these interventions and implant survival within this evaluation.

Figure 3.2c: Kaplan-Meier survival curve comparing implant survival in patients who received radiotherapy with those that did not.
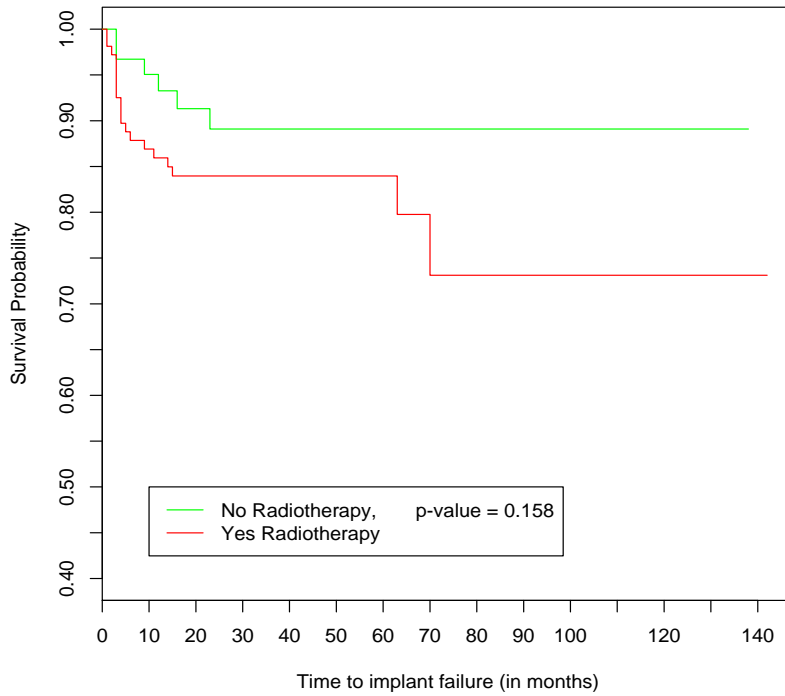
Figure 3.2d: Kaplan-Meier survival curve comparing implant survival in patients who received chemotherapy with those that did not.
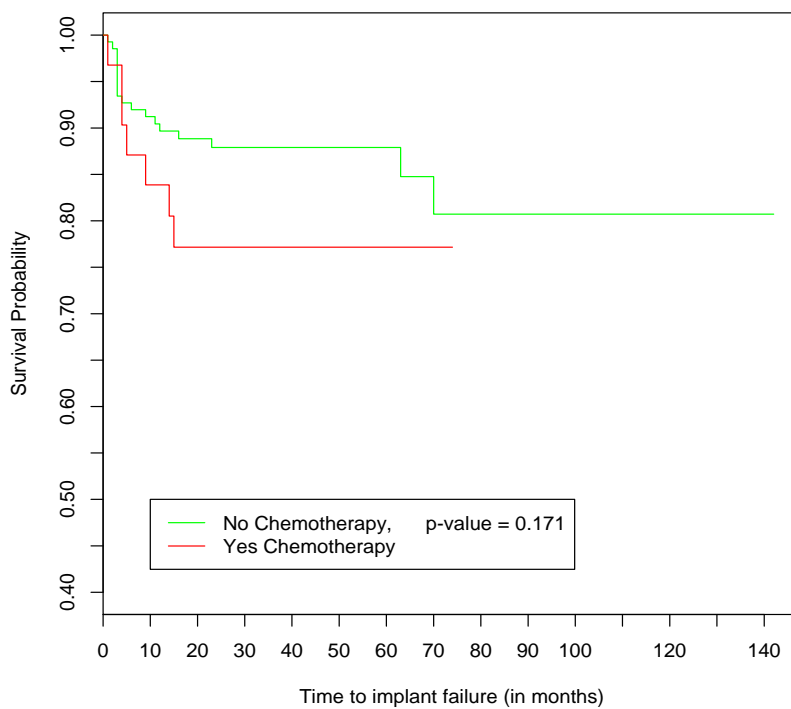
3.7.4.5 Implant system and implant geometry

Implant failure with each implant system was calculated and showed varying failure rates (Table 3.10) however, it would be inappropriate to draw rigid conclusions from this data due the small numbers of both patients and implants used with some of the implant systems. The most common implant to fail was Brånemark implants with unknown dimensions, with 8 failures, this was followed by Straumann RN 4.1mm diameter 10mm length implants with 7 implant failures and Straumann RN 4.1mm diameter 12mm length implants with 6 implant failures. However, it would be inappropriate to draw conclusions from this data due incomplete data (164 implant dimensions/lengths were unknown in the 779 implants placed) and the small numbers of some of the implant dimensions used. No real statistical or descriptive analysis of the implant diameter or length can be drawn and thus in this retrospective evaluation no conclusion, can be drawn on the relationship between implant length/diameter and implant survival.

Table 3.10: Implant system and implant failure

Implant system	No. of Patients	No. of Implants	No. of Implant failures	Implant Failure (%)
Straumann	140	679	24	3.5%
Brånemark	16	63	8	12.7%
Astra Tech	11	36	2	5.6%
Oktagon	1	1	0	0.0%
TOTAL	168	779	34	96.5%

3.7.4.6 Cancer staging

Patient level implant failure for cancer staging was calculated. Data may indicate a correlation between higher cancer staging and increased patient implant failure

(Table 3.3). However, it would be inappropriate to draw rigid conclusions due to the small size of some of the groups.

3.7.4.7 Surgical complications

Implant failure was higher when surgical complications were experienced during implant fixture placement. In total, 24 patients experienced surgical complications during implant placement, of these, 9 patients experienced implant failure (37.5% of patients with surgical complications). This led to 12 implant failures in total of the 100 implants that were placed in this patient group (with an implant failure rate of 12% in patients that experienced surgical implant complications).

This is higher than for patients that had no documented surgical complications during implant placement with implant failure occurring in 15 of 143 patients (10.5% of patients with no documented surgical complications) and led to 22 implant failures in total of the 679 implants that were placed in this patient group (with an implant failure rate of 3.2% of implants with no documented surgical complications).

3.8 Conclusion

This service evaluation of a regional patient cohort found high rates of implant survival when used as part of routine oral rehabilitation of H&N oncology patients with a median follow-up of 38 months. Implant survival estimates at 3 years were 95.7% [95%CI 94.3-97.2%] and 95.5% [95%CI 93.9-97.0%] at 5 years. Survival analyses for specific covariates showed non-significant trends for increased implant failure in patients receiving radiotherapy (p=0.16), chemotherapy (p=0.17) and being

male (p=0.09). Implant survival however was found to be affected by the bone type, with implant failure being higher for implants placed into autogenous bone grafts/free flaps in comparison to implants placed into native bone (p=<0.001). Reported surgical complications noted at the time of implant placement were high with 14.4% of patients experiencing such events. Such complications appeared to increase the risk of implant failure (at the patient level).

Overall this service evaluation supports the use of dental implants in the oral rehabilitation of this complex patient group, but it is important to recognise that this is an analysis of a complex care-pathway with a large number of confounding variables. The findings should not be considered as generalisable beyond the specific environment in which this service evaluation was conducted. However, the findings highlight the urgent need for prospective multi-centre standardised data recording in order to generate robust data to enable potentially important treatment covariates to be explored.

CHAPTER 4:

SERVICE EVALUATION OF OUTCOMES OF IMPLANT BASED PROSTHESES IN THE ORAL REHABILITATION OF HEAD AND NECK ONCOLOGY PATIENT IN A LARGE REGIONAL COHORT

4. Service evaluation of outcomes of implant based prostheses in the oral rehabilitation of head and neck oncology patients in a large regional cohort

4.1 Background

Prosthodontic treatment of H&N cancer patients is a challenging undertaking. This is due to multiple factors including altered anatomy, irradiation- induced xerostomia and associated fragile mucosa, presence of vulnerable tissues, impaired oral function and, in some patients, a lack of emotional resilience to tolerate such treatment. [Eckert et al., 1996], [Visch et al., 2002], [Barrowman et al., 2011] Conventional prostheses are of limited use in such patients, therefore, implant-retained or supported prostheses are often necessary [Mericske-Stern et al., 1999], [Weischer & Mohr, 1999] and are being increasingly used in the oral rehabilitation of H&N oncology patients. [Müller et al., 2004], [Schoen et al., 2004], [Hessling et al., 2015]
The success of such rehabilitation has been reported previously. [Mericske-Stern, 1990], [Granstrom, 2005], [Hessling et al., 2015] However, the majority of the literature reporting on outcomes of oral rehabilitation in H&N cancer patients has focused on implant survival and quality of life measures after rehabilitation, as opposed to prosthesis success or survival. Therefore, given the increasing use of dental implants in the oral rehabilitation of H&N cancer patients, [Alani et al., 2009] there is a need for such literature to better inform clinicians and patients.

4.2 Aims & Objectives

The aim of this service evaluation is to present survival and complication-free survival rates of both fixed and removable implant-based oral prostheses in a large cohort of H&N cancer patients. In addition, this service evaluation aims to report on the causes and frequency of such failures and complications for each prosthesis type.

4.3 Methods

4.3.1 Service evaluation approach and setting

The overall service approach and setting are described in section 3.2.1.

Prosthodontic treatment and follow up protocol

The prosthodontic restoration of the dental implants is undertaken by the Restorative team at Birmingham Dental Hospital (BDH) under the supervision of a lead specialist Restorative Consultant.

The type of prosthesis the patient is to receive is in the main pre-planned during the process of implant surgery planning. All technical/laboratory work was carried out or prescribed by laboratory technicians at BDH who are accustomed to this patient group.

During this service evaluation, the provision of the prostheses and maintenance of the implants and prostheses was undertaken under the care or supervision of a single specialist Restorative clinical lead. Patients were reviewed at least annually, where possible, but the recall interval was determined by the treating clinician at the most recent appointment. Each recall visit included updating the medical history and

carrying out a clinical examination, with the prosthesis and implants assessed clinically and radiographically as deemed appropriate.

4.3.2 Eligibility criteria

Inclusion criteria

1. Patients who had suffered with H&N cancer.

2. Patients who completed oral rehabilitation with an implant retained fixed or removable intra-oral prosthesis.

3. Patients who had been followed up on at least one occasion after delivery/fitting of the prosthesis.

4. The service evaluation was limited to include only the first implant retained intra-oral prosthesis provided for the patient.

Exclusion criteria

1. Patients who did not suffer with H&N cancer.

2. Patients who did not complete oral rehabilitation with an implant retained fixed or removable intra-oral prosthesis.

3. Patients who were not followed up after delivery/fitting of the prosthesis.

4. Any subsequent replacement or additional implant retained intra-oral prosthesis other than the first prosthesis that was provided to the patients.

5. Patients where the minimum data-set could not be collected.

4.3.3 Clinical endpoints

Prosthetic survival

Prosthetic survival was defined separately for both fixed and removable prosthesis as;

- Removable prosthesis survival - prosthesis being utilised by the patient.
- Fixed prosthesis survival - prosthesis in situ.

The prosthetic survival time was defined as the time from the date of restoration of the implant(s) to the date of the first prosthetic failure or last follow-up date, whichever occurred first.

Prosthetic complication-free survival

Prosthetic complication free-survival was defined as a prosthesis deemed to have survived without encountering a complication requiring adjustment, modification or partial replacement of the prosthesis.

The prosthetic complication-free survival time was determined as the time from the date of restoration of the implants, to the date of the first prosthetic complication or last follow-up date, whichever occurred first without the prosthesis failing prior to this date.

Prosthetic complications were grouped into;

- Implant and implant based prosthetic components.
- Repair of prosthesis.
- Adjustment of prosthesis.

4.3.4 Variables considered in the service evaluation

The minimum data-set for study inclusion required; patient gender, age, oncological diagnosis, the oncological management (surgery; radiotherapy; chemotherapy; or combinations), the nature of any surgical reconstruction (soft tissue graft, non-vascularised bone graft and composite free flap), date of implant placement, date of restoration of the implants, the site of the oral rehabilitation (maxilla or mandible), the classification of the prosthesis (fixed or removable), the details of the prosthesis provided (fixed - single implant crown or bridgework, removable - the retention system used). The date of prosthetic failure, the type/cause of the prosthetic failure, the date of the 1st prosthetic complication, the type/cause of all reported prosthetic complications and the date of last follow up. Additionally, the TNM staging and patient date of death were also recorded where possible.

4.4 Ethical approval

See section 3.4 and appendix 1.

4.5 Data collection

The process of data collection and the data that was collected is described in section 3.5.

4.6 Statistical analysis

Differences in categorical and continuous data were assessed for statistical significance using Pearson Chi-square, t-test, Fisher's exact test and analysis of variance (ANOVA) as appropriate. Cox proportional hazards (PH) regression models were fitted to evaluate the association between prostheses type (fixed and removable) and clinical/medical factors (grafting, radiotherapy, chemotherapy) and survival and complication-free survival, independent of potential confounders of age and sex. The PH assumption was tested using graphical methods. Descriptive statistics were used to analyse the frequency and type of prosthetic complications. The timing of prosthetic failure and the time to the 1st prosthetic complication was calculated from the date of prosthetic restoration to the date of the event.

Analyses were carried out using Stata/IC version 14.0 (StataCorp LP).

4.7 Results

4.7.1 Population demographics

A total of 167 patients were identified for inclusion within this study. 14 patients were excluded from the analysis due to the minimum data set not being met or no follow-up having occurred after delivery of their prostheses. Therefore, a total of 153 patients were included for analysis.

4.7.1.1 Patients

Of the 153 patients included in the analyses, 101 (66.0%) were male and the mean age of this cohort at the time of inception i.e. delivery of prosthesis, was 63.3 years (Range: 32-88 years). The mean follow-up time for the prostheses was 2.6 years (S.D. 1.9 years, range 0.1-8.8 years). Patients had a variety of benign and malignant H&N tumours with varying anatomical sites and TNM stagings (Table 4.1). These patients received a range of treatments for their H&N cancer including surgical resection, radiotherapy and chemoradiotherapy. Some of the patients who underwent surgical resection were also reconstructed with a variety of soft tissue flaps, non-vascularised bone grafts and composite free flaps (Table 4.1).

Table 4.1: Demographics of study population

Demographics	N=153
Age	63.3 years (Range:32-88)
Male	N= 101 (66%)
Cancer Type	
SCC	118 (77.1%)
Adenoid Cystic Carcinoma	7 (4.6%)
Ameloblastoma	5 (3.3%)
Unspecified carcinoma/tumour	5 (3.3%)
Malignant Melanoma	2 (1.3%)
Osteogenic sarcoma	2 (1.3%)
Mucoepidermoid	2 (1.3%)
Pleomorphic Adenoma	2 (1.3%)
BCC	2 (1.3%)
Adenocarcinoma	2 (1.3%)
Primitive Neuroectodermal Tumour	1 (0.7%)
Chondrosarcoma	1 (0.7%)
Odontogenic keratinocyst	1 (0.7%)
Lymphoma	1 (0.7%)
Dendritic Cell Sarcoma	1 (0.7%)
Pindburg Tumour	1 (0.7%)
TNM Staging	
I	20 (13.1%)
II	20 (13.1%)
III	12 (7.8%)
IVA	55 (35.9%)
IVB	1 (0.7%)
IVC	1 (0.7%)
Unknown	44 (28.8%)
Treatment Modality	
No Surgery[1]	18 (11.8%)
Surgery and no Reconstruction	51 (33.3%)
Surgery and Reconstruction with Free Flap/Autogenous bone graft	84 (54.9%)
Radiotherapy	72 (47.0%)
Chemo-radiotherapy	25 (16.3%)
Chemotherapy	0 (0.0%)
Neither (Radiotherapy or Chemotherapy)	56 (36.6%)
Type of tissues used for Surgical Reconstruction	
Fibula	26
Radial	29
DCIA	11
Scapula	8
ALT	6
Iliac crest (Non-Vascular)	3

Pectoralis Major	2
Type of prostheses	
Maxillary Fixed	51 (23.1%)
Mandibular Fixed	52 (23.5%)
Maxillary Removable	52 (23.5%)
Mandibular Removable	66 (29.9%)

1. No Surgery: these patients did not received surgical intervention for their cancer but were treated by other means such as radiotherapy and chemotherapy or a combination of these treatment modalities.

   (Please Note: one patient was reconstructed with both an ALT and a Fibula free flap reconstruction)

4.7.1.2 Implants

713 intra-oral implants were placed with 30 implant failures during the observation period in this patient cohort. Implants were placed into a variety of bone types including native bone, resected bone and autogenous bone grafts, with some of these sites receiving radiotherapy or chemo-radiotherapy (Table 4.1).

4.7.1.3 Prostheses

Of the 153 patients rehabilitated, 68 (44.4%) patients had bi-maxillary reconstructions, 51 (33.3%) had mandibular reconstructions and 34 (22.2%) had maxillary reconstructions.

153 patients were provided with 221 prostheses in total and were grouped into prosthesis types (maxillary fixed (n=51), mandibular fixed (n=52), maxillary removable (n=52) and mandibular removable (n=66)). Patients in these groups did

not vary significantly in their age, sex or the need for grafting. However, patients who were rehabilitated with a mandibular fixed prosthesis were much less likely to have received radiotherapy, compared with the other groups (Table 4.2).

Table 4.2: Univariate analysis of prosthesis demographics

	Prostheses (n=221)	Max Fx (n=51)	Mand Fx (n=52)	Max Rem (n=52)	Mand Rem (n=66)	p=
Age (years)	63.7 (11.1)	62.8 (11.4)	64.5 (10.6)	65.9 (10.0)	65.9 (11.1)	0.081
Male %	70.7	68.6	63.5	76.9	69.7	0.518
Radiotherapy %	70.1	78.4	50	71.2	78.8	*0.003
Grafted %	53.9	60.8	59.6	48.1	48.5	0.370

(Differences in categorical and continuous data were assessed for statistical significance using Pearson Chi-square, t-test, Fisher's exact test and analysis of variance (ANOVA) as appropriate. All numbers are means (SD) unless stated otherwise).

4.7.2 Prosthesis survival

The Kaplan-Meier survival curve shows the reduction in survival for all prosthesis types over time (Figure 4.1). Cox's proportional hazard regression models were used to report the 5-year survival and identify the hazard ratio for each prosthesis type. This revealed that the 5-year survival was highest for maxillary fixed prostheses (87%) followed by mandibular fixed (79%), maxillary removable (66%) and the lowest survival for mandibular removable (50%) (Figure 4.2).

Figure 4.1: Kaplan-Meier survival curve: Survival for each prosthesis type.
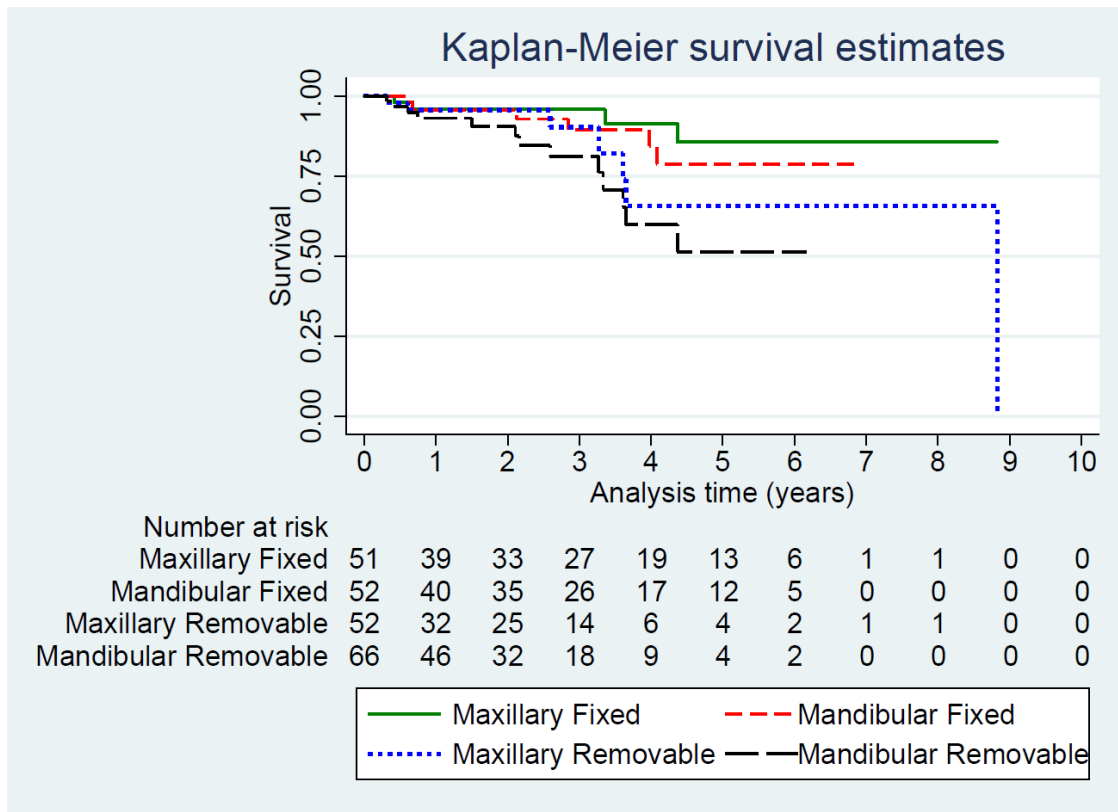
Figure 4.2: Cox proportional hazards regression: Overall influence of prosthesis type on prosthesis survival & 5-year survival for each prosthesis type.
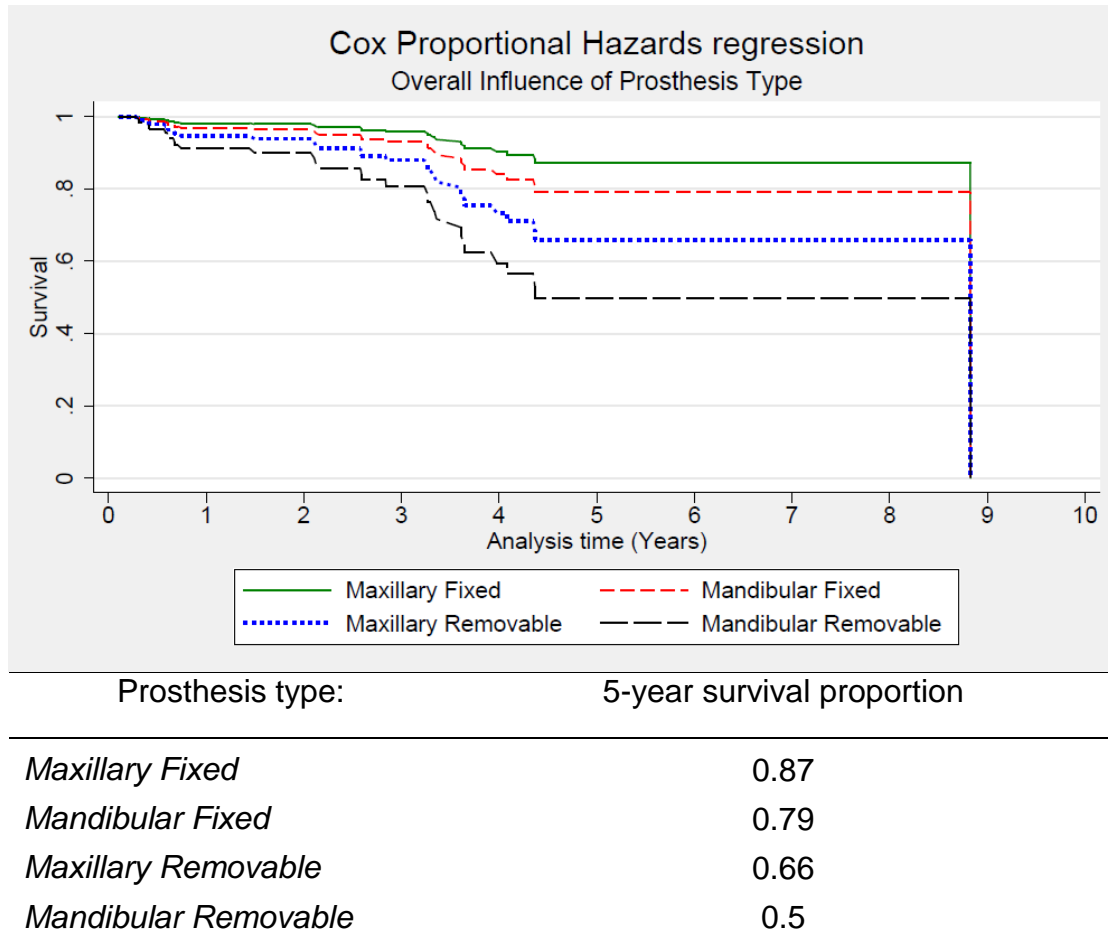
Prosthesis type:	5-year survival proportion
Maxillary Fixed	0.87
Mandibular Fixed	0.79
Maxillary Removable	0.66
Mandibular Removable	0.5

For the calculation of hazard ratios, the maxillary fixed prosthesis was used as the reference [HR=1.0]. The results show that the maxillary fixed prostheses [HR = 1] had the lowest hazard ratio followed by, mandibular fixed [HR=1.71; 95% Confidence Interval (CI) 0.47-6.21], maxillary removable [HR=3.05; 95%CI 0.83-11.15] and mandibular removable prosthesis [HR=5.1; 95%CI 1.60-16.25]. However, the only statistically significant result was related to the mandibular removable prosthesis (P=0.006) (Table 4.3).

Variables of radiotherapy, grafting, age and sex were assessed for their effect on overall prosthesis survival using the cox proportional hazard regression model. These variables were not found to have a statistically significant effect on the overall survival of the prosthesis (Table 4.3).

Table 4.3: Hazard ratios (Cox proportional hazards regression) for prosthesis survival and prosthesis complication-free survival for prosthesis type, radiotherapy, grafting, age & sex.

Variables	HR for Survival	95% CI		p=	HR for Complication-free Survival	95% CI		p=
Prosthesis type								
Max Fx	1				1			
Mand Fx	1.71	0.47	6.21	0.414	0.88	0.43	1.79	0.717
Max Rem	3.05	0.83	11.15	0.092	1.91	1.01	3.66	*0.048
Mand Rem	5.1	1.60	16.25	*0.006	2.29	1.23	4.25	*0.009
Radiotherapy								
No	1				1			
Yes	1.23	0.49	3.08	0.662	1.06	0.61	1.85	0.833
Grafting								
No	1				1			
Yes	1.65	0.75	3.65	0.213	0.72	0.46	1.14	0.161
Age	0.97	0.93	1.01	0.113	0.99	0.97	1.01	0.466
Male								
No	1				1			
Yes	0.85	0.34	2.13	0.726	1.34	0.77	2.31	0.3

4.7.3 Prosthesis complication-free survival

Cox's proportional hazard regression models were used to report the 5-year complication free-survival and identify the hazard ratio for each prosthesis type. This revealed that the 5-year complication free-survival was highest for mandibular fixed prosthesis (62%) followed by maxillary fixed (58%), maxillary removable (36%) and

the lowest complication free-survival for mandibular removable (29%) (Figures 4.3 &
4.4).

**Figure 4.3: Kaplan-Meier survival curve: Complication-free survival for each
prosthesis type.**
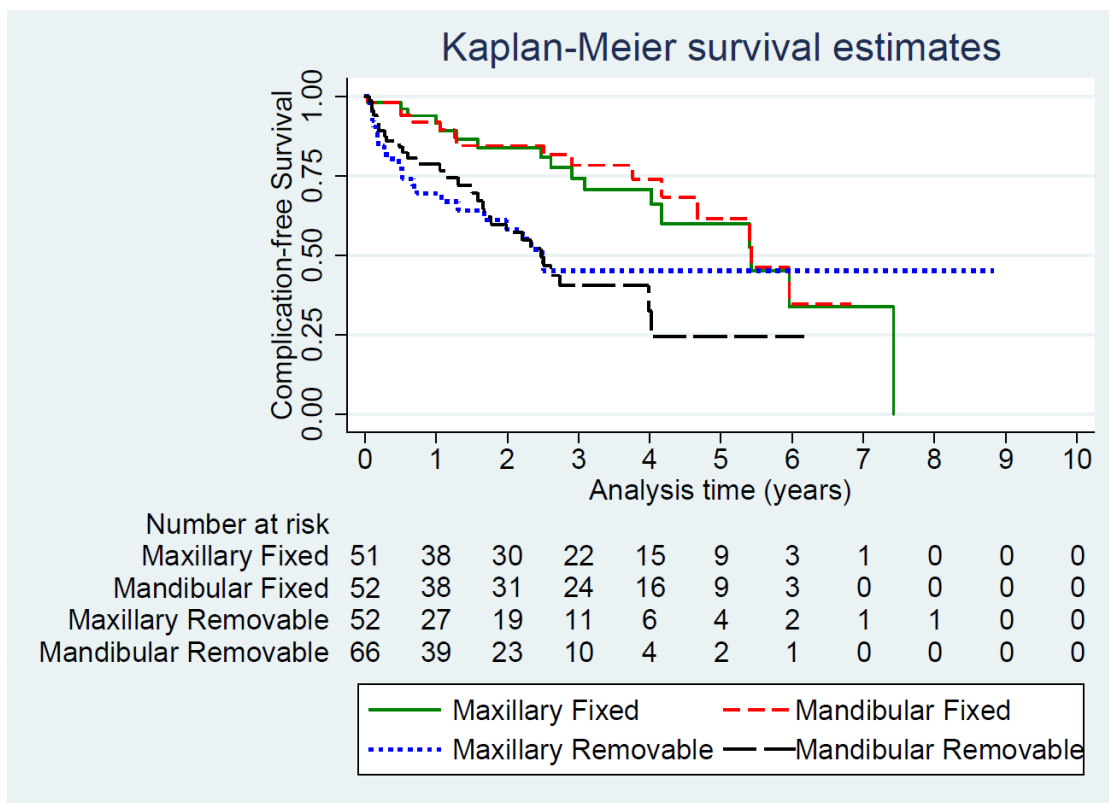
Figure 4.4: Cox proportional hazards regression: Overall influence of prosthesis on prosthesis complication-free survival.
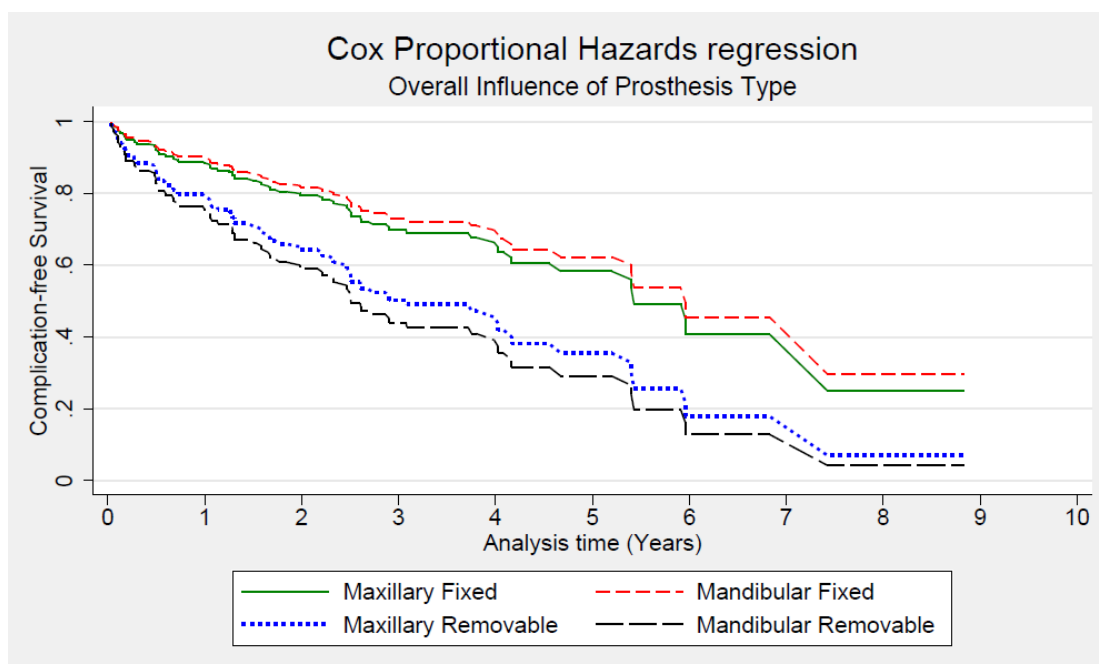
Prosthesis type:	5-year complication-free survival proportion
Maxillary Fixed	0.58
Mandibular Fixed	0.62
Maxillary Removable	0.36
Mandibular Removable	0.29

For the calculation of hazard ratios, the maxillary fixed prosthesis was used as the reference [HR=1.0]. Results demonstrated that, mandibular fixed [HR=0.88; 95%CI 0.43-1.79] had a highest complication free-survival, followed by maxillary fixed [HR = 1.0],

maxillary removable [HR=1.91; 95%CI 1.01-3.66] and mandibular removable prosthesis [HR=2.29; 95%CI 1.23-4.25]. The statistically significant results were related to the mandibular removable (P=0.009) and maxillary removable prosthesis (p=0.048) (Table 4.3).

Variables of radiotherapy, grafting, age and sex were assessed for their effect on overall complication-free survival of the prosthesis using the cox proportional hazard regression model. These variables were not found to have a statistically significant effect on the overall complication-free survival of the prosthesis (Table 4.3).

4.7.4 Causes of prostheses failure & type of complications for each prosthesis type

4.7.4.1 Fixed maxillary prostheses

51 fixed maxillary prostheses were provided (50 cases were fixed implant bridgework (fixed partial dentures) and 1 case was single unit implant crowns). The follow up period of time for fixed maxillary prostheses was 3.2 years (S.D. 2.1 years, range 0.2-8.8 years).

Fixed maxillary prostheses: Failure

In total 2 fixed maxillary prostheses failed during the observational period. Both of these prostheses failed due to fracture of the prosthesis and both were replaced with a removable implant retained prosthesis (Table 4.4).

Fixed maxillary prostheses: Complications

A number of complications were reported for maxillary fixed prostheses during the observational period as shown in Table 4.4. The most common complication was related to fracture of the prostheses. This complication affected 9 prostheses and occurred on 20 occasions demonstrating the recurrence of such complications within

the same prosthesis. Other complications included loosening of the abutment screw which affected 4 prostheses and occurred on 4 occasions, and also the need to adjust 2 prostheses on 2 occasions to improve oral hygiene measures around the prosthesis.

4.7.4.2 Fixed mandibular prostheses

In total 52 fixed mandibular prostheses were provided, all of which were fixed implant bridgework (fixed partial dentures). The follow-up period of time for fixed mandibular prostheses was 3.1 years (S.D. 2 years, range 0.19-6.8 years).

Fixed mandibular prostheses: Failure

In total 5 fixed mandibular prostheses failed during the observational period. 3 of these prostheses failed due to fracture and were replaced with another fixed implant prosthesis. 1 prosthesis was removed and replaced with a removable implant prosthesis to improve oral hygiene measures and 1 prosthesis was removed and not replaced as there was cancer recurrence around the site of the prosthesis (Table 4.4).

Fixed mandibular prostheses: Complications

A number of complications were reported for mandibular fixed prostheses during the observational period as shown in Table 4.5. The most common complication was related to fracture of the prostheses. This complication affected 6 prostheses and occurred on 14 occasions demonstrating the repetition of such complications within the same prostheses. Other complications included, loosening of the abutment screw

which affected 5 prostheses and occurred on 7 occasions. There was also 1 prosthesis that had to have the distal section of the fixed bridgework partially sectioned and removed (leaving the distal implant as a sleeper) due to soft tissue trauma and discomfort; however, the prosthesis was still functional.

4.7.4.3 Removable maxillary prostheses

In total 52 removable maxillary prostheses were provided. All of these cases were implant overdentures retained by Locator® abutments (Zest Dental, CA, USA). The follow up period of time for removable maxillary prostheses was 2.1 years (S.D. 1.8 years, range 0.15-8.8 years).

Removable maxillary prostheses: Failure

In total 5 removable maxillary prostheses failed during the observational period. 2 of these prostheses failed due to a lack of patient tolerance with one of these prostheses being removed and not replaced and the other prosthesis being removed and replaced with a fixed implant prosthesis. The other 3 prostheses were replaced with another removable implant prosthesis for a variety of reasons including: the patient losing their prosthesis, implant failure and technical inadequacies of the current prosthesis (Table 4.5).

Removable maxillary prostheses: Complications

A number of complications were reported for maxillary removable prostheses during the observational period as shown in Table 4.5. The most common complication was related to the Locator® male insert (Zest Dental, CA, USA); this retentive element

within the prostheses needed to be replaced in 12 prostheses on 20 occasions demonstrating the recurrence of such complications within the same prosthesis. For 3 prostheses (on 3 occasions) the Locator® abutment (Zest Dental, CA, USA) had to be retightened as it had become loose. For 2 prostheses (on 2 occasions) the Locator® denture cap (Zest Dental, CA, USA) which houses the retentive male insert within the prosthesis had to be replaced. Overall 4 prostheses fractured, 2 of these prostheses had a minor fracture and 2 prostheses had a major fracture (through and through). 1 prosthesis required adjustment and relining due to cancer recurrence which was carried out on 3 occasions for the same prosthesis. 2 prostheses needed adjustment after implant failure and 4 prostheses (on 4 occasions) required gross adjustment of the prosthesis after delivery.

4.7.4.4 Removable mandibular prostheses

In total 66 removable mandibular prostheses were provided. All of these cases were implant retained overdentures retained by Locator® abutments (Zest Dental, CA, USA). The follow up period for removable mandibular prostheses was 2.1 years (S.D. 1.6 years, range 0.11-6.2 years).

Removable mandibular Prostheses: Failure

In total 13 removable mandibular prostheses failed during the observational period. 5 of these prostheses failed due to a lack of patient tolerance with 3 of these prostheses being replaced with a fixed implant prosthesis and 2 of these prostheses being removed and not replaced during the observation period. Additionally, 2 prostheses failed due to the lack of patient tolerance after implant failure and these

prostheses were not replaced during the observational period. The other 6 removable mandibular prostheses that failed were replaced with another removable implant prosthesis for a variety of reasons including: the patient losing their prosthesis (2 prostheses), implant failure (1 prosthesis) and technical inadequacies of the current prosthesis (3 prostheses) (Table 4.5).

Removable mandibular Prostheses: Complications

A number of complications were reported for mandibular removable prostheses during the observational period as shown in Table 4.5. The most common complication was related to the Locator® male insert (Zest Dental, CA, USA) which needed to be replaced in 14 prostheses on 27 occasions demonstrating the repetition of such complications within the same prosthesis. For 4 prostheses (on 5 occasions) the Locator® abutment (Zest Dental, CA, USA) had to be retightened as it had become loose. For 1 prosthesis one of the Locator® abutments (Zest Dental, CA, USA) had to be removed due to soft tissue trauma and the prosthesis had to be modified. For 1 prosthesis (on 1 occasion) the Locator® denture cap (Zest Dental, CA, USA) had to be replaced. 4 prostheses fractured, of which 2 of these prostheses (on 3 occasions) had a minor fracture and 2 prostheses (on 2 occasions) had a major fracture (through and through). 1 prosthesis required adjustment and relining due to cancer recurrence (on 1 occasion) and a further prosthesis required relining due to poor fit of the prothesis. 1 prosthesis required adjustment after further implant placement and 4 prostheses (on 4 occasions) required gross adjustment after delivery.

Table 4.4: Type of complications and failures associated with maxillary and mandibular fixed implant-based prostheses

Type of Complication/Maintenance associated with a Fixed Reconstruction	MAXILLARY FIXED PROSTHESES			MANDIBULAR FIXED PROSTHESES		
	No. of Prostheses	% of all Maxillary Prostheses	No. of events	No. of Prostheses	% of Mandibular Prostheses	No. of events
TOTAL NUMBER OF PROSTHESIS	51			52		
COMPLICATION						
Implant Components						
Loose Abutment screw	4	7.8	4	5	9.6	7
Repair of Prosthesis						
Fracture of prosthesis	9	17.6	20	6	11.5	14
Adjustment of Prosthesis						
Adjustment to prosthesis to improve oral hygiene measures	2	3.9	2	0	0	0
Fixed reconstruction sectioned and reduced posterior extension as uncomfortable for patient	0	0	0	1	1.9	1
TOTAL COMPLICATIONS	15		26	12		22
PROSTHESIS FAILURE						
Loss & Replacement of the Prosthesis						
Replaced with a fixed implant prosthesis - due to repeated fracture of teeth	0	0	0	3	5.8	3
Replaced with a removable implant prosthesis - due to repeated fracture of teeth	2	3.9	2	0	0	0
Replaced with a removable implant prosthesis - to improve access for oral hygiene measures	0	0	0	1	1.9	1
Loss of Prosthesis						
Fixed reconstruction removed due to cancer recurrence	0	0	0	1	1.9	1
TOTAL FAILURE	2	3.9	2	5	9.6	5

Table 4.5: Type of complications and failures associated with maxillary and mandibular removable implant-based prostheses

Type of Complication/Maintenance associated with a Removable Reconstruction	MAXILLARY REMOVABLE PROSTHESES			MANDIBULAR REMOVABLE PROSTHESES		
	No. of Prostheses	% of all Prostheses	No. of events for Prostheses	No. of Prostheses	% of Mandibular Prostheses	No. of events for Mandibular Prostheses
Total No. of Prosthesis	**52**			**66**		
COMPLICATION						
Implant Components						
Locator abutment required tightening	3	5.8	3	4	6.1	5
Locator insert (male component) replaced	12	23.1	20	14	21.2	27
Locator abutment removed	0	0	0	1	1.5	1
Locator Denture Cap (housing) replaced	2	3.8	2	1	1.5	1
Repair of Prosthesis						
Fracture of prosthesis - minor	2	3.8	2	2	4.5	3
Fracture of prosthesis - major (through and through)	2	3.8	2	2	4.5	2
Adjustment of Prosthesis						
Adjustment of prosthesis after implant failure	2	3.8	2	0	0	0
Adjustment of prosthesis after further implant placement	0	0	0	1	1.5	1
Reline of prosthesis - due to poor fit	0	0	0	1	1.5	1
Reline of prosthesis - due to cancer recurrence	1	1.9	3	1	1.5	1
Gross adjustment of prosthesis	4	7.7	4	4	6.1	4
TOTAL COMPLICATIONS	**28**		**38**	**31**		**46**
PROSTHESIS FAILURE						
Loss & Replacement of the Prosthesis						
Replaced with a removable implant retained prosthesis - due technical inadequacies	1	1.9	1	3	4.5	3
Replaced with a removable implant retained prosthesis - due to implant failure	1	1.9	1	1	1.5	1
Replaced with a removable implant retained prosthesis - due to patient losing their prosthesis	1	1.9	1	2	3	2
Replaced with a fixed implant prosthesis - due to patient intolerance with a removable implant prosthesis	1	1.9	1	3	4.5	3
Loss of Prosthesis						
Patient unable to tolerate removable implant prosthesis - patient opted for no further treatment	1	1.9	1	2	3	2
Patient unable to tolerate removable implant prosthesis - after implant failure	0	0	0	2	3	2
TOTAL FAILURE	**5**	**9.6%**	**5**	**13**	**19.7%**	**13**

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4.8 Conclusion

This service evaluation highlights the failures and complications of implant prostheses in this patient cohort. Overall, fixed implant prostheses had a higher 5-year survival and 5-year complication-free survival; they also experienced fewer complications in comparison to removable implant retained prostheses within this evaluation. This was statistically significant in the 5-year survival of mandibular removable prostheses (P=0.006) and in the 5-year complication-free survival of both mandibular removable (P=0.009) and maxillary removable prostheses (p=0.048).

Variables of radiotherapy, grafting, age and sex were assessed for their effect on 5-year survival and 5-year complication free-survival of the prosthesis however, these were not found to be statistically significant.

This service evaluation demonstrates the risk of prosthetic failure and complications in a well-planned treatment group and demonstrates that implant based prosthetic treatment for this patient group can be unsuccessful and present a high maintenance burden in the form of management of complications.

CHAPTER 5:

SERVICE EVALUATION OF PROSTHODONTIC COMPLICATIO DURING IMPLANT BASED ORAL REHABILITATION OF HEAD AND NECK ONCOLOGY PATIENTS IN A LARGE REGIONAL COHORT

5. Service evaluation of prosthodontic complications during implant based oral rehabilitation of head and neck oncology patients in a large regional cohort

5.1 Background

Many of the studies assessing implant based prosthodontic rehabilitation in H&N cancer patients focus only on implant-based outcomes such as implant survival. However, there is evidence albeit infrequently documented to suggest that a number of implants placed into this patient group are deemed unrestorable [Chan et al., 1997], [Chang et al., 1998], [Smolka et al., 2008], [Hundepool et al., 2008], [Barrowman et al., 2011]. A dental implant is worthless even if it successfully osseointegrates unless it can be prosthodontically loaded and used in the rehabilitation. Implant based prosthodontic treatment in this patient group is often challenging, expensive and protracted and not always successful, [Hundepool et al., 2008] [Fierz et al., 2013], [Katsoulis et al., 2013], with some authors reporting an inability to complete such treatment [Garrett et al., 2006], [Roumanas et al., 2006], [Smolka et al., 2008], [Hundepool et al., 2008], [Korfage et al., 2010], [Fierz et al., 2013]. A number of reasons have been given for this including; recurrence or metastatic disease [Garrett et al., 2006], [Roumanas et al., 2006], [Smolka et al., 2008], refusal of implant therapy [Garrett et al., 2006], [Hundepool et al., 2008], patients lost to follow-up [Garrett et al., 2006], patient death [Garrett et al., 2006], [Hundepool et al., 2008], [Korfage et al., 2010], [Fierz et al., 2013], non-cooperative patients [Smolka et al., 2008], patients refusing further treatment [Smolka et al.,

2008], [Hundepool et al., 2008], [Korfage et al., 2010], poor general health of the patient [Hundepool et al., 2008], poor anatomical conditions unfavourable for treatment [Smolka et al., 2008], [Hundepool et al., 2008], and implant failure [Smolka et al., 2008]. Those patients that do undergo implant based prosthodontic rehabilitation present an increased workload and technical difficulty in comparison with non-oncology patients [Cuesta-Gil et al., 2009], [Fierz et al., 2013], [Fang et al., 2015] which can prolong or even lead to treatment being ceased [Garrett et al., 2006], [Roumanas et al., 2006], [Smolka et al., 2008], [Cuesta-Gil et al., 2009], [Fierz et al., 2013], [Fang et al., 2015]. Despite the complexity of such care there is a clear deficit within the literature reporting on the complications that occur during the prosthodontic phase of implant based oral rehabilitation in this patient group. Complications can and do occur and it is essential that clinicians are able to appreciate and alleviate or minimise these complications where possible. Furthermore, these complications need to be at the forefront of discussion with patients receiving such treatment so that they are aware of the complexity of the treatment and the lengthy time it can take to successfully rehabilitated; indeed, in some cases rehabilitation may not be completed [Garrett et al., 2006], [Roumanas et al., 2006], [Smolka et al., 2008], [Hundepool et al., 2008], [Fierz et al., 2013]. With the increasing use of dental implants in the oral rehabilitation of H&N cancer patients, a stronger evidence base is required to help inform clinical decision making.

5.2 Aims & Objectives

The overall aim of this service evaluation is to describe the range of complications and issues that affected the oral rehabilitation treatment pathway in H&N oncology

patients who completed implant based prosthodontic rehabilitation in a well-controlled tertiary treatment centre. The primary objective was to determine what standard of care was achieved in this service?

5.3 Methods

5.3.1 Service evaluation approach and setting

The overall service approach and setting are described in section 3.2.1.

The clinical process of oral prosthetic rehabilitation (restoration of the dental implants) was undertaken at BDH. The required laboratory work was prescribed by the treating clinician and all laboratory work was either carried out or supervised by onsite laboratory technicians at BDH who are accustomed to this patient group. All treatment is provided at no cost to patients.

Implant planning and Surgical implant placement technique

Implant planning and surgical implant placement technique is described in section 3.2.1.

Prosthodontic treatment protocol

The prosthodontic restoration of the dental implants is undertaken by the Restorative team at BDH under the supervision of a lead specialist Restorative Consultant.

Within this service all implants are conventionally loaded and are left for at least 3-months after surgical placement to allow osseointegration to occur prior to beginning

the process of restoration. The type of prosthesis the patient is to receive is in the main pre-planned during the stages of implant planning.

5.3.2 Eligibility criteria

Inclusion criteria

1. Patients who had suffered with H&N cancer.

2. Patients who were provided an implant retained fixed or removable intra-oral prosthesis.

Exclusion criteria

1. Patients who did not suffer with H&N cancer.

2. Patients who were not provided with an implant retained fixed or removable intra-oral prosthesis.

3. Patients where the minimum data-set could not be collected.

All H&N oncology patients who had completed oral rehabilitation and been provided with a definitive implant retained prosthesis during the census period were included. The end point of data collection was deemed to be the successful completion of oral rehabilitation in this evaluation period.

5.3.3 Clinical endpoints

In this study, implant survival was defined as an implant fixture still in situ and implant failure defined as implant fixture not in situ due to the loss or removal for clinical

reasons. Implant survival time was defined as the time interval from date of implant placement to the date of implant failure or last follow-up date, whichever occurred first.

Implant success was defined as an implant fixture still in situ which was prosthodontically utilised and loaded. Those implants that were not in situ or were not prosthodontically utilised and loaded were deemed to be unsuccessful.

A complication was defined as a circumstance or event that lead to increased complexity, time or need to repeat/restart stages of treatment.

5.3.4 Variables considered in the service evaluation

The minimum data-set required for study inclusion required; patient demographics (age, gender), tumour diagnosis and TNM classification and staging, treatment received for H&N cancer (surgery - tumour ablation, reconstruction, radiotherapy and chemotherapy). Adjunctive surgeries (implant site augmentation, soft tissue modification – debulk of soft tissue flap, sulcoplasty), location of implant placement (site - maxilla, mandible, bone type - native bone, resected native bone, autogenous bone grafts vascularised and non-vascularised), implant manufacturer, implant planning (two or three dimensional imaging), implant surgery variables (use of CAD-CAM (computer aided design-computer aided manufacture) surgical guides, laboratory made surgical guides or freehand implant placement). Dental rehabilitation (type – fixed (crown or bridgework), removable (type of retention system), site - maxilla, mandible, and timing) and the documented complications during implant based prosthodontic rehabilitation and their consequences, which were grouped into the following; patient complications, clinician and laboratory complications, implant

complications (including implant survival & implant success), peri-implant soft tissue complications and clinical prosthodontic complications.

5.4 Ethical approval

See section 3.4 and appendix 1.

5.5 Data collection

The process of data collection and the data that was collected is described in section 3.5.

5.6 Statistical analysis

Complications reported during the process of prosthodontic rehabilitation are reported and analysed in a descriptive manner to avoid over-interpretation.

5.7 Results

5.7.1 Population demographics

A total of 167 patients were identified for inclusion within this study. 4 patients were excluded from the analysis due to the minimum data set not being available. Therefore, a total of 163 patients were included for analysis.

5.7.1.1 Patients

Of the 163 patients included in the analyses, 107 (65.6%) were male and the mean age of this cohort at the time of inception i.e. delivery of prosthesis, was 63.0 years (Range: 27-88 years). Patients had a variety of benign and malignant H&N tumours with varying anatomical sites and TNM stagings. These patients received a range of treatments for their H&N cancer including surgical resection, radiotherapy and chemoradiotherapy. Some of the patients who underwent surgical resection were also reconstructed with a variety of soft tissue flaps, non-vascularised bone grafts and composite free flaps. (Table 5.1)

Table 5.1: Demographics of study population

Demographics	N=163
Age	63.0 years (Range:27-88)
Male	N= 107 (65.6%)
Cancer Type	
SCC	124 (76.1%)
Adenoid Cystic Carcinoma	7 (4.3%)
Ameloblastoma	7 (4.3%)
Unspecified carcinoma/tumour	5 (3.1%)
Malignant Melanoma	3 (1.8%)
Osteogenic sarcoma	3 (1.8%)
Mucoepidermoid	2 (1.2%)
Pleomorphic Adenoma	2 (1.2%)
BCC	2 (1.2%)
Adenocarcinoma	2 (1.2%)
Primitive Neuroectodermal Tumour	1 (0.6%)
Chondrosarcoma	1 (0.6%)
Odontogenic keratinocyst	1 (0.6%)
Lymphoma	1 (0.6%)
Dendritic Cell Sarcoma	1 (0.6%)
Pindburg Tumour	1 (0.6%)
TNM Staging	
I	21 (12.9%)
II	20 (12.3%)
III	12 (7.4%)

IVA	60 (36.8%)
IVB	1 (0.6%)
IVC	1 (0.6%)
Unknown	48 (29.4%)
Treatment Modality	
No Surgery	19 (11.7%)
Surgery and no Reconstruction	55 (33.7%)
Surgery and Reconstruction with Free Flap/Autogenous bone graft	89 (54.6%)
Radiotherapy	74 (45.4%)
Chemo-radiotherapy	28 (17.2%)
Chemotherapy	0 (0.0%)
Neither (Radiotherapy or Chemotherapy)	61 (37.4%)
Site of Prosthetic Restoration	
Bi-maxillary	71 (43.6%)
Mandible	57 (35.0%)
Maxilla	35 (21.5%)
Type of prostheses	
Fixed	111 (47.4%)
Maxillary Fixed	55 (23.5%)
Mandibular Fixed	56 (23.9%)
Removable	123 (52.6%)
Maxillary Removable	54 (23.2%)
Mandibular Removable	69 (29.5%)

5.7.1.2 Implant imaging, planning & placement

Of the 163 patients, 135 patients (82.8%) had CBCT images taken and reformatted for SIMPLANT® Computer-Guided Implant Treatment Software (Dentsply Sirona, York, PN, USA). SIMPLANT® Surgical Guides (Dentsply Sirona, York, PN, USA) were then constructed from this scan and used at the time of surgical implant placement. For 2 patients conventional CBCTs were taken, for 22 patients conventional radiographs were taken and for 4 patients it was unclear what radiographic imagery was taken for implant planning purposes.

763 implants in total were placed in 163 patients. 121 patients had 569 implants placed by the Oral & Maxillofacial surgery Team (OMFS) at UHB, and 42 patients

had 194 implants placed by the Oral Surgery and Restorative Departments at BDH. A variety of implant systems were used which included; 663 Straumann implants (Institut Straumann, Basel, Switzerland), 63 Brånemark implants (Nobel Biocare, Zurich, Switzerland), 36 Astra Tech implants (Dentsply Implants, Mannheim, Germany) and 1 Oktagon implant (Dental Ratio, Langenfeld, Germany) implant with a range of 1 to 11 implants per patient. Of these, 368 (48%) implants were placed in the maxilla and 395 (52%) implants in the mandible.

9 patients had primary implant placement with 19 implant fixtures placed and 154 patients had secondary/delayed placement with 744 implant fixtures placed.

5.7.1.3 Prosthodontic rehabilitation

All 163 patients that started the process of implant based prosthodontic rehabilitation were definitively restored as per the inclusion criteria. Of the 163 patients that were prosthetically restored, 71 (43.6%) patients had bi-maxillary reconstructions, 57 (35.0%) had mandibular reconstructions and 35 (21.5%) had maxillary reconstructions.

234 prostheses were provided in total. 111 were fixed prosthesis (47.4% of prosthesis) of which 55 prostheses were provided in the maxilla and 56 prostheses in the mandible.123 were removable prosthesis (52.6% of prosthesis) of which 69 prostheses were provided in the maxilla and 56 prostheses in the mandible (Table 5.1).

For fixed prosthesis, 109 prostheses were implant supported fixed partial dentures (fixed implant supported bridgework) and 2 prostheses were single unit implant crowns.

For removable prosthesis, 122 prostheses were retained using Locator® abutments (Zest Dental, CA, USA) and 1 prosthesis was retained by a CAD-CAM titanium bar (Atlantis™, Dentsply Sirona, PA, USA) and Titanium clip.

The average (mean) time for prosthetic rehabilitation was 9.7months (from the date implant placement to definitive restoration of the implant/s) with a range of 4 to 38 months. It took 8.49months (mean) to restore the implants with a fixed prosthesis and 10.45months (mean) for a patient to be restored with a removable prosthesis.

5.7.2 Complications

5.7.2.1 Patient complications

In total 14 patients (8.6% of all patients) had a documented complication that affected implant based prosthodontic rehabilitation. 8 patients had trismus related to oncological interventions in the form of surgery and/or radiotherapy. 5 patients had microstomia as a result of surgical intervention and 1 patient had tumour recurrence with nodal spread (Table 5.2).

5.7.2.2 Clinician and laboratory complications

In total 5 patients (3.1% of all patients) had a documented clinician-based complication that affected implant based prosthetic rehabilitation; this included prosthetic implant components not being available in 4 cases and in 1 case, laboratory work was not ready for the treatment appointment as it had not been booked in correctly (Table 5.2).

In total 7 patients (4.3% of all patients) had a documented laboratory-based complication that affected implant-based prosthodontic rehabilitation. In 3 cases laboratory work was not completed or ready for the patient's appointment, and in 4 cases laboratory work had to be re-done as the laboratory work provided was not to the clinician's prescription (Table 5.2).

Table 5.2: Patient, clinician & laboratory reported complications and issues

Complication Type	No. of patients (% of all patients)
Patient Based Complications	
Trismus	8 (4.9%)
Microstomia	5 (3.1%)
Tumour Recurrence	1 (0.6%)
TOTAL	14 (8.6%)
Clinician & Laboratory Based Complications	
Lab work booked incorrectly	1 (0.6%)
Prosthodontic implant components not available	4 (2.5%)
Lab work not completed or ready for patient appointment	3 (1.8%)
Lab work incorrect and required to be re-done	4 (2.5%)
TOTAL	**12 (7.4%)**

5.7.2.3 Implant based complications

Implant based complications are summarised in table 5.3. Overall implant survival was 95.8%, (32 implants failed in the 763 implants placed) with a mean follow up of 42.1months (range: 1-142 months). Implant failure occurred in 13.5% of patients (22 patients experienced implant failure) (see chapter 3).

These 32 implants failed for a variety of reasons which included; 20 implant failures due to a lack of osseointegration (in 15 patients); 6 implants failed due to failure of the bone graft (composite free flap) into which they were placed (in 2 patients); 5 implants failed due to perimplantitis (in 4 patients); and 1 implant (in 1 patient) the

implant was explanted at the patient's request as the implant could not be prosthodontically restored and was causing soft tissue trauma.

Overall implant success was 94.5%, (42 implants were not prosthetically restored over the observational period – which occurred in 30 patients (18.4% of patients)).These 42 implants were unsuccessful due to the following reasons; 32 implants failed and were subsequently removed/lost (as described above); 7 implants (in 6 patients) were deemed to be prosthodontically unrestorable and were left as sleepers; 2 implants (in 1 patient) experienced ORN at the implant site (irradiated native mandible) and were left as sleepers; and for 1 implant (in 1 patient) the cover screw was not able to be removed from the implant fixture despite repeated attempts to remove and was left as a sleeper.

Other implant complications were reported and included, the prosthetic challenge of restoring 12 implant fixtures (in 9 patients) due to unfavourable implant position/angulation; however, these implants were successfully utilised and loaded as part of the prosthodontic rehabilitation. For 3 implants the cover screw could not be removed using conventional methods. In 2 of these cases specialist equipment and support from the implant manufacturer was needed to remove the cover screw, however, in the other case the cover screw was unable to be removed and was left as a sleeper (as previously reported) and was not restored (albeit in this case the overall prosthodontic treatment plan remained unchanged). In 1 case during the uncovering of the implant fixture to allow restoration it was noted that there was necrotic bone present around the implant fixture. This necrotic bone was removed, the site grafted with a xenograft (Giestlich Bio-Oss® and Bio-Gide®) and the implant re-submerged. On uncovering another implant fixture (which had osseointegrated) it

was noted that there was a lack of buccal bone around the implant fixture. This site was grafted with a xenograft (Giestlich Bio-Oss® and Bio-Gide®) and the implant re-submerged. Both of these implants were later uncovered and used as part of the prosthodontic reconstruction. There were also 2 cases (with 2 implants) of the healing abutment becoming loose which required re-tightening and 2 cases (with 2 implants) where the healing abutment had been lost after becoming loose, which required subsequent replacement during the process of prosthodontic rehabilitation.

5.7.4.2 Peri-implant soft tissue complications

Peri-implant soft tissue complications which hindered prosthodontic rehabilitation were reported in 16 patients (9.8% of all patients).

In 3 cases deep soft tissue associated with the soft tissue component of a vascularised free flap required surgical debulking to reduce the depth of the peri-implant soft tissues around the implant fixture to allow restoration. In another 2 cases, a sulcoplasty/vestibuloplasty procedure adjacent to the implant fixture/s was required to provide a sulcus to allow restoration of the implant/s whilst also improving the peri-implant soft tissue profile. The surgery required for these 5 cases was carried out after implant placement and therefore delayed restoration of the implants. In the majority of cases, such issues are identified at the implant planning stages and the appropriate surgical procedures are carried out by the OMFS team at the time of surgical implant placement. In 7 patients, peri-implant soft tissue overgrowth was noted and required surgical removal to allow restoration of the implants. For a further 4 patients deep soft tissue around the implant fixtures was documented, however, no further treatment was carried out to alleviate this.

Table 5.3: Implant and peri-implant complications

Implant Complications	No. of Patients (% of all Patients)	No. of Implants (% of all Implants
Implant Failure		
Implant failure due to lack of osseointegration & explanted	15 (9.2%)	20 (2.6%)
Implant failure due to free flap failure & explanted	2 (1.2%)	6 (0.8%)
Implant failure due to peri-implantitis & explanted	4 (2.5%)	5 (0.7%)
Implant failure due to it being deemed unrestorable & explanted	1 (0.6%)	1 (0.1%)
OVERALL: Implant Failure	22 (13.5%)	32 (4.2%)
Lack of Implant Success		
Implants deemed unrestorable and left as sleepers	6 (3.7%)	7 (0.9%)
ORN around implants. Implants unrestored and left as sleepers	1 (0.6%)	2 (0.3%)
Unable to remove cover screw from implant fixture. Implant unrestored and left as sleeper	1 (0.6%)	1 (0.1%)
OVERALL: Unsuccessful Implants (which include failed implants)	30 (18.4%)	42 (5.5%)
Other Implant Complications		
Unfavourable implant position. Implant restored	9 (5.5%)	12 (1.6%)
Difficulty in removing cover screw	3 (1.8%)	3 (0.4%)
Loose healing abutment – required tightening	2 (1.2%)	2 (0.3%)
Lost healing abutment - required replacement	2 (1.2%)	2 (0.3%)
Necrotic bone around implant fixture on exposure - this removed and grafted with a xenograft	1 (0.6%)	1 (0.1%)
Lack of bone around implant fixture on exposure - grafted with a xenograft	1 (0.6%)	1 (0.1%)
TOTAL: Other Implant Complications	18 (11.0%)	21 (2.8%)
Peri-implant Soft Tissue Complications		
Soft Tissue - Deep around Free Flap that required debulk (after implant placement)	3 (1.8%)	5 (0.7%)

Lack of sulcus or implants close to adjacent tissues - required sulcoplasty (after implant placement)	2 (1.2%)	4 (0.5%)
Deep Soft tissue around a free Flap	4 (2.5%)	Unknown
Soft tissue overgrowth around implant that required resection	7 (4.3%)	unknown
TOTAL: Peri-implant Soft Tissue Complications	16 (9.8%)	N/A

5.7.4.3 Clinical prosthodontic complications

Clinical prosthodontic complications during the rehabilitation process were relatively common. On 49 occasions the clinical/laboratory work had to be re-perfomred and in some cases restarted in 46 patients (28.8% of patients) (Table 5.4).

The most frequent stage of treatment that was repeated was the prosthetic try-in stage, with the most common reason for this being an inaccurate occlusal scheme in 17 cases, unacceptable aesthetics in 11 cases and a lack of freeway space being provided in 5 cases.

Impressions were retaken on 16 occasions. For the fabrication of a fixed implant prosthesis this occurred on 7 occasions. In 3 of these cases master impressions were retaken due to the verification jig being non-passive on intra-oral try-in (demonstrating that the master model was inaccurate) and required a repeat fixture level secondary impression. In 3 cases the try-in of the metal framework substructure was not passive on intra-oral placement and a new fixture level secondary impression was required, and in 1 case, a single implant crown did not fit, and a repeat fixture level impression was required.

For fabrication of a removable implant prosthesis, impressions had to be re-taken on 9 occasions. In 3 cases master pick up impressions were retaken as the housing of

implant retention system within the acrylic base plate of the removable prosthesis did not accurately fit onto the Locator® abutment/s (Locator® Zest Anchors LLC, California, USA). In 3 other cases repeat master impressions were required due to the cobalt chromium metal framework not fitting accurately. In 1 case, a laboratory based reline of the acrylic base plate for an implant retained overdenture at the try-in stage was required due to poor fit and lack of retention of the acrylic base plate. In another case primary impressions were repeated as the special trays were inadequate due to poor initial primary impressions and in another case primary impressions had to be retaken as the laboratory work had been lost.

Table 5.4: Prosthetic laboratory work repeated and reasons why

Lab Work Re-done & Reasons why	No. of Events	No. of Patients (% of all patients)
Impressions		
Start from Beginning 1st impressions - lost lab work	1	1 (0.6%)
Repeated 2nd Impression - verification jig not passive/fitting	3	3 (1.8%)
Repeated 2nd Impression – implant fixed metal framework not passive/fitting	3	3 (1.8%)
Repeated 2nd Impression - implant crown didn't fit	1	1 (0.6%)
Repeated 2nd Impressions - complete denture with locators not seating correctly	3	3 (1.8%)
Repeated 2nd impression – cobalt chromium metal denture framework didn't fit	3	3 (1.8%)
Repeated 1st Impression - for new special tray	1	1 (0.6%)
Reline impression in prosthesis due to poor	1	1 (0.6%)

retention		
Registration/Try-In		
Re-Try – due to aesthetics	11	11 (6.7%)
Re-Try – due to the occlusion/occlusal plane being incorrect	17	16 (9.8%)
Re-Try - due to lack of Free Way Space	5	3 (1.8%)
TOTAL	49	46 (28.2%)

5.8 Conclusion

This service evaluation indicated that complications arising during the process of implant based prosthetic rehabilitation in this patient group are variable and common. Such complications can delay the process of treatment and can lead to clinical and laboratory stages of treatment needing to be repeated or restarted despite the expertise of clinicians and laboratory technicians at this regional centre, who are well versed in treating this patient group. This evaluation provides some form of understanding of the type and frequency of complications arising during the process of implant based prosthetic treatment in this patient cohort, which the literature is currently lacking, despite the challenges of prosthetically rehabilitating this patient group being widely recognized and reported. [Garrett et al., 2006], [Smolka et al., 2008], [Hundepool et al., 2008], [Cuesta-Gil et al., 2009], [Fierz et al., 2013], [Katsoluis et al., 2013], [Fang et al., 2015]

CHAPTER 6:

DISCUSSION

6. Discussion

6.1 Summary of results and comparison with the literature

6.1.1 Systematic Review: Survival of dental implants placed in autogenous bone grafts and bone flaps in head and neck oncology patients

The discussion of the systematic review has been reported in section 2.5.

6.1.2 Service evaluation of outcomes of implants placed for the oral rehabilitation of head and neck oncology patients in a large regional cohort

The results obtained from this service evaluation of a regional centre demonstrate that implant survival rates were high and surgical treatment relatively reliable in this challenging patient group. When comparing the implant survival rate of this evaluation with others, findings appear consistent with previous literature which reports implant survival ranging from 75 to 97.1% with average follow-up ranging from 30.9 months to 5.4 years. [Shaw et al., 2005], [Teoh et al., 2005], [Yerit et al., 2006], [Hessling et al., 2015], [Ch'ng et al., 2016], [Linsen et al., 2012].

The bone type into which the implants were placed influenced survival. A trend can be observed suggesting higher implant survival when placed within the native mandible/maxilla in comparison with implants placed into autogenous bone grafts

and vascularized free flaps. This is consistent with the majority of the reported literature [Hessling et al., 2015] [Watzinger et al., 1996], [Shaw et al., 2005], [Ch'ng et al., 20016] however, equivalent implant survival in native and autogenous bone grafts/vascularized free flaps has been reported in some centres. [Schliephake et al., 1999] [Chiapasco et al., 2008]

Radiotherapy is commonly reported as a risk factor for implant failure. Here, radiotherapy did not (statistically) significantly affect implant survival either alone or in combination with chemotherapy. There was, however, a trend towards higher numbers of failures in both of these treatment groups (Figures 3.2c & 3.2d). In this cohort the majority of patients received radiotherapy and/or chemotherapy prior to implant placement. The existing evidence base suggests that in particular, timing of radiotherapy can affect implant survival, with increased failure reported when radiotherapy is carried out before implant placement. [Fierz et al., 2013], [Buddula et al., 2012], [Granström et al., 2005] The data quality is poor, however, and a systematic review by Nooh (2013) concluded that timing of radiation therapy in relation to implant placement had no significant effect on implant survival. [Nooh, 2013] The combined use of chemoradiotherapy appeared to influence implant survival with higher levels of implant failure seen in the reported cohort when compared with patients who received either treatment modality in isolation. This observation supports a report by Hessling et al (2015) who found a statistically significant correlation between implant loss and adjuvant combined radiotherapy and chemotherapy. [Hessling et al., 2015]

Patients with a higher cancer staging exhibited a trend towards increased implant failure (at the patient-level of assessment). However, there is little evidence in the

literature to support this with Granström et al (2005) reporting no correlation between tumour type, size, stage, nodes or metastasis and implant outcomes. [Granström et al., 2005] The complexity of surgery will undoubtedly influence the subsequent environment into which implant placement is planned, and it was clear from this service evaluation that surgical complications at the time of implant placement were frequent and varied. A trend between implant failure and reports of surgical complications was observed but could not be statistically tested due to the large number of confounding factors. Surprisingly, there appears to be no literature reporting this concept and with which to compare this observation.

Implant survival within this study did not appear to be affected by patient demographics of age or sex. In relation to some of the factors that were considered, definite conclusions could not be reached due to small patient/implant numbers within comparator groups and also incomplete data capture due to the retrospective nature of this service evaluation. This included the implant system and implant dimensions. When assessing the literature with regard to implant dimensions, Buddula et al., (2012) and Klein et al., (2009) reported that implant dimensions had no effect on implant survival [Klein et al., 2009], [Buddula et al., 2012]; however, these studies had a relatively short follow up. Shaw et al., (2005) on the other hand found that implants of less than 13mm length had a higher rate of failure over longer implant lengths in this patient group. [Shaw et al., 2005]

6.1.3 Service evaluation of outcomes of implant-based prostheses in the oral rehabilitation of head and neck oncology patients in a large regional cohort

This service evaluation retrospectively reports on a cohort of 153 head and neck oncology patients who were restored and reviewed with 221 implant retained prostheses.

Survival

It was found that there was a reduction in survival for all prosthesis types over time. The 5-year survival was highest for maxillary fixed prostheses (87%) followed by mandibular fixed (79%), maxillary removable (66%) and the lowest survival for mandibular removable (50%) however, the only statistically significant result was related to the mandibular removable prostheses (p=0.006)

On reviewing the literature relating to the survival of implant-retained prostheses in this patient group, there are very few studies, and those that do so report on this aspect as an additional rather than a primary outcome of their study. Shaw et al., (2005) reported failure of 12 implant retained prostheses from 71 implant prostheses that were provided to H&N oncology patients (17% prosthesis failure) during a median follow-up of 3.5 years. Nelson et al., (2007) reported 100% survival of the 78 removable- and 25 fixed-implant retained prostheses that were provided over a mean follow-up period of 10.3 years in a cohort of H&N cancer patients. However, comparing this service evaluation to the literature is difficult due to a lack of studies in general and also poor standardisation in the definition of prosthetic failure/survival within these studies. Furthermore, other studies have reported prosthetic failure in

this patient group but have not quantified such events to allow comparison. [Cotic et al., 2016], [Barrowman et al., 2011]

Within this service evaluation, fixed implant prostheses were shown to have a higher 5-year survival in comparison to removable implant prostheses; this has also been reported in the literature. [Shaw et al., 2005], [Barrowman et al., 2011], [Cotic et al., 2016]

The most commonly reported reason for failure of removable retained implant prostheses in this service evaluation was related to a lack of tolerance and/or an inability to adapt to the prosthesis. These are commonly reported causes of prosthetic failure in the literature. [Shaw et al., 2005], [Barrowman et al., 2011], [Cotic et al., 2016] In response to this, within this evaluation, two broad treatment strategies were adopted; namely either converting the patient to a fixed implant prosthesis or providing no further treatment. Both of these treatment strategies have also been used in other studies reporting on such events. [Shaw et al., 2005], [Barrowman et al., 2011], [Cotic et al., 2016]

Variables of radiotherapy, grafting, age and sex were assessed for their effect on overall prosthesis survival; however, none of these were found to be statistically significant. Such variables and their effects on prosthetic survival have not previously been reported within the literature. It would, however, be reasonable to assume that both radiotherapy and grafting would have an impact on prosthetic survival due to the fact that both of these treatment modalities can lead to a less favourable intra-oral environment that does not lend itself well to prosthetic rehabilitation, which is well documented within the literature. [Eckert et al., 1996], [Visch et al., 2002], [Barrowman et al., 2011]

Complication-free survival

A reduction of complication-free survival for all prosthesis types with time was observed. 5-year complication free-survival was highest for mandibular fixed prostheses (62%) followed by maxillary fixed (58%), maxillary removable (36%) and the lowest complication free-survival for mandibular removable (29%). However, the only statistically significant results were related to removable prostheses, both maxillary (p=0.048) and mandibular (p=0.009) prostheses.

This higher frequency of complications associated with removable retained implant prostheses within this patient group has previously been reported [Nelson et al., 2007], [Doll et al., 2015], [Fang et al., 2015]. Nelson et al., (2007) and later (with the same patient group), Doll et al., (2015) reported higher prosthetic complications and an increased maintenance need for implant retained overdentures in comparison to implant supported fixed prostheses, with the latter prosthesis type experiencing no complications or maintenance issues over their observational period (10.3years). This has also been shown in a study by Fang et al., (2015) who reported higher rates of complications in patients restored with removable- (12 complications in 17 patients) in comparison to fixed-implant prostheses (8 complications in 57 patients) during their observation period of 12.8years.

Variables of radiotherapy, grafting, age and sex were assessed for their effect on overall complication free-survival however, none of these were found to be statistically significant. Such variables and their effects on prosthetic complications have not previously been reported within the literature with which to compare.

Causes of prosthesis failure & type of complications for each prosthesis type

In the cohort studied all removable prostheses used the Locator system for retention which is a common approach in this patient group. [Cotic et al., 2016] This was selected for a number of reasons, including; its ease of use, ability to compensate for unfavourable implant position/angulation, the ability to easily modify or adjust the prosthesis (particularly if implant failure occurs), and there is also reduced soft tissue overgrowth/hyperplasia around non-splinted vs splinted retention systems. [Teoh et al., 2005] Despite these advantages, the most common complications with a removable implant overdenture in this study was related to the Locator retention system; both to the Locator abutment within the implant fixture and the Locator housing and its insert within the prosthesis. Such complications with the retention system in H&N cancer patients have also been reported by Nelson et al., (2007) who reported the need to replace the matrix retainer in 11 of the 78 removable implant prostheses during the observational period of the study.

The need for gross modification and relining of removable implant prostheses was required on a frequent basis within this service evaluation. This was commonly due to the prosthesis having a sub-optimal fit or due to intra-oral soft tissue overgrowth (both cancerous and non-cancerous). The need for regular adjustment is well documented with Linsen et al., (2012) and Mericske-Stern et al.,(1999), reporting a need for frequent relining of the prosthesis and also the need for correction/adjustment of the prosthesis as part of regular maintenance [Mericske-Stern et al.,1999]. Additionally, studies by both Shaw et al., (2005) and Teoh et al., (2005) reported that soft tissue overgrowth led to failure of the prosthesis and the need for replacement. Other causes of prosthesis failure both within this service

evaluation and within the literature include, implant failure and the inability of the patient to tolerate an implant retained removable prosthesis. [Shaw et al., 2005]

A number of prostheses within the service evaluation fractured during the observational period. This is again a well reported but uncommon complication. Prabo et al.,(2013), Fang et al.,(2015) and Cuesta-Gil et al., (2009) reported fracture of the denture base and the prosthetic teeth in this patient group with Cuesta-Gil et al., (2009) attributing this to excessive occlusal forces being applied as a result of the loss of proprioception and recommending the use of metal reinforcement in such prostheses. [Cuesta-Gil et al., 2009]

When assessing the maintenance and complications associated with fixed implant retained prostheses in this service evaluation, the most common complication related to fracture of the prosthesis. This was found to be a recurring event within the same individual patients. Fracture of fixed implant prostheses in this patient group has been reported by Zou et al., (2015) who reported fracture of 4 fixed implant retained prostheses in 32 patients included in the study who underwent surgical resection and were then reconstructed with an iliac bone graft of the mandible. Fracture of the prosthesis in this study occurred between 3 and 8 years after delivery of the prosthesis. [Zou et al., 2015] Fang et al., (2015) also reported fracture of fixed implant prosthesis with 'chipping' of the porcelain in 4 patients and worn/fractured acrylic in 1 patient of the 57 patients who were rehabilitated with fixed implant reconstructions, in a cohort of patients who had undergone surgical resection and reconstruction with a fibula free flap of the mandible. [Fang et al., 2015]

Loosening of an abutment screw was another common complication within this service evaluation which has also been reported in the literature by Zou et al., (2015).

Furthermore, Fang et al., (2015) reported fracture of an abutment screw in 3 of the 57 patients rehabilitated with fixed implant prostheses. [Fang et al., 2015] However, such an event did not occur within this service evaluation.

Adjustment of fixed implant prostheses was required infrequently to improve access for oral hygiene measures in this evaluation. Such a need has also been reported by Shaw et al., (2005) who carried out refinement and alteration of design of the prosthesis over time to allow access for oral hygiene measures with inadequate oral hygiene being a common problem leading to loss of the prosthesis. [Shaw et al., 2005]

In this service evaluation there were several patients where prosthetic failure occurred. This was predominantly in removable implant prostheses and mainly due to a lack of tolerance by the patients to adapt to a removable implant retained prosthesis. As a result, modification or replacement of the prosthesis was required. This lack of tolerance and dissatisfaction has also been reported in the literature, with Cuseta–Gill et al.,(2009) reporting 2 dissatisfied patients as a result of worsened function after rehabilitation with use of an implant retained dental prostheses, with both prostheses requiring removal [Cuseta–Gill et al., 2009]. Shaw et al., (2005) also reported removal of 2 patients' prostheses despite technically satisfactory reconstructions, implants, and prostheses, as the patients deemed their oral function to be inadequate.[Shaw et al., 2005]

6.1.4 Service evaluation of prosthodontic complications during implant based oral rehabilitation of head and neck oncology patients in a large regional cohort

Implant based prosthodontic treatment in this patient cohort comes with multiple complications which can prolong and delay treatment. The challenging nature of this treatment is well reported within the literature, and it is observed that such treatment brings with it an increased workload and technical difficulty in comparison with non-oncology patients. [Fierz et al., 2003], [Cuesta-Gil et al., 2009], [Fang et al., 2015]

Multiple complications were reported within this service evaluation during the process of prosthodontic oral rehabilitation. Such complications commonly led to clinical stages of treatment and laboratory work needing to be repeated or restarted which subsequently delayed prosthodontic rehabilitation. Only patients who completed implant based prosthetic rehabilitation were included and as such the effect of these complications on the discontinuation of treatment cannot be reported upon.

The time taken from the date of surgical implant placement to completion of prosthodontic rehabilitation within this service evaluation was on average (mean) 9.74 months; however, this ranged from 4 to 38months. A variety of documented reasons for delays in prosthodontic treatment include; the need for additional pre-prosthetic surgery, recurrence of H&N cancer, implant failure, unfavourable implant position/angulation, poor general health of the patient and the ability of the patient and the service to attend/provide the appointments to allow such treatment to be carried out.

Within the literature the length of time to restore these patients was quantified by Katsoulis et al.,(2013) who reported that it took on average between 8 and 16months

to prosthodontically restore H&N cancer patients with implant based prostheses; however, for some patients prosthetic treatment took over 2 years to complete with a variety of reasons being reported including; complications after tumour surgery and radiotherapy, comprising osteomyelitis, disturbed soft tissue healing, sequestration of grafts, caries, early loss of implants as well as recurrence of tumours. [Katsoulis et al.,2013] Other reported causes delaying or leading to a discontinuation of prosthetic rehabilitation within the literature include; unfavourable implant positioning, implant failure, tumour recurrence/metastatic disease, poor general health of the patient, patients lost to follow-up, patient death, patients' poor cooperation, caries, radiotherapy, poor soft tissue healing, unfavourable hard and soft tissues, trismus, unfavourable intermaxillary relationship, failure of autogenous bone grafts and patients refusing further surgery [Hundepool et al., 2008], [Garrett et al., 2003], [Smolka et al., 2008], [Katsoulis et al.,2013].

Implant success (ability to restore the implant) was high at 94.5%; however, where there was a lack of success (implant failure and an inability to prosthodontically use the implant fixture(s)), this commonly led to changes in the proposed prosthodontic treatment plan. In total there were 7 implants (0.92%) in 6 separate patients where the implant fixture(s) were deemed to be unrestorable as a result of unfavourable implant positioning or angulation. This was despite optimal implant planning in all 6 of these patients who were planned using a CBCT which had been reformatted for SIMPLANT® implant planning software (Dentsply Sirona, York, PN, USA) and subsequent use of SIMPLANT® Surgical Guides (Dentsply Sirona, York, PN, USA). The issue of implants being prosthetically unrestorable is common in this patient group and widely reported within the literature. [Chan et al., 1997], [Chang et al.,

1998], [Hundepool et al., 2008], [Smolka et al., 2008], [Barrowman et al., 2011] The inability to restore the implant fixture does not necessarily mean that the treatment planning and surgical execution of implant placement was inadequate. In most cases it is a challenge to place implants in an optimal position in this patient group due to the unfavourable bony structures that have been previously resected, irradiated and reconstructed with bone grafts/composite free flaps. [Barrowman et al., 2011] Intra-oral access is often compromised as a result of microstomia, and trismus leading to restricted mouth opening which is frequently reported in this patient group. [Hundepool et al., 2008], [Fierz et al., 2013] [Katsoulis et al.,2013] This can make the surgical placement of the implant fixture/s and their subsequent prosthetic restoration challenging and, in some cases, impossible. [Fierz et al., 2013], [Katsoulis et al.,2013] These restrictions and the lack of suitable sites often lead to implant fixtures being placed where there is adequate bone volume and surgical access rather than the implant fixture being placed in the optimal prosthodontic position for restoration as reported in the literature. [Chan et al., 1997], [Chang et al., 1998], [Ozan et al., 2008], [Essig et al., 2011]

Peri-implant soft tissue complications also hindered prosthodontic restoration of the implant fixtures in 16 patients (9.8% of all patients) within this service evaluation. Such issues are commonly reported in this patient group within the literature with peri-implant mucosal hyperplasia. [Chan et al., 1997], [Kovács et al., 2000], [Fang et al., 2015], [Mericske-Stern et al., 1999], [Korfage et al., 2010] and deep soft tissue around the implant fixtures (particularly implants placed into/passing through soft tissue flaps) being widely reported. [Mericske-Stern et al., 1999], [Schultes et al., 2002], [Blake et al., 2008], [Wang et al., 2015] As a result of these soft tissue

challenges, surgical intervention was required in a number of cases which included surgical resection of hyperplastic tissue, debulking of soft tissue flaps and the need for sulcoplasty/vestibuloplasty procedures to improve the peri-implant soft tissue profile and allow the prosthetic restoration of the implant fixtures. These surgical procedures are routinely carried out within this service and are well reported surgical procedures. [Hessling et al., 2015], [Shaw et al., 2005], [Teoh et al., 2005]

When assessing the literature relating to complications arising during the process of implant based oral rehabilitation in this patient cohort, and their consequence on the process of implant based prosthodontic treatment, there appears to be no literature with which to compare the findings of this service evaluation. It is however, well described in the literature that treatment in this patient cohort is complex with technical difficulties that can prolong or even lead to treatment being ceased [Cuesta-gil et al.,2009], [Fierz et al., 2003], [Fang et al.,2015] and that there is a need for individualised and often imaginative solutions to treat this challenging patient group. [Cuesta-gil et al., 2009]

6.2 Limitations of study

6.2.1 Systematic Review: Survival of dental implants placed in autogenous bone grafts and bone flaps in head and neck oncology patients

The limitations of the systematic review are reported in sub-section 2.5.2 Limitations.

6.2.2 Service evaluation of the complications and outcomes of implants and their prosthesis placed for the oral rehabilitation of head and neck oncology patients in a large regional cohort

Some of the principal limitations of this service evaluation are its retrospective nature, the limited follow-up period and also the inability to eliminate confounding variables due to heterogeneity of the patients, treatments and follow up. These are common limitations within the literature reporting on such outcomes in this patient cohort which can be expected.

As the service evaluation reported on a specific regional centre, the results cannot be extrapolated beyond this environment, thereby reducing its external validity and generalisability to H&N cancer patients restored with an implant-based prosthesis. The retrospective nature also means that some data was not recorded and there is also a risk of reporting bias.

A major issue generally within the literature is the lack of, or a lack of standardisation and consensus on defining outcome measures. The outcome measures that were used within this service evaluation such as implant and prosthetic survival/failure etc. either lacked a definition or there was no consensus agreement on what defines these outcomes. As such there is a need to clearly define these outcome measures via a consensus process to allow standardisation.

Additionally, some outcomes that would have been useful to assess such as peri-implant health and maintenance regimes to assess long term outcomes were not able to be assessed, as this data was not available for collection within our service as it was either not assessed or not recorded. This is true not only within this service evaluation but also within the literature. There is therefore a need for some form of

consensus on the standardisation of a minimum data set required for measuring outcomes, analysing end-points and the most appropriate way to statistically analyse the data. This would allow and enable comparison of studies including statistical analysis via a meta-analysis.

CHAPTER 7:

CONCLUSIONS AND FUTURE RESEARCH

7. Conclusions and future research

7.1 Conclusions

The main findings identified by the systematic review , with the exception of a small number of studies was that implant survival (at an implant level) in autogenous bone grafts was clinically promising (>85%) in a H&N cancer cohort but was still lower than implants placed into native bone in the same group. Weak evidence was identified to suggest that radiotherapy and the type of autogenous bone graft donor site is a prognostic factor affecting implant survival in this patient cohort. Implant survival did not appear to be affected by the type of H&N tumour (malignant vs. benign). Implant success was shown to be lower than implant survival and was related to peri-implant bone loss, peri-implant hyperplasia and prosthetic complications with restoration of the implants. This was primarily related to composite (bone and soft tissue) free flaps and specifically the soft tissue component. Implant success is starting to become the more accepted outcome measure with implant 'survival' being a measure of implant success or failure.

The service evaluation of a patient cohort from a regional centre demonstrated high implant survival rates when used as part of routine oral rehabilitation of H&N oncology patients, with a median follow-up of 38 months. Implant survival estimates at 3 years were 95.7% [95%CI 94.3-97.2%] and 95.5% [95%CI 93.9-97.0%] at 5 years. Survival analyses for specific covariates showed trends for increased implant failure in patients receiving radiotherapy (p=0.16), chemotherapy (p=0.17) and being male (p=0.09) but were not found to be statistically significant in this population.

Implant survival, however, was found to be affected by the bone type, with implant failure being significantly higher for implants placed into autogenous bone grafts/free flaps in comparison to implants placed into native bone (p=<0.001). These findings are consistent with the conclusions of the systematic review. Reported surgical complications noted at the time of implant placement were high with 14.8% of patients experiencing such events. Such complications appeared to increase the risk of implant failure (at the patient level). Overall this service evaluation supports the use of dental implants in the oral rehabilitation of this complex patient group, but it is important to recognise that this is an analysis of a complex care-pathway with a large number of confounding variables. The findings should not be considered as generalisable beyond the specific environment in which this service evaluation was conducted.

The service evaluation also highlighted the failures and complications of implant prostheses in this patient cohort. Overall, fixed implant prostheses had a higher 5-year survival and 5-year complication-free survival, and they also experienced fewer complications in comparison to removable implant prostheses within this evaluation. This was statistically significant in the 5-year survival of mandibular removable prostheses (p=0.006) and in the 5-year complication-free survival of both mandibular removable (p=0.009) and maxillary removable prostheses (p=0.048).

Variables of radiotherapy, grafting, age and sex were assessed for their effect on 5-year survival and 5-year complication free-survival of the prosthesis; however, these were not found to be statistically significant. This service evaluation demonstrates the risk of prosthetic failure and complications in a well-planned treatment group and

demonstrates that implant based prosthetic treatment for this patient group can be unsuccessful and lead to a high maintenance burden in the form of complications.

It is evident that complications ongoing during the process of implant based prosthetic rehabilitation in this patient group are variable and not uncommon. These complications can delay the process of treatment and can lead to clinical and laboratory stages of treatment needing to be repeated or restarted, despite the expertise of clinicians and laboratory technicians at this regional centre who are well versed in treating this patient group. The evaluation provided some form of understanding of the type and frequency of complications arising during the process of implant based prosthetic treatment in this patient cohort, which the literature is currently lacking, despite the challenges of prosthetically rehabilitating this patient group being widely recognised and reported.

7.2 Suggestions for further research

- There is a clear need for international consensus agreement on defining outcome measures such as implant survival and implant success. There is also a need for a consensus on the standardisation of what minimum date set is required for measuring outcomes, analysing end-points and the most appropriate way to statistically analyse the data. This would facilitate standardisation and enable the comparison of studies, including statistical analysis, via a meta-analysis.

- In order to understand these treatment modalities in this patient cohort, larger, well designed prospective studies are required. In assessing survival and prognostic factors, prospective observational studies would be the most

appropriate study design to assess these. However, this study design has a number of limitations for such a study which include; the length of time required to follow up these patients to assess the outcomes over extended time periods (minimum 5 year follow up but ideally longer). Patient drop-out would be anticipated to be high due to fact that this patient group will generally have a reduced life expectancy due to their cancer diagnosis. Additionally, large patient numbers would be required to assess prognostic factors due to the high survival rates reported in this patient group within the evaluation and within the literature. There would also be additional resources, training, expertise and funding that would be required to conduct such a study.

- Consideration for prospective data collection of implants and their prostheses within the service during the processes of treatment. This would minimise the challenges of retrospective data collection, such as being unable to identify patients, missing data and also biases such as recall and reporting bias commonly associated with retrospective data. The process of collecting data to assess outcomes is something that is currently being considered within our service and will include all patients who have had dental implants provided.

- There is a need for studies with extended follow up periods preferably beyond 5 years. This service evaluation and the studies considered herein are commonly shorter than this. With such short follow up periods, long term outcomes cannot be assessed. Where possible, follow-up of at least 5 years would be beneficial to assess longer term outcomes. However, reduced follow up of studies would be expected with patients within this cohort due the fact

that this patient group will generally have a reduced life expectancy due to their cancer diagnosis.

- There is a need to assess other outcome measures such peri-implant health and maintenance regimes to assess long term outcomes, both with regard to implant and prosthetic based outcomes.

- Consideration of studies reporting on quality of life improvements in H&N cancer patients who have undergone implant based prosthodontic treatment, to understand what provides better patient based outcomes in this patient cohort. This may be extremely challenging due to extensive heterogenicity within this patient cohort such as patient demographics, patient expectations, treatment modalities received for their H&N cancer and the prosthodontic treatment that is provided etc.

- Consideration of studies assessing/comparing different patient pathways and journeys in order to better understand the time taken for treatment and the resource allocation to provide such treatment against the outcomes of treatment and QoL improvement. This could include studies comparing primary vs secondary implant placement, different treatment modalities for maxillary reconstruction e.g. comparing obturating a defect with a removable prosthesis vs zygomatic implants and an implant retained prosthesis vs surgical reconstruction for example.

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APPENDICES

9.1 Ethical Approval: Email - NHS R&D approval as a service evaluation.
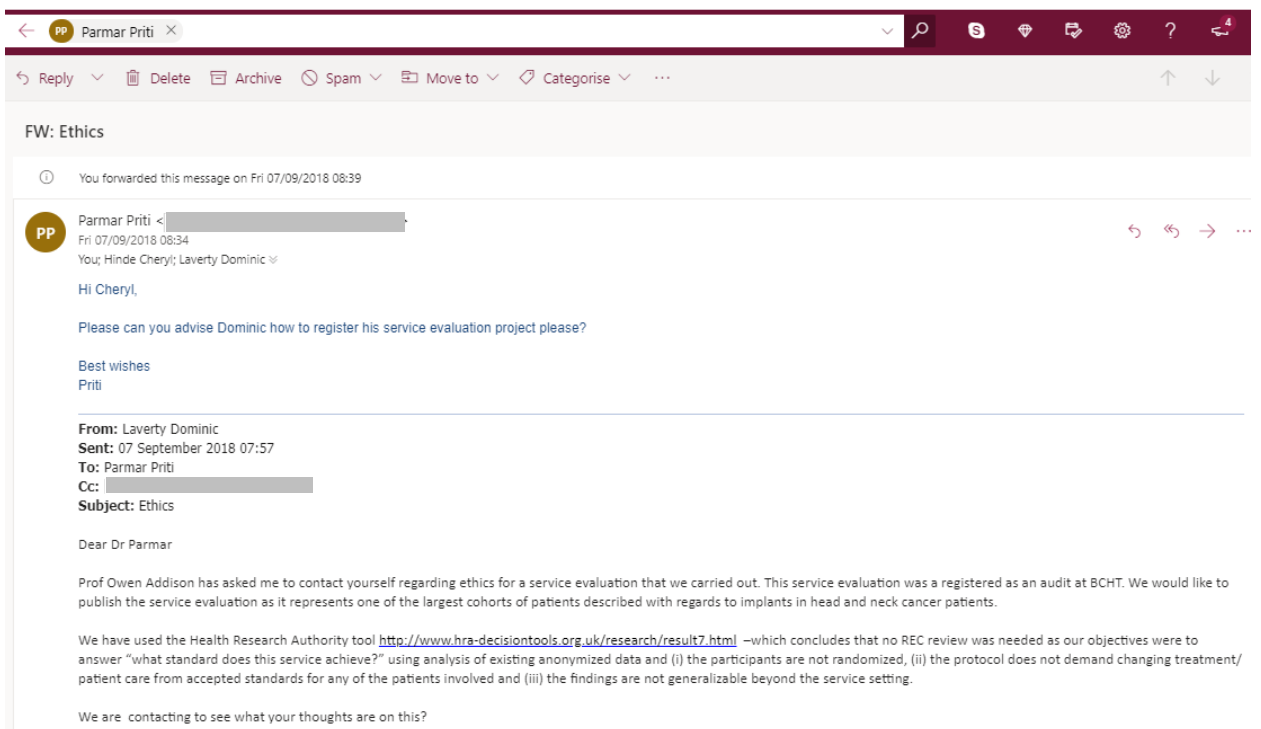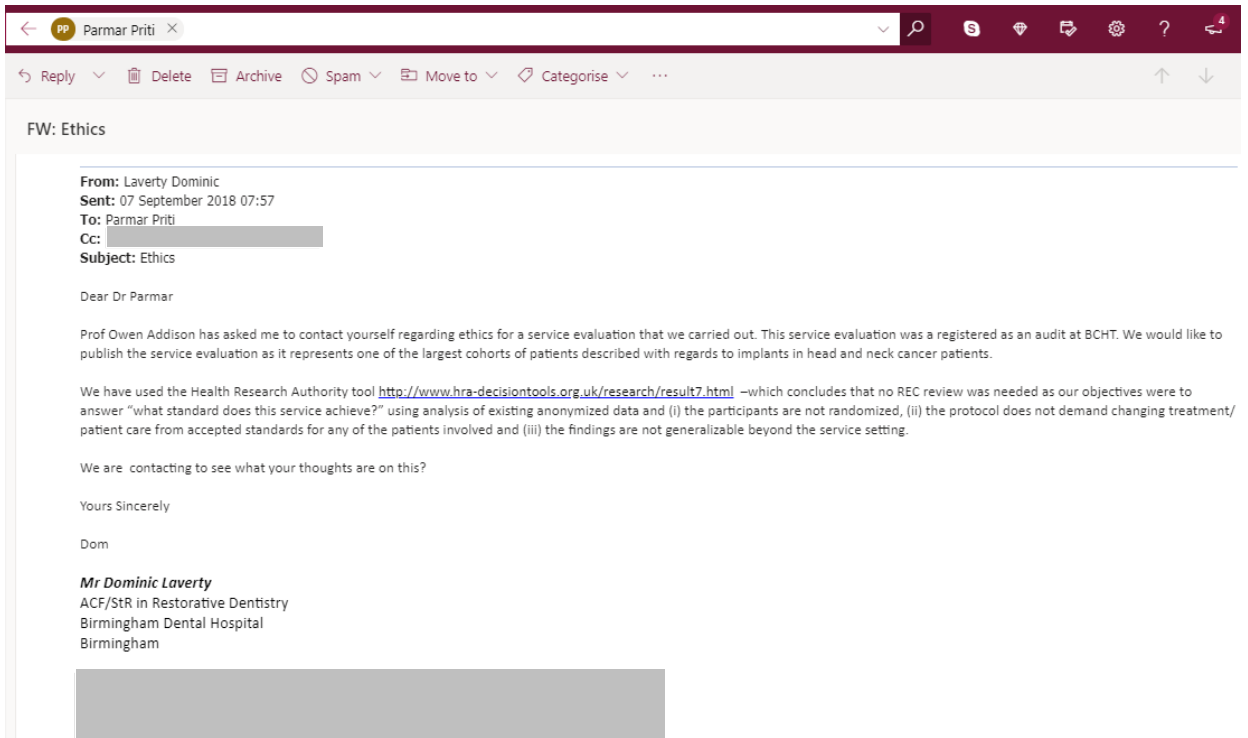
9.2 Copy of Book Chapter

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Oral Prosthodontic Rehabilitation of Head and Neck Cancer Patients

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Introduction

When patients are first diagnosed with Head and Neck (H&N) cancer, their main concern is with survival. However, following cancer treatment their concerns can rapidly shift towards re-obtaining and maintaining a good Quality of Life (QoL) [1]. Oral prosthodontic rehabilitation forms a major component of QoL improvement contributing not only functionally but also psychologically. H&N cancer treatment can leave the patient with significant disability and deformity. Oral prosthodontic rehabilitation aims to address the acquired functional and cosmetic deficits by providing treatment to restore the defect, re-establish oral function, improve cosmetic appearance and allow the patient to interact in society with confidence. Rehabilitation should be patient-centred aiming to meet each individual's unique and specific needs.

Oral rehabilitation of H&N cancer patients often occurs towards the end of the overall care pathway however planning should begin early. Treatment is challenging and requires a multidisciplinary team (MDT) approach to optimise outcomes. [2,3] The dental practitioner involved in the patient care pathway should have received specific training to meet the complex needs of this patient group. The nature of the acquired defect and associated oral conditions following cancer treatment as well as the patient's general health, social, psychological, and economic aspects determine the final treatment outcome of prosthetic rehabilitation. [4] With patient survival following H&N cancer improving, prosthodontic rehabilitation is becoming increasingly important in the post-operative care of these patients and is an integral part of the "success" of their cancer treatment.

Impact of H&N Treatment on the oral environment

Treatments for H&N cancer result in modification of the patient's oral environment which can impact on QoL and general wellbeing. Prevention or reduction of these side effects is a matter of increasing importance especially due to the improvement in H&N cancer survival. Early effects include xerostomia, mucositis and trismus with radiation caries and osteoradionecrosis (ORN) developing later. There is a need to appreciate all of the consequences of H&N cancer treatment on the oral environment and have an understanding of how these can be prevented or reduced.

Osteoradionecrosis

Osteoradionecrosis (ORN) is best defined as "exposed and necrotic bone associated with ulcerated or necrotic surrounding soft tissue which persists for greater than three months in an area that had been previously irradiated (not caused by tumour recurrence)" [5]. Typically, ORN manifests as a breach of the oral mucosa, but more recently it has been recognized that early stages can be revealed radiographically prior to any breach the oral mucosa or cervicofacial skin [6]. In any event, there is a wide spectrum of clinical presentations from slowly progressive bone erosion to pathological fracture that may be early onset *de novo* (within 2 years, especially after administrations in excess of 70Gy) or later after a surgical insult such as dental extractions.

Risk factors for the development of ORN may be patient-dependent or treatment-dependent. Patient-dependent risk factors include a poor dental status, continued alcohol and/or tobacco consumption, advanced age, hypertension, diabetes mellitus

and collagen disorders amongst others. Treatment-dependent factors include the use of hyperfractionation and brachytherapy and the number of surgeries. Concomitant chemotherapy is currently not thought to be a significant risk factor and there is weak data emerging to support the idea that intensity-modulated radiation therapy (IMRT) may be beneficial when compared to other modalities of radiation therapy[7,8]. A number of classification systems exist for ORN. The Marx classification hinges on the theory of a triad of hypoxia, hypocellularity and hypovascularity being responsible for ORN and is subdivided based upon the response of the condition to hyperbaric oxygen (HBO) treatment[9]. Possibly the most widely used classification system for ORN is that published by Notani et al.,[10]:

- Grade 1: ORN confined to alveolar bone
- Grade 2: ORN alveolar bone and/or mandible above the level of the inferior alveolar nerve
- Grade 3: ORN involving the mandible below the level of the inferior alveolar nerve or cutaneous fistula or pathologic fracture

Good dental care and oral hygiene pre- and post-radiotherapy (RT) is of paramount importance in preventing ORN. The restorative dentist is a core member of the H&N MDT and should be involved in planning extractions of teeth that are of doubtful prognosis or are at risk of dental disease in the future and are in an area where there would be a risk of ORN [11]. Beumer et al.,[12] reported that 45% of cases of ORN associated with post-RT extractions required radical resection, compared with 12% of those cases of ORN associated with pre-RT extractions, highlighting the importance of such planning.

For early stages of ORN, management is largely conservative or medical, with the use of regular antimicrobial mouthrinses (such as chlorohexidine digluconate 0.2%) and low dose maintenance antibiotic therapy (most commonly doxycycline 100mg once daily PO) advocated. The use of pentoxifylline and vitamin E (α-tocopherol) is something that has received more attention in recent years as a possible treatment option. Pentoxifylline is a methylxanthine derivative with an anti-TNF- α activity that increases collagenase activity in vitro, as well as inhibiting inflammatory reactions and dermal fibroblast proliferation [13]. Tocopherol scavenges reactive oxygenation species generated during oxidative stress and inhibits TGF- α and procollagen gene expression. The PENTOCLO trial by Delanian and colleagues [14] demonstrated a reduction of exposed bone in 54 patients when combination therapy with pentoxifylline and tocopherol was given along with oral steroids and antibiotics. Hyperbaric oxygen (HBO) therapy is another treatment option for ORN patients that may not always be available due to issues surrounding funding and the proximity of hyperbaric chambers. The rationale arises from Marx's original theory regarding the development of ORN in which he demonstrated a 5.4% incidence of ORN following dental extractions in RT patients given HBO, compared with 29.9% in a group of comparable patients given penicillin alone [15]. These results have not been replicated elsewhere however, with most notably Annane et al.,[16] having to stop their trial early as HBO showed no impact on disease progression or pain relief in a randomized double-blind trial of ORN patients. Gal et al., [17] even went so far as to demonstrate that advanced ORN requiring free flap reconstructions showed worse outcomes when given HBO as this tended to delay definitive treatment. Other trials are under way including DAHANCA-21 looking at the management of established ORN with

HBO and the Cancer Research-UK HOPON trial examining the role of HBO in the prevention of ORN in at-risk patients [18].

With regard to the placement of implants in particular the evidence is controversial. Schoen et al., [19] found that in their small group of 26 patients rates of implant loss were higher in the HBO group (15% compared with 6%). In contrast, Granstrom et al., [20] showed that HBO significantly improved implant survival. A large series of 364 osseointegrated implants published by Shaw et al., [21] showed that HBO had no impact either way on the rate of implant loss. A recently published Cochrane review on the subject has suggested that HBO may offer no benefit but concluded that due to the paucity of data the authors were unable to make firm recommendations either way [22]. Interestingly, the study by Shaw et al., [21] also demonstrated that the use of radiotherapy before placement was not associated with a higher rate of implant loss. This stands in contrast to the systematic review by MacInnes et al., [23] of 10,150 implants across 15 trials that revealed implant failure to be statistically significantly higher in irradiated patients compared to patients who had not undergone radiotherapy.

Xerostomia

Xerostomia is one of the most common late side effects of RT to the head and neck. The effects of xerostomia can be quantified using toxicity criteria provided by the Radiation Therapy Oncology Group and European Organisation for Research and Treatment of Cancer (RTOG/EORTC) [24]. H&N radiotherapy damages the salivary glands, decreasing salivary flow and altering composition. In particular, Moller et al., [25] demonstrated a decrease in the buffering capacity of saliva to 67% of the pre-radiotherapy value and a change to an acidic pH. Glandular changes may be transient and recover over several months or may be permanent. The extent of damage depends on the volume of salivary gland tissue irradiated and the radiation dose and fractionation regimen [26]. Management of xerostomia is typically aimed at addressing symptoms and includes encouraging sipping sugarless fluids frequently, chewing sugarless gum and using carboxymethyl cellulose saliva substitute. Acidic salivary stimulants such as Glandosane™ are not recommended for dentate patients due to their pH being below the critical 5.5. Pilocarpine (a parasympathomimetic that stimulates residual salivary gland function) may also be prescribed [11]. Recent modifications to the way RT is delivered have aimed to maintain or even improve effectiveness, whilst reducing side effects. Nutting et al., [27] have demonstrated a significant reduction of radiation-induced xerostomia for patients treated with parotid-sparing intensity-modulated radiation therapy (IMRT) compared with conventional therapy.

Mucositis

Mucositis is inflammation and ulceration of the oral cavity mucosal lining that can be related to radiotherapy and systemic chemotherapy. Oral mucositis may be associated with significant morbidity with complaints including pain, odynophagia, dysphagia, dysgeusia and malnutrition. Between 30% and 60% of H&N cancer patients receiving radiotherapy will develop oral mucositis and this increases to 90% when given with concomitant chemotherapy [28]. Mucositis can be quantified using the RTOG/EORTC grading system [24]. Alternative indices in common use include, the World Health Organization (WHO) grading of mucositis and the National Cancer

Institute common toxicity criteria [29]. Epithelial cells show a biphasic radiation response in terms of reduction in cell density with a steep decrease exhibited in the first week following radiotherapy and then a more gradual decline as the rapid suppression in cell production is offset by a restoration of cellular proliferation [30]. Mucositis is of particular importance in perioperative care of the H&N cancer patient as it may result in weight loss that cannot be counteracted by nutritional counselling alone. Enteral tube feeding (nasogastric tube or gastrostomy insertion) may be required if mucositis is anticipated that would interfere with swallowing and should be pre-empted and discussed with the multidisciplinary team and the patient and family prior to embarking on treatment [31]. Management options for symptomatic relief of mucositis are varied and can include ice, benzydamine mouthwash and hydrolytic enzymes amongst others [11]. The repair of ill-fitting dental prostheses, effective oral hygiene and removal of compromised teeth may reduce the incidence and severity of mucositis [28]. A recent Cochrane systematic review by Worthington et al., [32] identified ten interventions that had an evidence base: aloe vera, amifostine, cryotherapy, granulocyte-colony stimulating factor (G-CSF), intravenous glutamine, Manuka honey, keratinocyte growth factor, laser, polymixin-tobramycin-amphotericin (PTA) antibiotic pastille/paste and sucralfate.

Trismus

Radiotherapy may cause problems such as fibrosis with resultant trismus in up to 47% of patients, which may also be contributed to by surgical scarring. Trismus can limit the ability to secure a safe airway, oral intake, dental rehabilitation and tumour surveillance [33]. Options for treatment may include intensive physical therapy and coronoidectomy. It has been recommended that frequent dental reviews should be mandated and dental work that had been deferred by RT should be completed as soon as feasible [11]. Limitations in mouth opening can severely compromise dental rehabilitation. When recognised the patient should be instructed to begin exercises to maintain mouth opening as soon as possible. The use of wooden tongue depressors has been shown to be effective. The patient should stack the tongue depressors on top of each other positioning them between the upper and lower front teeth and introducing as many as possible to stretch the facial soft tissues. This position should be held for greater than 15 minutes several times a day. Occlusal splint devices such as the Therabite™ have been also shown to result in improvement in maximum interincisal opening (MIO) with sustained outcomes [34].

Dental Caries

Rampant dental caries may be multifactorial in the H&N cancer patient but is due in no small part to the xerostomia caused by radiotherapy, as well as possibly direct radiogenic damage to the amelo-dentinal junction. Involvement of the dental team should begin early and include intensive oral hygiene advice, a comprehensive dental assessment prior to radiotherapy, dietary advice with regards to caries prevention, fluoride mouthrinses, consideration of topical fluoride therapy or alternative remineralisation agents and regular dental reviews [11, 35]. (Figure 1)
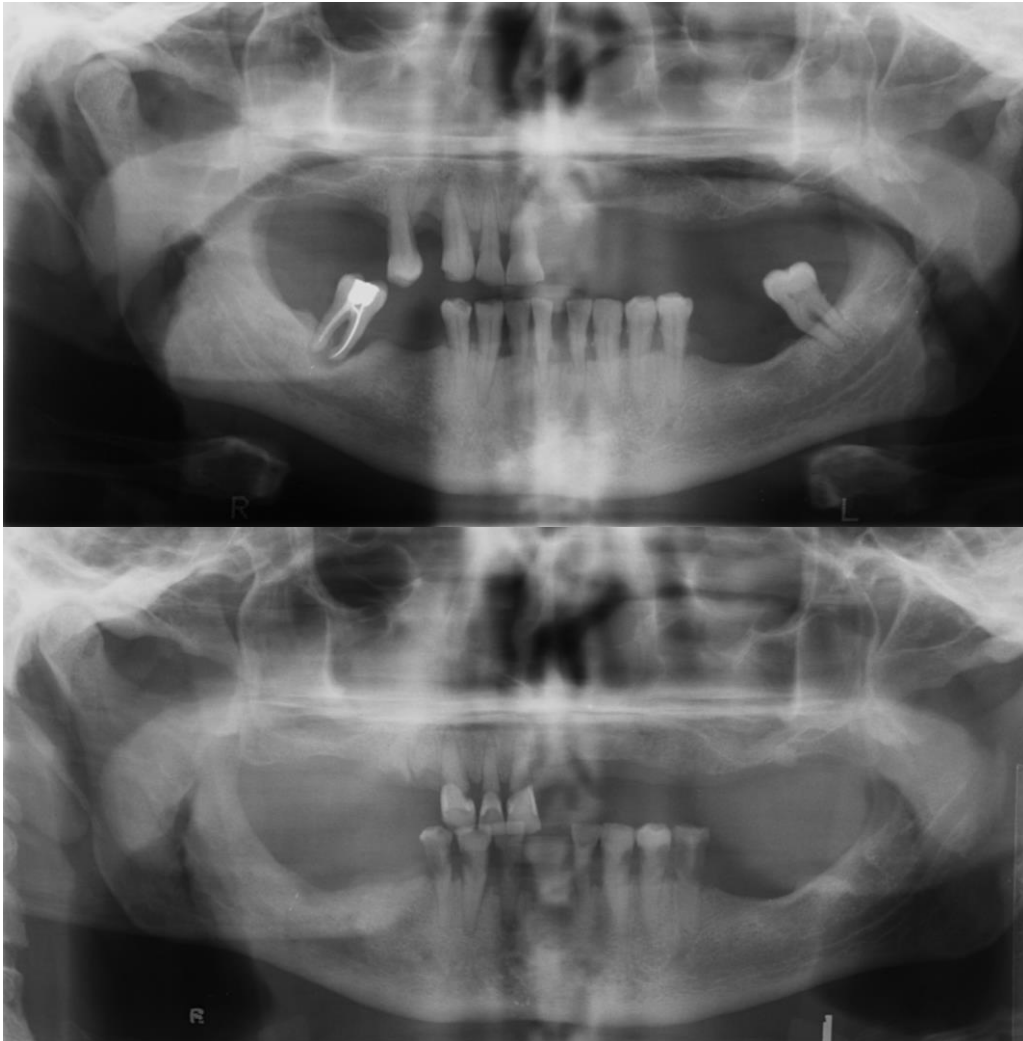
Figure 1: OPT radiograph before and after radiotherapy showing dental caries as an indirect consequence of radiotherapy which rendered the patient edentate.

Opportunistic Infections

Oral *Candida* infections in particular are common following chemotherapy and radiotherapy and opportunistic infections such as this and others (e.g. herpes) should be identified and treated early [36]. Qualitative changes in the oral flora are well-documented following chemotherapy in particular [37]. *Candida albicans* is the commonest opportunistic pathogen in this patient cohort (Figure 2), but less common species may be found, such as *C. glabrata, C. krusei, C. africana and C. guilliermondii* [38]*.* Other opportunistic pathogens in the H&N cancer patient may include *Staphylococcus* and *Pseudomonas* species. There is a propensity for resistance to antimicrobials in this patient population, with a high proportion of *Staphylococcus aureus* isolates being methicillin-resistant (MRSA). Other drug-resistant organisms may include methicillin-resistant coagulase-negative streptococci (MRCNS) such as *Strep epidermidis* and *Strep sciuri* [39]. National guidelines highlight the role for antifungal drugs in preventing oral candidiasis, but nystatin does not appear to work effectively. Chlorohexidine gluconate may have a role but its alcohol content may aggravate mucositis, as well as taking into account its other side effects such as alteration of taste and staining of teeth, which may outweigh benefits [11].

Figure 2: Clinical photograph of the edentulous maxilla of a H&N oncology patient denture induced stomatitis (candida infection) due to over wearing of a removable prosthesis, inadequate denture hygiene and radiotherapy induced xerostomia.

Psychological Impact

As many as 20-30% of H&N cancer patients experience symptoms of clinical depression during their illness, but this may be a conservative figure [40]. Reasons for under diagnosis may include a reluctance to complain, busy outpatient facilities and a worry on the part of the patient that they might become a "burden" for clinicians [41]. Various QoL tools have been designed to elicit psychosocial problems sooner rather than later in H&N cancer. These may include the University of Washington Quality of Life instruments (UW-QoL)[42], the Hospital Anxiety and Depression Scale (HADS) and the patients concern inventory (PCI) [43] amongst others, that may help focus consultations to address patient concerns as well as targeting MDT members that may be best suited to address an individual's key concerns at an outpatient appointment. Psychosocial issues may be easily overlooked by H&N clinicians, with Detmar et al.,[43] highlighting that 25% of patients were only willing to discuss emotional functioning at the initiative of their physician. This trend is particularly pronounced in older and less well educated patients. Prior to surgery, anxiety is greatest, whilst depression tends to be more pronounced following surgery [44]. Anxiety may be heightened by factors such as poorly controlled pain, malnutrition, poor support networks and fear of recurrence [40,44]. Reducing and controlling these contributors, whilst simultaneously providing patients' access to key team members such as clinical psychologists and emotional support therapists, may go a long way to alleviating and underappreciated but important aspect of the H&N patient's journey.

The role of the dentist in the H&N cancer care pathway

Prior to H&N cancer therapy

A significant proportion of patients diagnosed with H&N cancer have less than optimal oral hygiene and have been irregular attendees to a dental practitioner [46, 47]. At the time of cancer diagnosis the majority of patients will require some form of

dental treatment [46,47,48] with a high percentage of dentate patients requiring dental extractions mainly due to periodontal disease [46]. All patients should receive a comprehensive dental examination prior to H&N cancer treatment. It is of paramount importance that an appropriate dental professional performs the clinical examination for H&N cancer patients. Ideally this will be an experienced dental practitioner that specialises in or who has considerable experience of dentally managing and treating this patient group. In an ideal structure the dentist is part of the core of the MDT. This arrangement facilitates prompt management of oral health problems to ensure that H&N cancer treatment is not delayed.

The main purpose of the initial pre-therapy screening is to:

1. Identify and eliminate any dental pathology, by carrying out simple restorative treatment or extractions.
2. Provide oral hygiene instruction and put an oral hygiene and disease prevention regimen in place.
3. Inform the patient of the oral consequences of H&N cancer treatment.
4. Provide a brief discussion on the potential oral rehabilitation treatment(s) following their cancer treatment.

A thorough history, clinical examination and review of special investigations including relevant radiographs should be carried out. Minimizing the risk of oral and dental infection before cancer therapy is performed through stabilisation treatments which include:

- Providing simple oral/dental prophylaxis including oral hygiene instruction.
- Simple treatment of carious teeth that have a good long term prognosis.
- Extracting symptomatic teeth, teeth with questionable prognosis and teeth with active infection that cannot be dealt with in a timely fashion.
- Providing dentures with a simple atraumatic design.

Deciding which teeth to extract and which to restoratively treat or leave is a challenging process and involves an assessment of the risk of long-term complications for each tooth in each individual patient. Whilst there appears to be consensus for extraction of teeth with gross dental pathology, there is very little to aid the decision making process in teeth with intermediate dental disease and the majority of decision are based primarily on clinical experience and opinions rather than evidence-based clinical guidelines [49-51]. This decision making process takes into consideration not just dental factors but also the patient's age, patients preferences, dental awareness and previous motivation and compliance with dental care. Cancer related factors such as clinical staging and tumour location, whether treatment is of a curative or palliative intent, the proposed cancer treatment, the dose and field of radiotherapy, and the immediacy of cancer treatment must also be considered as these will impact on the extent and range of functional deficits that the patient will subsequently acquire. [51]

Treatment planning should happen as part of MDT activities and effectively communicated to all team members. Teeth within the radiation field carry with it a risk of ORN after extraction [52] so in general teeth with doubtful long-term prognosis that lie in the radiotherapy fields should be extracted ahead of radiotherapy commencing. Extractions should be carried out as early as possible: ideally before or at the time of primary surgery if adjuvant radiotherapy is planned and at least 21 days before radiotherapy begins. [53,54] Minimally traumatic extraction techniques are essential and

primary closure of surgical sites should be achieved wherever possible.[55] There is an emphasis on the importance of good daily oral hygiene, and consideration should be given to the patient's compliance and their dexterity. A lack of motivation or compliance in some patients may require careful re-assessment of the long-term likelihood of tooth survival. Dentures should be assessed to ensure a good fit and any sharp edges of teeth smoothed to reduce the risk of trauma to the mucosa which may become more friable following surgery and/or radiotherapy. The patient should also be warned that they may struggle to wear their prosthesis during and after treatment due to discomfort, particularly if undergoing radiotherapy.

The oral and dental side-effects of cancer treatment should be explained to the patient and the family and preventive advice given. Patients should be given instruction on good oral hygiene measures with emphasis on caries prevention. This will include the provision of toothpaste and mouthwash with high fluoride content and provision of fluoride applicator trays which the patient uses with high fluoride supplements. Dietary advice should be given with emphasis on the frequency and quantity of sugar intake. However, care needs to be taken as some patients may struggle to eat and drink before, during or after treatment and may find a sugary diet or use of supplements high in sugar vital to maintaining weight. A careful balance needs to be struck so discussions with the dietician involved in the MDT may be warranted.

The main purpose of the dental assessment is to ensure that unscheduled interruptions to primary treatment as a result of tooth related problems are avoided. Importantly there is evidence to show a reduced survival in patients who have cancer treatment interrupted [56]. The initial assessment stage is also the time to begin planning oral rehabilitation. Useful records that can be acquired include pre-surgical dental study casts for aiding treatment/implant planning and the construction of an obturator; records of the shade and shape of the natural teeth and clinical photographs of the mouth and face to assist meeting cosmetic objectives later on during oral prosthodontic rehabilitation. At the MDT meeting, the dentist should discuss with surgeons, oncologists and radiologists, the proposed H&N cancer treatment plan to understand the dimensions of the proposed resection and express their views on which hard and soft tissue structures would be useful to retain without compromising the tumour resection. Finally, a frank discussion with the patient and if appropriate the family, with regards to oral rehabilitation should be undertaken. Here, gauging the patient's wishes and desires and managing their expectations is essential. Ultimately no promises with a definitive treatment plan can be given due to the unpredictable nature of cancer and its management, but an understanding of a potential proposed plan or an understanding that oral prosthodontic rehabilitation can be carried out at an appropriate time is useful.

During H&N cancer treatment

Comprehensive case planning and pre-emptive dental treatment should result in little dental treatment need during H&N cancer treatment. Wherever possible, active dental care should be delayed until after active cancer treatment however supportive dental care should not be forgotten and oral hygiene maintenance and advice and support on making the oral environment as clean and as comfortable during treatment should be facilitated. Inevitably access to a trained dental care professional may be limited at this stage so awareness of oral care is essential amongst the

general nursing and support team. In some instances, direct input from the dentist is needed such as the provision of an obturator if reconstruction and closure of the defect is not planned and also the planning and placement of implants at the time of surgery (primary implant placement). These will be discussed in later sections.

After H&N cancer treatment

The primary objective is always to maintain the current dentition and where required begin or continue oral rehabilitation. All patients should continue on a strict disease prevention regimen and been seen often by a dental care professional. The frequency of recall of patients who are not receiving active care should be determined by assessing the patient's risk factors. Patients requiring more frequent monitoring include: those with unstable oral health prior to cancer treatment, those who cannot maintain good oral hygiene, and those with significant trismus and xerostomia [57]. Patients who have received radiotherapy are at risk of ORN so extractions should be avoided where possible. Patients with xerostomia as a result of surgery or radiotherapy may require advice on how to relieve symptoms (see xerostomia section) and how to prevent dental disease. Patients who present with new dental caries following dental treatment should be given active prevention which can include the use of topical fluoride in close fitting dental trays. (Figure 3)

Figure 3: Vacuum formed thermoplastic fluoride trays on stone dental models. The trays are designed to hold a reservoir of fluoride gel or high fluoride tooth-paste at the tooth surface and are worn by the patient overnight.

It is important to recognise that only 5–25% of patients require oral rehabilitation after treatment for oral cancer [21, 58, 59], which should be carried out by dental practitioners and technicians with specialist maxillofacial prosthodontic skills to help restore the function and aesthetics lost as a result of the H&N cancer treatment.
(See Figure 4 for a flow chart through the pre, during and post-treatment Restorative management of H&N oncology patients)

Figure 4: Flow-chart of the oral rehabilitation pathway for patients receiving treatment for H&N cancer that result in an oral deficit.
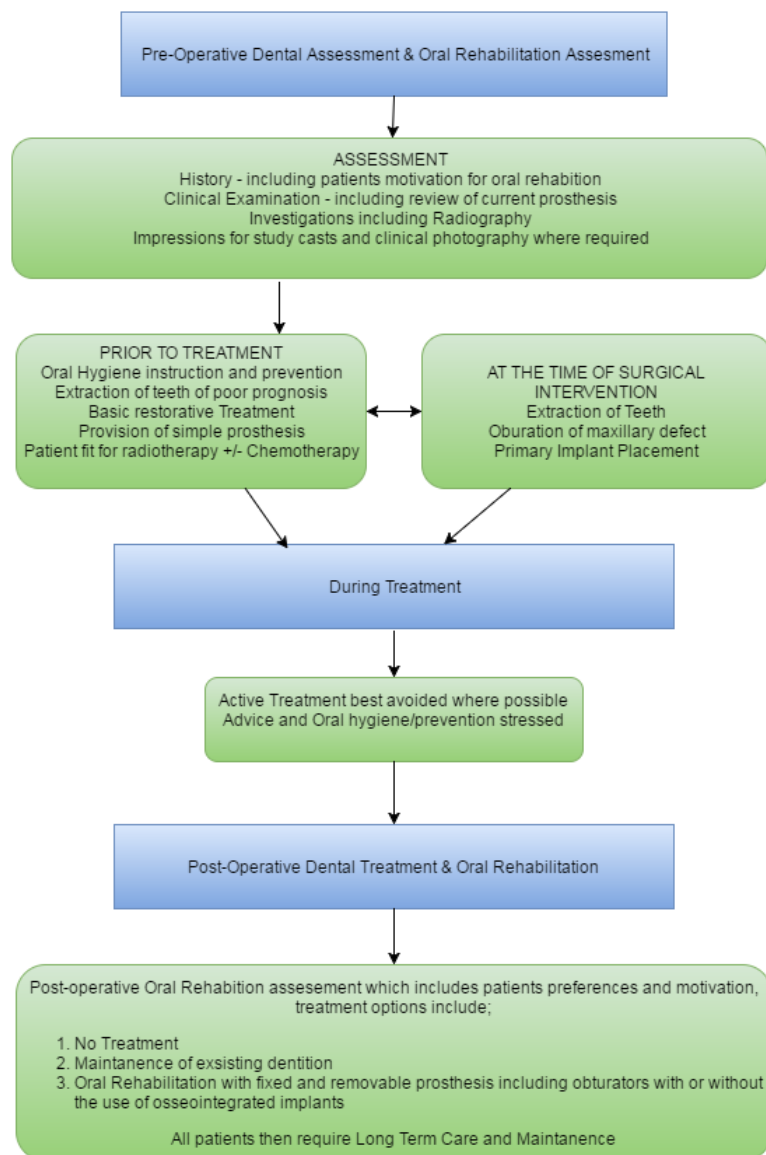
History and emerging trends of dental implants in oral rehabilitation

History of dental implants

The history of modern dental implants begins at the time of World War II when in army service Dr. Norman Goldberg considered applying metals that were used as implants in other parts of the body as anchors in the facial skeleton [60]. In 1948 with Dr. Aaron Gershkoff, he placed the first successful sub-periosteal implant [60]. However, the foundation of implant dentistry as we know it today began in 1957, when the Swedish orthopaedic surgeon Per-Ingvar Brånemark in studying bone healing and regeneration, discovered that bone in contact with titanium formed a robust structural and functional interface without being rejected and this was termed as osseointegration. Further studies were carried out and eventually the first titanium 'root form' dental implant was placed in a human in 1965[60-62]. A number of different dental implant designs have been developed and used in clinical dentistry and are included here as patients with these devices are still encountered.

- **Subperiosteal Implants** - described in 1949 by Drs. Goldberg and Gershkoff [63]. Defined as an implant framework that sits directly onto the bone but is not implanted. It has a saddle shaped design to fit to the buccal or lingual cortical plates and can be used in the mandible and the maxilla. These implants had low survival and success rates [64,65] and are no longer used today. (Figure 5)

- **Transosteal Implants** –described by Dr Small in 1968. Its name is derived from the fact that the implant transverses the superior and inferior borders of the mandible. The implant is inserted underneath the chin with a flat bone plate fixed against the inferior border of the mandible. Several threaded posts projected into the anterior mandible from the plate to be used to retain prosthesis. [66,67] To place this type of implant is highly invasive, requires extensive surgery and is rarely used today. (Figure 6)

- **Ramus frame implant** – used only in an edentate mandible, it comprises a metallic tripoidal device designed to provide a denture-bearing surface. It is inserted into the mandible at the right and left ascending ramus and the symphyses of the mandible[68].

- **Endosteal/Endosseous Implants** – are implants that are inserted directly into the bone and are the main implant type used today. There are a large number of manufacturers with subtle differences in design but generically they are screw and similar in form to the natural tooth root they replace. They have been shown to have high survival and success [69]. Other designs that have historically been used include the blade implant designed by Dr Linklow in 1966. [70] This implant is inserted into a groove machined into the alveolar bone. One or more posts are attached to the fin-shaped plate, which anchors the prosthesis. The blade shaped implant system had poor success but still is occasionally encountered.[71,72]

Figure 5: A subperiosteal implant and bar supra-structure manufactured for an edentulous mandible.

Figure 6: An Orthopantomogram (OPT) radiograph showing a transosteal 'Bosker' implant used to secure a bar retained mandibular complete denture. The implant at the time of the OPT has been in place > 25 years and functions well.

The conical/screw 'root form' endosseous implant forms the mainstay of modern dental implant based rehabilitation due to its high success and survival, [73-75] ease of placement in comparison to other designs and flexibility in its prosthodontic restoration and 'simple' maintenance. Dental implant technologies are constantly being developed to improve clinical outcomes. Innovation is actively being sought to improve surgical techniques, ensure quicker and more predictable healing and osseointegration times, achieve earlier restoration times and improve long-term implant survival. However, dental implants do and will fail and practitioners should be well versed in dealing with this consequence and patients should be fully aware of this before they enter into this type of treatment.

Development of dental implantology as a treatment modality oral prosthodontic rehabilitation

Oral prosthodontic rehabilitation has radically changed over the past 20 years. Defects created as a result of surgical intervention for H&N cancer treatment were often left and rehabilitation relied on using a removable prosthesis to obturate the

defect, replace missing structures including the teeth and restore function and aesthetics [76]. Over the past decade there has been a clear shift towards surgically reconstructing the defect site to close communications between facial compartments and then using dental implant anchorage to retain prostheses to restore the lost function and appearance.

Dental implants began to be used in oral rehabilitation in H&N cancer patients in the mid-1980s with promising long-term observations being first reported by the late 1980s. These revealed that rehabilitation with implants could be successful with improved outcomes in comparison with conventional tissue-supported prostheses.[76,77] Conventional removable prostheses are often poorly tolerated, are difficult for the patient to maintain and can fail to meet the intended design function such as swallowing and chewing. The key deficiencies include poor adaption and stabilisation of the prosthesis due to altered post-surgical anatomy, low salivary flow and a lack of emotional resilience of the patient rendering it difficult, if not impossible to prosthodontically rehabilitate these patients even with the use of reconstructive surgery. [78-81]. A UK study identified that the number of individuals receiving surgical reconstructions has increased from 38% to 91% between 1995 and 2009, with the use of microvascular free flaps becoming more common and the use of dental implants to rehabilitate increasing from 43% to 93%.[82] This shift has also been well reported in the literature in most developed countries. [81, 83-85]. In comparison with removable prosthodontic reconstructions, implant based oral rehabilitation has been shown to be more effective, have a high clinical success with good patient satisfaction. [73, 86, 87] Implants strategically placed are now proven as a therapeutic option to compensate – at least in part – both hard and soft tissue defects of the mandible.

This change in practice has coincided with a decrease in the need for traditional prosthetic obturator provision. [88,89] However despite this shift in practice reconstructive surgery and placement of dental implants may not be appropriate for all patients, such as those patients with significant medical co-morbidities, those lacking suitable donor sites or patients that do not want to embark on this often lengthy treatment pathway. Conventional prosthetic rehabilitation can therefore still be more appropriate and should be appreciated and considered when treatment planning. [81] Dental implant based rehabilitation is certainly more expensive and time consuming often taking several years to complete the definitive treatment. It also requires practitioners that are trained in carrying out the surgical and prosthodontic procedures and with this increasing complexity the need for a multi-disciplinary approach is essential. [2, 90]

Surgical management of H&N cancer and resulting challenges for oral rehabilitation

Reconstruction of H&N cancer patients after ablative surgery has been revolutionized since the introduction of microvascular composite tissue transfer reconstructive techniques since the 1980s which are being increasingly used to rehabilitate this patient cohort. Ablative oncologic defects created to ensure safe surgical margins pose issues for the reconstructive surgeon in terms of restoring form, aesthetics, function and psychological wellbeing of the patient. Maxillectomy defects in particular are challenging with the main two options for rehabilitation being provision of either

an obturator or autologous tissue transfer. The latter option may involve nonvascularised grafts, local flaps, regional flaps or free tissue transfer [91]. Obturators are quick, low cost, and associated with low morbidity and enable regular direct examination of the ablative defect to aid in detection of early recurrence (although there is limited evidence to substantiate this providing a survival advantage) [92]. As defects become larger however (Brown class III defects and above), issues with retention arise, even with implant support. Free flaps aim to overcome the problems of obturators, sealing nasal leakage and the skull base in larger resections, obviating the need to repeatedly clean and revise the prosthesis and may be more acceptable to patients [93]. Patients with poor manual dexterity and/or visual impairment, as well as those with significant trismus following ablative treatment, may have issues with handling obturators. Offset against this is the donor site morbidity of free flaps, longer operating and hospital stays and the potential for failure. A wide array of different options for tissue transfer may be available. Low-level maxillectomy defects may be rehabilitated with options as simple as the buccal fat pad and free calvarial bone grafts with pedicled temporoparietal fascial flaps [93, 94]. Vascularised free tissue transfer options include the deep circumflex iliac artery (DCIA) flap with internal oblique muscle, the scapula flap (figure 7 & 8), the fibula flap and the composite radial [95-98]. Making the choice can be aided by classifying the defect according to its horizontal and vertical components [99] as well as exploring patient expectations in terms of rehabilitation. The flap choice may be further guided by patient factors and co-morbidities (e.g. free fibula flap contra-indicated in instances of peripheral vascular disease and compromised blood flow to the lower limb as revealed on magnetic resonance angiography) (Figure 9).

Figure 7: The tip of the scapula may be a very good match in terms of shape for large maxillectomy defects.

Figure 8: Intra-oral view of a hemimaxillectomy defect repaired with a scapula flap.

Figure 9: A low level hemi-maxillectomy defect in a patient with peripheral vascular disease that precluded the use of a fibula flap

Some authors have argued that defect reconstruction provides better outcomes in terms of swallowing, mastication and speech, particularly for larger defects in the horizontal component [100,101]. Whilst Rogers et al., [93] demonstrated that larger maxillectomy defects had an impact on QoL as determined by the University of Washington questionnaire, no difference between outcomes in terms of QoL have been demonstrated when comparing obturated patients with those receiving free tissue transfer. This has been echoed in a recent paper by Breeze and colleagues [102] who again demonstrated that whilst QoL decreased post-treatment in both groups and patients receiving either an obturator or free tissue transfer scored equivocally. (Figure 10 & 11)
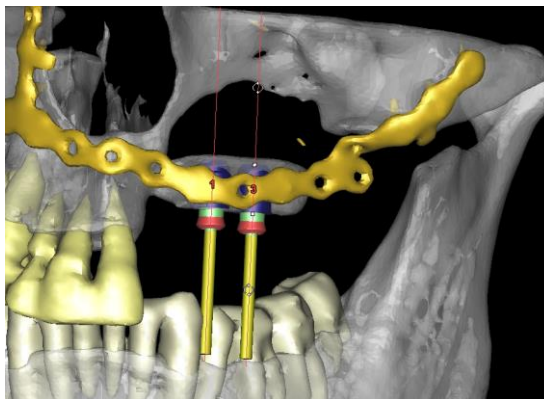

Figure 10: Digital planning for placement of osseointegrated implants in a composite radial flap with custom reconstruction plate.

Figure 11: The definitive implant supported prosthesis in-situ.

Free flap solutions may provide challenges in later prosthetic rehabilitation in terms of scarring of the soft tissue envelope, paucity of keratinized mucosa around prospective implants, disparity in bone quality and quantity among different free flap options and excessive bulk of soft tissue. Subsequent surgeries may be required to debulk soft tissue paddles, restore sulcus depth (sulcoplasty) and/or optimize the peri-implant mucosa through the use of palatal mucosal grafts or split thickness skin grafts as second stage procedures [103]. Smaller maxillectomy defects (Brown class I and posterior class IIb) may require only soft tissue reconstructions such as the fasciocutaneous radial forearm flap with the remaining teeth being sufficient to retain a prosthesis. Adequate soft tissue bulk to "cushion" the tooth-borne prosthesis may be better provided by the anterolateral thigh flap, the thickness of which reduces dead space and the risk of dehiscence [99]. This is one example of planning for the final prosthodontic rehabilitation being a factor in the flap selection. Similarly, the use of muscle in the DCIA flap to obturate larger maxillectomy defects (Brown class III and IV) provides a surface that epithelializes to leave a natural oral mucosal surface with a favourable implant-soft tissue interface in need of little further preparation [92]. Implant planning is certainly a consideration when selecting vascularized free tissue options for mandibular reconstruction. All flaps are not created equal in terms of their ability to support implant-retained prosthodontics solutions and cadaveric studies have highlighted the iliac crest as being the most consistently implantable donor site, with composite radial flaps being significantly less so [104,105]. For reconstruction following segmental mandibulectomy, classification systems such as those published by Urken [106] are again key in helping the surgeon decide on the reconstructive options. Ultimately the decision is tailored to the individual case in terms of the defect, patient co-morbidities and fitness for lengthy surgery, clinician preference and patient expectations. Issues faced by patients with segmental mandibulectomy defects may include alteration of the mechanics of mastication, tethering of the lip and tongue with resultant oral incompetence, dysarthria, dysphagia and alteration of facial appearance, all problems that are aggravated further by adjuvant radiotherapy. Aims of mandibular reconstruction include:

- Optimizing tongue bulk and mobility
- Achieving oral competence
- Maintaining proper occlusal relationships
- Providing bone stock for osseointegrated implants
- Providing a neomandible capable of withstanding occlusal forces
- Re-establishing the lower facial contour

The DCIA offers a pleasing contour at the angle region and also provides sufficient height of a neomandible that can match the dentate native mandible, rendering prosthodontics rehabilitation easier with a more favourable crown-to-root ratio of osseointegrated implants. In addition, it offers lip support and gives a better chance of achieving oral competence [108]. By contrast, the fibula flap matches only the edentulous atrophic mandible in terms of height but is capable of providing sufficient length to address near total mandibulectomy defects and is of particular value when resections involve the condyle of the mandible [103] (Figure 12 & 13). In addition, modifications of the fibula flap (such as the double-barrel fibula or use of vertical distraction osteogenesis of a single-barrel fibula) can optimize its properties to support osseointegrated implants [109]. A further consideration in mandibular reconstruction has an impact on prosthodontics rehabilitation and function are those cases where the mandibular condyle must be resected to ensure oncological safety. The fibula is often the flap of choice as it can be shaped to fit the glenoid fossa and a temporalis fascia flap interposed. Other options include costochondral rib grafts, the sternoclavicular joint, metatarsal and alloplastic temporomandibular joint (TMJ) replacements [103]. Staged approaches using either temporary alloplastic condyles and subsequent rib grafts or alternatively immediate condylar reconstruction and delayed ilium corticocancellous block grafts to custom reconstruction plates on the body of the mandible are also described [110]. Such approaches may further delay prosthodontics work and we favour definitive reconstruction at the time of ablative surgery as rule.
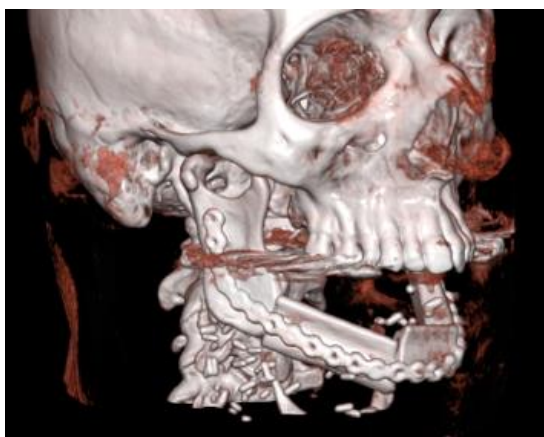

Figure 12: Segmented CT demonstrating a large segmental mandibulectomy defect reconstructed with fibula flap with multiple osteotomy sites, secured with custom pre-bent reconstruction plate.

Figure 13: Clinical photograph demonstrating the mandibular prosthesis supported by implants placed into both native and non-native bone.

General principles of oral prosthodontic rehabilitation

The primary objective of oral prosthodontic rehabilitation is to preserve and restore function, aesthetics, oral competence, swallowing, speech, mastication and the patient's ability to interact effectively within society and maintain psychological well-being [111]. In general, the prosthodontic rehabilitation of H&N cancer patients is challenging and brings with it increased work-load, technical complexity [112,113] in comparison with non-oncology patients [112]. There are a number of principles that should be considered when planning and providing treatment:

The process of rehabilitation begins at the time of initial diagnosis and treatment planning: Treatment planning oral rehabilitation begins early on as part of a MDT approach including surgeons, oncologists and radiologists. Alongside the proposed H&N cancer treatment plan discussion of the state of the remaining dentition and plans to remove diseased or heavily restored tooth units should occur. The dimensions of the proposed resection should be discussed and will guide the development of a provisional oral prosthodontic rehabilitation treatment plan. The plan should then be discussed with the patient and their family. Early planning helps manage patient expectations and can speed up the oral rehabilitation process which can sometimes takes years to achieve the final results. [114]

The dentition should be preserved if possible: This is discussed in more detail elsewhere in the chapter however in general no matter how good the oral prosthodontic rehabilitation is it cannot truly replace the hard and soft tissue structure lost as a result of treatment and therefore all structures should be preserved were possible without compromising the H&N cancer treatment.

Rehabilitative treatment plans should be based on fundamental principles of prosthodontics including a philosophy of preventive dentistry and conservative restorative dentistry [115]: The mainstay of treatment will be based around preserving and maintaining the current dentition. Where the patient requires treatment including prosthodontic rehabilitation this should be based on sound fundamental prosthodontic principles and like any treatment plan were possible should be as simple and conservative as reasonably possible.

Multidisciplinary cancer care is required to achieve the optimal function [2, 115]: An MDT approach is vital to successfully treat this challenging and complex patient group. Input from all parts of the surgical and allied health professional team is essential to help the patient transition through this very difficult journey effectively addressing as best as possible all aspects of their loss of function and appearance.

Each patient is an individual and treatment should be specific to that patient: No "one size fits all" template can be applied to the oral rehabilitation of H&C patients. Each case is individual and decision making is based upon balancing evidence, resources, clinical experience and the patient's wishes. Oral Rehabilitation should be patient centred and patient directed and meets the individual patients' unique and specific needs. Rehabilitation should be discussed early with the patient to understand their motivation and desire for treatment for oral rehabilitation. When assessing patients for oral rehabilitation it is important to appreciate there are a number of factors that can affect decision making and the treatment outcome;

- The prognosis and systemic status of the patient.
- The size and site of the defect – and whether this site has been reconstructed or not; the availability of hard and soft tissues in the defect to support the prosthesis and proximity to vital structures.[116, 117]
- Adjunctive therapy such as radiotherapy that may compromise the surgical result and adjust the treatment plan.
- Patient concerns/issues with function such as oral function, speech, swallowing and aesthetics and the patient's availability, accessibility, and cost of rehabilitative procedures.
- Patient's attitude, resilience and adaptability to cope with a prosthesis. [116,117]
- Patient's ability to maintain good oral hygiene.

All factors should be considered when treatment planning patients to ensure that optimal results are achieved however, even with the best planning there are often changes in the original treatment plan and/or delays in prosthodontic treatment due to the nature cancer or to the patient's recovery from the original treatments. Any potential challenges or complications should be identified and appreciated early on in planning stages whereby it can be alleviated or minimised to ensure optimisation of prosthodontic rehabilitation. [2, 112] When treatment planning the opposing arch should always be considered, along with the presence or absence of natural teeth, residual alveolar ridge form, previous denture-wearing experience, and extent of ablative surgery. For example, success in the mandible with an implant-retained prosthesis may not always be matched by a conventional maxillary denture due to the result of relatively high occlusal forces generated from the mandibular implant prosthesis and a lack of neuromuscular function following surgery affecting muscular control of a maxillary denture and in some cases there may be a case of prescribing implant-retained prostheses in both arches. [118]

Prosthodontic treatment options

There are usually a number of different treatment approaches to provide prosthodontic rehabilitation. Deciding which approach to choose is often not clear and therefore it is an essential part of comprehensive patient assessment to understand the functional and cosmetic deficits and also the individuals' expectations of what oral rehabilitation will provide. It is important that when treatment is provided that it is predictable, and readily maintainable.

In general, prosthodontic options to rehabilitate the oral form and function lost as a result of H&N cancer treatment fall into four main categories;
- Maintenance of a functional dental arch (maintaining the remaining teeth).
- Provision of fixed prostheses using natural tooth structure as the support.
- Provision of removable prostheses.
- The use of implant retained fixed or removable prostheses.

For many patients, maintenance of their existing dentition is the clear treatment of choice with no requirement for prosthetic replacement of missing teeth and/or supporting structures [88,119, 120]. In this particular patient group who often did not possess excellent dental health prior to their cancer diagnosis, it is important to recognise that provision of complex treatments can require considerable behaviour change (oral hygiene, attendance for protracted courses of treatment) to achieve a

predictable treatment outcome. Careful patient selection is essential and as part of informed consent it is important that the patient understands that treatment will often be lengthy and not always successful. A wide variation in the percentages of patients who complete oral and dental rehabilitation following H&N oncology treatment has been reported in the literature (22–91%). [121]

Nowadays in many treatment centres, the final goal of treatment after ablative surgery for oral cancer is considered to be the provision of implant-based oral rehabilitation [81]. Implant-based rehabilitation has been shown to be often more effective than conventional rehabilitation with in particular removable prostheses [122]. Many patients who have had no previous denture-wearing experience prior to ablative cancer surgery find adapting to a removable prosthesis extremely difficult, particularly when there is loss of neuromuscular function and creation of unfavourable denture bearing anatomy following the initial surgery. [118] Implant-based rehabilitations are not suitable for all patients and indeed many patients want to avoid further surgeries after their initial cancer management. In these cases, careful assessment is needed to determine whether a conventional removable prosthesis will adequately address the patient's functional and cosmetic deficiencies. It has been shown that treatment with conventional prostheses can be highly successful. [165, 123, 124] If conventional treatment cannot be implemented due to anatomical barriers, or if treatment has been tried and is has been poorly tolerated then patients may subsequently be considered for secondary implant-based treatment.

The implant retained fixed prosthesis

A fixed implant reconstruction is a prosthesis that is supported and retained by osseointegrated implants and permanently secured in position so that it cannot be removed by the patient. A fixed implant prosthesis can be used to replace single teeth or multiple missing units (implant-retained fixed partial dentures (bridgework)). Fixed reconstructions are generally thought to be the preferred options for most patients [118] with improved patient comfort, psychological well-being and superior chewing performance being reported in comparison to implant retained removable prosthesis.[125] Fixed reconstructions are particularly useful in patients that have had radiotherapy which makes the soft tissues friable and more susceptible to trauma particularly when the patient suffers from xerostomia.[118, 126] Fixed reconstructions are often more challenging to plan and execute than removable reconstructions and the success of a fixed prosthesis is dependent on an increased implant number and the precise positioning and angulation of the implants in comparison to its removable alternative. [118] Optimal implant positioning is more readily achievable when implants are placed secondarily to ablative surgery due to the increased time available for planning. General principles dictating the number, type and position of dental implants required has been gained from evidence based on rehabilitation of "healthy" mouths not associated with oncology. For fixed full-arch reconstructions placement of 6 to 8 implants is recommended for the maxilla [127,128] and a minimum of 6 in the mandible.[129] However this is a guide and ultimately whatever the prosthetic approach is decided upon the prosthesis must be adequately supported by an appropriate number of implants to ensure longevity of the implants and the prosthesis. As fixed in comparison to removable reconstructions require mores supporting implants there must be an adequate volume of bone to accommodate the implant fixtures. When

this is lacking bone grafting procedures for implant site preparation may be required which is not be appropriate for all patients. [130,131]

Correct implant angulation and positioning is important to ensure that implants are placed within the "prosthodontic envelope" with a good anterior-posterior spread to provide even favourable biomechanical loading. Implants should be loaded along their long axis and where this isn't achieved there is risk of implant and/or prosthetic failure. Implants should be placed parallel to one another so there is a common path of insertion of the prosthesis into the implant fixtures. Small divergences between implants can be compensated for by tolerances built into the prosthetic implant components but wherever possible this should be avoided. A common finding in the implant outcomes literature for this particular patient group is the report of unfavourable positioning and/or angulation of implants [132] leading to fixtures being deemed unrestorable and unusable in the final reconstruction. The prosthesis design should where possible incorporate features that allow it to be both cleansable and allow direct visualization of the underlying tissue to assess for tumour recurrence. Whilst this is often possible in the posterior dentition, anteriorly it may not always appropriate for either a functional or cosmetic reasons. [125] Fixed reconstructions are typically more expensive, take longer to complete and therefore may not be appropriate when finances and time are restricted. [130,131] (Figure 14 & 15)
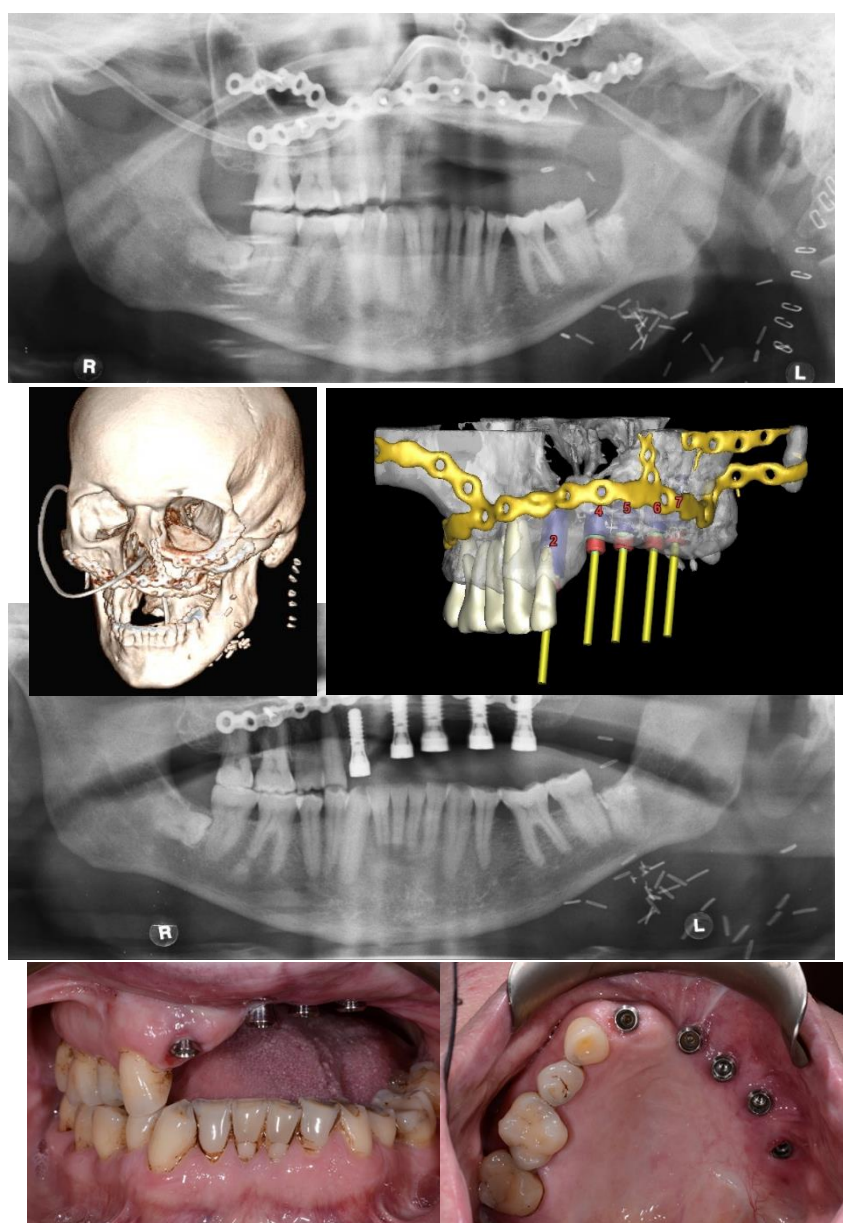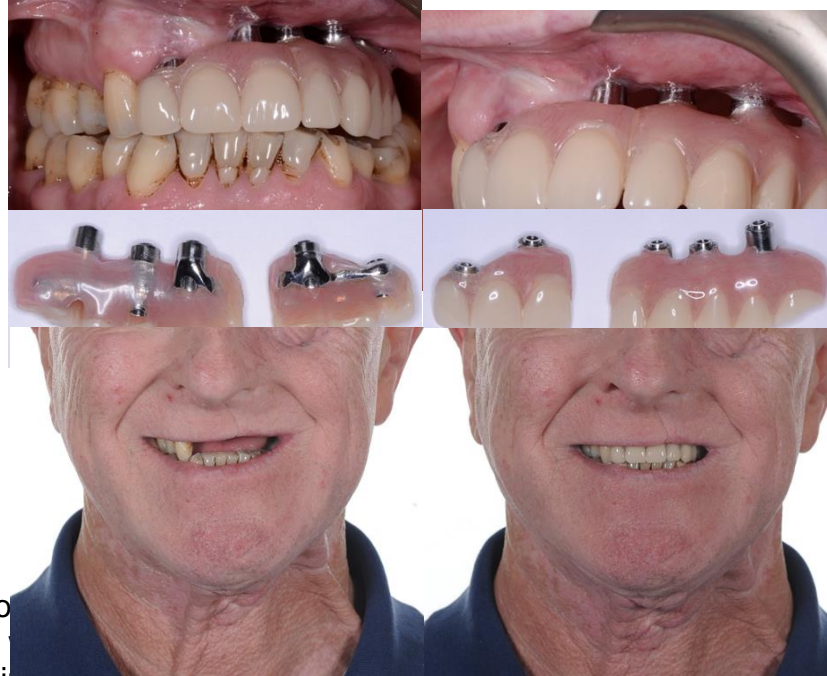
Figure 14: sho... ...section and reconstruction ... ...noma of the left maxillary sinus. Implants planned using a reformatted CBCT for SIMPLANT planning software and Straumann Standard Plus RN (Tissue level) Implants placed and restored with screwed retained fixed prosthesis on an ATLANTIS (Dentsply) ISUS CAD/CAM superstructure HYBRID TITANNIUM Framework.

Figure 15: showing fixed implant retained reconstruction after surgical resection and reconstruction with a DCIA flap of the left maxilla due to an SCC of the left maxillary sinus. Straumann Standard Plus RN (Tissue level) Implants placed and restored with screwed retained cantilevered fixed prosthesis on an ATLANTIS (Dentsply) ISUS CAD/CAM superstructure HYBRID TITANNIUM Framework. Note the lack of keratinised tissue surrounding the implant fixtures.

Removable implant retained prosthesis

A removable implant retained prosthesis is supported and retained to varying degrees by both the implants and the denture bearing tissues and can be removed by the patient for cleaning. When considering the choice between fixed and removable implant based reconstructions it is essential not only to consider the replacement of missing teeth but also of the supporting structures. Frequently clinical situations present in this patient group where there is excessive alveolar ridge resorption, large acquired defects in the denture bearing areas or unfavourable anatomy particular, when there is a loss of facial support of the lips and soft tissues of face. Additional volume can be incorporated into removable prostheses to replace these supporting structures. It has also been reported that removable prostheses in comparison to fixed have been shown to be associated with fewer problems with regards to phonetics and saliva control.[118]

A removable prosthesis is also preferable where reconstruction or resection of bone creates a large vertical discrepancy between the bone and the proposed occlusal plane. This is particularly true in mandibular resections and reconstructions with a single barrel fibula free flap placed on the inferior border of the mandible in order to re-establish symmetry in the lower third of the face (Figure 16).[125] Fixed reconstruction may not be ideal in such cases due to lack of bone height leading to

the use of shorter length implants, lack of bone volume to accommodate a reasonable number of implants, the amount of hard and soft tissue that needs to be replaced by a fixed reconstruction and also their being an unfavourable implant–crown ratio due to the vertical discrepancy whereby the implants need to support long crowns to reach the occlusal plane, with the risk of unfavourable forces being loaded and potentially jeopardizing long-term implant survival.[132, 133] Removable reconstructions in general require fewer implants to support the prosthesis. For an implant retained complete overdenture it is generally accepted that in the mandible 2 implants in canine region is the minimum number of implants required. [134,135] In the maxilla more implants are required to support the overdenture with preferably 4 to 6 implants utilised with a reasonable anterior-posterior spread. [135] Removable reconstructions are also favoured when there is inadequate clinical access to enable surgical placement and restoration of implants (usually in more posterior regions of the mouth) and when patients are unable to maintain good oral hygiene around the implants/prosthesis as a result of poor motivation or lack of dexterity.

A variety of retention systems can be used to retain an implant retained overdenture. The retentive systems can be classified as to whether the implants are splinted together or free standing.[136] Splinted implants utilise some form of interconnected bar to connect/splint the implants whereas free standing anchorage abutments are not directly linked together. The most suitable retention system should be hygienic; able to atraumatically and evenly distribute stresses both mechanically and biologically [137]; should retain the prosthesis but enable simple insertion and removal and should be easy to adjust or replace components as and when they fail. The design of the prosthesis and the retention system needs to be considered especially following radiotherapy [21] where loading on dry and friable tissues may lead to discomfort and inflammation. Bars connecting multiple implants are generally preferred around these areas with an aim to reduce the load on the vulnerable soft tissues. There are a numerous systems available that include; Locators, Bars and Clips, Stud attachment and magnet attachments. The decision on which system is going to be utilised should be considered early in treatment planning as this will dictate the number and positioning of the implants. (Figure 17 & 18)
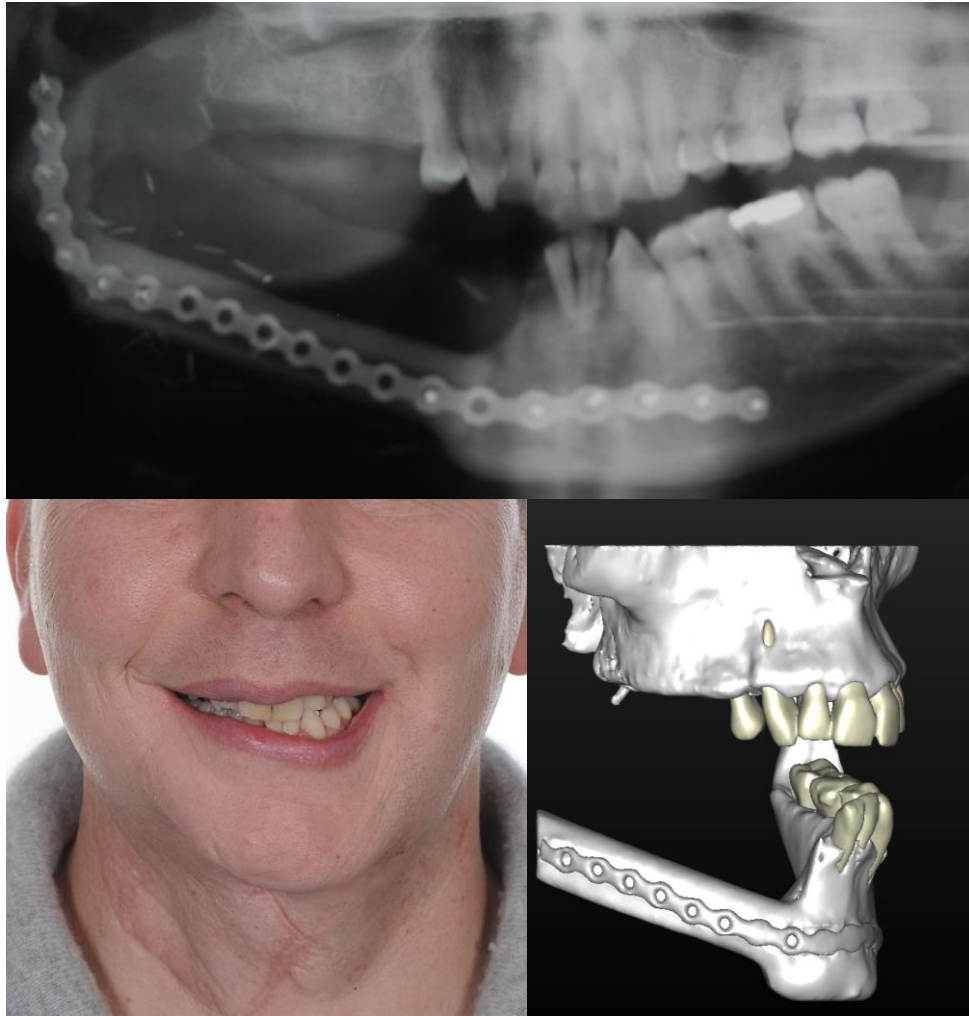
Figure 16: CT scan and OPT radiograph showing sectional mandibuloectomy and reconstruction with a single barrel fibula free flap – note the vertical discrepancy between he fibula bone and the remaining native mandible as the fibula bone is placed along the inferior border of the mandible to provide a good facial profile. Also notes the deep soft tissue overlying which is unfavourable for restoration and required surgical debulk at the time of implant placement.
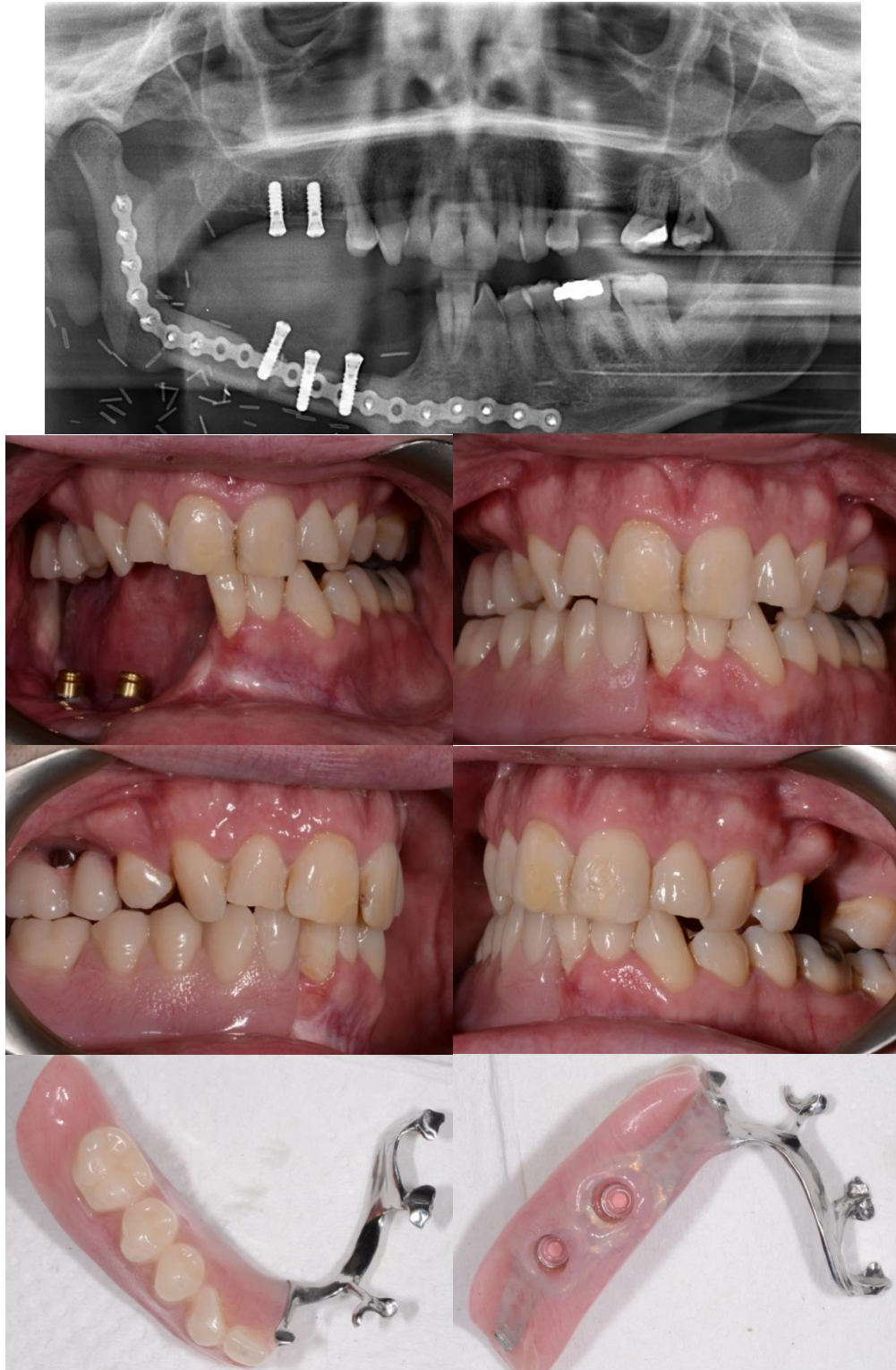
Figure 17: A mandibular implant retained removable prosthesis on Locators (Zest) note the amount of hard and soft tissue that required restoring due to the vertical discrepancy between the fibula bone and the occlusal plane. The upper right maxilla was restored with a fixed prosthesis and designed to allow easy access for oral hygiene.

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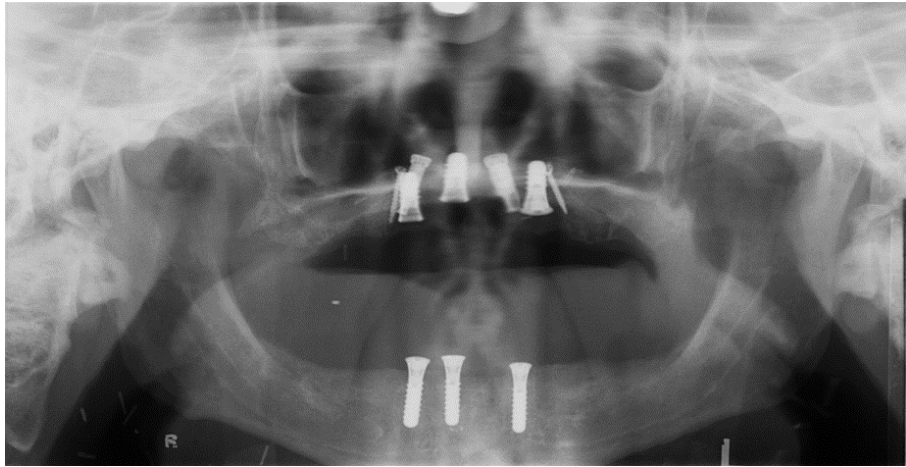
Figure 18: Upper and lower implant retained overdentures. Due to a lack of bone of available to accommodate implants the hard palate was unconventionally used. Implants were also placed for a nasal prosthesis. The patient had previously had an SCC nose requiring a rhinectomy and reconstruction with a radial composite flap to upper lip.

Conventional removable prostheses

To provide a conventional prosthesis can be challenging despite the advancement of surgical reconstructive techniques. Patients often have a reduced ability to control conventional dentures due to the effects of treatment for H&N cancer, as the surgery and radiotherapy can lead to an unfavourable denture bearing anatomy, friable soft tissues and xerostomia [83]. Furthermore, the loss of sensory and motor functions which are important in attaining neuromuscular control are unpredictable at the

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commencement of treatment. In general patients who have never used a removable prosthesis previously tend to struggle to adapt most. The unfavourable denture bearing tissues can include a lack of alveolar ridge height and width or even loss of denture bearing tissues altogether. Reduced sulcus depths make it more difficult to attain a peripheral seal for the denture base and tightly bound or firm tissues or conversely thick and mobile overlying soft tissues impact on prosthesis stability (Figure 19). Composite tissue flaps which commonly present an abundance of soft tissues can be highly unfavourable for prosthodontic loading and further surgical intervention to debulk these tissues may be required.

The ability of the patient to cope with a removable prosthesis varies and is dependent on the configuration of soft and hard tissues, the presence and distribution of teeth, the presence or obliteration of the sulci, tissue support, extent of mouth opening, the maxillo-mandibular relationship, the quantity and quality of saliva, oral sensation and musculature, and the function of the residual tongue. [51] Previous to the now routine use of dental implants, conventional prostheses were the mainstay of prosthodontic rehabilitation and should always be considered as the first line of treatment (Figure 20). Due to the abnormal anatomy of the denture bearing tissues, the distribution of loading should be considered in particularly in irradiated sites which are more vulnerable to soft tissue trauma and to a small risk of osteoradionecrosis [138]. Loading must also be minimised at the tumour site so that any changes in this site are recognised early and not considered to be related to poorly fitting prosthesis.
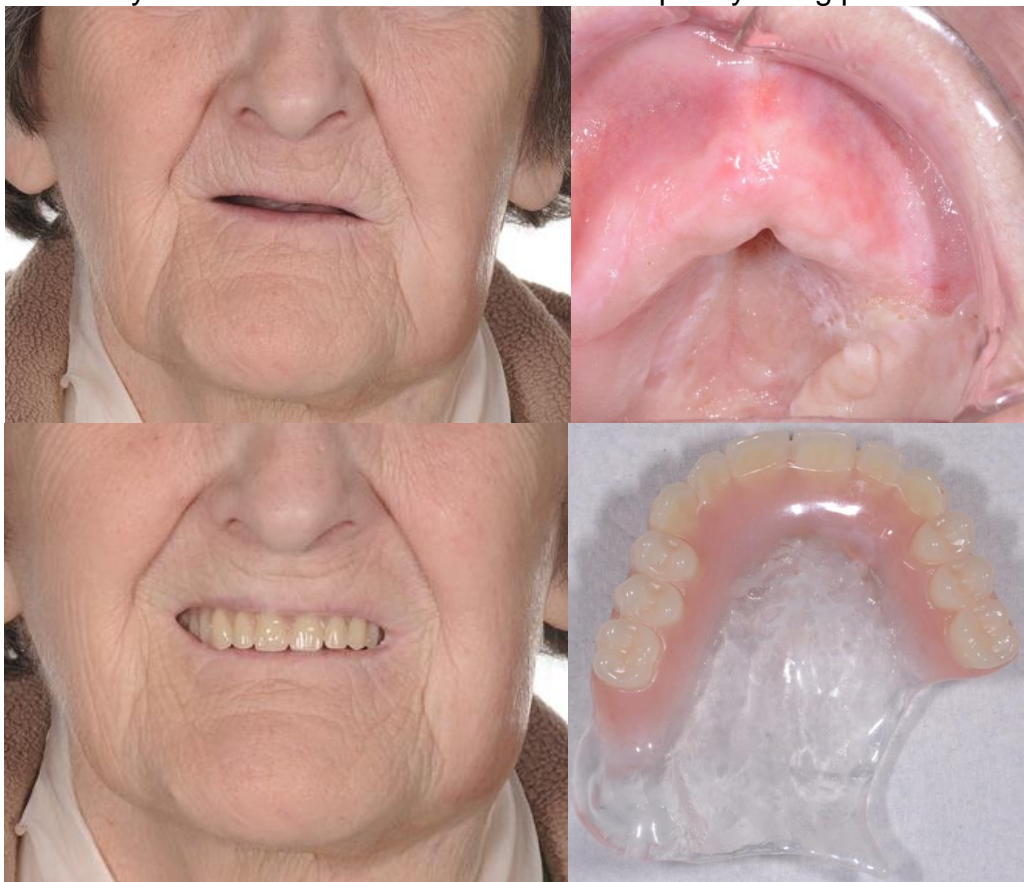
Figure 19: A patient with a sectional coverage complete upper complete conventional denture replacing the maxillary dentition following SCC of the left retromolar trigone and reconstructed with a soft tissue flap. This site was not loaded

due to the unfavourable denture bearing anatomy of flabby and mobile soft tissue and a lack of sulcus. The patient opted not to have implants placed due to the risk of ORN.

Figure 20: Historical prosthodontic models showing a patient restored with a complex two-part removable conventional prosthesis after surgical resection of the anterior mandible and glossectomy

Obturators

An obturator is a removable prosthesis that is used to close a defect of the maxilla as a result of a partial or total removal or a congenital defect. It can either be retained conventionally or by implants. Surgical removal of the palate by ablative surgery creates a significant anatomical defect that allows the oral cavity, maxillary sinus, nasal cavity and nasopharynx to become one confluent chamber. This impacts on speech, swallowing, and chewing. It allows the passage of food and liquids to pass from the oral into the nasal cavity and creates an unnatural hypernasal speech due to air movement from the oral cavity into the nasal passages.[139] Post-resection management of the defect can be either surgical closure or prosthetic rehabilitation with an obturator. The clinical decision is multi factorial and requires an MDT approach. [113,140,141] Ideally patients with such defects are surgically reconstructed. However, this may not be appropriate for all patients due to significant medical co-morbidities, lack of suitable donor sites or the patient is unwilling to have further

surgery. For these patients, prosthetic obturation may be more appropriate. Dental/zygomatic implants can be utilised to improve the retention of a maxillary obturator.

Some of the advantages of obturating a maxillary defect include the provision of an immediate set of teeth, the ability to restore cheek support with the prosthesis, the ability to gain support/retention from within the resected site and also ability to remove the prosthesis to visualise the surgical site for re-occurrence. However, obturators often require adjustments and replacement soon after initial surgery. [142] Patients may also feel an uncomfortable reminder of the cancer as a result of the defect [143] and can be totally dependent on the obturator for eating and speech. Fabricating a retentive prosthesis over the reconstruction can be difficult and implant anchorage may subsequently be required [142]. Factors which contribute to the retention of an obturator include:

- Number of position of teeth to help retain/support the prosthesis.
- The size of the ablative surgery the larger the resection particularly of the denture bearing tissues
- Design of the Prosthesis;
- The amount of undercuts within the surgical defect to retain the prosthesis conventionally.
- The use of dental/zygomatic implants.

The use of implants can dramatically improve the retention and function of obturator prostheses and especially in edentulous patients. However, the use of implants is complicated by the age of the patients, the use of radiotherapy and high recurrence and mortality rates within this patient population and so needs to be carefully considered. [144,145]. The most desirable site for implants in most edentulous maxillectomy patients is the residual pre-maxillary segment. This is a preferred site due there usually being an ample volume of bone to accommodate implant placement and the fact that the anterior maxillary segment is diagonally opposite the most retentive portion of the defect which is the skin-lined posterior lateral wall. The maxillary tuberosity, posterior alveolar ridge, and the zygoma are considered secondary implant sites. (Figure 21)
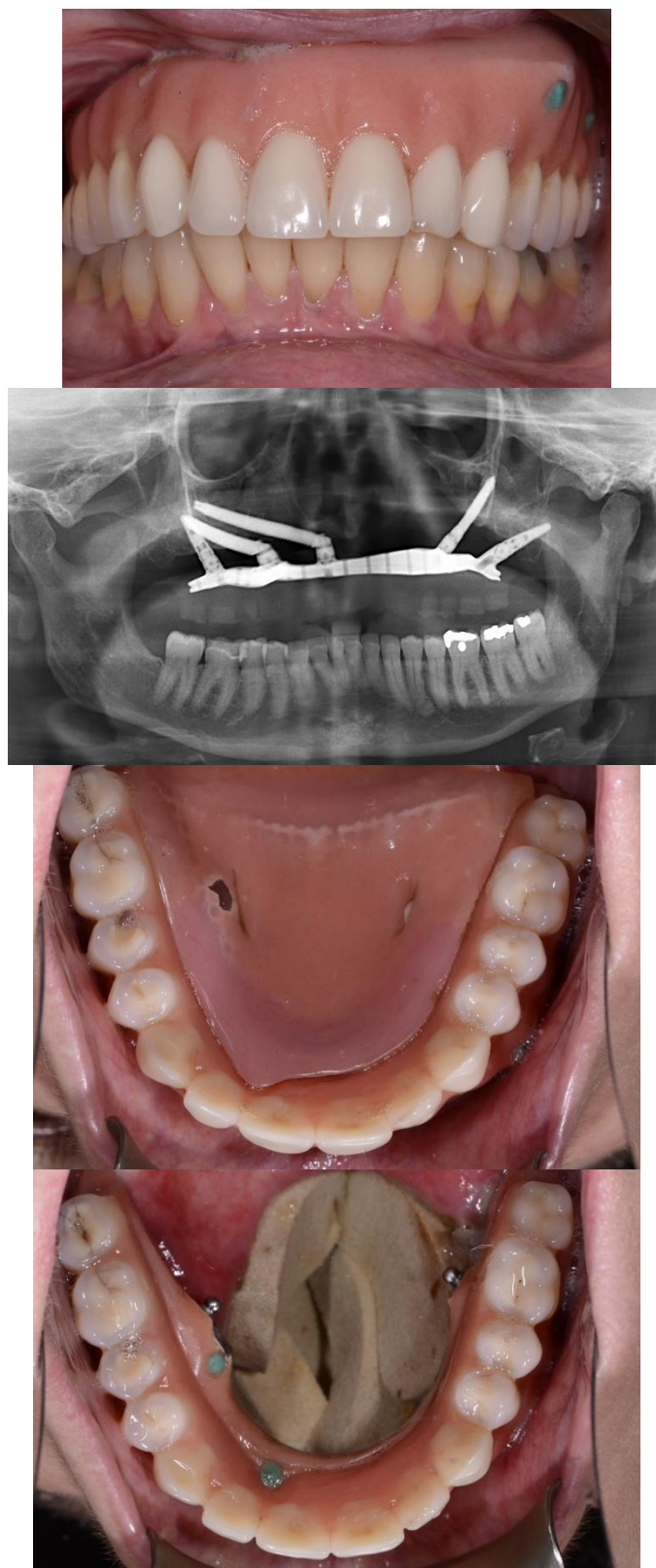
Figure 21: shows a fixed full arch maxillary implant retained prosthesis on zygomatic/pterygoid implants with a removable section in the mid maxillary region retained by precision ball attachments to act as an obturator and also allow surgeons to visualise the surgical resected site. The patient was historically treated with surgical resection for a Wegners granulomatosis

Surgical obturators

The immediate surgical obturator serves as the initial interim prosthesis to restore vital oral functions and to a lesser degree aesthetics. It can preserve he patient's morale and the surgical cavity and facial form. The prosthesis is constructed from a pre-operative cast or a copy of an existing satisfactory complete maxillary prosthesis. It is important at the pre-surgical planning stage to discuss with the surgeon the approximate surgical boundaries of the resection and discuss any area that may provide natural undercuts to help aid retention and support for the appliance without compromising the resection itself. The obturator is fitted by the prosthodontist or a maxillofacial technician using materials such as silicone putty or impression compound. It is important to ensure it is well adapted, can be fully seated and supports the normal facial contours to minimise scar contracture and disfigurement.[51] The obturator is then fixed in position using either titanium anchorage screws, clasps engaging the remaining teeth or transnasal and zygomatic wires.[146] After 7−10 days, the surgical obturator can be removed.[115] Impressions can then be taken if needed for a further interim obturator to be made.

Interim obturators

After a period of healing of at least 7-10 days and preferably 6-8 weeks the immediate obturator is replaced by an intermediate prosthesis. This is required as the will be rapid remodelling of the adjacent tissues during the first stages of wound healing and the immediate obturator will become loose and less effective. The aim of this procedure is to develop a stable and comfortable intermediate prosthesis. Once provided the patient should be reviewed regularly every 2−4 weeks as further soft tissue changes will occur during the first 6−12 months post resection.[147] The interim obturator will need periodic modification for better adaptation as the healing progress using tissue conditioners and denture reline materials. Good oral hygiene is essential to prevent soft tissue inflammation and denture stomatitis.

Definitive obturator

After a period of 6-12 months post-resection a clinical assessment needs to be made that the surgical site is stable and local cancer recurrence has been excluded. At this point only can the definitive obturator be considered and this time-period is inevitably a range as surgical healing will differ between patients.[148] Although obturator provision is challenging due to the absence of suitable abutment teeth, trismus, reduced denture support area and other co-morbidities, a well-made prosthesis can significantly improve a patient's QoL (Figure 22). Where possible the prosthesis should be supported on a firm base which include the teeth, the remaining denture bearing tissues and any other appropriate anatomical structure including the floor of the orbit, pterygoid plate and nasal septum.[116] The section of the obturator filling the acquired void is term the 'bulb' and obturators bulbs can either solid or hollow and the latter may have an open or closed tops. [51] Hollow bulbs reduce the weight of the prosthesis which is better for the soft tissues at the surgical site and improves retention of the prosthesis and comfort for the patient (Figure 23). [149]
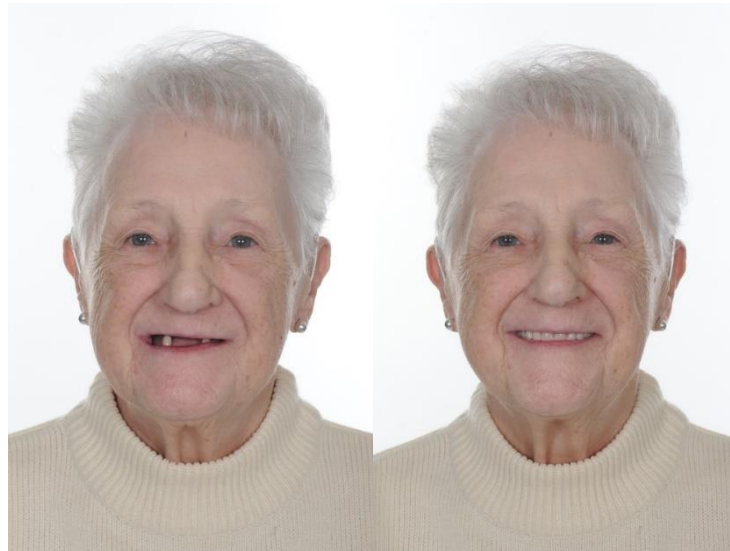
Figure 22: Demonstrating a small defect post-surgical removal of a mucoepideroidmid carcinoma resulting in an oro-nasal communication. A complete denture obturator was provided to seal off the defect.

Figure 23: An upper complete definitive (hollow box) obturator and lower complete removable prosthesis. (note the hollow box portion has 2 holes – the hollow portion was created using pumice/plaster to fill the hole of the defect for acrylic to cured around it. The 2 holes are then created to remove the plaster/pumice in the defect to create a hollow space, making the prosthesis much lighter.)

Challenges and complications in achieving oral rehabilitation

As previously outlined there are many challenges in the prosthodontic rehabilitation of H&N cancer patients. These challenges often lead to changes in the original treatment plan and/or delays in prosthodontic treatment. Any potential challenges or complications should be identified and appreciated early on and were possible in planning stages however this is not always possible. The following are some of the most common issues faced by the dentist and the patient care team.

Patient and family expectations. Expectations can be high and need to be carefully managed. No matter how well the surgical and prosthodontic rehabilitation is executed, it will never truly replace the hard and soft tissue that that patient has lost nor restore the patient to how they were cosmetically and functionally before their cancer diagnosis. Good communication is essential and the patient must understand the limitations of what can be achieved and the difficulty of the task of carrying out prosthodontic rehabilitation. Patients must also be aware of the long term care and maintenance that is required and their central role in maintaining good oral health. Building a strong rapport with the patient and their family is one of the most important factors influencing the progress and often outcome of treatment.

Sub-optimal implant positioning and angulation. This is well reported in the literature as a common problem in this patient cohort. Implants are often placed where there is adequate bone rather than in the optimal position for prosthodontic rehabilitation (Figure 24) [118,150,151] and is particularly true at reconstructed sites. It also may be impossible to place implants in certain anatomical sites due to the inadequate access to surgically place the fixture and a compromise alternative site may need to be agreed upon. [76] By ensuring good pre-operative planning the likelihood of implant being placed in an unrestorable position is minimised. Some of the challenges experienced when implant planning include a lack of bone volume, the presence of reconstruction screws in the ideal implant site, anatomical structures such as the maxillary sinus, inferior dental nerve and irradiated sites. If implants have been placed in a sub-optimal position there are prosthodontic solutions which can be applied, however there are limitations and the final prosthodontic rehabilitation will be less predictable, more time consuming and more expensive.

Figure 24: These images show unfavourable implant angulation (image 1) and unfavourable implant positioning (image 2)with the upper right implant being placed too far buccally and outside the prosthodontic envelope leading to a bulky prosthesis in this region.

Lack of Bone volume for implant placement. Implants can only be placed where there is adequate bone volume. Where there has been surgical resection or reconstruction there may be a lack of bone volume to accommodate an implant fixture. Careful consideration is required to assess if other sites would be amenable to implant placement or whether further surgery to enhance the bone volume prior to implant placement is indicated. Good pre-operative planning and use of CBCTs with implant planning software can help improve the predictability of transferring planned positioning into clinical reality. (Figure 25)
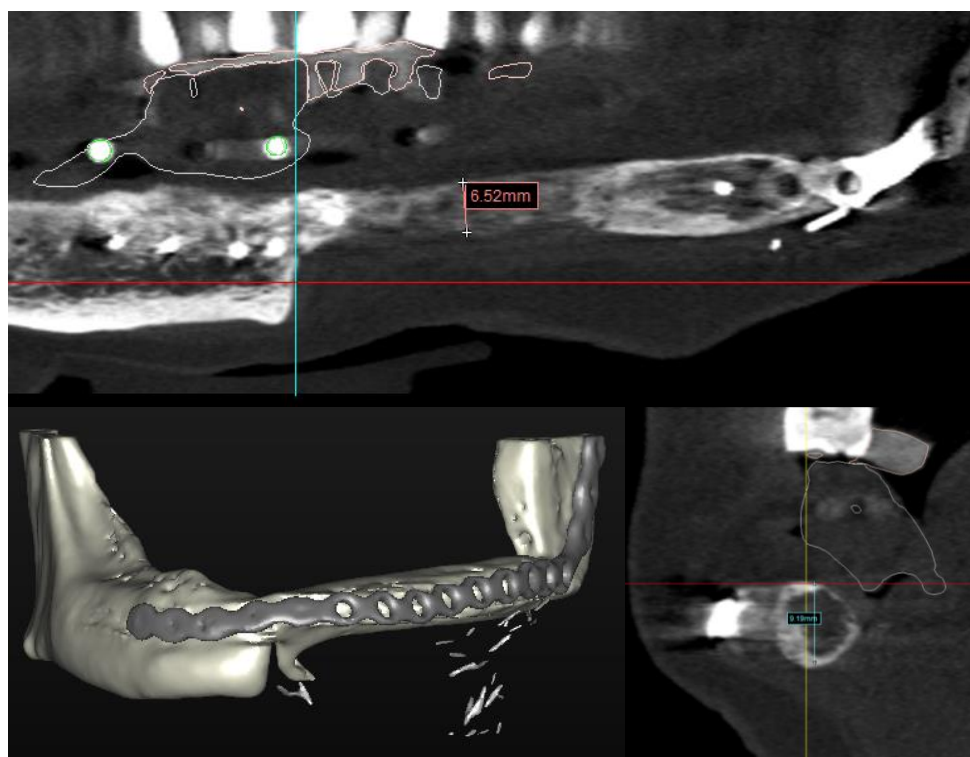
Figure 25: CBCT imaging of fibula free flap being used to assess and confirm in this instance a lack of bone height to accommodate implant placement.

Microstomia/Trimsus. Trismus commonly occurs as a result of surgery and/or radiotherapy and can lead to restricted of intra-oral access [152] making prosthodontic rehabilitation more challenging. It is important to monitor and record mouth opening and note its restriction as part of the treatment planning process. Many implant providers will supply an intra-oral guide to assess whether there is adequate intra-oral access to place an implant fixture. (Figure 26)

Figure 26: A Straumann diagnostic T Tool which can be used to gauge whether there is adequate intra-oral access to prepare the implant bed and place the dental implant.

Peri-implant tissue health and hygiene maintenance. Poor oral hygiene is commonly reported in this patient group [118,153] and these patients are at a higher risk of dental disease including dental caries and periodontal disease. Poor oral hygiene and plaque accumulation around implants can lead to peri-implant mucositis (Figure 27), and subsequently to peri-implantitis –which can be defined as peri-implant inflammation associated with progressive peri-implant bone loss. Peri-implantitis in H&N oncology patients has been shown to be higher than in the general population. [154,155] There is also a tendency for peri-implant soft tissue overgrowth particular around implants penetrating soft tissue flaps with a characteristic doughnut like lesion of hypertrophic tissue observed. Treatment is aimed at maintaining good oral hygiene at these sites but in some cases surgical debulking may be required and long term soft tissue grafting to improve the peri-implant tissue biotype indicated [21].

Figure 27: Clinical images showing poor oral hygiene around implants leading to a tissue response of peri-implant mucositis and hyperplasia.

Failure of autogenous grafts. The autogeneous grafts that are used to reconstruct the acquired defect or to prepare a site before implant placement can fail. This may be as a direct consequence of implant placement into the graft area or due to unrelated factors. Graft failure will limit implant site options and may lead to a clinical decision to not proceed with implant based reconstruction.

Xerostomia. The quality and quantity of saliva have been shown to play a significant role in retention of dentures. [156] Lack of saliva can also increase the likelihood of infection within the mouth which can be uncomfortable and also makes the tissues

less lubricated and increase the risk of trauma, all of which make prosthodontic rehabilitation challenging.

Implant failure. Implant failure is understood to be slightly higher in this patient cohort in comparison to the general population. This is particularly true where implants have been placed into reconstructed sites [21, 157] and in sites that have received radiotherapy. [158,159] Implant failure also appears to higher when placed into the native maxilla then in the native mandible in this patient group [21].It must be noted that the quality of evidence for implant success and survival remains poor.

Unfavourable denture bearing anatomy. [87] In general the larger the defect is the more challenging it is to prosthodontically restore. As a result of surgical intervention there may be anatomical complications to overcome including deep soft tissues which impacts on the ability to load these sites and maintain healthy soft tissues in the long term. [154] Surgeries can also lead to a lack of sulcus depth and the tethering of soft tissue structures which limit the extension of the prosthesis (which is normally desired to provide tissue support and a peripheral seal and hence retention). (Figure 28)

Figure 28: Demonstrates unfavourable denture bearing anatomy in the lower right quadrant of the mouth.

The impact of oral rehabilitation on quality of life

Patients with H&N cancer not only live with the potential of that their diagnosis is life threatening, but also with the consequences of the cancer and its treatment, which can lead to disfigurement, impaired speech, swallowing and masticatory function and also other problems such as concern over finances, socializing and family worries; all of which impact on the patients' QoL. [160] There are a multitude of QoL indicators and tools that have been applied to assess outcome of prosthodontic rehabilitation following H&N cancer treatment. Studies tend to assess the physical, functional, psychological and social well-being of patients. QoL studies ascertain the outcomes of prosthodontic rehabilitation, with the aim of identifying the rehabilitation needs of patients and guiding appropriate provision of treatment to this patient group. However, there can be considerable individual variation in the priority the individual patient places on oral prosthodontic rehabilitation, and what is technically possible might not be acceptable or sought after by some patients. Similarly, sometimes what the patient wants is often unachievable for the clinical team and therefore managing expectations becomes an essential part of the overall care pathway. It is key to have

good insight into the patient's goals and value system to help guide treatment [161] as it has been shown that this patient group is not homogenous [162] and therefore providing an individual treatment plan that meets the patients' needs is vital. [160] There is a clear need not only to just address the physical consequence of the H&N cancer treatment but to also deal with the emotional consequences to ensure oral prosthodontic rehabilitation goes smoothly. [162] When deciding on removal of teeth either prior, during or after H&N cancer treatment, it needs to be acknowledged that loss of teeth has been shown to be detrimental to the patients QoL, which is in turn in direct correlation with an increasing number of missing teeth [163-165]. Patients that are rendered edentulous by H&N cancer treatment and have no functional occlusion have been shown to have reduced QoL with increased psychological consequences, [166] and are less likely to wear dentures, [167] which can be challenging for both the patient and prosthodontist undertaking the treatment. Where possible retaining the patient's dentition even in just one jaw can have a positive effect on the patient's psychological well-being, [163] and can also aid oral rehabilitation. Some of the most common issues reported by patients in terms of QoL after H&N cancer treatment are oral function, [168] chewing, speech, swallowing and appearance. [169] When these are impaired, the impact upon the patient's QoL is detrimental but can be reversed by prosthodontic rehabilitation. In general, studies assessing the impact of prosthodontic rehabilitation on H&N cancer patients QoL have shown that the successful completion of oral rehabilitation after H&N cancer improves the patient's QoL. [162,170,171] Some of the factors that affect the success of prosthodontic rehabilitation with regard to QoL include radiotherapy, which has been shown to reduce the improvement of QoL in patients after prosthodontic rehabilitation, in comparison to patients that have not undergone radiotherapy. [83,170] The use of dental implants to retain prosthesis has shown to greatly increase QoL of H&N cancer patients when compared to conventional rehabilitation with [83,170] with particular improvement in masticatory outcome [172].

Adjunctive surgeries to enable restorative management

The peri-implant environment in the H&N patient is a challenging one. Reconstructive surgery may force the hand of the implantologist and restorative dentist in terms of bone availability for implant placement and the condition of the surrounding soft tissues as a result of cancer treatment. This is particularly true where surgical intervention has occurred and implants are to be placed into a reconstructed site. Free flap reconstruction may be an excellent solution to reconstruct tissue defects and re-establish mandibular continuity, but the flap may require adjustment when it comes to implant restoration. Skin paddles, raised with composite flaps, exhibit morphology that differs significantly from the native oral mucosa [154]. For this reason, we may opt to raise our composite flaps without skin as a fascia-only paddle, allowing this to "mucosalize" inside the mouth (Figure 29,30,31). Excessive bulk of any free tissue transfer may be an issue and this may be deliberate as adjuvant radiotherapy in particular will cause tissue shrinkage, meaning that the reconstructive surgeon may err on the side of providing a bulky repair in anticipation of this. In addition, in composite flaps muscle may be left deliberately bulky to optimize bone

perfusion from secondary segmental arterial supply, as in the free fibula flap, a typical type V Mathes and Nahai flap [154, 173].

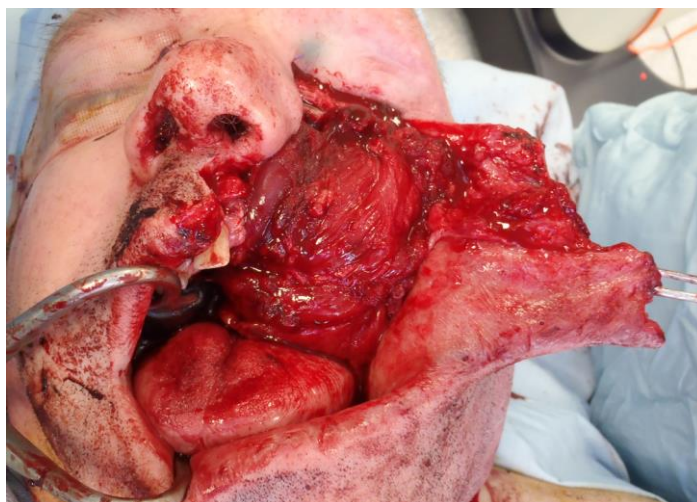
Figure 29: Insetting of DCIA flap without a skin paddle following maxillectomy via a Weber-Ferguson approach which will be left to mucosalize.
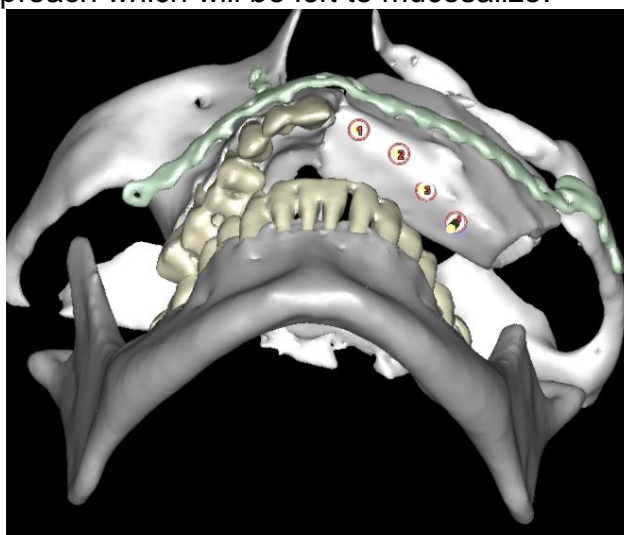
Figure 30: Software-assisted planning for implant placement for the case shown in figure 29.
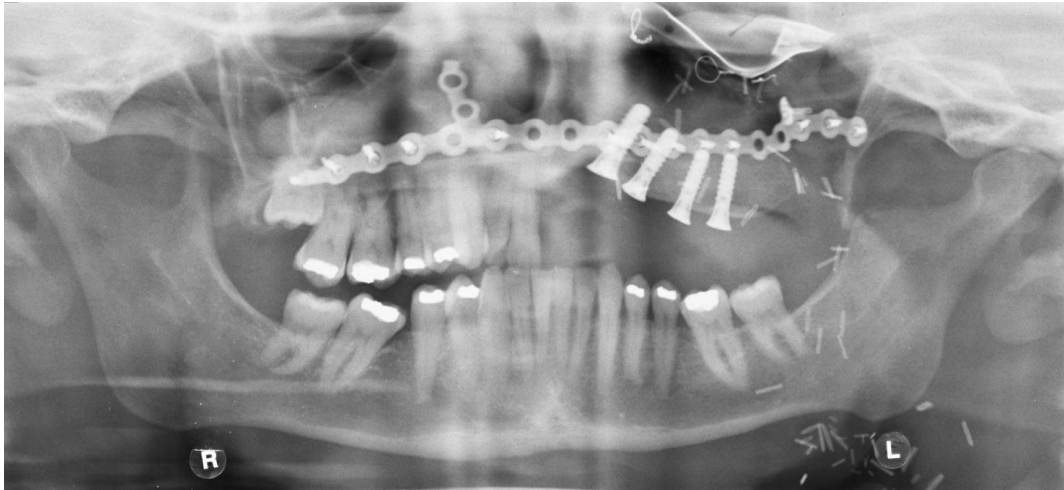
Figure 31: Final OPT radiograph with implant fixtures placed into DCIA ready for prosthodontic reconstruction for the case shown in figure 29.

As a result of surgical intervention there may be anatomical complications to overcome including deep soft tissues which impacts on the ability to load these sites and maintain healthy peri-implant soft tissues. It can also lead to a lack of sulcus depth and the tethering of soft tissue structures which can impose limits on the extension of the prosthesis impacting on support, stability, peripheral seal and hence retention. As a result there is often the need for adjunct soft tissue modifications around these sites including the debulking of free flap skin paddles and vestibuloplasty prior to oral rehabilitation [21, 157].

Debulking of the flap tissue involves careful remove of some of the excessive soft tissue prior to definitive oral rehabilitation. It is recommended that this is carried out by the surgeons who carried out the reconstruction as they are more aware of the anatomical structures present to minimize the risk of flap failure. A vestibuloplasty involves deepening the gingivolabial or gingivobuccal tissues. This often requires the use of a split thickness skin graft to provide the soft tissue needed to extend the sulcus depth. Some form of soft tissue stent is then required to hold the soft tissues in position during healing, [21, 157]. Our current practice is to use an acrylic soft tissue stent relined intra-operatively with Coe-Pak™ periodontal dressing. The dental implants themselves can be used to help retain the stent. [21]

The peri-implant soft tissue profile is important to maintain good hygiene and tissue health. Natural oral mucosa surrounding the implants is preferred to skin grafts which have unpredictable behaviour during healing and after abutment connection. [83] It is recommended that if possible 1.5mm of keratinised tissue should remain around the implant fixture. It has been shown that this provides the epithelial and connective tissue elements needed for soft tissue integration to the implant and the development of circumferential biological width to help prevent soft-tissue recession, facilitate oral hygiene measures [174-177] thereby reducing local inflammation which could lead to bone [178]. Where this is lacking it needs to be considered whether further surgery is warranted and occasionally the free mucosa or skin present around the implants may be replaced. [83, 118] Autogenous tissue grafts using a free gingival graft or a subepithelial connective tissue graft are considered the gold standards in soft tissue augmentation procedures although allogenic and xenogenic products can be used.

Adjunctive soft tissue surgeries can be particularly helpful in patients with: chronic inflammation despite hygiene efforts; continued recession or attachment loss despite periodontal intervention; sites with soreness upon brushing; a predisposition toward periodontitis or recession; and those patients who want to improve the soft tissue aesthetics around the implant. [179]

Distraction osteogenesis (DO) is used extensively in craniofacial surgery and in correcting congenital malformations of the mandible in particular. DO spares donor site morbidity and obviates the need for free tissue transfer. It comes with its own set of problems however such as the need for prolonged treatment, well-motivated patients and the possibility of facial scarring in the use of external distractors [21]. It may however, represent a treatment option in overcoming some of the problems with free flap reconstruction where bone height is an issue, as vertical distraction osteogenesis has been used with some success in increasing bone height in both fibula and scapula flaps [180,181]. That said, implant failure rates are often higher, the evidence base is restricted to isolated case series and it is best regarded as being a high-risk endeavour. Our practice is often to opt for the deep circumflex iliac artery (DCIA) flap when reconstructing the hemi-mandible, as this provides bone quality and quantity sufficient to support implants. Fibula flaps may however be "double-barrelled" to provide added bone height to support implants from the outset, without the need for later free tissue grafting or DO [109]. Anticipating the need for implant-supported prosthodontics may be equally addressed however by the simple solution of siting a single-barrelled fibula flap at a higher level to enable the implants to sit at a comparable to the remaining dentition (Figure 32).

The key tenet behind H&N surgery is ablation of disease to optimize survival and minimize the chances of recurrence. Reconstructive surgery aims to return the patient to form and function, with an attempt to restore quality of life. In focusing on the bigger picture, one should be mindful of the need for "fine-tuning" when approaching pre-prosthetic surgery to achieve those secondary goals. The good reconstructive surgeons will have an armamentarium of techniques at his or her disposal to optimize implant health and survival in pursuing oral rehabilitation.
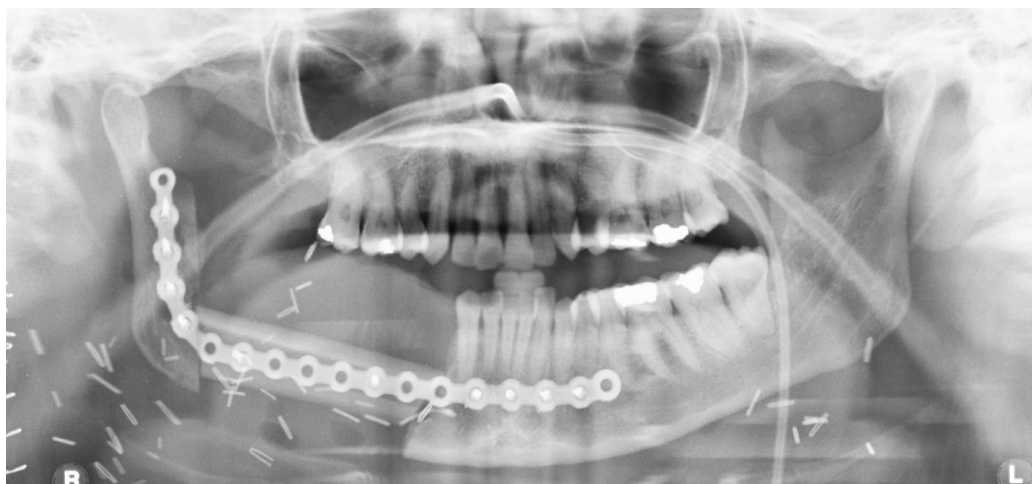

Figure 32: Orthopantomogram (OPT) showing single-barrelled fibula free flap set to height of remaining native alveolar bone to optimize implant-supported prosthodontic rehabilitation.

Planning for dental implants

If planning osseointegrated implants to anchor the definitive prosthesis is a treatment option, then it must be considered early in the treatment planning process. Surgical and post-surgical management of the patient's pathology defines the reconstructive space and in most cases limits the options (number, type, size and position) for implant anchorage. It is therefore essential in this limited environment, that the implant anchorage strategy is discussed as part of multidisciplinary team planning. [82] Decision making on the number, type and position of dental implants should be prosthodontically driven. This is to ensure that fixtures are placed in biomechanically appropriate and restorable positions.

Timing of implant placement can vary with implants placed at the time of surgical removal of the tumour or later on in the patient's treatment. Placement of the implant at the time of tumour resection is known as primary implant placement, whereas delayed placement is termed secondary implant placement. [182] Traditionally, implants have been selectively placed secondarily to tumour resection and reconstruction allowing for a period of healing and for the patient's prognosis and functional deficits to be assessed. [21] However, primary placement at the time of tumour resection is increasingly reported and is proposed to reduce the number of surgical interventions and to accelerate the patient's functional and cosmetic rehabilitation. Currently timing of implant placement is a matter of personal preference of the surgical team [183] and there is little outcome-based evidence to select either approach. [184]

Planning for primary placement

It can be argued that planning for primary placement has the greatest technical complexity and careful patient selection is necessary to achieve predictable outcomes. Close teamwork between surgeons and maxillofacial prosthodontists is required. [83] A key pressure-point is the understandable urgency to carry out ablative surgery which limits time for prosthodontic planning. Teams using primary implant placement in their routine patient care pathway typically have prosthodontists integrated in their service.

Radiographic imaging is needed for implant planning. Intra- and extra-oral radiographs may be sufficient for simple cases but typically three dimensional data are required to assess available bone volumes, bone quality and the relationships with key anatomical structures. When CT scans are requested as part of tumour diagnosis and surgical work-up widening the image field to ensure that information for implant planning is available is recommended. As the ablative surgery occurs at the same time as the implant placement pre-operative assessment of the acquired defect is not possible. Access to digital 3D images and stereolithic planning models can be useful to help communication between surgical and prosthodontic teams. It must be accepted that this approach cannot be completely accurate due to intra-operative decision making and outcomes will be sensitive to operator experience and skill. The advantages of primary implant placement include:

- Implants placed prior to the bone irradiation may lower the risk of ORN. [83, 185]
- A reduction in the interval between surgical resection and oral rehabilitation. [83, 78, 185]

- Improved access to the implant site at the time of respective surgery. [51]
- A reduction in the number of surgical procedures. [78]

When primary implant placement has been carried and radiotherapy is planned, typically a 3-4 week healing time is required prior to commencing radiotherapy [186]. This healing period rarely constitutes a delay to the patient's overall care as it coincides with the amount of time required to heal after ablative surgery [83, 185].

Planning for secondary placement

Secondary implant placement allows increased time to plan implant placement and has been shown to result in more accurate implant positioning with an increased ability to utilise the implants in the subsequent prosthodontic rehabilitation [182]. In common with implant planning in all populations' careful patient selection is essential. Shaw et al., [21] proposed six criteria for selection of patients following H&N cancer treatment for implant-based oral rehabilitation:

1. Adequate patient motivation, expectation, and resources.
2. Reasonable oncologic prognosis.
3. Good oral hygiene.
4. Bone of adequate quality and volume and within suitable arch relationship.
5. Adequate oral function (particularly tongue and swallowing).
6. No medical contraindications to further surgery.

The advantages of secondary implant placement include
- Improved accuracy in implant positioning. [182]
- Reduction in delays to commencement of rehabilitation and a reduced risk of complications immediately after surgery. [187,188]
- Better appreciation of the patient chance of cancer recurrence and survival. [182]
- More accurate assessment of the patient's oral health and postoperative function which will guide prosthodontic treatment planning. [182]
- Addresses reported concerns about backscattering from titanium implants during radiotherapy, and possible localised tissue damage. However, the exact limits and mechanisms of potential backscatter remain to be established. [189]

When secondary implant placement is planned there must be an appropriate period of healing following respective and reconstructive surgeries. In general, there is no reason to delay placement of implants into an unaffected native bone from a biological perspective as osseointegration remains predictable. When an implant is planned into a resected and/or reconstructed site the period of healing will be sensitive to the nature of the surgery. In all case it is essential that histopathology results demonstrate successful tumour removal prior to implant placement. For patients that have received radiotherapy, guidance regarding implant timing from reported evidence is inconsistent but waiting at least 18 months to 2 years appears to result in the most favourable outcomes. For patients who have undergone reconstruction with an autogenous bone graft including a vascularised free flaps and non-vascularised bone grafts it is suggested to wait at least 6 months before secondary implant placement. All proposed timings have no strong evidence to support them but would be considered conservative in the opinion of the authors. The

secondary implant placement planning process is similar to what it would be carried out in a healthy patient taking into consideration the additional complexities of abnormal anatomy and frequently restricted access.
(See Figure 33 for summary on the pathway for implant planning and treatment)
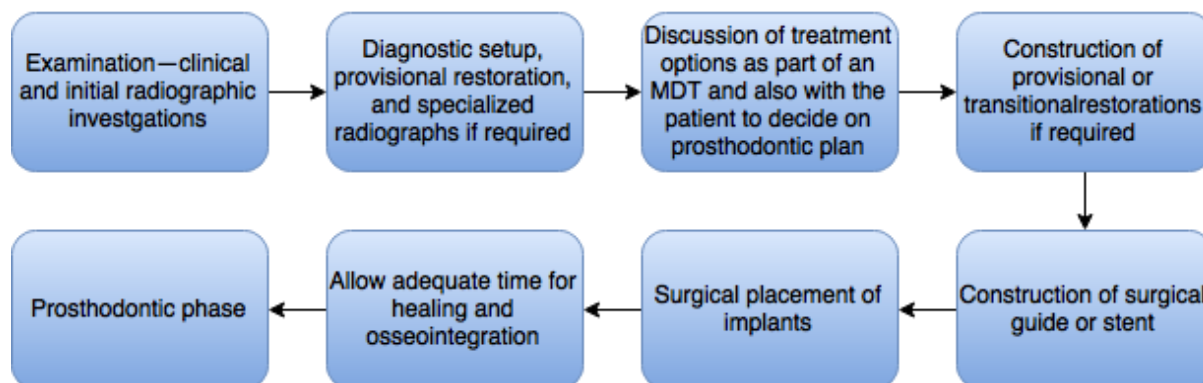
Figure 33: Flow-chart summarising the pathway for implant planning and treatment

The Diagnostic Work-up

Prosthodontically led implant planning should ensure the correct positioning and angulation of the implants within a so-called "prosthodontic envelope". The prosthodontic envelope refers to a three dimensional space in which the implants and attachments to the implants can be positioned in the confines of the desired definitive prosthesis. Failure to place implants within the prosthetic envelope can lead to a need for implant removal or leaving the implant in-situ unused as a "sleeper". Typical errors leading failure to use an implant relate to its angulation (too buccal or lingual) or insertion height (usually insufficient vertical height above the implant to restore the fixture). It is useful to consider implant planning as being carried out in a reverse order. This means that optimal tooth positioning (and associated supporting structures) represents the starting point. Subsequently these idealised positions are related to the patients remaining soft and hard tissues to determine if or where implants can and should be placed.

Implant planning should consider
- The facial profile
- Support of upper and lower lips and lip competence
- Tooth position and number of desired tooth units (which can vary from case to case)
- Hard and soft tissue profiles
- How much of the prosthesis is revealed during function.
- Occlusal relationships.
- Any adjunctive features of the prosthesis e.g. obturating oro-nasal communications.

Pre-operative study casts (prior to ablative surgery) and post-operative study casts with a diagnostic wax up of the teeth (a simulation of tooth position fabricated on a stone model in dental wax) and supporting structures or a prosthesis can be used to help gauge and plan treatment (Figure 34). The diagnostic setup can then be

adjusted if necessary as a compromise between fulfilling optimal rehabilitative requirements and the feasibility of implant placement in desired positions. Diagnostic set-ups are useful but it is not until prosthesis insertion that information such as facial support and appearance can be assessed by the clinician and the patient alike. Where patients already have an acceptable prosthesis worn prior to or following ablative surgery, this can be used without the need for any further diagnostic wax-up. By assessing the ideal position of the teeth and the surrounding structures implants can then be placed in the correct position/angulation so that the implant fixtures sit within the prosthodontic envelope. Diagnostic templates do not take into consideration the underlying bone anatomy and should be used in conjunction with radiographic imagery. Preferably the diagnostic template can be converted into a radiographic stent worn during two or three dimensional radiographic imaging to assess the tooth position in relation to the underlying bone. [190]The diagnostic casts and provisional prostheses can also serve as a model for the fabrication of a surgical stent/guide to assist the surgeon in the optimal placement of the implants and a transitional restoration during the treatment program.
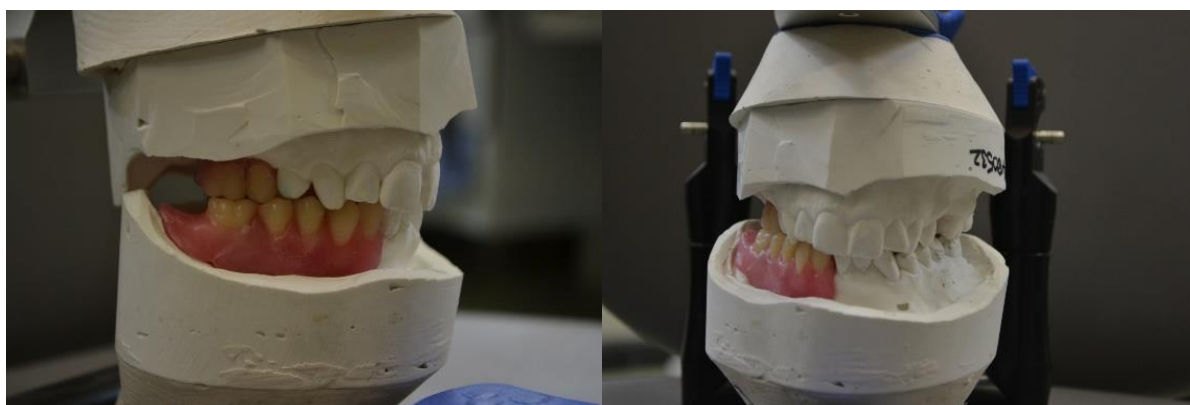
Figure 34: Mounted study casts with a partially constructed prosthesis which is being constructed to help aid implant planning in a patient who had surgical resection and reconstruction of the right posterior mandible.

The key limitation to place dental implants is the availability of sufficient bone volume to adequately stabilise the implant so that a direct interface between the implant surface and the bone is formed. Frequently following resective surgery and even after reconstruction there is a lack of bone volume with a recommended minimum volume being 10 mm depth and 6 mm width of well-vascularized bone [191]. Importantly the bone volume must also enable to the implant to be placed with an appropriate angulation so that it lies within the prosthodontic envelope. The number of implants is dictated by the type of prosthesis it has to retain. Implant number and positioning is a biomechanical consideration which has been extensively researched. For an implant retained complete overdenture (replacing all teeth with a removable prosthesis) it is generally accepted that in the mandible 2 implants in canine region are the minimum number of fixtures required. [134,135] In the maxilla more implants are required to support an implant retained overdenture with preferably 4 to 6 fixtures used with ideally an even anterior posterior spread [192]. For a fixed full arch reconstruction (replacing all teeth with a fixed prosthesis) placement of 6 to 8 implants is recommended in the maxilla [127,128] and a minimum of 6 in the mandible.[129]

However these recommendations are based on non H&N cancer patients and biomechanical evidence in this latter population is poor. Often more implants rather than a minimum number to support a prosthesis are planned in the event of an implant failure or inability to use an implant thereby safeguarding against the need for additional surgery. [125]

Imaging and radiographic stents

Radiographic imaging

A two dimensional screening radiograph(s) should be taken to the give the clinician an indication of the overall anatomy of the maxilla and mandible after resection and ahead of rehabilitation. Imaging should comprehensively cover the overall status of the remaining teeth and supporting bone. Imaging will be used to distinguish between sites where it is possible to place implants; sites where it is unlikely that implants can be placed without additional grafting and those sites where it is inadvisable to recommend implants. In many instances the orthopantomogram (OPT) is the radiograph of choice for initial screening to assess whether any further radiographic imagery is required for definitive implant planning (Figure 36). To improve the usefulness of two dimensional radiographic imaging (primarily to allow foreshortening and elongation magnification effects to be accommodated for) radiopaque markers of known dimensions such as metal spheres and guide-tubes can be incorporated into the patients pre-existing prosthesis so that the depth and dimension of the implants can be calculated. [193] However frequently three-dimensional imaging of in this patient group is essential due to the anatomical complexity of their remaining bone.
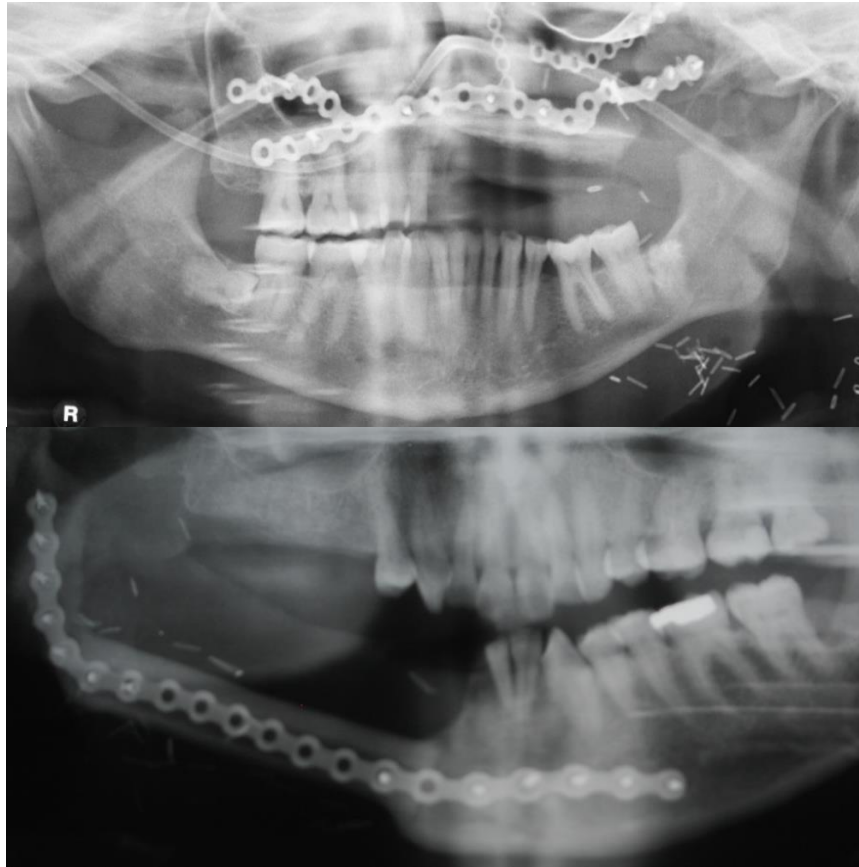
Figure 36: Pre-implant screening OPTs showing the complexity of the residual bony sites following ablative surgery and reconstruction

Cone beam computerised tomography (CBCT)

A cone beam computerised tomography (CBCT) is a radiographic imaging technique used to produce a 3D image (Figure 37). It produces high resolution images that are associated with fewer artefacts than a conventional CT scan due to quicker exposures and reduced patient movement. A CBCT can help improve diagnosis, allows virtual (digital) implant planning and allows construction of 3D stereolithographic models. CBCT imaging can help specifically identify the position of key structures to avoid such as the inferior dental nerve (Figure 38), reconstruction plates and screws (Figure 39) and teeth and can also help identify sites where it may be possible to place implants with or without any adjunctive surgical intervention. Planning software allow image segmentation to aid this process. CBCT scans can be taken with the patient wearing a radiographic stent in-situ to help relate the supporting anatomy with the idealised tooth position, occlusion, form and contour of missing teeth/structures. Stents are usually provided in the form of radio-opaque markers incorporated into a provisional prosthesis derived from the planning stages (Figure 40). [194,195]
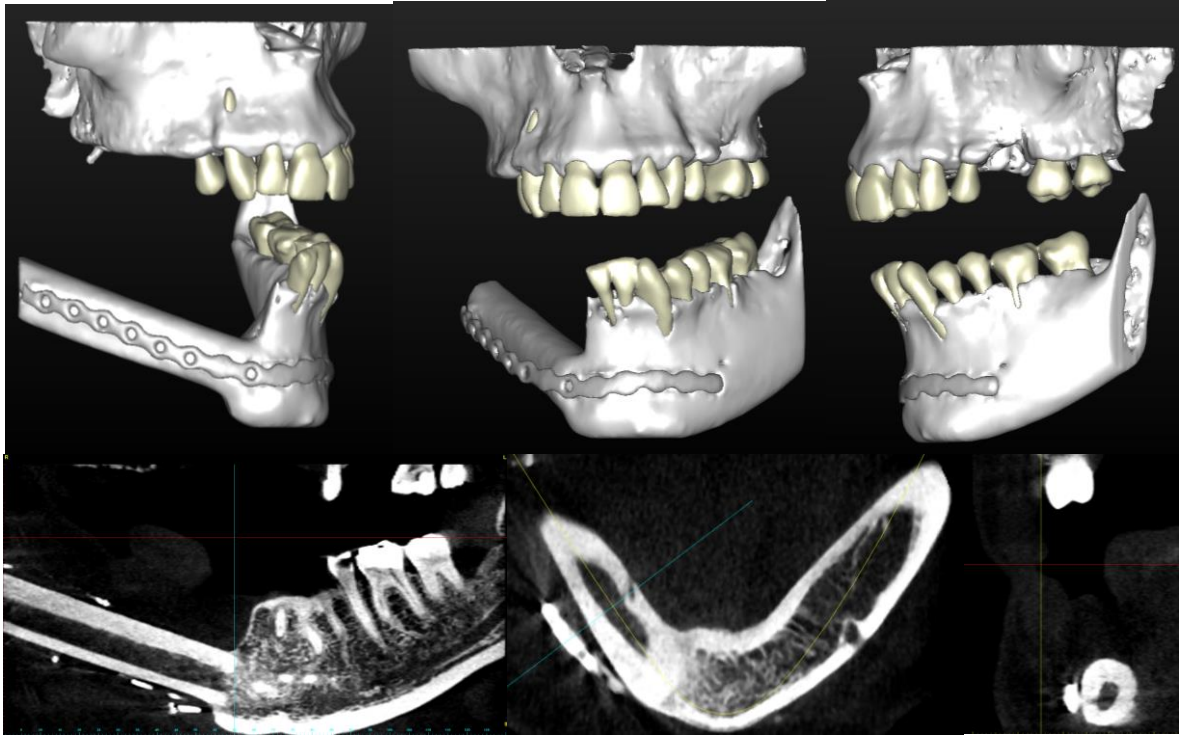
Figure 37: CBCT of H&N oncology patient reconstructed with a single barrel fibula free flap showing the 3D reconstructed image and the CT scan viewed in coronal, transverse and sagittal sections.
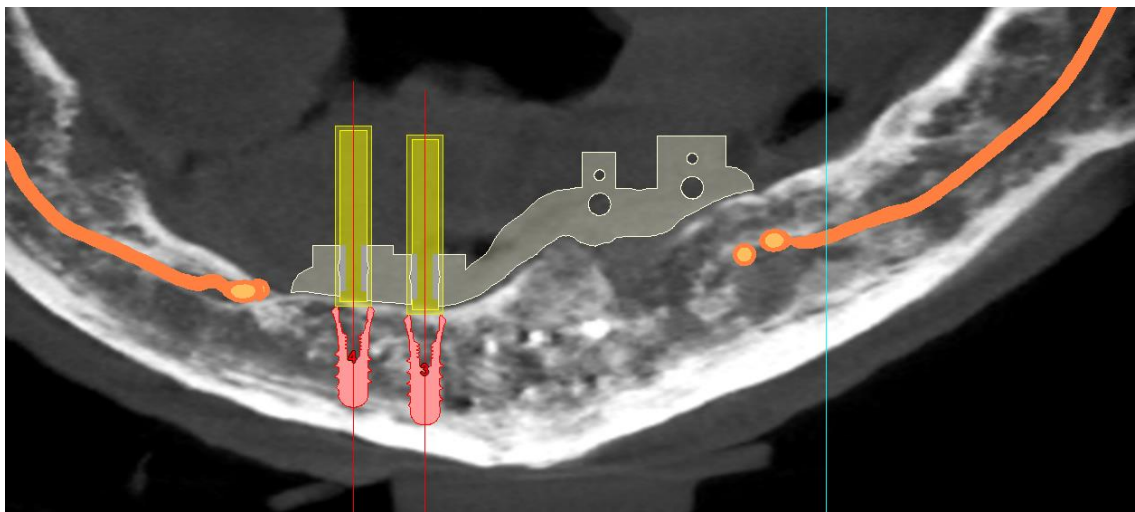
Figure 38: CBCT image segmented in digital planning software to highlight the inferior dental nerve and mental foramina (marked in orange) so these can be avoided when planning implant placement.
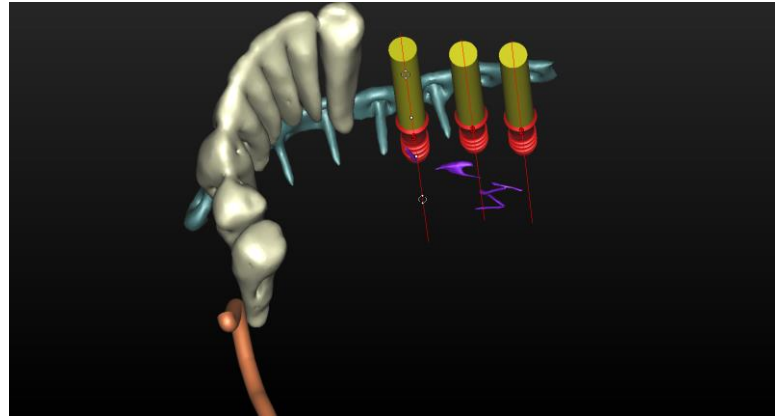
Figure 39: CBCT image segemented in digital planning software with the bone removed allowing visualisation of the planned implant placement avoiding the reconstruction screws and plates (blue).
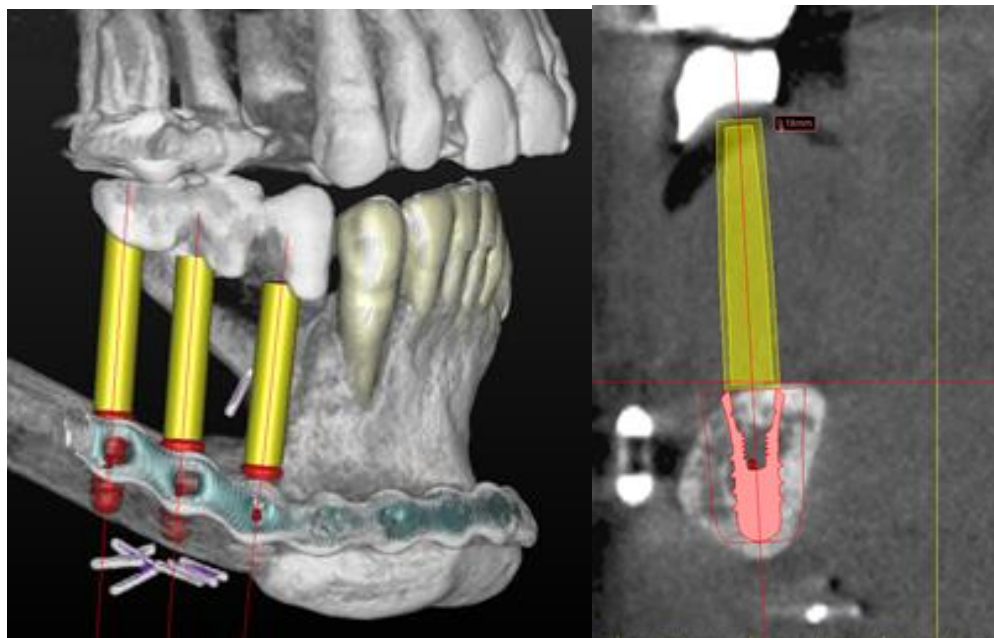
Figure 40: CBCT reformatted for SIMPLANT planning software with a radiographic stent in the form of a prosthesis with radiopaque teeth (barium sulfate) showing the relationship between required tooth position and planned implant fixtures into a single barrel fibula flap.

Implant planning software and dual scan CBCT imaging

A number of commercial software programs have been developed to aid implant planning and placement including Nobel Guide (Nobel Biocare™,Zurich, Switzerland), iDent (iDent Imaging Inc, New York, USA), Blue Sky Plan (Blue Sky Bio LLC, USA) and SIMPLANT (Materialise Dental, Leuven, Belgium) (Figure 41). The implant planning software is used to analyse CT or CBCT data and accurately plan implant positioning. This software allows clinicians to view and interact with 3D scan data, to choose implant dimensions and place the implant body virtually on the reconstructed digital image of the patient's facial skeleton. Typically, CT scan data

needs to be reformatted to be compatible with the software which can incur additional costs.
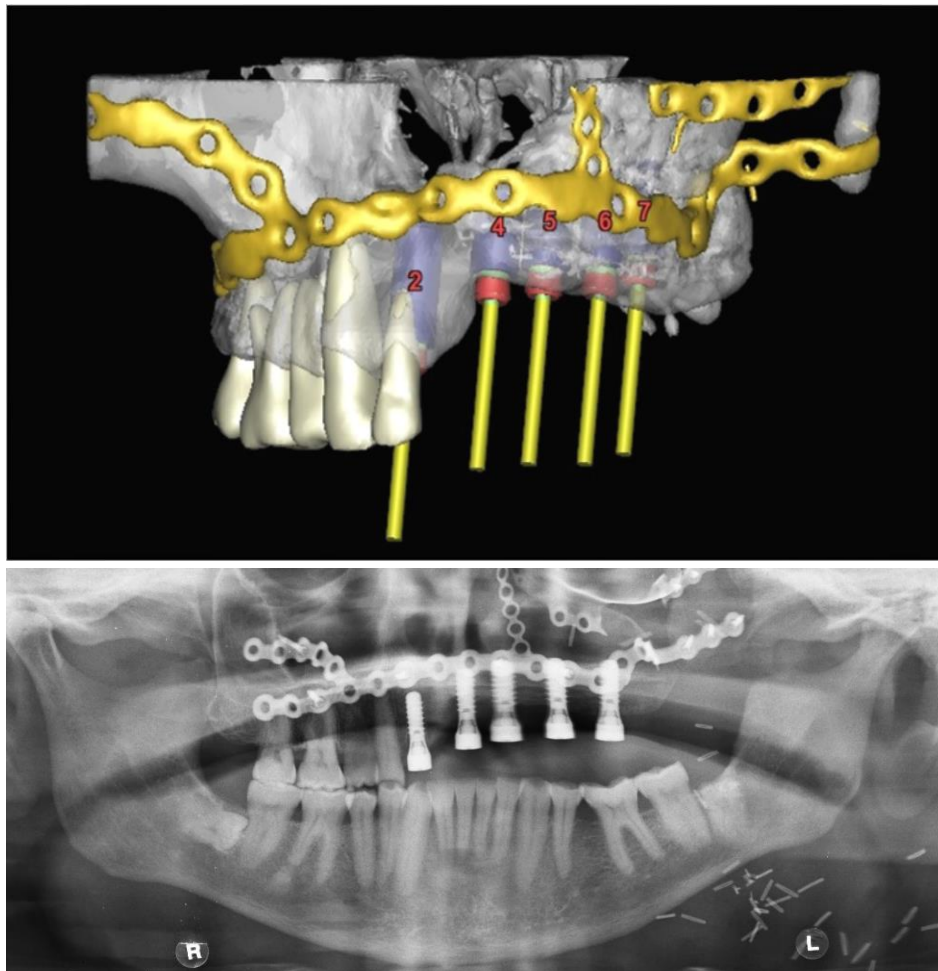
Figure 41: Demonstrating the use of SIMPLANT planning software with a reformatted CBCT to plan implant placement into a DCIA flap and into native bone. Post-operative OPT radiograph shows optimal implant position for restoration as planned.

A dual scan is becoming an increasingly popular tool in planning implant placement in this patient group. The process entails constructing a conventional prosthesis with idealised tooth position and radiographic markers placed with prosthesis. Two separate CBCT scans are carried out. The first is taken with the prosthesis in-situ and the second is a scan of the prosthesis separately. These two CBCT scans are then reformatted and brought together with the scans being co-located using the radiopaque markers. This type of scan is expensive but allows more accurate and precise implant planning. Once this the implant plan has been approved on the software a stereolithographic surgical stent can be constructed to be used at the surgical implant placement (Figures 42 & 43).
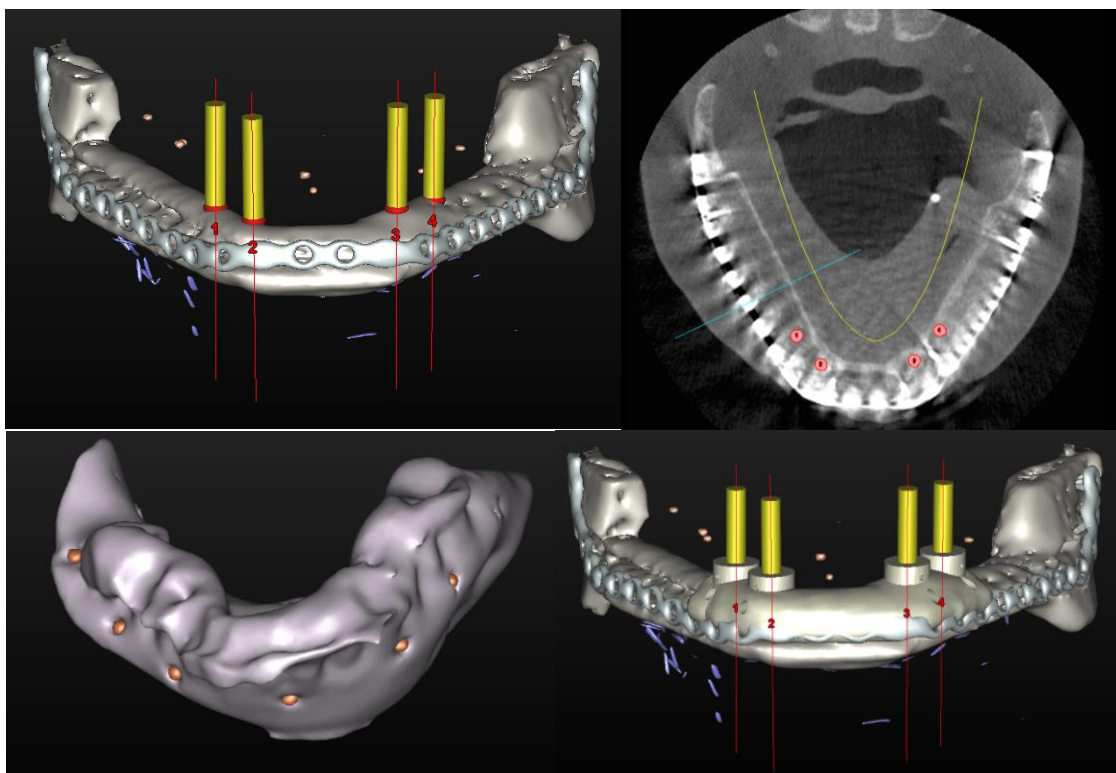
Figure 42: A patient with partial mandibulecomty and reconstruction with fibula free flap. A complete mandibular prosthesis was constructed to idealise tooth positioning. The prosthesis was copied and radiographic markers (Simplant Dual Scan Markers) placed and used as a radiographic stent. A polyvinylsiloxane bite record was so the stent can be accurately located during the CBCT. The CBCT shows markers (orange) to help guide implant placement from the scanned prosthesis.
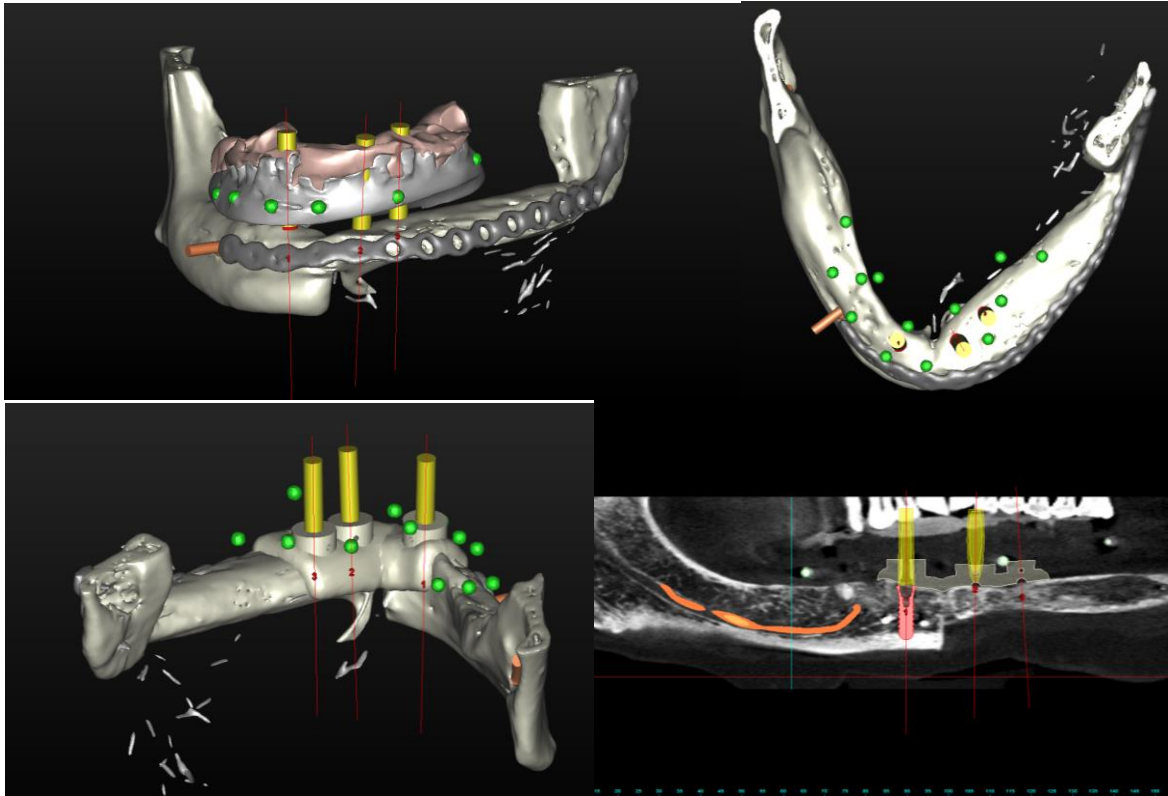
Figure 43: A dual CBCT scan using a radiographic stent in the form of a prosthesis with Simplant Dual Scan markers placed (green balls) that is worn during the scan. There is Futar bite registration paste (pale pink) used to help patient locate prosthesis in relation to the maxillary arch to ensure correct positioning during the CBCT Scan. Images shown 3D scan with prostheses in situ with planned implant placement and shows the implants sitting within the prosthetic envelope (within the green balls),

Surgical stents

Implant placement can be carried out "free-hand" or with the assistance of surgical guides/stents to improve placement accuracy. A surgical stent is a guide used to assist in proper surgical placement and angulation of dental implants.[196] The main objective of the stent is to direct the implant drilling system and to more closely reproduce the placement position determined from implant planning. Guides can be constructed with increasing accuracy from the diagnostic wax up/prosthesis, customized from conventional radiographic stents or most accurately designed and fabricated using CAD-CAM from three dimensional imaging data.[197] Surgical stents can be supported during the surgical procedure either by the teeth, the mucosa, the underlying bone, or a combination (Figures 43 & 44).
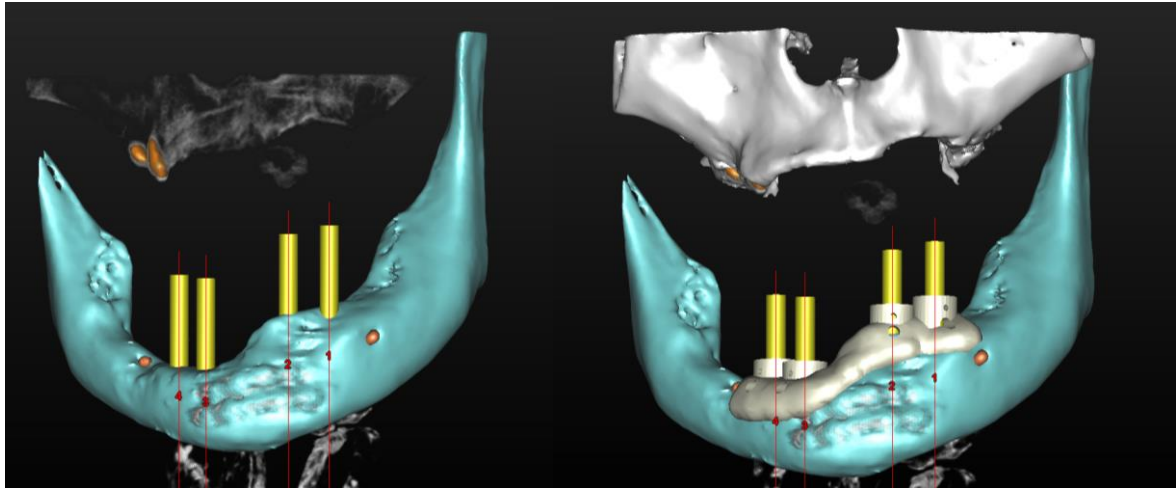
Figure 43: Demonstrates the design of the planned surgical bone stent planned in digital planning software using CBCT scan data.
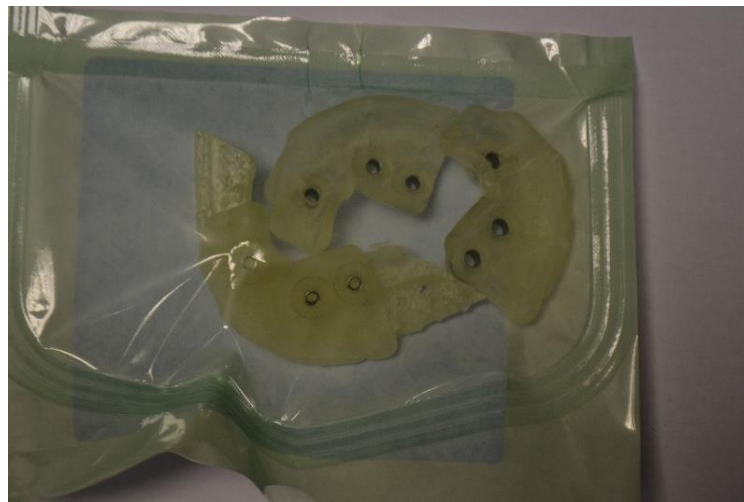
Figure 44: Surgical bone fitted implant guides to be used at time of implant placement that were produced from a dual Scan CBCT from patient.

Implant survival in H&N oncology patients

The overall treatment that this patient group undergo does not lend itself well to implant survival and in general implants in patients placed following management of H&N cancer have a lower survival rate than those who have not undergone cancer treatment. [73] Due to the huge variability in patient health, diagnosis, surgical and post-surgical management the majority of evidence relating to implant survival is provided by small retrospective case series.

From the evidence there is currently no strong indication that implant survival is affected by chemotherapy irrespective of whether implants have been placed before or after chemotherapy was provided [198]. Radiotherapy has been studied as a factor in many retrospective studies and there is an indication that implants placed into irradiated bone have a greater risk of failure than those in non-irradiated bone, [158, 199,200] with the maxilla in particular having a higher implant failure rate than the mandible. [201,202] When assessing the literature on implant failure in irradiated patients

there appears to be a higher failure rate prior to 2007 and it has been proposed that this relates to a transition from machined implant surfaces to micro-roughened implant surfaces at this time. This would suggest that the implant surface has an effect in general but more so in irradiated bone. [203] Following radiotherapy there is no consensus on the time period for implant placement that optimises implant survival. The type of bone the implant is placed into can affect implant survival with implants placed into native bone frequently reported to have a higher survival rate when compared with implants placed into vascularized free flaps (Figure 45). [21, 79, 157, 204] This is also true in irradiated patients with higher survival rate of implants in irradiated native bone than in irradiated grafted bone. [159] Patients that undergo radiotherapy are at risk of ORN after implant placement. ORN is discussed in more detail elsewhere in the chapter. Overall when reviewing the literature on implant survival in H&N cancer patients implant survival rates of between 81-99% are typically reported with a follow up ranging from 0 to 10 years.[21, 79, 152, 153, 157, 206-209] Despite such a high survival rate being reported there is currently considerable discussion regarding definitions of implant survival and success in this patient group and there is clearly a lack of good quality prospective long-term survival studies with sufficient implant and patient numbers provide strong evidence.
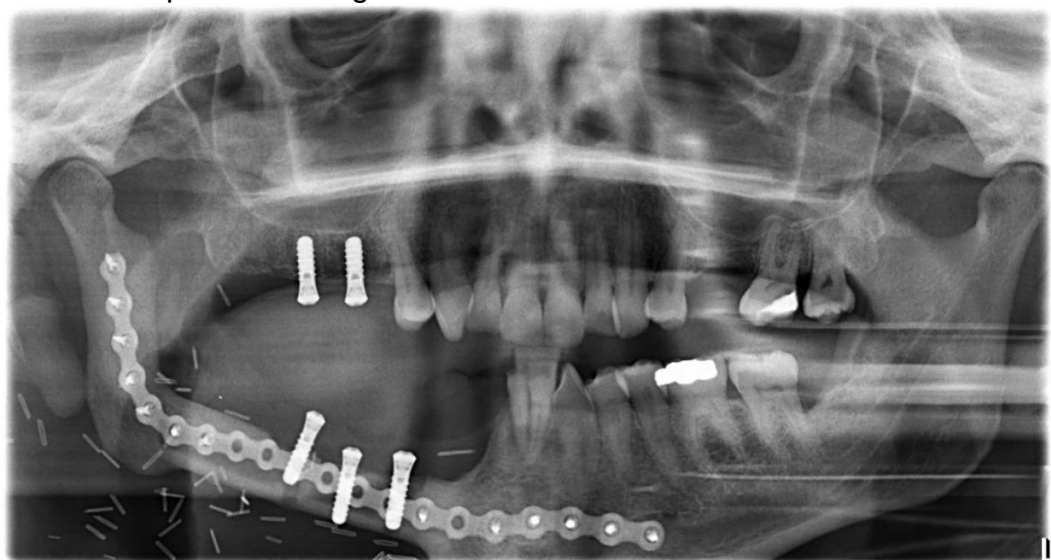
Figure 45: Showing implant failure of the distal implant in a fibula flap in the reconstructed mandible.

Zygomatic implants

Zygomatic implants were initially designed for use in the severely resorbed maxilla but have found favour in recent years in the rehabilitation of H&N patients with larger maxillectomy defects with a paucity of bone who are receiving obturator rehabilitation rather than composite free tissue transfer (Figure 46). High survival rates and stability have been demonstrated in the literature for zygomatic implants and immediate loading is possible [210,211].
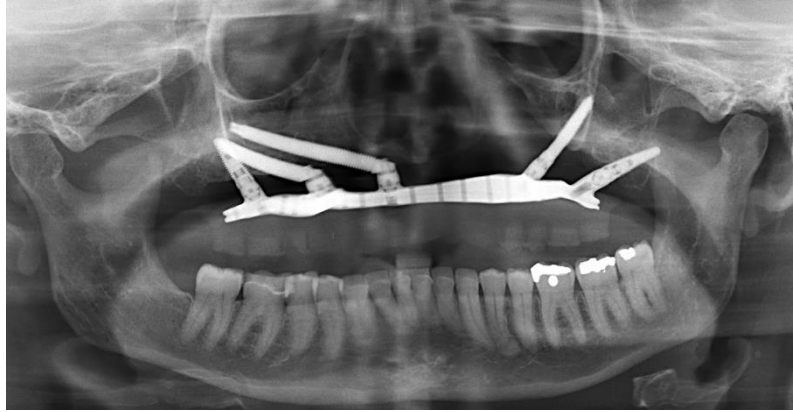
Figure 46: Prosthetic rehabilitation using zygomatic and pterygoid implants with an interconnecting bar for a fixed prosthesis after historical surgical intervention for Wegners granulomatosis.

The zygoma exhibits poor trabecular density but strong cortical bone ensuring good primary stability and enabling immediate loading [212]. The zygomatic implants are placed from the palate through the maxillary sinus to engage bone at the junction between the temporal and frontal processes of the zygoma, with direct vision through an antrostomy in the anterior sinus wall facilitating placement. Implant placement to support a prosthesis may be done in a tripod fashion with bilateral zygomaticus implants and further conventional endosteal implants in the anterior maxilla (Figure 47). Alternatively, Schmidt described placement of two zygomatic implants at either zygomatic buttress to allow rehabilitation of the near total maxillectomy defect (Figure 48) [213].

Figure 47: Prosthetic rehabilitation using zygomatic implants bilaterally and conventional implants in the anterior maxilla in a "tripod" approach.

Figure 48: Alternative design of particular use in near total maxillectomy defects whereby two zygomatic implants are placed on either side and loaded at 4-6 months.

Computer tomography (CT) scans allow for exclusion of sinus pathology prior to placement, an estimate of residual volume of maxillary bone and concavity of the sinus wall. Dedicated software allows for planning with virtual simulation of implant placement and fabrication of surgical guides to allow flapless surgery [214]. Complications of zygomatic implants include peri-implantitis, implant failure and a 5% rate of chronic sinusitis in the literature [215]. In our own experience in Birmingham, a 9.5% failure rate of zygomatic implant placement was seen, principally related to insufficient bone at insertion [216]. This is comparable to experience elsewhere in the literature where failure rates of up to 25% have been reported [213,215,216]. Fewer zygomatic implants have been placed within our unit in recent years owing to our practice moving in favour of composite free tissue transfer for larger maxillectomy defects (Brown class III and IV defects) and conventional implants using 3D stereolithographic model planning, custom reconstruction plates and cutting guides for deep circumflex iliac artery (DCIA) flaps [95, 217] (Figure 49).
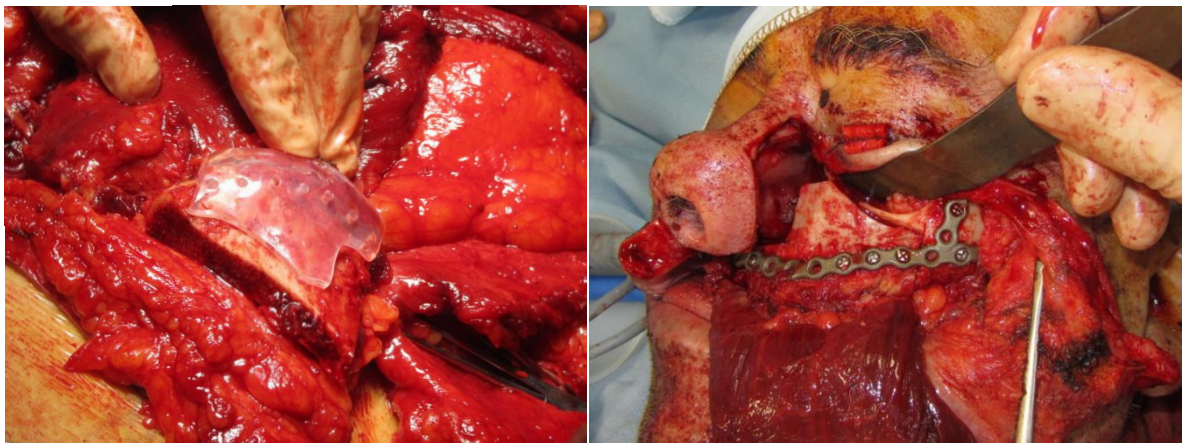
Figure 49: Custom cutting guide for DCIA flap in situ and DCIA flap inset with custom reconstruction plate which will enable placement of conventional endosteal implants, obviating the need for zygomatic implants.

Maintenance of dental and oral health

All patients whether prosthodontic rehabilitation has been carried out or not should be regularly reviewed. The frequency of dental recalls and oral examination depends on an assessment of the patient's risk factors for oral and dental disease coupled with evaluating their compliance with oral hygiene measures and dietary advice. Frequently patients struggle to maintain oral hygiene at a sufficient level and therefore regular short recall intervals should be considered as part of the patient's lifelong care pathway. The risk of uncontrolled dental disease after cancer treatment continues indefinitely following radiotherapy, as does the risk of ORN. Without regular reinforcement of preventive regimes and timely care, destruction of the dentition can be rapid and difficult to control. Thus, regular oral heath monitoring is imperative to avoid complex treatment in a challenging patient group. Regular review appointments also offer an opportunity for dental professionals to reinforce advice on life style changes with respect to smoking cessation and alcohol reduction; it also allows early identification of the development or recurrence of pathology so appropriate intervention can be provided.

Help and advice may be sought regarding other compilations associated with the oral environment after treatment including xerostomia which the dental practitioner can assist with. Regular maintenance of any maxillofacial prosthesis will also be required, which can include adjustments, relines and partial/complete replacement of the prosthesis and or its components, which commonly occurs. Those patients that have had implants placed will require regular review and professional cleaning and maintenance. Peri-implantitis has anecdotally been shown to higher in this patient group although no robust prospective studies have been reported. Cleaning around implants can be more challenging for these patients due to the altered intra-oral environment and therefore regular review and professional cleaning is essential to maintain health peri-implant soft tissues. When an adequate level of oral hygiene cannot be achieved to ensure peri-implant health a removable prosthesis should be routinely considered.

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9.3 Copy of systematic review for chapter 2

Laverty DP, Kelly R, Addison O. Survival of dental implants placed in autogenous bone grafts and bone flaps in head and neck oncology patients: a systematic review. Int J Implant Dent. 2018;4(1):19.

9.4 Copy of service evaluation for chapter 3

Laverty DP, Addison O, Wubie BA et al. Outcomes of Implant Based Oral Rehabilitation in Head and Neck Reconstruction oncology patients - a retrospective analysis of a large, single-centre cohort. Int J Implant Dent. 2019;5(1):8.

REVIEW　　　　　　　　　　　　　　　　　　　　　　　　**Open Access**

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Survival of dental implants placed in autogenous bone grafts and bone flaps in head and neck oncology patients: a systematic review

Dominic P. Laverty[1*], Robert Kelly[2] and Owen Addison[2,3]

Abstract

Using implants to retain prostheses as part of the oral rehabilitation of head and neck cancer patients is an increasingly common treatment modality, particularly in transported bone which is used to reconstruct defects following oncological surgical resection. The aim of this systematic review is to evaluate the survival of dental implants placed into autogenous bone grafts and flaps, in head and neck cancer patients. MEDLINE, EMBASE, CENTRAL and Science Direct databases were searched (1980-August 2017) for studies evaluating intra-oral implant placement into autogenous bone grafts and flaps in H&N cancer patients. Twenty articles were included reporting on 1905 implants placed into autogenous bone in head and neck cancer patients. Implant survival varied from 54 to 100% within the studies with 11 studies reporting implant survival of over 90%. In conclusion, intra-oral implant survival in autogenous bone grafts in head and neck oncology patients is promising, however inconsistencies in data reporting and in outcome definitions precludes formal meta-analysis.

Keywords: Dental implants, Autogenous bone graft, Head and neck oncology, Implant survival

Review
Introduction
Rationale
The use of implants to retain prostheses as part of oral and dental rehabilitation of head and neck (H&N) cancer patients is becoming an increasingly common treatment approach [1–3]. A number of benefits advocating implant anchorage over conventionally secured prostheses have been proposed [4] but importantly include a significant improvement in the reported quality of life (QoL) of patients [5].

Patients with H&N cancer often undergo ablative surgery with or without surgical reconstruction, radiotherapy and chemotherapy [4, 6]. Both surgical and non-surgical interventions can lead to significant disability, including facial deformity, loss of hard and soft tissue, impaired speech, swallowing and mastication [7]. Oral and dental

rehabilitation has conventionally required the use of removable prostheses to obturate defects, to replace missing tissue structures and to restore function and aesthetics. In this patient group, removable prostheses are often poorly tolerated, are difficult for the patient to maintain and frequently fail to fully achieve the intended functional improvement. The use of dental implants has been proposed to enable secure anchorage for prostheses, reduced loading on vulnerable tissues and provide a better functional and cosmetic solution [8].

However, dental implants can only be placed if there is sufficient bone to encase the implant so that a direct interface between the implant surface and bone can be achieved. Frequently following resective surgery, insufficient bone volume remains and bony reconstruction of the surgical defect is required to enable successful dental implant placement [9]. Patients are commonly reconstructed with either a non-vascularised bone graft or a composite free flap. A non-vascularised bone graft is a free piece of non-vascularised bone (or bone substitute) that is placed in the tissues. A free flap is a vascularised piece of

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bone (pedicled), which is being increasingly used to reconstruct tumour patients.

High 'survival' and 'success' rates have been reported in the literature for dental implants placed into autogenous bone grafts in healthy patients but notably the success rates remain lower for implants placed into healthy native bone [10, 11]. With the increasing use of complex reconstructive techniques in rehabilitation following H&N cancer and the placement of dental implants into transported bone, there is a need to appraise the highly varied evidence that is currently available in order to help inform clinical decision making.

Objectives
It is the aim of this systematic review to evaluate the survival of dental implants placed into autogenous bone grafts, in H&N oncology patients.

Methods
Protocol
The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [12, 13] for describing and summarising the results of our review was used [12, 13].

A quality assessment of all selected full-text articles was performed using the Methodological Index for Non-Randomized Studies (MINORS) [14] assessment tool to assess the risk of bias of the included studies. The MINORS scoring list consists of 12 items, eight apply to non-comparative studies, and a further four apply to comparative studies. Items are scored as 0 (not reported), 1 (reported but inadequate), and 2 (reported and adequate) with this then totalled up to give a score with the higher scores representing a reduced risk of bias [14]. This was chosen over the Cochrane collaborations' tool for assessing risk of bias for randomised controlled studies since none of the studies included were randomised control trials.

Eligibility criteria
Inclusion criteria
Studies that met the following criteria where included:

1. Dental implant placement into patients with cancer of the H&N.
2. Dental implants placed into autogenous bone grafts.
3. Studies performed on humans.
4. Patients over 18 years old, or if there are patients under 18 years old within the study that these patients and their data can be removed from the analysis.
5. English language articles.
6. Any study design reporting on at least 35 dental implants or 20 patients who have had implants placed into autogenous bone.

7. Data related to implant number and implant survival in autogenous bone grafts that was either directly reported or can be calculated from data within the study.

Exclusion criteria
Studies were excluded if they met the following criteria:

1. Studies that reported on craniofacial or extra-oral implants only.
2. No reported implant survival or an inability to calculate implant number or survival from reported data.
3. Studies reporting on patients under 18 years old where there no ability to remove these patients and their data from the analysis.
4. Laboratory or animal-based studies.
5. Studies with less than 20 patients or 35 dental implants placed into autogenous bone grafts.
6. Review articles.

Information sources
Four electronic databases were used to systematically search the available literature: (1) The National Library of Medicine (MEDLINE via PubMed), (2) EMBASE, (3) Cochrane Central Register of Controlled Trials and (4) Science Direct. The searches were limited to studies involving human subjects and publication dates from January 1980 to August 2017 that satisfied the inclusion criteria.

Search
The following search terms were used: *Population*: (<[text words] dental implant OR dental implant* OR oral implant OR oral implants OR osseointegrated implants OR endosseous implant OR dental implantation <[MeSH terms/all subheadings] AND (<[text words] head neck OR squamous cell carcinoma OR oncology OR tumour OR cancer OR malignant OR neoplasm <[MeSH terms/all subheadings] AND *Intervention*: free flap OR vascularized flap OR hard tissue graft OR micro vascularized flap OR micro anastomosed flap OR anastomosed flap OR native bone OR DCIA OR deep circumflex iliac artery OR radial OR scapula OR fibula OR iliac OR rib OR costochondral <[MeSH terms/all subheadings].

Study selection
Two reviewers (DL and RK) carried out the primary search by screening independently the titles and abstracts and identifying the studies appearing to meet the inclusion criteria. Studies with insufficient information in the title and abstract to make a clear decision were identified and the full paper was reviewed. Those studies selected for evaluation of the full manuscript were carried out independently by the same reviewers who determined the final

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inclusion. Any disagreement was resolved by discussion with a third independent reviewer (OA). The reasons for rejecting studies at this or subsequent stages were recorded.

Data collection process

Two reviewers (DL and RK) then independently extracted the data using a bespoke data extraction form. Any disagreement was resolved by discussion with a third reviewer (OA). Studies with missing or incomplete data were excluded and reference lists of the selected studies were checked for cross-references to search for papers that might meet the eligibility criteria for inclusion.

Data items

Data was collected for implant survival, implant success, implant failure, implant complications, surgical implant placement protocol, implant system used, clinical follow-up, how the author defined success/survival, the type of autogenous bone graft, implant site, the prosthodontic rehabilitation and type of cancer, and the use of radiotherapy were documented where possible.

Risk of bias in individual studies

A quality assessment of all selected full-text articles was performed using the Methodological Index for Non-Randomised Studies (MINORS) [14] assessment tool.

Summary measures

The main outcome measure was implant survival. This review will define implant survival as an implant still in situ that has not been removed or lost at the census date

and thus implant failure defined as an implant that has been removed or lost and is no longer in situ.

Synthesis of results

The survival and success figures documented where possible are taken directly from the study; however, where the study did not specifically document the survival or success of implants placed into autogenous bone as a percentage, this was calculated from the data provided (as a function of surviving or successful implants from total reported as placed), and studies that lacked data to calculate this were rejected as part of the secondary screening process.

Additional analyses

No further analyse was carried out.

Results

Study selection

Searches of EMBASE, the Cochrane Central Register of Controlled Trials, Science Direct and MEDLINE generated 619 articles. After duplicate articles were removed, 566 unique articles were remaining. After the review of the titles and abstracts, 151 articles were accepted for further consideration, and 415 were rejected. After the full text was attained and reviewed for the 151 articles, 131 articles were rejected leaving 20 articles to be included in the systematic review (Fig. 1).

Study characteristics

The following data was extracted from the studies; study design, centres (single vs multiple centres), patient demographics (patient age, H&N cancer diagnosis), treatment
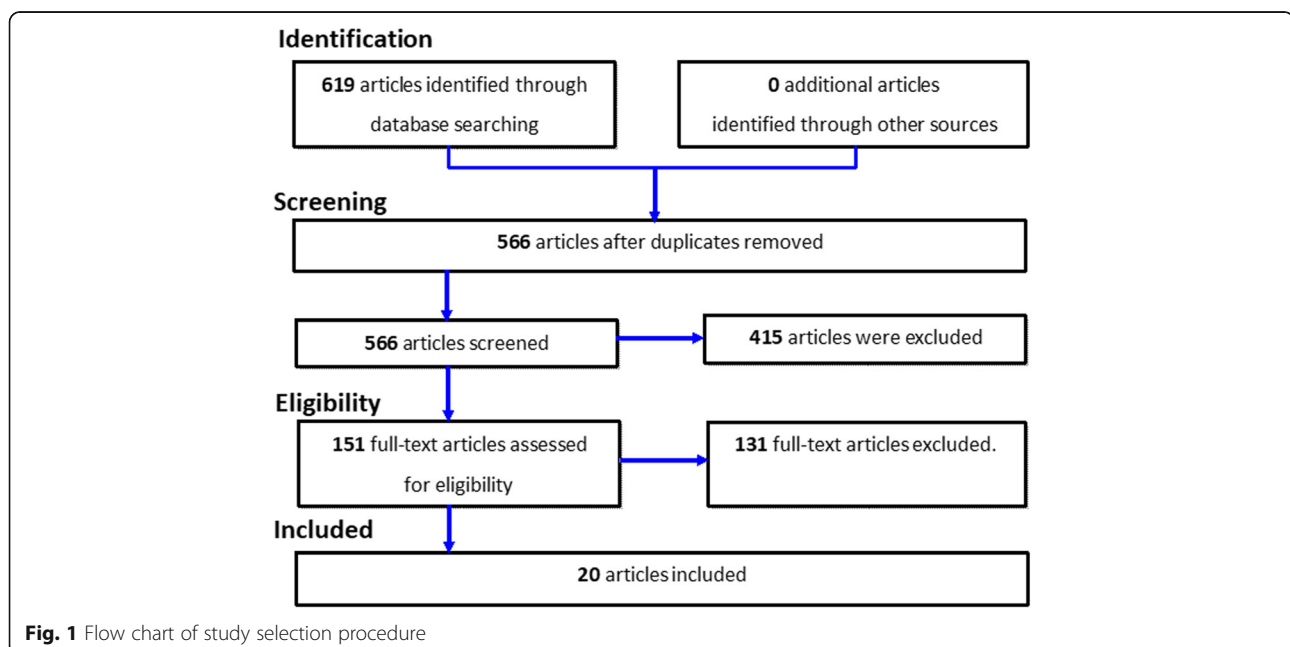

Fig. 1 Flow chart of study selection procedure

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modalities (surgery, radiotherapy, chemotherapy), donor site of autogenous bone graft, outcome measures, implant details (implant system, implant number, implant site, type of bone implant placed into (non-vascularised vs vascularised/ free flap), implant placement surgical protocol implant survival/success/failure figures), implant definitions (implant survival/success/failure), type of prosthetic rehabilitation (fixed vs removable), and any reported complications.

Risk of bias within studies

There were varying scores attained by the studies using the MINORS assessment tool, ranging from 7/16 to 13/16 representing varying degrees of bias within the studies (Table 1).

Statistical analysis

Due to the lack of controlled studies and the heterogeneity of the studies concerning patient selection, surgical protocols, implant loading, follow-up and prosthetic rehabilitation, implant survival definitions and figures, measurement protocols, and inconsistency in data reporting a formal meta-analysis would be statistically inappropriate and was not conducted. Descriptive statistics where used to interpret and present the data from these studies.

Results of the studies

Descriptive data extraction was carried out for the 20 studies and is summarised in Tables 1 and 2. All studies were retrospective observational studies in design with the majority undertaken at single centres; however, for 3 studies, this was unclear (Schultes et al. [15], Yerit et al. [16], Linsen et al. [17]). These 20 studies were published over a range of 21 years (1996 to 2017) and provide cumulative data on 1905 implants placed into autogenous bone grafts in H&N cancer patients with both benign and malignant tumours being reported. The exact patient number for this intervention within some of the studies was unclear as a result of the studies reporting on implant rather than patient number or there was an inability to identify which population received dental implants to identify patient numbers. One study (Chiapasco et al. [18]) included reported on patients under 18 years old (two patients in total); however, these patients and their data could be removed from the analysis.

Implants were placed into both vascularised and non-vascularised autogenous bone grafts, with a number of donor sites being reported. (Tables 2 and 3) These implants were placed in a variety of intra-oral sites with implants placed into autogenous bone grafts within the mandible reported in eight studies and bi-maxillary placement in nine studies, and in three studies, it was unknown where the implant fixtures were placed other than that they were placed into autogenous bone grafts (Linsen et al. [17], Fenlon et al.

[19], Ch'ng et al. [20]). There were no studies where implants were placed solely in the reconstructed maxilla.

Radiotherapy to the autogenous bone graft/implant site was reported in 16 studies. Two studies (Wang et al. [21], Zou et al. [22]) reported that radiotherapy was not carried out on the study population and in 1 study (Yerit et al. [16]) bone graft sites were not irradiated. One study (Chiapasco et al. 2008 [23]) failed to report whether radiotherapy was carried out or not on the study population. Of 20 studies included in the systematic review, only 7 studies reported on outcomes related to implant survival in irradiated autogenous bone grafts (Barrowman et al. [7], Fenlon et al. [19], Ch'ng et al. [20], Buddula et al. [24], Fierz et al. [25], Teoh et al. [26], Burgess et al. [27]).

The surgical and loading implant protocols were reported in 17 studies with no description given in 3 studies (Barrowman et al. [7], Fierz et al. [25], Hessling et al. [28]). The implant placement protocols were diverse with variables including the use of surgical templates/guides, primary and/or secondary implant placement following autogenous bone grafting, and immediate and/or delayed implant loading; however, the majority of the studies reported on delayed implant placement following initial healing of the transported bone graft and delayed loading of the implant fixtures. Six studies reported primary implant placement (Fenlon et al. [19], Ch'ng et al. [20], Zou et al. [22], Burgess et al. [27], Wu et al. [30], Watzinger et al. [29],) and one study reported immediate implant loading (Chiapasco et al. [18]). Additional procedures were also reported which include removal of reconstruction plates and screws at the time of implant placement, bone condensing to enhance the bone density, and further peri-implant surgery in the form of debulking of soft tissues, gingivoplasty/vestibuloplasty and free mucosal grafts to optimise the soft tissue conditions (Table 1). Prosthodontic reconstruction of the implant fixture was reported in 15 of the studies which included fixed and removable prosthesis and is summarised in Table 1.

Overall implant survival

The overall implant survival of implants placed into autogenous bone grafts varied highly (both at implant and patient levels) between the included studies ranging from 100% with a mean follow-up of 3.5 years ± 0.3 years in a study by Wang et al. [30] to 54% with a mean follow-up 5.4 years ± 3.2 years by Yerit et al. [16].,(at an implant level) (Table 2).

Eleven studies compared implant survival in autogenous bone grafts to that in native bone within their studies. Nine of these studies (Barrowman et al. [7], Yerit et al. [16], Linsen et al. [17], Fenlon et al. [19], Ch'ng et al. [20], Hessling et al. [28], Watzinger et al. [29], Shaw et al. [31], Klein et al. [32]) reported higher implant failure rates

Table 1 Study characteristics and MINORS scores

Author	Year of publication	Study design	Outcome measure	Criteria—survival	Criteria—success	Quality assessment using the MINORS assessment tool	Head and neck cancer diagnosis	Patients age range	Follow-up period	Implant site	Implant system	Implant placement protocol	Prosthodontic rehabilitation
Studies with an average follow-up of 3 years or greater													
Watzinger et al. [29]	1996	Retrospective observational	Implant survival in irradiated mandibles and Outcomes of Peri-implant bone	Not defined	N/A	7/16	SCC	Range = 41–79 years	Up to 3 years	Mandible	IMZ	Primary and secondary implant placement. Secondary placement 6 months after oncological reconstruction. Delayed loading of implants of at least 6 months.	Removable
Teoh et al. [26]	2005	Retrospective observational	Implant survival in the reconstructed mandible and prognostic factors.	Own—implant not removed then survived.	N/A	12/16	SCC, Osteogenic sarcoma, Benign tumours, mucoepidermoid carcinoma and other sarcomas	Mean = 42 years (range = 67–80.5 years)	Mean = 51.7 months (range = 1.3–138 months)	Mandible	Nobel and Osseotite	Delayed loading of implants 6 months after placement. Fixations screws removed prior to implant placement	Fixed and removable
Wu et al. [30]	2008	Retrospective observational	Clinical outcomes of dental implants placed in fibula free flaps for orofacial reconstruction	Own—implants still functioning with no mobility, pain or infection, but with peri-implant bone resorption more than 2 mm were classified as survived.	Albrektsson et al.1986	9/16	Benign and malignant head and neck tumours	Average 47.1 years	Average 47.8 months	Maxilla and mandible	ITI and Branemark	19 patients had primary implant placement 10 patients had secondary placement after oncological reconstruction. Delayed loading of implants of at least 3 months after placement.	Fixed and removable
Fenlon et al. [19]	2012	Retrospective observational	Implant survival	Poorly defined—implant osseointegrated and in situ then survived (usefulness of implant assessed using own 4-point index)	N/A	12/16	Cancer	Unknown	At least 3 years	Unknown	Nobel Biocare, Endopore, Astra and unknown implants	95 implants were primarily placed and 50 implants had secondary placement 3 months after oncological reconstruction.	Unknown
Ch'ng et al. [20]	2014	Retrospective observational	Implant survival, assess effect of risk factors associated with poor healing.	N/A	Own—implant success was defined as a painless and stable fixture without evidence of peri-implant infection or radiographic	12/16	SCC, recurrence, osteosarcoma, desmoid tumour, adenoid cystic carcinoma, adenocarcinoma, fibrosarcoma, melanoma, MEC, hemangioma-endothelioma	Median age = 59 years	Mean = 3.1 years	Unknown	Astra	Primary and secondary implant placement. Patients had implants placed prior to radiotherapy. Reconstruction plates and screws	All removable

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Table 1 Study characteristics and MINORS scores (Continued)

Author	Year of publication	Study design	Outcome measure	Criteria—survival	Criteria—success	Quality assessment using the MINORS assessment tool	Head and neck cancer diagnosis	Patients age range	Follow-up period	Implant site	Implant system	Implant placement protocol	Prosthodontic rehabilitation
					lack of osseointegration							removed if hindering implant placement. Debulking of soft tissues and vestibuloplasty also carried out as required.	
Shaw et al. [31]	2005	Retrospective observational	Implant survival and complications and surgical complications	N/A	Own—implant success was defined as remaining function, no mobility, pain or infection.	10/16	80% of patients SCC, other 20% unknown	Mean = 58 year (range = 15–80 years)	Mean = 3.5 years (range = 0.3/14 years)	Maxilla and mandible	Frialit II, IMZ, Branemark, and IMTEC	Secondary implant placement 1 year after oncological reconstruction. Delayed loading of implants of 3–6 months. Debulking of soft tissue and mucosal grafts carried out as required.	Fixed and removable
Wang et al. [21]	2015	Retrospective observational	Vertical bone Height—double barrel vs vertical distraction Osteogenesis in Fibula Free Flaps, Implant Survival and Success	Poorly defined - implant still in situ then survived.	Albrektsson et al.1986	12/16	Ameloblastoma and OKC	Range = 28–55 years	Mean = 42.5 months ± 4 months	Mandible	Straumann	Secondary implant placement after oncological reconstruction. Delayed loading of implants 3–5 months after placement. Distraction osteogenesis devices used as implants and restored.	All fixed
Yerit et al. [16]	2006	Retrospective observational	Implant survival in the mandible after radiotherapy and radical surgery in oral cancer patients.	N/A	Own - Implant Success when no complaints of the patient, no mobility, no peri-implant tissue inflammation and no peri-implant bone loss exceeding one-third of implant length was observed	10/16	Cancer of oral cavity (majority of the subjects having destructive oral squamous cell carcinomas stage T2–T4)	Range = 16–84.1 years	Mean = 5.42 years ± 3.21 years	Mandible	IMZ, Frialit II and Xive	Implant insertion at various intervals with the mean at 1.41 years after reconstruction. Delayed loading of implants of at least 6 months. Gingivoplasty and vestibuloplasty procedures carried out as required.	Removable
Linsen et al. [7]	2009	Retrospective observational	Survival of implants and implant-retained prostheses in patients after ablative surgery of oral cancer with or without	N/A	Kaplan et al. 1958	9/16	SCC, Ameloblastoma, Adenoid Cystic Carcinoma, OKC, Carcinoma of other origins	Mean = 55.7 year (range = ± 16.25 years)	Mean = 47.99 months ± 134.31 months)	unknown	Branemark and Straumann	Delayed implant placement with an average of 41 months after oncological treatment. Delayed loading of implants of	Fixed and removable

Table 1 Study characteristics and MINORS scores (Continued)

Author	Year of publication	Study design	Outcome measure	Criteria—survival	Criteria—success	Quality assessment using the MINORS assessment tool	Head and neck cancer diagnosis	Patients age range	Follow-up period	Implant site	Implant system	Implant placement protocol	Prosthodontic rehabilitation
			adjunctive radiation therapy.									4.9 months (average).	
Studies with an average follow-up of less than 3 years or no average follow-up reported													
Fierz et al. [25]	2013	Retrospective observational	Reports on surgical and prosthodontic rehabilitation after resection for oral oncology resection	Own—implant not removed then survived, those functioning given a 'survival rating'	N/A	9/16	SCC, Adenocarcinoma and Others tumours	Mean = 57 year (range = ± 7.2 years)	Range = Less than 12 months up to 5 years	Maxilla and Mandible	Unknown	No described protocol.	Fixed and removable
Barrowman et al. [7]	2011	Retrospective observational	Audit experience of implant placement in jaws after oral cancer resection, Success of Prosthodontic Rehabilitation	Poorly defined - implant still in situ then survived	N/A	10/16	SCC, Verrucous Carcinoma, Osteosarcoma and Adenoid Cystic Carcinoma	Range = 20–76 years	Up to 15 years	Maxilla and Mandible	Branemark	No described protocol.	Fixed and removable
Zou et al. [22]	2013	Retrospective observational	Long-term clinical outcomes on immediate or staged Implant Placement in iliac bone for restoring defects after tumour resection.	Own - Implants provided supportive function and were stable when torque tested	Albrektsson et al.1986	7/16	SCC, Ameloblastoma, OKC, Myxoma	Range = 24–61 years	Up to 12 years	Mandible	Nobel and Straumann	17 patients had primary implant placement 15 patients had secondary placement after oncological reconstruction. Delayed loading of implants of 5–6 months. Bone condensing was performed to enhance the bone density.	Fixed and removable
Schultes et al. [15]	2002	Retrospective observational	Stability of implants in microvascular free flaps	Poorly defined - implant still in situ then survived	N/A	8/16	Alveolar crest carcinoma T4	Average 58.2, 53.6 years	Up to 12 months	Mandible	SIS (Austria)	Implants placed 4 months after radiotherapy Delayed loading of implants of 4 months	All removable
Buddula et al. [24]	2010	Retrospective observational	Implant survival in irradiated bone	Own—implant present in oral cavity at time of data collection then deemed to have survived.	N/A	13/16	SCC, adenoid cystic carcinoma, BCC and unknown	Mean = 60.2 years	Up to 7 years	Maxilla and mandible	Unknown	Median time from ending radiotherapy to implant placement was 3.4 years.	Unknown
Klein et al. [32]	2009	Retrospective observational	Prognostic parameters for the rehabilitation of mandibular continuity	N/A	Naert et al. 1992	11/16	SCC	Mean = 55.7 years	Not documented	Mandible	Unknown	Implants were principally placed into the following 4 tissue conditions:	Unknown

Table 1 Study characteristics and MINORS scores (*Continued*)

Author	Year of publication	Study design	Outcome measure	Criteria—survival	Criteria—success	Quality assessment using the MINORS assessment tool	Head and neck cancer diagnosis	Patients age range	Follow-up period	Implant site	Implant system	Implant placement protocol	Prosthodontic rehabilitation
			defects with free autologous bone and dental implants for patients after intra-oral squamous cell carcinoma									non-irradiated local bone, irradiated local bone, osteoplastic in non-irradiated tissue and osteoplastic in irradiated tissue.	
Burgess et al. [27]	2017	Retrospective observational	Implant survival in a variety of composite free flaps	Own—implant not removed then survived	N/A	10/16	Head and neck neoplasia	Average age at implantation was 51 years (range, 18–77 years)	At least 6 months follow-up	Maxilla and mandible	Neoss, Straumann Dentsply Sirona, South Africa - Head Office implants	Primary and secondary implant placement. The mean time to implant placement from reconstruction was 19 months (range, 0–141 months) with 2 patients (7 implants) having their implants placed into the fibula 6 weeks before harvesting.	Unknown
Chiapasco et al. [18]	2006	Retrospective observational	Fibula Free flap survival, implant survival	Albrektsson et al.1986	Albrektsson et al.1986	9/16	Rhabdomyosarcoma, sarcoma, SCC, osteosarcoma and ameloblastoma	Range = 13–66 years	Range = 24–106 months	Maxilla and mandible	Branemark, ITI and 3i	Placement using surgical guides. Secondary implant placement 3–12 months after oncological reconstruction. Implants immediately loaded in 2 patients. Delayed loading for the all other patients 3-6 months after placement.	Fixed and removable
Chiapasco et al. [23]	2008	Retrospective observational	Bone graft success, implant success, patient satisfaction	Own—similar to Albrektsson et al.1986 authors allow greater bone loss around implants.	Albrektsson et al.1986	7/16	Ameloblastoma, ossifying fibroma, cementoblastoma, myxoma, SCC, gigantocellular tumour, OKC and rhabdomyosarcoma.	Range = 17–54 years	Range = 48–132 months	Mandible	Straumann, Nobel biocare and Branemark	Placement using surgical guides. Secondary implant placement 4–7 months after oncological reconstruction. Delayed loading of implants 4-6 months after placement.	All fixed

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Table 1 Study characteristics and MINORS scores *(Continued)*

Author	Year of publication	Study design	Outcome measure	Criteria—survival	Criteria—success	Quality assessment using the MINORS assessment tool	Head and neck cancer diagnosis	Patients age range	Follow-up period	Implant site	Implant system	Implant placement protocol	Prosthodontic rehabilitation
Chiapasco et al. [33]	2000	Retrospective observational	Bone resorption of bone grafts, behaviour of bone around implants, implant failure	Albrektsson et al.1986	Albrektsson et al.1986	10/16	Ewing sarcoma, epidermoid carcinoma, cylindroma, desmoplastic fybroma, chondroblastic sarcoma, cementoblastoma, ameloblastoma, chondrosarcoma, ossifying fibroma, myxoma and giantocellular tumour	Range = 20–58 years	Range = 14–34 months	Maxilla and mandible	Branemark and ITI	Placement using surgical guides. Secondary implant placement 4–8 months after oncological reconstruction. Delayed loading of implants 4-6 months after placement.	Unknown
Hessling et al. [28]	2015	Retrospective observational	Implant survival, peri-implantitis	Poorly defined—implant still in situ then survived.	N/A	8/16	SCC and odontogenic tumours with malignant degeneration	Range = 18–77 years	Range = 3–82 months	Maxilla and mandible	Xive and templant	No described protocol.	Fixed and removable

The characteristics and MINORS (Methodological Index for Non-Randomized Studies) score for each of the 20 studies included within the review divided into those studies with a mean follow-up of 3 years or greater and those studies with a mean follow-up of less than 3 years or where no mean follow-up was reported within the study

Those marked with an asterisk have had the survival percentages calculated by the authors due to their being adequate information/data within the studies to calculate this

Abbreviations: SCC squamous cell carcinoma, *BCC* basal cell carcinoma, *ACC* adenoid cystic carcinoma, *OKC* odontogenic keratinocyst, *RDX* radiotherapy, *chemo* chemotherapy, *ORN* osteoradionecrosis, *DCIA* deep circumflex iliac artery flap, *MINORS* Methodological Index for Non-Randomized studies

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Table 2 Summary of implant survival and implant success in autogenous bone grafts

Author	Year of publication	Donor site of autogenous bone graft	Radiotherapy/ chemotherapy to bone graft site	Complications	Implant survival				Implant success				Reasons for a lack of implant success
					No. of patients who had implants placed into autogenous bone grafts (and failures)	Overall patient implant survival in autogenous bone grafts	No. of implants placed into autogenous bone grafts (and failures)	Overall implant survival in autogenous bone grafts	No. of patients who had implants placed into autogenous bone grafts (and unsuccessful)	Overall patient implant success in autogenous bone grafts	No. of implants placed into autogenous bone grafts (and unsuccessful)	Overall implant success in autogenous bone grafts	
Studies with an average follow-up of 3 years or greater													
Watzinger et al. [29]	1996	Vascularised iliac bone graft and non-vascularised iliac and rib bone graft	Yes—all patients had chemotherapy and RDX	Marginal bone loss, periodontal pocketing, gingival index and sulcus bleeding index showed wide variation	Not reported	N/A	52 (14)	73.1%*	Not reported	N/A	52 (22)	57.7%*	Non-functioning implants (not prosthetically loaded)
Teoh et al. [26]	2005	Vascularised fibula free flap	Yes—5 patients had chemotherapy, 1 patients had chemo/RDX (pre-implant placement), 6 patients had pre-op RDX and 1 patient had post-op RDX.	13 patients had soft tissue hyperplasia that need debulking or skin grafting	22 (2)	90.9%*	71 (3)	95.8%*	Not reported	N/A	Not reported	N/A	N/A
Wu et al. [30]	2008	Fibula free flap	Yes—3 patients had RDX (unsure if pre or post-op)	Soft tissue hyperplasia needed surgical removal in 6 patients (17 implants).	29 (not reported)	N/A	100 (9)	91.0%	29 (not reported)	N/A	100 (14)	86.0%	Unfavourable local soft tissue and implant left as sleepers. Peri-implant bone loss greater than 2 mm
Fenlon et al. [19]	2012	Vascularised free flap—DCIA, radial, fibula and rib	Yes—35 implants had RDX	High rate of poor implant positioning in primary implant placement.	41 (10)	75.6%*	145 (18)	87.5%*	Not reported	N/A	145 (34)	76.6%*	Implants osseointegrated but prosthetically unusable
Ch'ng et al. [20]	2014	Vascularised fibula free flap	Yes—66/243 patients had RDX (43 patients pre-op RDX, 23 patients post-op RDX)	ORN 7.7% of all implants (19 patients, 4 cases in vascularised fibula free flap and 15 in native bone) smoking was shown to be a significant risk factors. Also modification of peri-implant soft tissue required such as debulking of soft tissue and vestibuloplasty as required.	54 (10)	81.5%*	243 (20)	91.8%	Not reported	N/A	Not reported	N/A	N/A
Shaw et al. [31]	2005	Vascularised composite DCIA, fibula and radius and non-vascularised bone grafts	Yes—47% of patients had RDX	Soft tissue overgrowth in 3 patients (5 implants). Also, surgical debulk of soft tissue reported in number of cases.	33 (12)	63.6%*	123 (32)	69.0%	Not reported	N/A	Not reported	N/A	N/A

Table 2 Summary of implant survival and implant success in autogenous bone grafts (Continued)

Author	Year of publication	Donor site of autogenous bone graft	Radiotherapy/chemotherapy to bone graft site	Complications	Implant survival				Implant success				
					No. of patients who had implants placed into autogenous bone grafts (and failures)	Overall patient implant survival in autogenous bone grafts	No. of implants placed into autogenous bone grafts (and failures)	Overall implant survival in autogenous bone grafts	No. of patients who had implants placed into autogenous bone grafts (and unsuccessful)	Overall patient implant success in autogenous bone grafts	No. of implants placed into autogenous bone grafts (and unsuccessful)	Overall implant success in autogenous bone grafts	Reasons for a lack of implant success
Wang et al. [21]	2015	Vascularised fibula free flap (double barrel or vertical distraction osteogenesis techniques)	NO	Implant hygiene and bleeding increased over time. 6 patients (11 implants) required soft tissue reduction however recurrence of soft tissue overgrowth occurred.	19 (0)	100%	51 (0)	100%*	Not reported	N/A	51 (7)	86.3%*	Peri-implant bone loss greater than criteria (radiographic assessment)
Yerit et al. [16]	2006	Vascularised and non-vascularised iliac bone graft	No—No RDX to bone graft sites	None noted only documenting causes of implant loss	Not reported	N/A	78 (13)	54.0%	Not reported	N/A	Not reported	N/A	N/A
Linsen et al. [17]	2009	Avascularised iliac bone graft	Yes—39 implants had RDX, 44 implants did not have RDX	Peri-implantitis in 12 patients (31 implants).	Not reported	N/A	79 (8)	89.9%*	Not reported	N/A	Not reported	N/A	N/A
Studies with an average follow-up of less than 3 years or no average follow-up reported													
Fierz et al. [25]	2013	Vascularised free flap—fibula, radius, scapula	Yes—20 out of 46 implants had RDX	Frail patients limited treatment, and prosthetic rehabilitation was challenging	Not reported	N/A	46 (8)	82.6%*	Not reported	N/A	Not reported	N/A	N/A
Barrowman et al. [7]	2011	Vascularised free flap—iliac, DCIA and fibula and non-vascularised bone graft.	Yes—15 implants in to irradiated vascularised free flap	Inability of patients to tolerate prosthesis. Peri-implantitis and lack of integration of some implants.	Not reported	N/A	38 (5)	86.8%*	Not reported	N/A	Not reported	N/A	N/A
Zou et al. [22]	2013	Vascularised iliac bone graft	No	Increase in plaque index over time. Prosthodontic complications overtime after prosthesis fitted also tumour recurrence	32 (not reported)	N/A	110 (4)	96.4%	Not reported	N/A	110 (9)	91.8%	Severe gingival hyperplasia and bone resorption in peri-implant area
Schultes et al. [15]	2002	Vascularised scapula and iliac bone graft	Yes—all patients had RDX 60 Gys.	Increased pocket depth around implants placed into non-native bone in comparison to native bone. 7 implants with pocketing greater than 5 mm were all in vascularised free flaps	38 (2)	94.7%*	96 (2)	97.9%*	Not reported	N/A	96 (4)	95.8%*	Implants inadequately positioned and could not be used for further prosthetic treatment
Buddula et al. [24]	2010	Bone graft—fibula, iliac and scapula (unsure of	Yes—all patients had RDX	None noted only documenting implant survival	Not reported	N/A	59 (8)	83.3%	Not reported	N/A	Not reported	N/A	N/A

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Table 2 Summary of implant survival and implant success in autogenous bone grafts (Continued)

Author	Year of publication	Donor site of autogenous bone graft (vascularised or non-vascularised)	Radiotherapy/chemotherapy to bone graft site	Complications	Implant survival				Implant success				
					No. of patients who had implants placed into autogenous bone grafts (and failures)	Overall patient implant survival in autogenous bone grafts	No. of implants placed into autogenous bone grafts (and failures)	Overall implant survival in autogenous bone grafts	No. of patients who had implants placed into autogenous bone grafts (and unsuccessful)	Overall patient implant success in autogenous bone grafts	No. of implants placed into autogenous bone grafts (and unsuccessful)	Overall implant success in autogenous bone grafts	Reasons for a lack of implant success
Klein et al. [32]	2009	Avascular iliac bone graft	Yes—some patients had RDX	None noted only documenting implant survival	Not reported	N/A	128 (22)	78.4%	Not reported	N/A	Not reported	N/A	N/A
Burgess et al. [27]	2017	Vascularized bone grafts—fibula, DCIA, scapula and radial	Yes—some patients had RDX	None noted only documenting implant survival	59 (not reported)	N/A	199 (11)	93.6%	Not reported	N/A	Not reported	N/A	N/A
Chiapasco et al. [18]	2006	Vascularised fibula free flap	Yes—some patients had RDX and chemo—unknown number	Soft tissue overgrowth in 2 patients that required removal and palatal mucosal graft placed	14 (1)	92.9%*	62 (1)	98.3%*	14 (2)	85.7%*	62 (5)	91.9%*	Peri-implant bone loss greater than criteria (radiographic assessment)
Chiapasco et al. [23]	2008	Non-vascularised—Calvarium or iliac bone graft	Unknown	Soft tissue grafting required around 3 implants in 3 patients	16 (1)	93.8%*	60 (2)	96.7%	16 (2)	87.5%*	60 (4)	93.3%	Peri-implant bone loss greater than criteria (radiographic assessment)
Chiapasco et al. [33]	2000	Non-vascularised—ilieum and fibula, and vascularised free flap—ilieum and fibula	Yes—3 patients had RDX (unknown if pre or post)	Soft tissue grafting required around 3 implants in 3 patients	18 (2)	88.9%*	72 (3)	95.8%*	18 (2)	88.9%*	72 (3)	95.8%*	N/A
Hessling et al. [28]	2015	Free iliac crest, microvascular iliac, microvascular fibula, microvascular scapula, calavarial bone graft	Yes—some patients had RDX and chemo (pre- and post-op) unknown number	67% peri-implantitis due to a lack of attached gingivae	Not reported	N/A	93 (8)	91.4%*	Not reported	N/A	Not reported	N/A	N/A

Implant survival and implant success in autogenous bone grafts was extracted on a patient and implant level (where applicable) for all 20 studies included within this review
Those marked with an asterisk have had the survival/success percentages calculated by the authors due to their being adequate information/data within the studies to calculate this
Abbreviations: RDX radiotherapy, chemo chemotherapy, DCIA deep circumflex iliac artery flap, pre-op pre-operative, post-op postoperative

Table 3 Implant survival in autogenous bone grafts placed in vascularised and non-vascularised bone grafts

Author	Year of publication	Non-vascularised bone graft				Vascularised bone graft			
		No. of patients who had implants placed into non-vascularised autogenous bone grafts (and failures)	Overall patient implant survival in non-vascularised autogenous bone grafts	No. of implants placed into non-vascularised autogenous bone grafts (and failures)	Overall implant survival in non-vascularised autogenous bone grafts	No. of patients who had implants placed into vascularized autogenous bone grafts (and failures)	Overall patient implant survival in vascularised autogenous bone grafts	No. of implants placed into vascularised autogenous bone grafts (and failures)	Overall implant survival in vascularised autogenous bone grafts
Studies with an average follow-up of 3 years or greater									
Watzinger et al. [29]	1996	Not reported	N/A	33 (13)	60.6%*	Not reported	N/A	19 (1)	94.7%*
Teoh et al. [26]	2005	N/A	N/A	N/A	N/A	22 (2)	90.9%*	71 (3)	95.8%*
Wu et al. [30]	2008	N/A	N/A	N/A	N/A	29 (not reported)	N/A	100 (9)	91%
Fenlon et al. [19]	2012	N/A	N/A	N/A	N/A	41 (10)	75.6%*	145 (18)	87.5%*
Ch'ng et al. [20]	2014	N/A	N/A	N/A	N/A	54 (10)	81.5%*	243 (20)	91.8%
Shaw et al. [31]	2005	2 (1)	50%*	8 (2)	75%*	31 (11)	64.5%*	115 (30)	73.9%*
Wang et al. [21]	2015	N/A	N/A	N/A	N/A	19 (0)	100%	51 (0)	100%*
Yerit et al. [16]	2006	Not reported	N/A	Not reported	N/A	Not reported	N/A	Not reported	N/A
Linsen et al. [17]	2009	Not reported	N/A	79 (8)	89.9%*	N/A	N/A	N/A	N/A
Studies with an average follow-up of less than 3 years or no average follow-up reported									
Fierz et al. [25]	2013	N/A	N/A	N/A	N/A	Not reported	N/A	Not reported	N/A
Barrowman et al. [7]	2011	Not reported	N/A	6 (0)	100%*	Not reported	N/A	32 (5)	84.4%*
Zou et al. [22]	2013	N/A	N/A	N/A	N/A	32 (not reported)	N/A	110 (5)	96.4%
Schultes et al. [15]	2002	N/A	N/A	N/A	N/A	38 (2)	94.7%*	96 (2)	97.9%*
Buddula et al. [24]	2010	Not reported	N/A	Not reported	N/A	Not reported	N/A	Not reported	N/A
Klein et al. [32]	2009	Not reported	N/A	128 (22)	82.8%*	N/A	N/A	N/A	N/A
Burgess et al. [27]	2017	N/A	N/A	N/A	N/A	59 (not reported)	N/A	199 (11)	93.6%
Chiapasco et al. [18]	2006	N/A	N/A	N/A	N/A	14 (1)	92.9%*	62 (1)	98.3%*
Chiapasco et al. [23]	2008	16 (1)	93.8%*	60 (2)	96.7%*	N/A	N/A	N/A	N/A
Chiapasco et al. [33]	2000	10 (1)	90%*	41 (2)	95.1%*	8 (1)	87.5%*	31 (1)	96.8%*
Hessling et al. [28]	2015	Not Reported	N/A	62 (4)	93.5%*	Not reported	N/A	31 (4)	87.1%*

Implant survival in autogenous bone grafts was extracted on a patient and implant level (where applicable) for all 20 studies included within this review that specifically reported on implant survival in either vascularised or non-vascularised autogenous bone grafts

Those marked with an asterisk have had the survival percentages calculated by the authors due to their being adequate information/data within the studies to calculate this

within autogenous bone grafts than those within implants placed into the native bone; however, two studies (Buddula et al. [24], Teoh et al. [26]) reported no significant difference.

Autogenous bone graft type and implant survival

Seventeen studies reported on the specific bone graft type (non-vascularised or vascularised) into which the implants were placed. In the remaining three studies (Buddula et al. [24], Fierz et al. [25], Yerit et al. [16]), this distinction was not possible.

Of these 17 studies, 8 studies reported on implant survival in non-vascularised bone grafts and 14 studies reported on implant survival in vascularised bone grafts with 5 studies (Barrowman et al. [7], Hessling et al. [28], Watzinger et al. [29], Shaw et al. [31], Chiapasco et al. [33]), therefore reporting on implant survival in both non-vascularised and vascularised bone grafts within

their study (Table 3). Implant survival appears to be higher for those implants placed into vascularised bone grafts in comparison to non-vascularised bone grafts. Of the five studies reporting on both vascularised and non-vascularised bone grafts, three of these studies (Barrowman et al. [7], Watzinger et al. [29], Chiapasco et al. [33]) reported higher implant survival in vascularised bone grafts whereas the other two studies (Hessling et al. [28], Shaw et al. [31]) reported higher implant survival in non-vascularised bone grafts. Shaw et al. [31] reported that implants placed into 'vascularized bone graft were superior to non-vascularized bone. In particular, those implants in composite radial forearm flaps performed badly. With the proportion of patients with implant loss in these bone flaps within their study being 27% in iliac crest, 33% in fibula, and 100% in radius and that implants placed in composite fibula and iliac crest flaps performed approximately as well as in native maxilla within their study' [31].

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Twelve studies reported on the use of more than one autogenous bone graft donor site within their study (Barrowman et al. [7], Schultes et al. [15], Yerit et al. [16], Fenlon et al. [19], Chiapasco et al. [23], Buddula et al. [24], Fierz et al. [25], Burgess et al. [27], Hessling et al. [28], Watzinger et al. [29], Shaw et al. [31] and Chiapasco et al. [33]); of these, five studies reported on the effect of the autogenous bone graft donor site on implant survival. Two studies (Fenlon et al. [19], Burgess et al. [27]) reported no significant effect on implant survival in varying graft donor sites; however, three studies (Hessling et al. [28], Shaw et al. [31], Chiapasco et al. [33]) reported varying implant survival rates within different autogenous bone grafts but only one study (Hessling et al. [28]) reported that implant loss was significant with this being for implants placed into fibula bone grafts. Shaw et al,. [31] reporting that implants placed into 'vascularized bone graft were superior to non-vascularized bone. In particular, those implants in composite radial forearm flaps performed badly. With the proportion of patients with implant loss in these bone flaps within their study being 27% in iliac crest, 33% in fibula, and 100% in radius and that implants placed in composite fibula and iliac crest flaps performed approximately as well as in native maxilla within their study' [31].

Radiotherapy and implant survival

Seven studies reported on outcomes related to implant survival in irradiated autogenous bone grafts (Barrowman et al. [7], Fenlon et al. [19], Ch'ng et al. [20], Buddula et al. [24], Fierz et al. [25], Teoh et al. [26], Burgess et al. [27]) (Table 4). One study reported solely on irradiated patients (Buddula et al. [24]) the other six studies (Barrowman et al. [7], Fenlon et al. [19], Ch'ng et al. [20], Fierz et al. [25], Teoh et al. [26], Burgess et al. [27]) reported on both irradiated and non-irradiated patients. These six studies (Barrowman et al. [7], Fenlon et al. [19], Ch'ng et al. [20], Fierz et al. [25], Teoh et al. [26], Burgess et al. [27]) all reported higher implant failure (at an implant and a patient level (where applicable)) of implants placed into autogenous bone grafts in irradiated patients in comparison to those patients who did not received radiotherapy (Table 4).

All of these studies (Barrowman et al. [7], Fenlon et al. [19], Ch'ng et al. [20], Fierz et al. [25], Teoh et al. [26], Burgess et al. [27]) reported on the deleterious effect of radiotherapy on implant survival in autogenous bone grafts within their studies and was found to be statistically significant in two studies (Fenlon et al. [19], Ch'ng et al. [20]) with Fenlon [19] reporting a close correspondence of implant survival (in vascularised free composite grafts) and an absence of radiotherapy using a multiple correspondence analysis and Ch'ng et al. [20] who reported a statistical significance associated with higher implant failure in irradiated fibula free flaps in comparison to non-

irradiated fibula free flaps ($P = 0.041$). However, in two studies (Teoh et al. [26], Burgess et al. [27]), no statistical significance was found despite higher implant failure.

Primary and secondary implant placement and implant survival

Six studies clearly reported the use of both primary and secondary implant placement within their study (Fenlon et al. [19], Ch'ng et al. [20], Zou et al. [22], Burgess et al. [27], Watzinger et al. [29], Wu et al. [30]); however, only one study (Fenlon et al. [19]) reported on implant survival in primary and secondary implant placement within autogenous bone grafts. Felon et al. [19] reported on implant survival in immediate vs delayed placement of the implant fixtures into free vascularised grafts and found that implant survival of immediately placed implants was significantly worse than that of implants placed after a delay of 3 months in free vascularized grafts.

Cancer diagnosis and implant survival

With regards to cancer type (malignant vs benign), three studies (Schultes et al. [15], Watzinger et al. [29], Klein et al. [32]) reported exclusively on implant survival in patients with malignant H&N cancers with varying implant survival rates being reported, whilst one study reported exclusively on benign H&N cancer patients (Wang et al. [21]) with a 100% implant survival rate being reported (Table 2). Two studies (Fenlon et al. [19], Burgess et al. [27]) provided non-descriptive terms (cancer, head and neck neoplasia) for the type of H&N cancer of the patients within their studies and therefore differentiation between benign and malignant disease could not be made. The other 14 studies reported on both malignant and benign H&N cancers; however, the implant survival data was not reported or presented in a way in which comparison of implant survival in patients with malignant or benign H&N cancers could be made.

Implant survival and Peri-implant soft tissue

Only one study (Linsen et al. [17]) reported on the effect of the peri-implant soft tissue and implant survival of implants placed into autogenous bone grafts. Linsen et al. [17] reported a higher implant failure of implants placed into bone and soft tissue grafts in comparison to implants placed into a bone grafts with residual soft tissues. This difference, however, was not found to be statistically significant ($p = 0.436$).

In the other 19 studies, the effect of the peri-implant soft tissue was not directly reported as being a factor for implant survival. However, implant success appeared to be significantly affected by the peri-implant soft tissues (see the "Implant survival and Implant Success" and "Complications" sections – for further details).

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Table 4 Implant survival in autogenous bone grafts of irradiated & non-irradiated patients

Author	Year of publication	RDX				No RDX			
		No. of implants placed into autogenous bone grafts with RDX (and failures)	Overall implant survival of implants placed into autogenous bone grafts with RDX	No. of patients who had implants placed into autogenous bone grafts with RDX (and failures)	Patient based implant survival of implant placed into autogenous bone grafts with RDX	No. of implants placed into autogenous bone grafts with no RDX (and failures)	Overall implant survival of implants placed into autogenous bone grafts with no RDX	No. of patients who had implants placed into autogenous bone grafts with no RDX (and failures)	Patient-based implant survival of implant placed into autogenous bone grafts with no RDX
Teoh et al. [26]	2005	14(2)	85.7%*	4 (1)	75%*	57 (1)	98.2%*	22 (1)	95.4%*
Fenlon et al. [19]	2012	35 (15)	57.1%*	12 (8)	33.3%*	110 (3)	97.3%*	29 (2)	93.1%*
Ch'ng et al. [20]	2014	66 (11)	83.3%*	Not reported	N/A	177 (9)	94.9%*	Not reported	N/A
Fierz et al. [25]	2013	20 (6)	70.0%*	Not reported	N/A	26 (2)	92.3%*	Not reported	N/A
Barrowman et al. [7]	2011	15 (5)	66.7%*	Not reported	N/A	23 (0)	100%*	Not reported	N/A
Buddula et al. [24]	2010	59 (8)	83.3%	Not reported	N/A	N/A	N/A	N/A	N/A
Burgess et al. [27]	2017	45* (7)	84.4%*	Not reported	N/A	154 (4)	97.4%*	Not reported	N/A

Implant survival in autogenous bone grafts of irradiated and non-irradiated patients was extracted on an implant and patient level (where applicable) for seven studies that reported on implant survival of implants placed in autogenous bone grafts

Those marked with an asterisk have had the survival percentages calculated by the authors due to their being adequate information/data within the studies to calculate this

Abbreviations: RDX radiotherapy

Implant survival and implant success

In nine studies (Schultes et al. [15], Fenlon et al. [19], Wang et al. [21], Zou et al. [22], Chiapasco et al. [18], Chiapasco et al. [23], Watzinger et al. [29] Wu et al. [30], Chiapasco et al. [33]), both implant survival and success data was reported or provided (Table 2). When comparing implant survival and implant success in eight studies (Schultes et al. [15], Fenlon et al. [19], Wang et al. [21], Zou et al. [22], Chiapasco et al. [18], Chiapasco et al. [23], Watzinger et al. [29], Wu et al. [30], Chiapasco et al. [33]) implant success was found to be lower than implant survival but in one study (Chiapasco et al. [33]) implant survival and success were reported as being the same. The reasons for a lack of implant success within these eight studies (other than implant failure/loss) were related to excessive peri-implant bone loss in five studies (Wang et al. [21], Zou et al. [22], Chiapasco et al. [18], Chiapasco et al. [23], Wu et al. [30]), an inability to prosthetically restore the implants in four studies (Schultes et al. [15], Fenlon et al. [19], Watzinger et al. [29], Wu et al. [30]) and gingival hyperplasia in one study (Zou [22]). Six of these studies (Schultes et al. [15], Wang et al. [21], Zou et al. [22], Chiapasco et al. [18], Chiapasco et al. [23], Wu et al. [30]) reported some of this lack of success to the peri-implant soft tissue which was most frequently the soft tissue component of a combined bone and soft tissue free flap (most commonly the external skin).

Complications

A variety of implant-based complications were documented. Complications were often described within the study rather than being formal assessed, defined or used as outcome measures. Due to there being a lack of formal definition and variability in the documentation within the studies, the data cannot be considered robust to be collectively appraised but is described for information purposes. Common "complications" reported in the studies include soft tissue overgrowth/hyperplasia of the peri-implant tissues (Wang et al. [21], Chiapasco et al. [18], Teoh et al. [26], Wu et al. [30], Shaw et al. [31]), peri-implantitis and periodontal pocketing (Barrowman et al. [7], Schultes et al. [15], Linsen et al. [17], Burgess et al. [27], Hessling et al. [28]), the need for soft tissue debulking/modification around free flaps (Ch'ng et al. [20], Shaw et al. [31]) and the need for mucosal/soft tissue graft around implants to improve the soft tissue profile (Chiapasco et al. [23], Teoh et al. [26], Chiapasco et al. [33]). These peri-implant complications were most commonly seen when the soft tissue profile around the implant was related to a soft tissue graft and therefore did not have attached keratinised mucosa which is needed to provide a soft tissue profile that is conducive to peri-implant health. Other complications include poor oral hygiene (Wang et al. [21], Zou [22]), challenging

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prosthodontic rehabilitation/inability to tolerate the prosthesis provided (Barrowman et al. [7], Zou et al. [22], Fierz et al. [25]), poor implant position (Schultes et al. [15], Fenlon et al. [19], Watzinger et al. [29], Wu et al. [30]) and osteoradionecrosis (Ch'ng et al. [20]) (Table 2).

Discussion

Summary of evidence

Dental implants are now perceived to be a vital part of the clinician's armamentarium in the provision of oral and dental rehabilitation for patients with acquired deformity following management of their H&N cancer, and therefore, this systematic review is relevant to clinicians and stakeholders involved in the treatment and management of H&N cancer patients specifically with those involved in placing or utilising dental implants to assist in the dental/oral rehabilitation of H&N cancer patients.

The main findings from this systematic review did however identify, with the exception of a small number of studies, implant survival (at an implant level) in autogenous bone grafts was clinically promising (> 85%); however, this appears to be lower than implants placed into the native bone in H&N cancer patients. Weak evidence was identified which suggests that radiotherapy is a prognostic factor affecting implant survival in this patient cohort; however, this has also been reported as having a detrimental effect on implant survival in the native bone within the literature [34]. The type of autogenous bone graft donor site and implant survival was also reviewed within the included studies that compared varying autogenous bone graft donor sites and implant survival. There is some weak evidence from these studies to suggest that implants placed into vascularised bone grafts appear to have a higher survival rate in comparison to non-vascularised bone grafts within this review. This evidence however is unreliable, due to the clear lack of studies reporting on implant survival in non-vascularised bone grafts and thus the subsequent number of implants and patients included within this review. Implant survival did not appear to be affected by the type of H&N cancer type (malignant vs. benign); however, no studies within this review directly compared or enabled the authors of this manuscript to compare studies, and accordingly, no true conclusion can be made on this.

The implant placement protocol with regard to primary (immediate) or secondary (delayed) implant placement was also reviewed, and there is limited evidence from Fenlon et al. that implant failure is significantly worse in immediately placed implants in comparison with a delayed approach in free vascularized grafts.

Implant success was shown to be lower than implant survival and was related to peri-implant bone loss, peri-implant hyperplasia and an inability to prosthetically restore the implants. This was most commonly related to combined bone and soft tissue grafts, specifically the soft tissue component. This soft tissue component provides a suboptimal soft tissue profile which could contribute to implant failure (as a result of peri-implantitis); however, well-designed long-term studies are needed to fully comprehend the effect on implant survival.

Implant complications were also noted specific to autogenous bone grafts related to peri-implant soft tissue overgrowth/hyperplasia and the possible need for soft tissue debulking/modification and mucosal/soft tissue graft around implants, which occurred commonly in combined bone and soft tissue grafts. These finding, however, are limited to low-level evidence in the form of a small number of retrospective observational studies.

Limitations

This systematic review has identified that the quality of evidence to inform clinical decision making regarding the use of implants in transported bone in this patient group is currently deficient. All studies included in the review were retrospective observational studies and in general reported on low patient and implant number and found to be at moderate to serious risk of bias.

A lack of consistency in definitions of the primary (implant related) outcome measures was observed. The outcome measures used in the studies varied and implant survival/success was not necessarily the primary outcome measure. Only 14 of the 20 studies reported the primary outcome measure to be implant survival/success whilst the remainder reported free flap survival, graft success and bone resorption of bone grafts as the primary outcome.

A clear deficiency of many of the studies was the imprecise and inconsistent definitions of implant survival or implant success, as detailed in Table 1. In addition, in a number of studies, the terminology 'implant success' and 'implant survival' were used interchangeably within the narrative making comparison of the studies challenging and rendering statistical analysis of the survival data inappropriate.

The reporting of implant survival data varied between studies and was presented in a variety of ways which included cumulative survival and implant survival incidence. In some cases, no attempt to estimate survival was made but adequate data was documented to enable its calculation (Table 2). Best practice would be the reporting of cumulative survival to give context to survival (time) and account for patient drop-out which may be high in this particular patient group. Due to the variability in the methods of data reporting and their comprehensiveness, there was insufficient confidence in extracted data to report statistical findings. Notably, as all studies presented different deficiencies in data reporting or study definitions, there was no clear way to further exclude studies using these criteria.

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As such, there is a clear need for a consensus on what minimum data set is required for published articles reporting on implant survival in this patient cohort to allow further investigation via systematic reviews (e.g., effect of benign vs malignant H&N cancer and implant survival). The inclusion and exclusion criteria were highly variable, and in some studies, the criteria were such that there was a pre-disposition to selection bias and reporting higher implant survival rates. Patient follow-up was variable and also variably reported but in general was insufficient. Where possible, follow-up of at least 5 years is required to begin to evaluate the outcome of dental implant treatment. Unfortunately, information on long-term dental survival in this cohort is still scarce and the results of the present review should not be extrapolated beyond early implant survival.

Conclusion

Within the limitations of the current review, it can be concluded that implant survival in autogenous bone grafts in H&N oncology patients appears to be promising with implant survival being reported at over 80% in 16 of the 20 studies included with 11 of these reporting implant survival of over 90% in follow-up ranging from 3 months [28] to 15 years [5]. However, there is a lack of good quality evidence in the way of prospective studies and randomised control trials. A lack of long-term survival studies with sufficient implant and patient numbers was identified, and therefore, the results of the present review should not be extrapolated to longer follow-up times. Prognostic factors affecting implant survival in autogenous bone grafts were also reviewed with higher implant failure in autogenous bone grafts being reported in implants placed into irradiated autogenous bone grafts. Weak evidence suggesting implant failure was higher in non-vascularised in comparison with vascularised autogenous bone grafts and that implant failure was greater in primary placed implants in vascularised bone grafts in this cohort was identified. Implant success was lower than implant survival and was most commonly related to peri-implant disease and an inability to prosthetically to restore the implant. This was predominantly related to unfavourable peri-implant soft tissue which is frequently found around implants placed into combined bone and soft tissue flaps.

In order to understand the use of implants in autogenous bone grafts in H&N oncology patients larger, well-designed prospective studies are required. There needs to be clear set definitions of implant survival and success and appropriate presentation and statistical analysis of the data so that studies can be brought together to enable meta-analysis.

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Outcomes of implant-based oral rehabilitation in head and neck oncology patients—a retrospective evaluation of a large, single regional service cohort

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Abstract

Background: The study reports on implant survival outcomes in head and neck cancer patients who received implant-based oral rehabilitation in a regional service centre.

Methods: A retrospective analysis of implant survival outcomes in patients treated in a regional service from 2012 to 2017 was performed. The primary outcome measure was implant survival. The secondary outcome measure was to assess the effect of covariates associated with implant failure including bone type, radiotherapy, chemotherapy, gender and surgical implant complications. Kaplan-Meier survival curves were applied to compare differences in the survival rates of groups of variables. Cox proportional hazards models were applied to identify covariates associated with implant failure. p value was set at 0.05.

Results: The sample was composed of 167 head and neck cancer patients who had 779 dental implants placed. Implant survival estimates were calculated: 3 years, 95.7% [95%CI 94.3–97.2%] and 5 years, 95.5% [95%CI 93.9–97.0%], with a median follow-up of 38 months. Gender ($p = 0.09$), radiotherapy ($p = 0.16$) and chemotherapy ($p = 0.17$) did not significantly influence implant survival, whereas implant failure was higher in transported (reconstructed) bone sites in comparison with native bone ($p < 0.01$).

Conclusion: The result of this study suggests that overall implant survival as part of the routine oral rehabilitation is high in this patient cohort; however, implant failure was found to be statistically higher for implant placed into transported bone in comparison to native bone.

Keywords: Dental implant survival, Head and neck oncology, Autogenous bone graft, Microvascular free flap, Prosthodontics

Background

Oral rehabilitation with implant-retained prostheses can significantly improve the quality of life (QoL) for patients following the surgical management of head and neck (H&N) cancer [1], and this treatment modality is becoming more commonly used in this patient group [2–4]. Patients with H&N cancers often undergo ablative

surgery with or without reconstruction, radiotherapy and chemotherapy [5]. Such surgical interventions can lead to significant disability, including facial deformity, loss of oral hard and soft tissues, impaired speech, swallowing and mastication [6, 7]. Neither reconstructive surgeries nor conventional prosthodontic techniques are capable of addressing all of these problems successfully [7–9].

Oral and dental rehabilitation is provided to help facilitate mastication, facial support, oral comfort and oral competence and allow patients to speak, chew and appear in public with confidence [6, 10]. Rehabilitation with a removable prosthesis can often be difficult, if not impossible in

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some patients following surgical management of their H&N oncology. This is due to altered post-surgical anatomy, low salivary flow and a lack of emotional resilience of the patient [6]. For many years, removable prostheses have been central to conventional prosthodontic treatments; however, they have limited success and fail to address all of the problems that the patient may be facing [2, 5, 6, 10–12]. In many cases, a prosthesis may be provided for an aesthetic improvement only, with accepted limited function [6]. The use of osseointegrated dental implants has allowed improved retention of removable prostheses, reduced loading on vulnerable tissues and with this resulted in a reported improvement in the QoL for patients [2, 7, 13, 14].

Osseointegrated dental implants as a treatment modality have been shown to have high success and survival [15]. However, the reliability, safety and usefulness of implant placement in the H&N cancer population remains incompletely defined, mainly due to the limited availability of large, well-constructed studies in the literature [16]. The vast majority of evidence available, to guide clinicians, is formed from case reports and case series, using low patient numbers. Furthermore, the data is universally retrospective in nature which can be understood, as the service provided to this patient group does not lend itself to well-designed highly controlled trials.

With the increasing use of dental implants in the oral rehabilitation of H&N cancer patients [17], an improved evidence base is required to help inform clinical decision-making. The primary objective of this study is to present implant survival rates as part of a service evaluation of large H&N cancer patient cohort, where a consistent care pathway for oral and dental rehabilitation has been operative for the past 5 years. The cohort includes patients whose osseointegrated implants have been placed into a variety of bone types including native, native resected, autogenous non-vascularised and autogenous vascularised bone/free flaps. The secondary objectives are to assess the effect of covariates associated with implant failure such as radiotherapy and chemotherapy, which are frequently eluded to as prognostic factors for implant survival, and also to report the surgical complications during implant placement documented in this patient group.

Methods
Study design and setting
The service evaluation was performed by retrospectively examining treatment records of H&N oncology patients who were provided with an implant-retained prosthesis as part of an oral and dental rehabilitation. The study sample was taken from a population of H&N oncology patients that attended the Restorative Dentistry department at Birmingham Dental Hospital (BDH), Birmingham, UK (United Kingdom), for care following primary management of their H&N cancer, in a 55-month period

from November 2012 to May 2017. The H&N restorative service provided at BDH is a tertiary care service which covers a population of 5.5 million people within the West Midlands region of the UK. The service was led by a single specialist clinical lead during this period, and treatment was provided at no cost to the patients. Treatments were linked with Oral and Maxillofacial surgical (OMFS) teams at BDH or at University Hospitals Birmingham (UHB), Birmingham, UK. Despite the variability in disease presentation and in its management, a consistent co-ordinated care pathway leading to oral and dental rehabilitation including multi-disciplinary team (MDT) planning was followed. The treatment period for data collection included the care of patients who had received implant-based reconstructions within the same service at an earlier date but required prosthodontic maintenance or revision. These patients were included in the analysis subject to the completeness of the minimum data set.

All H&N oncology patients who had completed an oral rehabilitation that included the use of dental implants to retain a prosthesis, during the census period, were included. Patients were excluded if the minimum data set could not be collected. Restoration of the dental implant with a definitive prosthesis was the criterion for successful completion of the oral rehabilitation in this study.

Approval for this service evaluation was given by the Birmingham Community Healthcare NHS Foundation Trust R&D team (Birmingham, UK).

Eligibility criteria
Inclusion criteria

1. Patients who had suffered with H&N cancer
2. Patients who completed an oral rehabilitation with an implant-retained intra-oral prosthesis
3. Patients who had been followed up on at least one occasion after placement of dental implants

Exclusion criteria

1. Patients who did not suffer with H&N cancer
2. Patients who did not complete an oral rehabilitation with an implant-retained intra-oral prosthesis
3. Patients who were not followed up after dental implant placement
4. Patients in whom the minimum data set could not be collected.

Study variables
The minimum data set required for study inclusion required patient demographics (age, gender); tumour diagnosis; the oncological treatment carried out in the form of surgery (tumour ablation, reconstruction), radiotherapy (field and timing) and/or chemotherapy (drugs); adjunctive

surgeries (implant site augmentation); location of implant placement (maxilla, mandible, native bone, resected native bone, autogenous bone grafts vascularised and non-vascularised); dental rehabilitation (fixed, removable and timing) and the implant system used.

The primary outcome of this retrospective study was to assess the survival of dental implants in this patient group (at the patient level), and the secondary objective was to identify possible covariates on implant failure.

Data collection

Patients were identified from electronic patient management systems (iSoft Patient Manager (iPM) software, RiO (Servelec HSC)). The case notes of all potential patients were retrieved and reviewed at BDH. Records were comprised of a combination of paper medical records, scanned paper medical records (Iron Mountain Digital Record centre) and electronic medical records (Case Stream R4 Clinical+ Practice Management Software). In addition, the clinical notes of all patients were also reviewed at the UHB where primary management of their H&N cancer was undertaken using an electronic patient record system (Clinical Portal). Data were collected from the point of implant planning up until their most recent review appointment either at BDH or UHB.

Data were extracted in an anonymised format to a Microsoft Excel template. Data included gender, age, oncological diagnosis and TNM classification and staging; whether the patient had surgery; radiotherapy (dose and site); chemotherapy (drug types and dosages), nature of the surgical reconstruction and type of microvascular free flap/graft used; types of imagery taken for implant planning; whether surgical guides were used at the time of implant placement; the number of implants used; the sites of the implants placed; the types of bone into which the implants were placed; any documented surgical complications; the team who placed the implant(s); the date(s) of implant placement; the date(s) of implant failure; the number of implant failures and the clinically defined reasons for implant failure; the implant manufacturer and fixture dimensions; the site of the oral rehabilitation and whether the oral rehabilitation was fixed or removable. Finally, the date of the last follow-up was recorded or where appropriate the date of death.

For the purpose of this service evaluation, implant survival was defined as an implant fixture still in situ and implant failure defined as implant fixture not in situ which had been lost or removed for whatever reason. Implant survival time was defined as the time interval from the date of implant placement to the date of implant failure or the last follow-up date, whichever occurred first.

Implant planning

The majority of patients were planned for implant-based rehabilitation by a specialist restorative dentist in consultation with surgical teams from BDH and UHB. In the Birmingham service, patients are only provided with implants when conventional non-implant-retained prostheses are deemed inappropriate. As part of consent, patients understood the amount of time it would take for the planning, placement and restoring of dental implants and the need for multistage treatment and for regular review. All treatment costs were met by the service provider. Radiographic images were taken to assist in planning and included cone beam computed tomography (CBCT) with or without reformatting for implant planning software (SIMPLANT® Computer-Guided Implant Treatment Software (Dentsply Sirona, York, PN, USA) and conventional radiographs.

Surgical implant placement technique

Implants were placed by experienced surgical and restorative dental teams accustomed to placing a variety of implant systems in this patient group. Implants were placed into the native mandible/maxilla, resected mandible/maxilla or autogenous bone grafts. Implants were placed either free hand or using a surgical implant guide. Implant placement was both primary (at the time of surgical resection/reconstruction) or secondary/delayed (after surgical resection/reconstruction); however, within this service, primary implant placement was uncommon. At the time of restoring or uncovering the implants, the stability of the implants was assessed (manually). Any unstable implants were removed, not used or buried to allow a longer healing time and then potentially used at a later date. Any soft tissue modifications such as further free flap skin paddle debulking and sulcoplasty to provide a sulcus were carried out prior to oral prosthodontic reconstruction, usually at the time of implant placement.

Statistical approach

Statistical analyses using Kaplan-Meier survival curves were applied to compare differences in the survival rates of groups of variables. The log-rank test method was used to evaluate for significance of differences between groups of covariates on time to failure of implants. A Cox proportional hazards model was applied to identify the covariates associated with the time to failure of implants. The statistical analysis ($\alpha = 0.05$) was conducted considering the patients as the unit of analysis for patient-based variables (gender, chemotherapy, radiotherapy) and with the implant as the unit of analysis for nature of the implant site. Patients that died during the observational period were included in the analysis, but their data was censored beyond the date of their last follow-up appointment. Data were analysed using the statistical analysis software R version 3.3.2.

Results

Demographics

A total of 167 patients who had undergone implant-based oral rehabilitation from November 2012 to May 2017 were included in this service evaluation (Fig. 1). The study population comprised of 58 women (35%) and 109 men (65%) with a mean age of 63.2 years (range 27–88 years). The 167 patients had a variety of malignant and benign H&N tumours at various sites and stagings (Tables 1 and 2). Patients (from date of implant placement to their most recent review) were followed up for a median of 38 months (range 1–142 months). Seven hundred seventy-nine implants in total were placed in 167 patients. One hundred twenty-four patients had 583 implants placed at UHB, and 43 patients had 196 implants placed by at the BDH. A total of 148 patients (89%) had resective surgery, and of these, 92 patients had reconstructive surgery (55%) with a variety of microvascular free flaps and autogenous bone grafts as shown in Table 3 (note that a single patient received both an anterolateral thigh flap (ALT) and a fibula free flap (FFF) reconstruction). During the observation period, 28 patients included within this service evaluation died. As such, their data was censored from any further analysis beyond the date of their last follow-up appointment.

Implant imaging and planning

One hundred thirty-eight patients (83%) had a CBCT scan taken and reformatted for SIMPLANT® for implant planning purposes; once planned, this scan was used to construct SIMPLANT® Surgical Guides (Dentsply Sirona, York, PN, USA) for use at the time of surgical implant placement. For two patients, CBCTs were taken for implant planning (in both these cases, these acquired CBCTs were not reformatted for use with SIMPLANT® planning software); 23 patients had conventional plain radiographs taken for planning, and for four patients, it was unclear what radiographic imagery were taken for implant planning purposes.

Implants

A variety of implant systems were used which included 679 Straumann (Institut Straumann, Basel, Switzerland) implants, 63 Brånemark (Nobel Biocare, Zurich, Switzerland) implants, 36 Astra Tech (Dentsply Implants, Mannheim, Germany) Implants and one Oktagon (Dental Ratio, Langenfeld, Germany) implant, with a range of one to 11 implant used per patient. Of these, 373 (48%) implants were placed in the maxilla and 406 (52%) implants in the mandible (Table 4). Ten patients had primary implant placement with 26 implants, and 157 patients had secondary/delayed placement with 753 implants. Implants were placed into either non-resective native bone, resected native bone (which has not been reconstructed) or free flaps/autogenous bone grafts. Of the 92 patients who received reconstructive surgery with microvascular free flaps/autogenous grafted bone, 52 patients had implants placed into these reconstructed sites with 129 implants placed. In the remaining patients, 22 implants were placed into resected native bone (which has not been reconstructed) and 628 implants placed into non-resected native bone with 323
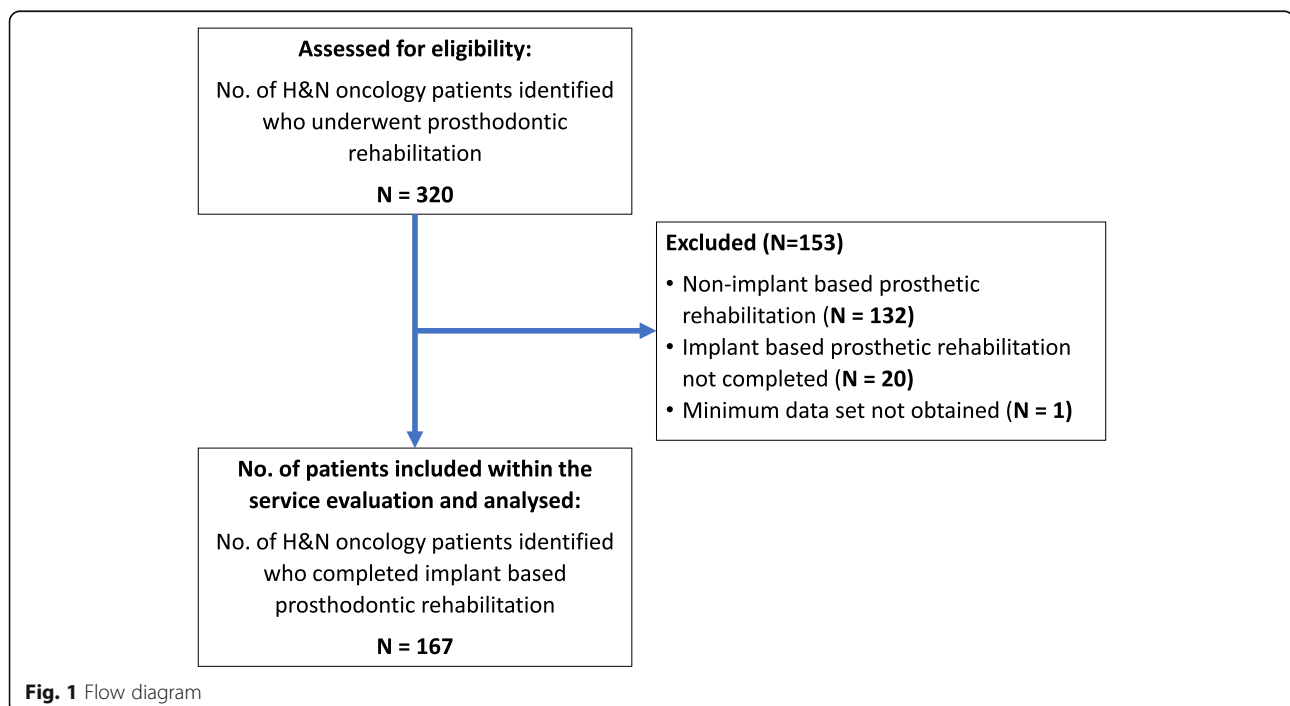

Fig. 1 Flow diagram

Table 1 Summary of cancer type and site of the study population

Cancer type	No. of patients										
	Buccal	FOM	Mandible	Maxilla	Nasal	Tonsil	Skin	Tongue	Pharynx	Not specified	Total
SCC	8	14	23	24	3	19	2	27	8	0	128
Adenoid cystic carcinoma	0	1	1	5	0	0	0	0	0	0	7
Ameloblastoma	0	0	5	2	0	0	0	0	0	0	7
Unspecified carcinoma/tumour	0	0	1	2	0	0	0	0	1	1	5
Malignant melanoma	0	0	1	1	0	0	0	0	0	1	3
Osteogenic sarcoma	0	0	1	2	0	0	0	0	0	0	3
Mucoepidermoid	0	0	1	1	0	0	0	0	0	0	2
Pleomorphic adenoma	0	0	0	2	0	0	0	0	0	0	2
BCC	0	0	0	0	1	0	1	0	0	0	2
Adenocarcinoma	0	0	0	2	0	0	0	0	0	0	2
Primitive neuroectodermal Tumour	0	0	1	0	0	0	0	0	0	0	1
Chondrosarcoma	0	0	0	1	0	0	0	0	0	0	1
Odontogenic keratinocyst	0	0	1	0	0	0	0	0	0	0	1
Lymphoma	0	0	0	0	0	0	0	1	0	0	1
Dendritic cell sarcoma	0	0	0	1	0	0	0	0	0	0	1
Pindburg tumour	0	0	1	0	0	0	0	0	0	0	1
Total	8	15	36	43	4	19	3	28	9	2	167

A summary of the head and neck cancer diagnoses and anatomical sites within the study population. *FOM* floor of the mouth, *BCC* basal cell carcinoma, *SCC* squamous cell carcinoma

implants in non-resected native mandible and 305 in non-resected native maxilla.

Radiotherapy and chemotherapy
A total of 105 patients (63%) received some form of radiotherapy with or without chemotherapy. Of these, 75 patients received radiotherapy (45%), 30 patients received chemoradiotherapy (18%) and no patients received chemotherapy in isolation (Table 5). Due to the retrospective nature of the study, the precise radiation fields could not be obtained in 30 patients and, therefore, it was not possible to estimate dosimetry to each of the implant sites. In the 75 patients in whom radiation fields were documented, the radiation dose for

Table 2 Description of cancer staging and implant failures

Cancer staging	No. of patients	No. of patients with implant failure	Patient implant failure (%)
I	22	1	4.5
II	20	3	15.0
III	12	2	16.7
IVA	63	12	19.0
IVB	1	0	0
IVC	1	0	0
Unknown	48	6	12.5
Total	167	24	14.4

Description of cancer staging and implant failures at the patient level

therapeutic radiotherapy ranged from 50 to 70 Gy in 72 patients. Two patients received palliative radiotherapy at 30 Gy with one of these patients stopping at a 7.5-Gy dose due to radiation-related complications and one patient received a higher dose of 88 Gy. A variety of adjunct chemotherapy drugs were used in 30 patients and shown in Table 6.

Pre-prosthetic surgery
In total, 19 patients required further surgery prior to oral rehabilitation. Eight patients required debulk of the soft tissue component of the microvascular free flap, ten patients required a sulcoplasty and one patient required surgery to release the tongue and improve its mobility to assist in oral rehabilitation.

Surgical complications during implant surgery
Surgical complications during the placement of the dental implants were noted in 24 of 167 patients (14.8% of patients). Complications have been categorised as treatment plan related, anatomy related, procedure related and other (according to Misch et al.,) [18] and are summarised in Table 7. Note that when CAD-CAM surgical implant guides (SIMPLANT® Surgical Guides (Dentsply Sirona, York, PN, USA) are referred to, these are from reformatted CBCTs and were planned using SIMPLANT® implant planning software.

Table 3 Summary of surgical interventions and tissue type used for head and neck reconstruction

Surgical intervention	No. of patients
No surgery	19
Surgery and no reconstruction	56
Surgery and reconstruction with free flap/autogenous bone graft	92
Total	167
Reconstructive tissue used	No. of patients
Fibula	31
Radial	30
DCIA	11
Scapula	9
ALT	7
Iliac crest (non-vascular)	3
Pectoralis Major	2
Total	93

Cancer staging and the number and percentages of patients experiencing implant failure for each cancer stage (where applicable). TNM tumour, node, metastasis

Implant failure

Thirty-four implant failures were observed out of 779 implants placed (median follow-up of 38 months, mean follow-up of 43 months and a range of 1–142 months). A Kaplan-Meier survival curve for overall implant survival is shown in Fig. 2. The median survival time is not attainable since the survival rate for the overall trend is better than 0.50. Survival rate estimates at 3 years and 5 years were 95.7% [95%CI 94.3–97.2%] and 95.5% [95%CI 93.9–97.0%], respectively.

Implant failure occurred in 24 of the 167 patients included (14.4% failure at a patient level). The mean age of study cohort was 63.2 years, and the mean ages of patients exhibiting implant failure or no failures were similar at 62.7 and 63.3 years, respectively. Of the 58 female patients within this cohort, five experienced implant

Table 4 Implant survival in specified bone type

Bone type	No. of implants	No. of implant failures	Implant survival (%)
All patients	779	34	95.6
Native maxilla/mandible (non-resected)	628	12	98.0
Native mandible (non-resected)	323	7	97.8
Native maxilla (non-resected)	305	5	98.4
Resected mandible/maxilla not grafted with autogenous bone	22	0	100
Native autogenous bone graft	129	22	82.9

Implant numbers, failures and implant survival percentages overall and divided into each type of bone into which the implants were placed which include; native bone, resected native bone and autogenous bone graft sites

failure (8.6%) whereas 19 of 109 male patients had implant(s) fail (17.4%) although this was not statistically significant ($p = 0.09$) (Fig. 3a).

Timing

The 34 implant failures were classified by the stage of treatment in which they failed, where stage II is the surgical uncovering of the implant fixture to allow prosthodontic restoration:

- Prior to stage II—3 implant failures
- At stage II and before prosthetic loading—22 implant failures
- After prosthetic loading—9 implant failures

For the 22 implants (in 17 patients) that failed due to a lack of initial osseointegration, the mean and median time to failure were 140 and 97 days, respectively. The mean and median time to failure of the five implants (in four patients) that failed due to peri-implantitis were 915 and 683 days, respectively. Of the six implants that failed due to free flap failure (in two patients), for one of these patients, failure occurred at day 16 after free flap reconstruction and primary implant placement and the other occurred at 451 days after implant placement when there was late failure (as a result of a pathological fracture due to osteoradionecrosis (ORN)). One implant (in one patient) was explanted as it was deemed to be in an unrestorable position and was causing soft tissue trauma after 366 days.

Bone type

Implant survival was high for implants placed into native bone (both resected and non-resected) (Table 4). Implant survival for implants placed into autogenous free flaps was 100% in scapula flaps, 83.0% in fibula free flaps (FFF), 80.0% in radial composite free flaps (RFF) and 76.0% in deep circumflex iliac artery flaps (DCIA). Implant survival in non-vascularised iliac bone graft was 80.0%. Implant survival in native bone associated with microvascular soft tissue flaps was 100% for anterolateral thigh flap (ALT). For pectoralis major flaps (PMF), no implant was placed through this soft tissue flap (Table 8). Kaplan-Meier survival curve comparing outcomes of a simplified comparison between implant failure in native and autogenous bone grafts/free flaps is shown in Fig. 3b. A statistically significant difference in implant failure was demonstrated with increased implant loss in transported bone (autogenous bone graft/free flap sites) in comparison to implant loss in native bone ($p < 0.01$). The majority of implant loss events were recorded in the first 6 months in native bone whereas loss in autogenous bone graft site was more progressive up until 24 months.

Table 5 Use and timing of radiotherapy, chemotherapy and implant failure

	No. of patients	No. of implants	No. of patients with failed implants	Patient-level implant failure (%)	No. of implant failures	Implant level failure (%)
Radiotherapy	75	382	11	14.7	15	3.9
Pre-operative	68	360	8	11.8	9	2.5
Post-operative	7	22	3	42.9	6	27.3
Chemoradiotherapy	30	143	7	23.3	11	7.7
Pre-operative	29	138	7	24.1	11	8.0
Post-operative	1	5	0	0	0	0
Chemotherapy	0	0	0	0	0	0
Neither	62	254	6	9.7	8	3.2
Total	167	779	24	14.4	34	4.4

The number of patients and implants placed into patients who recieved radiotherapy, chemoradiotherapy, chemotherapy (pre- and post-implant placement) and those that or did not receive radiotherpahy or chemotherapy and the number and percentage of patients and implants that failed in each of these groups

Radiotherapy and chemotherapy
In total, 105 patients received some form of radiotherapy with 525 implants placed into this patient group. Of these, 18 patients experienced implant failure with 26 implants failing in total with a patient implant failure rate of 17.1% and an implant failure rate of 5.0%. There were 62 patients that received 254 implants that did not receive any radio- or chemoradiotherapy; of these, 6 patients experienced implant failure with 8 implants failing in total with patient implant failure rate of 9.7% and an implant failure rate of 3.2%. Kaplan-Meier survival curves for radiotherapy and chemotherapy are presented in Fig. 3c, d. Both variables were not found using the log-rank test method to statistically have a significant effect on implant survival ($p = 0.16$ radiotherapy, $p = 0.17$ chemotherapy).

For patients receiving a combination of chemotherapy with radiotherapy, a higher implant failure rate than those patients who received radiotherapy without chemotherapy was observed. Thirty patients in total received chemoradiotherapy with 143 implants being placed into this patient group. Eleven implant failures occurred in 7 patients

Table 6 Chemotherapy agents used within the study population

Chemotherapy agents	No. of patients
Carboplatin	13
Cisplatin	10
Cetuximab	2
MAP chemo (methotrexate, doxorubicin, cisplatin)	2
R-CHOP (rituximab, cyclophosphoamide, doxorubicin, vincristine, prednisolone)	1
TPF (docetaxel, cisplatin, 5-fluorouracil)	1
Carboplatin and paclitaxel	1
Total	30

The drugs and regimes of chemotherapy agents used within the study population in the management of their head and neck cancer

(patient implant failure of 23.3% and an implant failure of 7.7%). This is in comparison with radiotherapy where 75 patients received radiotherapy and 382 implants placed with 15 implant failures occurring in 11 patients (patient implant failure of 14.7% and an implant failure rate of 3.9%) (Table 5). Despite this indication, a fitted Cox PH model for implant failure considering radiotherapy and chemotherapy factors and their combination identified no significant effect. The vast majority of patients received radiotherapy and/or chemotherapy prior to implant placement (Table 5), and therefore, it is not appropriate to discuss timing of these interventions and implant survival within this study.

Implant system and implant geometry
Implant failure with each implant system was calculated and showed varying failure rates (Table 9); however, it would be inappropriate to draw rigid conclusions from this data due to the small numbers of both patients and implants used with some of the implant systems. The most common implant to fail was Brånemark implants with unknown dimensions with 8 failures; this was followed by Straumann RN 4.1-mm-diameter and 10-mm-length implants with 7 implant failures and Straumann RN 4.1-mm-diameter and 12-mm-length implants with 6 implant failures. However, it would be inappropriate to draw conclusions from this data due to incomplete data (164 implant dimensions/lengths were unknown in the 779 implants placed) and the small numbers of some of the implant dimensions used. No real statistical or descriptive analysis of the implant diameter or length can be drawn, and thus, in this retrospective study, implant length/diameter cannot be considered to affect implant survival.

Cancer staging
Patient-level implant failure for cancer staging was calculated. Data may indicate a correlation between higher cancer staging and increased patient implant failure (Table 2). However, it would be inappropriate to draw

Table 7 Surgical complications reported during implant placement

Surgical complications	No. of cases
Treatment planning related	
During implant, placement reconstruction screw hit and reconstruction screw were removed to accommodate the implant	2
Implant position was changed during surgical procedure and the implant was placed free hand as the implant position from the surgical guide was deemed inappropriate	2
Anatomy related	
Difficult surgical access to place implants so implants were not placed	2
The implant was not placed as there is a high risk of inferior dental nerve damage	1
CAD-CAM surgical guide made access more challenging so it was not used to prepare posterior sites	1
Lack of bone volume to place implant—so an alternative site was used	3
Large incisions were required to attain surgical access to fit the CAD-CAM surgical guide which was deemed inappropriate and the implants were subsequently placed free hand	1
Procedure related	
Lack of primary stability of the implant so larger implant diameter was used to achieve primary stability	4
Lack of primary stability of the implant—implants left in situ	2
Lack of primary stability of implants—so the implant was not placed	1
Lack of primary stability of the implant—so the implant was placed in an alternative site	1
The implant was not placed due to being placed too deep	1
Other	
Inadequate fit of CAD-CAM surgical guide—either was not used or was used in to estimate the implant bed preparation site and angulation but then prepared and placed free hand	3
CAD-CAM surgical guide needed to be adjusted to allow it to fit	1
Total	24

The number of cases and type of surgical complications that were documented during the process of surgical implant placement in this study population. These were grouped into treatment planning-, anatomy-, procedure-related and other. CAD-CAM computer-aided design-computer-aided manufacture

rigid conclusions due to the small size of some of the groups.

Surgical complications

Implant failure was higher when surgical complications were experienced during implant fixture placement. In total, 24 patients experienced surgical complications during implant placement; of these, 9 patients experienced implant failure (37.5% of patients with surgical complications) and led to 12 implant failures in total of the 100 implants that were placed in this patient group (with an implant failure rate of 12% in patients that experienced surgical implant complications). This is higher in comparison with the patients that had no documented surgical complications during implant placement with implant failure occurring in 15 of 143 patients (10.5% of patients with no documented surgical complications) and led to 22 implant failures of the 679 implants that were placed (with an implant failure rate of 3.2% of implants with no documented surgical complications in patients that did not experience surgical implant complications).

Discussion

The use of dental implants as part of the oral and dental rehabilitation in H&N oncology patients is becoming increasingly popular [19, 20]. Implants enable rehabilitation in patients in whom conventional removable prostheses are not possible or provide an inadequate functional and cosmetic result. A UK national survey of OMFS surgeons' attitudes in the treatment and dental rehabilitation of oral cancer patients by Alani et al., which compared its finding with a study 15 years previously, reported that the use of dental implants had increased in the use to rehabilitate H&N oncology patients from 43 to 93%, between 1995 and 2009 [17]. The purpose of this article is to present the implant survival rates in a large H&N cancer patient cohort at a regional treatment centre. The results obtained demonstrate that implant survival is high and reliable in this challenging patient group. When comparing the implant survival rate of this study with others, findings appear consistent with previous literature which reports implant survival ranging from 75 to 97.1% with average follow-up ranging from 30.9 months to 5.4 years [5, 10, 12, 16, 21, 22].

In this study, the bone type into which the implants were placed influenced survival. A trend can be observed suggesting higher implant survival when placed within the native mandible/maxilla in comparison with implants placed into autogenous bone grafts and vascularized free flaps. This is consistent with the majority of the reported literature [5, 9, 10, 16]; however, equivalent implant survival in native and autogenous bone grafts/vascularized free flaps has been reported by some centres [23, 24]. Radiotherapy is commonly reported as a risk factor for implant failure. In this study, radiotherapy did not statistically significantly affect implant survival either alone or in combination with chemotherapy. There was, however, a trend towards higher numbers of failures in both of these treatment groups (Fig. 3c, d). In this cohort, the majority of patients received radiotherapy and/or
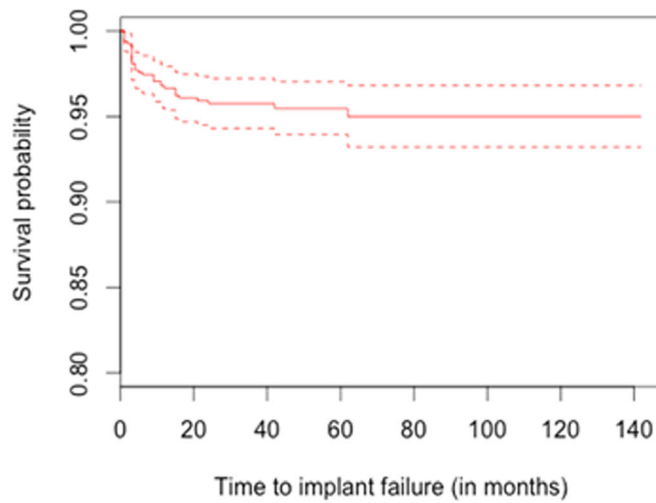
The survival rate at 3 and five years with the corresponding 95% confidence interval.

Time (in months)	Number at risk	Event	Survival rate	Standard Error	95% Confidence Interval for Survival rate	
3 years (36 months)	423	32	0.957	0.00738	0.943	0.972
5 years (60 months)	215	1	0.955	0.00784	0.939	0.970

Min. 1st Qu. Median   Mean   3rd Qu.   Max.

1.00 23.00   38.00   43.07 63.00   142.00

The Median follow-up time (in months) and its range

Fig. 2 A Kaplan-Meier survival curve for overall implant failure in this patient cohort. Implant survival rate at 3- and 5-year rates with corresponding CIs are shown. Median follow-up time and its range are also shown. CI confidence interval, Min. minimum, 1st Qu. first quartile, 3rd Qu. third quartile, Max. maximum

chemotherapy prior to implant placement. The existing evidence base suggests that in particular timing of radiotherapy can effect implant survival, with increased failure reported when radiotherapy is carried out before implant placement [14, 25, 26]. The data quality is however poor, and a systematic review by Nooh concluded that timing of radiation therapy in relation to implant placement had no significant effect on implant survival [27].The combined use of chemoradiotherapy appeared to influence implant survival with a higher implant failure seen in this cohort when compared with patients who received either treatment modality in isolation. This observation supports a report by Hessling et al. [5] who found a statistically significant correlation between implant loss and adjuvant combined radiotherapy and chemotherapy [5].

Patients with higher cancer staging showed a trend towards increased implant failure (at the patient unit of measurement level). However, there is little evidence in the literature to support this with Granström [26]

reporting no correlation between tumour type, size, stage, nodes or metastasis and implant outcomes [26]. The complexity of surgery will undoubtedly influence the subsequent environment into which implant placement is planned, and it was clear from this cohort analysis that surgical complications at the time of implant placement were frequent and varied. A trend between implant failure and reports of surgical complications was observed but could not be safely statistically tested due to the large number of covariates and confounding factors. Surprisingly, there appears to be no literature reporting on this concept with which to compare this observation.

Implant survival within this study did not appear to be affected by patient demographics of age or sex. In relation to some of the factors that were considered, definite conclusions could not be reached due to small patient/implant numbers within comparative groups and also the incomplete data capture due to the retrospective

Fig. 3 a Kaplan-Meier survival curves comparing implant survival according to gender. Implants placed into males had higher failure rate in comparison to those placed into females; however, this was not found to be statistically significant (*p* = 0.09). **b** Kaplan-Meier survival curves comparing implant survival in the native and transported bone. Implants placed into the transported bone had higher implant failure rate in comparison to implants placed into the native bone. This was found to be statistically significant (*p* ≤ 0.001). **c** Kaplan-Meier survival curves comparing implant survival in patients who received radiotherapy with those that did not. Implants placed into patients who received radiotherapy had a higher implant failure rate in comparison to implants placed into those patients who did not; however, this was not found to be statistically significant (*p* = 0.16). **d** Kaplan-Meier survival curves comparing implant survival in patients who received chemotherapy with those that did not. Implants placed into patients who received chemotherapy had a higher implant failure rate in comparison to implants placed into those patients who did not; however, this was not found to be statistically significant (*p* = 0.17)

nature of this study. This included the implant system and implant dimensions. When assessing the literature with regard to implant dimensions, Buddula et al. [25] and Klein et al [28] reported that implant dimensions had no effect on implant survival [25, 28]; however, these studies had a relatively short follow-up. Shaw et al. [10] on the other hand found that implants of less than

13 mm length had a higher rate of failure over longer implant lengths in this patient group [10].

The major strength of this study is the large patient and implant number with a reasonable follow-up period when compared with the previously literature. Some of the principal limitations of this study are its retrospective nature, the limited follow-up period which

Table 8 Type of microvascular free flap/autogenous bone graft implant placed into and implant survival

Type of microvascular free flap/autogenous bone graft—implant inserted into	No. of patients	No. of implants	No. of implant failures	Implant survival (%)
Scapula	5	12	0	100
Fibula	27	65	11	83.1
ALT	1	2	0	100
Radial	6	15	3	80.0
Pectoralis major	0	0	0	–
DCIA	10	25	6	76.0
Iliac crest (non-vascular)	3	10	2	80
Total	52	129	22	82.9

The number of patients and implants and percentage implant failure and survival for each autogenous bone graft that the implants were placed into. DCIA deep circumflex iliac artery flaps, ALT anterolateral thigh flap

unfortunately can be expected in this patient group which is also seen in the literature and also the inability to eliminate confounding variables due to heterogeneity of the patients, treatments and follow-up. When reviewing the literature on implant survival/failure in H&N patients, there is a lack of well-designed prospective studies with long-term follow-up, with the majority of the literature being retrospective with small patient numbers and short follow-up. These studies are hugely variable, and to make an effective comparison is difficult and in some cases inappropriate.

Accordingly, there is a clear need for a standardisation of reporting implant survival and failure. There is reasonable overall agreement on the criteria for implant survival and failure; however, there is no agreed minimum data set for collection to enable the comparison of studies, and furthermore there is no consensus on the best way to measure outcomes, analyse endpoints and the most appropriate way to statistically analyse the data.

Table 9 Implant system and implant failure

Implant system	No. of patients	No. of implants	No. of implant failures	Implant failure (%)
Straumann	140	679	24	3.5
Brånemark	16	63	8	12.7
Astra Tech	11	36	2	5.6
Oktagon	1	1	0	0.0
TOTAL	168	779	34	96.5

The number of patients, implants placed and implant failures and percentage implant failure for each implant system used in this patient cohort (note: one patient had both Straumann and Brånemark implants placed) (implant manufacturers: Straumann implants (Institut Straumann, Basel, Switzerland), Brånemark implants (Nobel Biocare, Zurich, Switzerland), Astra Tech implants (Dentsply Implants, Mannheim, Germany), Oktagon implants (Dental Ratio, Langenfeld, Germany)

Conclusion

This study reports high implant survival when used as part of the routine oral rehabilitation of H&N oncology patients with a median follow-up of 38 months. Implant survival estimates at 3 years was 95.7% [95%CI 94.3–97.2%] and 95.5% [95%CI 93.9–97.0%] at 5 years. Survival analyses for specific covariates showed trends for increased implant failure in patients receiving radiotherapy ($p = 0.16$), chemotherapy ($p = 0.17$) and being male ($p = 0.09$) but were not found to be statistically significant in this population. Implant survival however was found to be affected by the bone type with implant failure being higher for implants placed into autogenous bone grafts/free flaps in comparison to implants placed into native bone which was found to be statistically significant ($p \leq 0.001$). Reported surgical complications noted at the time of implant placement were high with 14.8% of patients experiencing such events. Such complications appeared to increase the risk of implant failure (at the patient level).

Overall, this service evaluation supports the use of dental implants in oral rehabilitation of this complex patient group, but it is important to recognise that this is an analysis of a complex care pathway with a large number of confounding variables. The findings should not be considered as generalisable beyond the specific environment in which this study was conducted. However, the findings highlight the urgent need for prospective multi-centre standardised data recording in order to generate robust data to enable potentially important treatment covariates to be explored.

and revising it. All authors approve this manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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