3D workflows in maxillary prosthodontic rehabilitation of head and neck cancer patients

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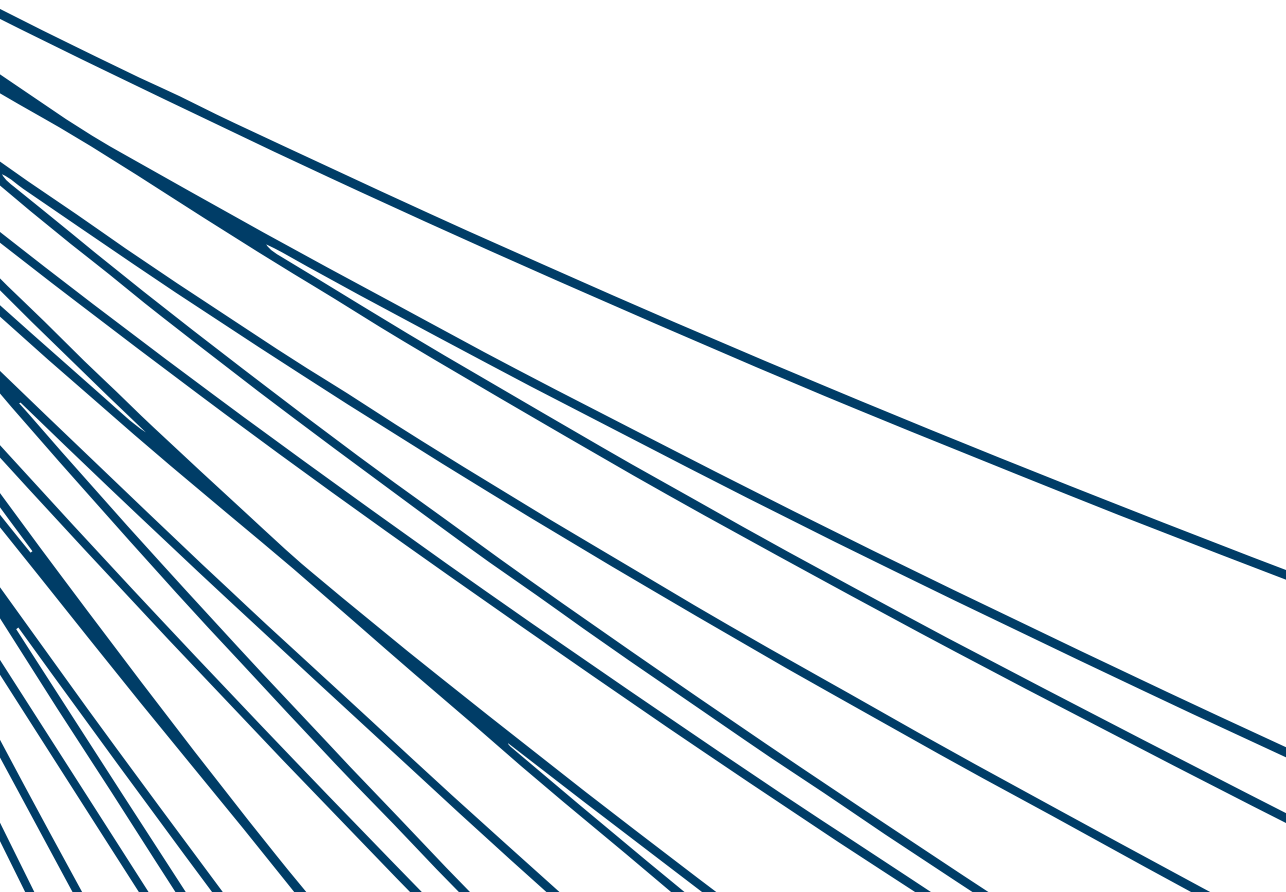


CHAPTER 1

General Introduction

GENERAL INTRODUCTION

Collaborative care of patients with head and neck cancer can be challenging particularly when it concerns diagnosis, treatment, and rehabilitation. Head and neck cancer doctors and dentists usually form a multidisciplinary team that care for the management of these cancers and develops individualized treatment plans for each patient. Oncological treatment options may include surgery, radiation therapy, chemotherapy or a combination of these treatments, depending on the stage, location and biological behaviour of the cancer, as well as the overall health of the patient[1].

Tumours of the maxilla, while relatively uncommon, require multidisciplinary involvement due to their effects on the aesthetic, functional and psychological aspects of the patients involved[2]. Although sequelae of tumour resection are comparable in the majority of patients, details in the intermaxillary relations, facial morphology and functional capacity can vary significantly[3].

Radiotherapy is a valuable treatment in the survival of head and neck cancer patients. When applied in the post operative setting, degeneration of oral functions after maxillectomy increase which can severely undermine the quality of life of the patients. The size and extent of the maxillary defect, patient factors, and comorbidities are decisive factors for the choice of surgical, prosthodontic, or combined rehabilitation after a partial maxillectomy. The use of classifications such as those by Brown[4] and Okay[5] are helpful tools to assist with surgical planning and decision-making in this complex area[6]. However, there is no clear or generally accepted recommendation to select the optimal method of obturation, reconstruction, and rehabilitation of the maxillary defects following tumour ablation[7].

The head and neck oncology team must make patient-specific decisions regarding rehabilitation based on the extent and position of the maxillary defect. The overall objective in patients with oronasal communication is to follow a surgical or prosthodontic reconstruction strategy with the aim to restore impaired oral functions[8]. From that perspective, dental rehabilitation is an important consideration for achieving a good outcome[9] and a major step toward enhancing quality of life after controlling the disease.

Obturator prostheses

Historically, rehabilitation with an obturator prosthesis has been the most common approach to restore maxillary defects[10]. This classic way of prosthetic management in general involves a three staged approach involving a surgical, interim and definitive obturator prosthesis[11]. The surgical obturator is placed subsequently after tumour resection in the operating room and enables immediate rehabilitation of oral function. This is achieved by peroperative adapting a prosthesis to the new anatomic situation.

Molding of a bulb extension secures obturation of the resection cavity. Fixation of the obturator in edentulous patients is generally ensured in the first weeks postoperative by screws in the palatal bone or zygomatic wiring, and when natural dentition remains after surgery clamps are used for retention. However, conventional obturator prostheses can have their drawbacks, mainly caused by lack of retention of the prosthesis[12].

Especially in more extensive resections, there may be no or hardly any maxillary bone or teeth present to provide obturator support. Placement of endosseous implants in the remaining native bone of the maxilla can provide a platform for the fabrication of a retention bar that supports and retains the overlying obturator prosthesis. Unfortunately the amount of maxillary bone is often limited or insufficient for reliable implant placement due to alveolar bone resorption as well as due to the ablative surgery.

Given the average high age among head and neck oncology patients prolonged edentulism is frequently seen with severe atrophic maxilla bone and the presence of pneumatic sinuses. This disables utilisation of conventional implants to gain retention and support the obturator prostheses.

Classic design of a surgical, interim and definitive obturator prosthesis

Zygomatic oncology implants

The development of the “remote bone anchorage” concept paved the way for the use of zygomatic implants in the management of patients with maxillary tumour defects with the high-quality bone of the zygoma providing excellent anchorage for long implants cantilevered into the defect to provide prosthetic support and retention. With advancing techniques in this field, zygomatic implant design has evolved from the traditional implant design developed by Professor PI Branemark with roughened threads throughout the entire length to “oncology-zygomatic implants” with threads only at the implant apex to allow osseointegration in the zygomatic bone. These modified implants are more cleansable when exposed into maxillary defects. Although good outcomes are reported over the years, zygomatic implants are still not widely used in complex

rehabilitation cases. Accurate placement of zygomatic implants, taking the preferred prosthodontic positioning into account, is considered difficult. In the absence of guiding anatomic references, it is challenging to place two zygomatic implants at the defect side because of the long drill path.

Prosthodontic virtual surgical planning

Advanced surgical techniques and the development of supportive care have contributed to improving outcomes and quality of life for patients with head and neck cancer. Among the emerging tools in Head and Neck cancer treatment is the use of three-dimensional virtual surgical planning (3D VSP), which has shown significant potential in the creation of accurate and patient-specific virtual models of the maxillofacial region. This technology enables surgical teams to simulate and plan surgical procedures with greater accuracy, by providing insight into the extent of the tumour and facilitating the planning of the surgical approach. The integration of 3D VSP into the management of head and neck cancer has been shown to improve the predictability and accuracy of surgical outcomes, while reducing the duration of surgery time. High-complexity oncological conditions often require prosthodontic rehabilitation and implant support. Therefore preoperative planning process should not only consider surgical oncological treatment and reconstruction but also include the seamless integration of prosthodontic rehabilitation into the virtual plan. After tumour resection, complex anatomic alterations demand individualized prosthodontic rehabilitation approaches, requiring the expertise of the maxillofacial prosthodontist. Therefore, a synergy of various digital workflows regarding treatment and rehabilitation should enhance the best possible care for patients with head and neck cancer. The integration of digital prosthodontic workflows is a crucial step towards personalized and precise management of maxillary malignancies, emphasizing the importance of teamwork in enhancing patient care.

AIM OF THE THESIS

The general aim of this PhD thesis is to develop a digital prosthodontic pathway for complex rehabilitation of maxillary defects in Head and Neck cancer patients, with preplanning the surgical resection and reconstruction with 3D virtual surgical planning (3D VSP). The progress of three-dimensional technology, the pre-treatment insight in overall prognosis and possibilities of surgical rehabilitation has led to many new applications in head & neck oncology. However, few new 3D supported strategies have been developed for supporting the prosthodontic rehabilitation after maxillectomies. In contrary to the 3D workflow of the surgical treatment, the prosthodontic rehabilitation of Head and Neck cancer patients commonly is an analog workflow with minor digitalized steps. A combined and complete virtual maxillary resection, reconstruction, and prosthetic rehabilitation planning will enable the maxillofacial prosthodontist to follow a digital prosthodontic workflow and to make balanced decisions with the

multidisciplinary Head and Neck Oncology team to shape and outline the prosthetic and dental rehabilitation in line with the surgical options. These topics will be addressed in this thesis.

The specific aims are:

- to systematically review the evolution of 3D techniques in prosthodontic rehabilitation of head and neck cancer patients. It offers a comprehensive overview of the prosthetic challenges in this patient group **(chapter 2).**
- to describe a complete 3D workflow for immediate implant-retained prosthetic rehabilitation following maxillectomy in cancer surgery. This workflow consist of a 3D Virtual Surgical Planning for tumour resection, zygomatic implant placement as well as for an implant-retained prosthetic-obturator to fit the planned outcome situation for immediate loading **(chapter 3)**.
- to assess the accuracy of the developed digital workflow for guided placement of zygomatic implants after maxillectomy and determine the usability of the procedure intraoperatively **(chapter 4).**
- to assess, in a prospective study, the implant survival and patient outcomes 1-3 year after guided placement of zygomatic implants in Head and Neck oncology patients. We visualize the tumour size and position and its direct impact on the radiation dose received by the zygomatic bone and implants **(chapter 5).**
- to combine the available 3D techniques of planning, designing and milling to produce a patient specific implant to support an obturator prosthesis. Our goal is to improve the severely impaired speech and swallowing, and a patient-specific sub-periosteal implant (psSPI) is designed that matched the remnants of the zygoma complex **(chapter 6).**

REFERENCES

1 Kitamura N., Sento S., Yoshizawa Y., Sasabe E., Kudo Y., Yamamoto T. Current Trends and Future Prospects of Molecular Targeted Therapy in Head and Neck Squamous Cell Carcinoma. *Int J Mol Sci* 2021;**22**(1):1–13. Doi: 10.3390/IJMS22010240.

2. Butterworth C. The prosthodontic management of the maxillectomy patient. *British Dental Journal 2022 233:9* 2022;**233**(9):744–8. Doi: 10.1038/s41415-022-5106-9.

3. Vissink A., Jansma J., Spijkervet FKL., Burlage FR., Coppes RP. Oral sequelae of head and neck radiotherapy. *Crit Rev Oral Biol Med* 2003;**14**(3):199–212. Doi: 10.1177/154411130301400305.

4. Brown JS., Shaw RJ. Reconstruction of the maxilla and midface: introducing a new classification. *Lancet Oncol* 2010;**11**(10):1001–8. Doi: 10.1016/S1470-2045(10)70113-3.

5. Okay DJ., Genden E., Buchbinder D., Urken M. Prosthodontic guidelines for surgical reconstruction of the maxilla: A classification system of defects. *J Prosthet Dent* 2001;**86**(4):352–63. Doi: 10.1067/MPR.2001.119524.

6. Butterworth CJ. Primary vs secondary zygomatic implant placement in patients with head and neck cancer—A 10-year prospective study. *Head Neck* 2019;**41**(6):1687–95. Doi: 10.1002/hed.25645.

7. Andrades P., Militsakh O., Hanasono MM., Rieger J., Rosenthal EL. Current strategies in reconstruction of maxillectomy defects. *Arch Otolaryngol Head Neck Surg* 2011;**137**(8):806–12. Doi: 10.1001/archoto.2011.132.

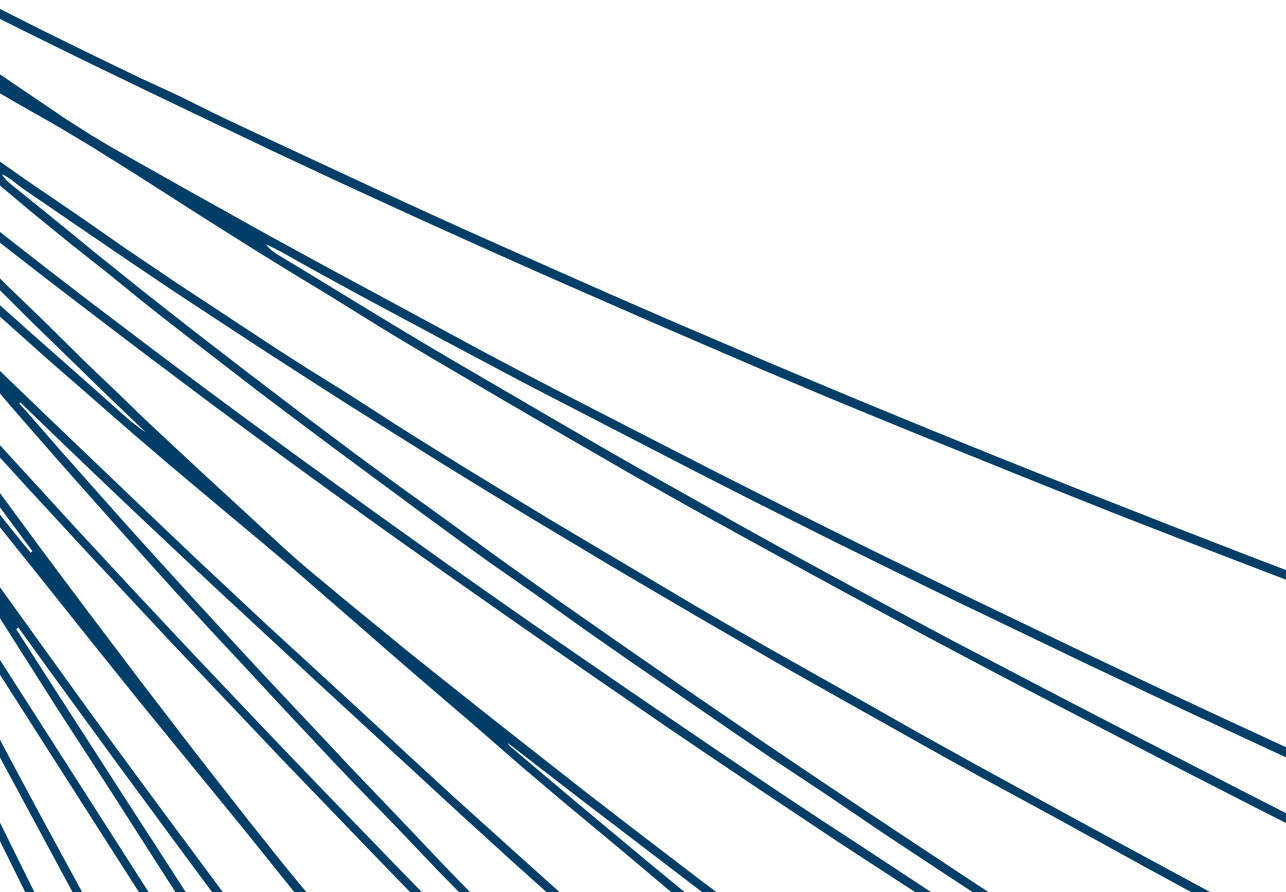
8. Witjes MJH., Schepers RH., Kraeima J. Impact of 3D virtual planning on reconstruction of mandibular and maxillary surgical defects in head and neck oncology. *Curr Opin Otolaryngol Head Neck Surg* 2018:108–14. Doi: 10.1097/MOO.0000000000000437.

9. Boonsiriphant P., Hirsch JA., Greenberg AM., Genden EM. Prosthodontic Considerations in Post-cancer Reconstructions. *Oral Maxillofac Surg Clin North Am* 2015;**27**(2):255–63. Doi: 10.1016/j.coms.2015.01.007.

10. Aramany MA. Basic principles of obturator design for partially edentulous patients. Part II: design principles. *J Prosthet Dent* 1978;**40**(6):656–62. Doi: 10.1016/0022-3913(78)90065-3.

11. Desjardins RP. Obturator prosthesis design for acquired maxillary defects. *J Prosthet Dent* 1978;**39**(4):424–35. Doi: 10.1016/s0022-3913(78)80161-9.

12. Buurman DJM., Speksnijder CM., Engelen BHBT., Kessler P. Masticatory performance and oral health-related quality of life in edentulous maxillectomy patients: A cross-sectional study to compare implant-supported obturators and conventional obturators. *Clin Oral Implants Res* 2020;**31**(5). Doi: 10.1111/clr.13577.



CHAPTER 2.1

Prosthodontic rehabilitation of head and neck cancer patients - challenges and new developments

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G.M. Raghoebar, H. Reintsema, A. Vissink, A. Korfage

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ABSTRACT

Head and neck cancer treatment can severely alter oral function and aesthetics, and reduce quality of life. The role of maxillofacial prosthodontists in multidisciplinary treatment of head and neck cancer patients is essential when it comes to oral rehabilitation and its planning. This role should preferably start on the day of first intake. Maxillofacial prosthodontists should be involved in the care pathway to shape and outline the prosthetic and dental rehabilitation in line with the reconstructive surgical options. With the progress of three-dimensional technology, the pre-treatment insight in overall prognosis and possibilities of surgical and/or prosthetic rehabilitation has tremendously increased. This increased insight has helped to improve quality of cancer care. This expert review addresses the involvement of maxillofacial prosthodontists in treatment planning, highlighting prosthodontic rehabilitation of head and neck cancer patients from start to finish.

INTRODUCTION

Head and neck cancer is the fifth most common cancer worldwide[1]. The course of the disease and its treatment have major effects on psychological well-being and functioning of the patients[2]. The treatment of head and neck cancers consists of different treatment modalities, typically being surgery, radiotherapy, chemotherapy or a combination of these modalities. Besides curing cancer, another important aim is to regain the oral function and aesthetics that got lost or altered due to the treatment.

Effects of primary oncology surgery can impede rehabilitation goals[3]. These effects include an altered oral anatomy, compromised soft tissue conditions like missing or scarred tissues and bulky flaps, altered muscle attachments and muscle balance, sensitivity disorders, loss of lip competence and trismus, loss of anatomical structures, loss of bony structures and/or teeth, and alterations in facial appearance. Regaining oral function and aesthetics is a challenge because of limitations in the restorative treatment options due to, e.g. poor support and lack of space for a prosthesis, impeded resilience of soft tissues, impaired tongue function, and loss of integrity and competence of the velopharyngeal complex[4].

Posteriorly situated tumours, tumour size, adjuvant radiotherapy and extensive soft-palate and tongue resections have been shown to be predictors for deterioration of oral functioning[5-7]. Studies that looked into the quality of life of head and neck cancer patients after completion of oncologic treatment reported that regaining oral function, including prosthetic rehabilitation, is of great importance[8-10]. Therefore, the oncological team is in need of specially trained, experienced dental professionals, preferably maxillofacial prosthodontists, to support the team with planning of the oral rehabilitating head and neck patients. This planning and treatment may include the use of osseo-integrated intra- and extra-oral implants to retain oral and/or facial prostheses .

As mentioned, to achieve rehabilitation goals, a close and open collaboration between ablative surgeons, reconstructive surgeons, radiation oncologists, maxillofacial prosthodontists and medical engineers is of utmost importance to move towards an optimal rehabilitation of the head and neck cancer patient. The purpose of this expert review is to emphasize the role of the maxillofacial prosthodontist in the treatment planning and oral rehabilitation of head and neck cancer patients as well as to discuss challenges and new developments in the prosthodontic rehabilitation of these patients.

Pre-treatment screening

Multidisciplinary first-day consultation intents to shorten time between diagnosis and treatment of oral cancer[11]. Maxillofacial prosthodontics should be included in the multidisciplinary first-day consultation. This first-day consultation aims to provide a preliminary plan stating the required diagnostic procedures and prosthetic involvement

(Figure 1) so that treatment can start as soon as and as effective as possible. The involvement of the maxillofacial prosthodontist includes a pre-radiation dental screening, and a pre-treatment dental and oral rehabilitation screening[12]. During this screening, all available information is gathered with regard to self-care, oral hygiene, dental situation, mouth opening, location of the suspected or confirmed tumour, presumed need for ablative surgery and/or radiotherapy, estimation of retention and bearing of a future (obturator, dental) prosthesis, and estimation of the pre-existent level of oral function[13,14]. This information is needed to design the best prosthetic treatment plan. This plan should be designed taking the patients' wishes, the tumour characteristics, extent of acquired resection for clean margins, possible types of reconstruction, need for (chemo)radiation, and dental and/or prosthetic possibilities into account.

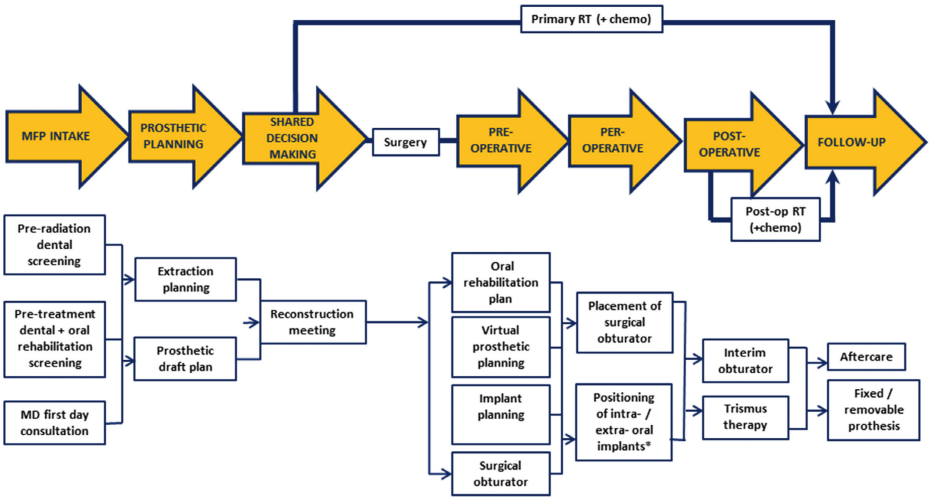


Figure 1. Involvement of the maxillofacial prosthodontist in treatment planning and rehabilitation of head and neck cancer patients focused on ablative surgery. MD: Multidisciplinary, MFP: maxillofacial prosthodontics; Post-op: Post-operative, RT: radiotherapy; chemo: chemotherapy.

*Preferably, implants are placed during ablative tumour surgery. When not feasible, implants can also be placed during follow-up. For details see Alberga et al. (2020).

Pre-radiation dental screening

In case radiotherapy might become involved, head and neck cancer patients in whom the oral cavity is within the radiation treatment portal are in need of a thorough dental examination. These patients have to complete any required dental treatment before the onset of radiotherapy[15]. Pre-radiation dental screening aims to locate and eliminate oral foci of infection, such as unrestorable caries, periodontal disease with pockets ≥6mm, periapical problems and (partially) impacted teeth[12].

Pre-treatment dental and oral rehabilitation screening

Although at the first day consultation the extent of the final oncologic treatment plan is uncertain, at this stage the maxillofacial prosthodontists should already estimate whether patients are in need of a prosthetic rehabilitation simultaneously with reconstructive surgery or after completion of cancer therapy, and what the patients' desires are. Implementing the results of pre-treatment screening into the prosthetic workflow ensures that all information is gathered and all needed care is provided to design a patient specific prosthetic rehabilitation draft plan. In some cases, prosthetic retentive considerations are critical to achieve successful prosthetic rehabilitation. The size of the defect and number of critical remaining teeth that may serve as anchorage for conventional clasp supported removable partial denture framework challenges the maxillofacial prosthodontists to obtain insight into the intended therapeutic isodosis fields in relation to the strategic important teeth. This sometimes results in a well-considered decision to leave teeth which are considered an oral focus of infection in situ (including a thorough discussion of the risk on development of osteoradionecrosis).

With regard to the future prosthodontic rehabilitation, an early decision whether there is a need to place implants is important. This allows for the preferred prosthodontic rehabilitation of head and neck patients. For example, choices in planning, positioning and amount of endosseous oral implants or oncology zygomatic implants are key factors for retention of the prosthetic construction[16,17]. Literature emphasizes the importance of an immediate implant procedure as it has been shown that placement of mandibular implants in edentulous patients during ablative surgery results in a higher number of patients with functioning mandibular dentures after completion of oncologic therapy[2,18,19]. Furthermore, an increasing trend is observed to early complete the prosthodontic rehabilitation for which an immediate implant procedure is often a prerequisite[16,20]. When implants are placed after radiation treatment, the anatomical site where the implants are placed seems to effect implant survival, as the implant survival rate is higher in the mandible than in the maxilla and in grafted bone[21,22]. Therefore, implant placement during ablative surgery is preferred, at least in selected cases[16].

When there is a need for per-operative prosthetics, the maxillofacial prosthodontist has to record the actual intra-oral situation through impression taking, intra-oral scanning and/or cone beam computer tomography (CBCT) imaging, all to capture the intra-oral pre-treatment situation and occlusal plane for fabrication of a surgical obturator, surgical guides and models, or an implant-supported prosthesis. A huge advantage of working with three-dimensional (3D) intraoral scanning is the ease to combine the data of the intra-oral situation, like the position of teeth and occlusion, with (CB)CT and magnetic resonance imaging (MRI) data of the surrounding tissues in an augmented model. This 3D virtual model provides more insight into the implications and complexity of surgical and prosthetic rehabilitation. This insight allows the surgical team to analyse the surgical and rehabilitation outcome and plan the treatment[23,24]. Although intraoral

scan techniques are widely used nowadays, some limitations can occur mostly due to poor intraoral access caused by, e.g., the tumour, trismus or pain. In those situations analogue impressions are the only feasible option. The produced plaster model can then in a second stage be digitallized in order to create the 3D virtual model.

When mutilating extra-oral defects are expected as a result of ablative surgery, extra-oral dimensions have to be recorded as well as to prepare for future extra-oral prostheses . Although analogue workflows still meet the quality standards of prosthetic care, digital technology has demonstrated ease and utility in design and construction workflows in prosthodontics[25]. The prosthodontic documentation can be completed by taking clinical photographs. In this way skin-, prosthetic- and facial characteristics are captured and aid with communication between the head and neck team. With all gathered information a prosthetic draft plan can be worked out in preparation of the necessary input of maxillofacial prosthodontists in choice of rehabilitation treatment.

Multidisciplinary approach

In the past, prosthodontic rehabilitation in the oncological treatment path was a stand-alone final procedure after completion oncological therapy. Nowadays, planning of surgical reconstruction starting with occlusion of teeth also safeguards a proper dental rehabilitation. This approach supports a thorough adjustment of the surgical and prosthetic planning and treatment before the oncologic treatment is started[23,26]. In a reconstruction meeting, the head and neck team can go through the available options of surgical, prosthetic or combined reconstruction. The input of maxillofacial prosthodontists in such a reconstruction meeting guards the feasibility from a prosthetic point of view, guided by a prosthetic draft plan, and includes the eventual need for implant placement. With the introduction of 3D planning and computer aided design (CAD) assistance, preoperative virtual augmented models provided by medical engineers at these meetings are a great asset to the surgical team and support shared decision making regarding favourable reconstruction option after oncology treatment.

Virtual planning

Once the final oncological treatment plan is agreed upon, having access to a pre-operative virtual surgical planning (VSP) can be of importance for the surgical team[24]. Three-dimensional planning enables a high accuracy of guided resection surgery and prosthetic driven reconstruction planning[27,28]. Besides a reliable intended outcome, the concept of backwards planning from occlusion maximizes the chances of completing oral rehabilitation of the patient. A 3D VSP can be very precisely executed, with the use of 3D printed guides creating the possibility of completing a full ablative and reconstructive plan in one surgery[23,26]. However, soft tissues are not very reliable reproduced yet by digital techniques. This is still an uncertain factor to be taken into account when it comes to planning prosthetic treatment. The risk of losing prosthetic retention options due to compromised soft tissues means critically assessing choices such as preservation

of a functional dental arch (shortened), planning a fixed or removable prosthesis, and indication of peroperative insertion of endosseous oral implants or oncology zygomatic implants. Tools to better reproduce soft tissues are in development.

Rehabilitation of mandibular defects

Smaller head and neck tumours can require resection of soft tissue only and can surgically be managed by primary closure. To overcome possible absence of vestibule or compromised neutral zone provision of individualized adapted prostheses is required. With such an approach oral function might reach a near normal level after ablative surgery and prosthetic rehabilitation[8].

Advanced tumours can result in large defects, requiring surgical reconstruction[29]. The resulting altered anatomy can be unfavourable because of flap positioning and presence of scar tissue. Such unfavourable conditions may impair the ability to speak, masticate and swallow. Loss of sensibility, a shallow or absent buccal vestibule, radiation-induced hyposalivation and trismus may further compromise oral function. Advanced tumour surgery requiring bone resection may further compromise oral function due to loss of the continuity of the mandible, loss of teeth and severe deformities. Most of all, an impaired motility of the tongue challenges the fabrication of a functional mandibular resection prosthesis as it compromises stability of this prosthesis during speech and mastication[30].

Many of the aforementioned problems can, at least in part, be reduced by the use of endosseous oral implants to retain prostheses (Figure 2). These implants contribute to stabilization of prostheses and reduce loading of the compromised soft tissues and underlying bone[31]. In many patients, an almost normal masticatory function can be achieved with a rehabilitation of the reconstructed side with implant-supported removable partial dental prostheses or implant-retained mandibular overdentures[32]. Maximization of dental rehabilitation significantly improves oral functioning, oral diet achievements and oral health related quality of life[2,33]. Several authors reported that a relatively low percentage of reconstructed patients complete prosthetic rehabilitation[34]. Causes of not completing the prosthetic treatment after implant placement are, vertical discrepancy between the graft and the remaining mandible, which leads to an unfavourable implant–crown ratio, poor quality of soft tissues (hypertrophy often appears after the placement of the abutments), and the type of the prosthesis (fixed or removable)[35]. As implant placement during primary reconstruction shortens the interval between surgery and dental rehabilitation, the number of orally rehabilitated patients will increase[16,36].

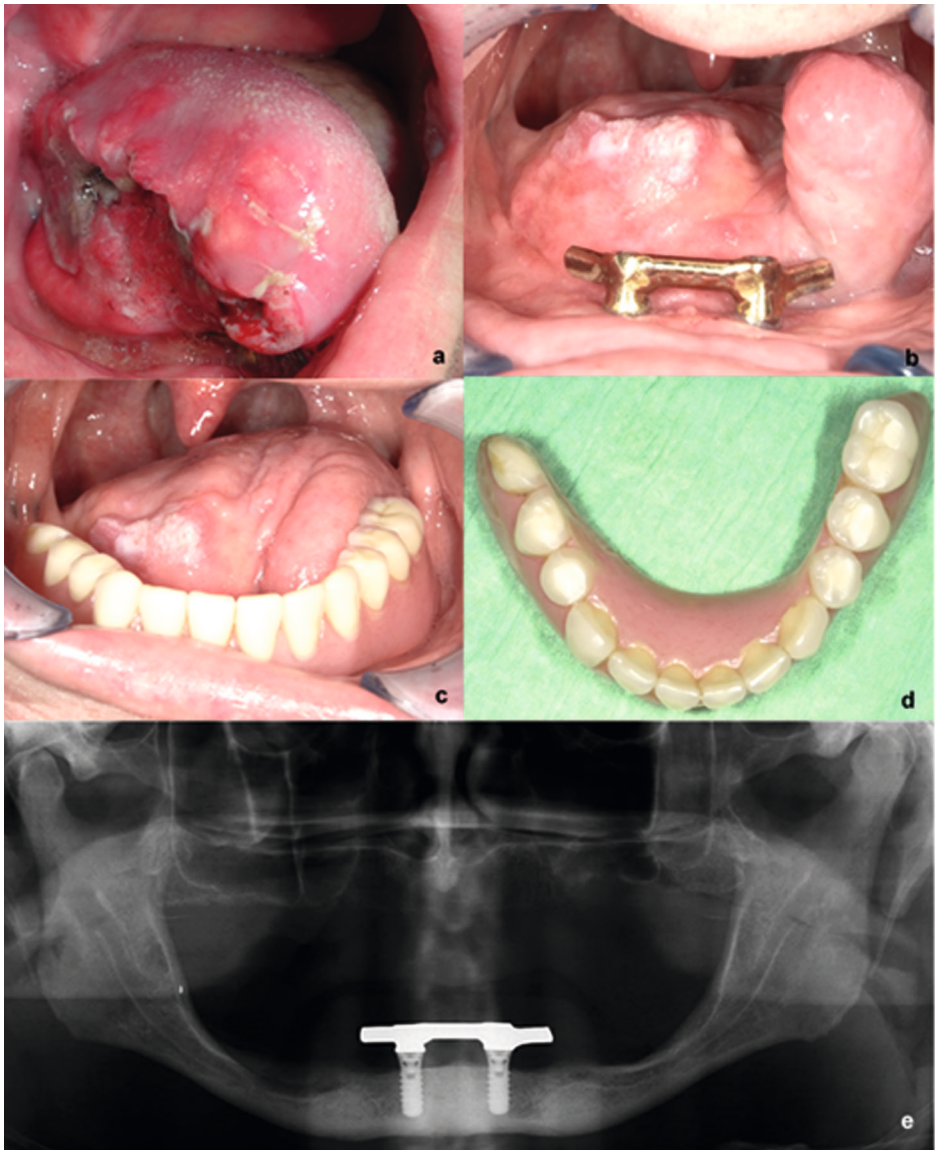


Figure 2. Patient diagnosed with squamous cell carcinoma of the tongue after hemiglossectomy and radial forearm free flap reconstruction.

a. Pre-operative image of tumour **b**. Intra-oral view after ablative surgery and postoperative radiotherapy. Bar suprastructure with distal extensions fixed on two endosseous implants **c,d**. Implant supported prosthesis with patient specific design to optimize tongue function during speech and mastication **e**. Orthopantomogram two years after reconstructive surgery showing good integration of endosseous implants.

Rehabilitation of maxillary defects

Management of maxillary, midface and skull-base tumours is challenging and complex when it comes to ablative surgery with a need for oral and facial reconstruction, and oral rehabilitation. Maxillary resections lead to a variety of oronasal defects, with a diversity of approaches for restoring oral functioning. Manifold maxillectomy classification schemes are mentioned in literature, all originating from the Brown classification published in 2000 [37]. These schemes categorize the range of maxillary defects by location, extension like the vertical and horizontal components, and biomechanical forces, and provide guidelines for surgical and prosthetic rehabilitation choices**.**

Restorative decision making

When tumour resection causes a minor oronasal fistula and primary closure is not feasible, surgical reconstruction with soft tissue flaps alone can lead to excellent functional and aesthetic results, as long as prosthetic retention of teeth replacement is guaranteed. For larger maxillary defects, the option of prosthetic rehabilitation with an obturator prosthesis is the standard of care in many institutions since decades[38,39]. This approach includes maxillary obturators for defects of the hard palate, pharyngeal obturators for defects of the soft palate, and maxillopharyngeal obturators for defects that include both structures. However, the discomfort of wearing, removing, and cleaning such a prosthesis, its poor retention in large defects, and the frequent need for readjustments often limit the value of this cost-effective method of restoring speech and mastication[40].

In case of even larger tumours, the defect size increases and the remaining dentition and supporting palatal bone will be more limited. Due to lack of retention and stability of a prosthesis, the interplay of forces further compromises functional rehabilitation and thereby overall success of treatment[41]. Placing endosseous implants in the native bone of the maxilla will allow to improve retention of the obturator prosthesis and thereby increase the success of prosthetic rehabilitation. Patients with implant-supported obturator prostheses have significantly better masticatory and oral function, and less discomfort during food intake than patients with a conventional obturator[42]. Studies which compared prosthetic obturation with reconstruction of a palatomaxillary defect demonstrated that there are some advantages to reconstruct the defects above obturation of these defects, in particular with regard to quality-of-life issues such as comfort, convenience, and feelings of self-consciousness[43]. However, especially in medically compromised and older patients, implant-supported obturator treatment is a viable alternative to surgical reconstruction after maxillectomy[42], although an obturator prosthesis is not obsolete and is still standard care in low-income and middle-income countries. With the benefits of digital techniques and surgical reconstruction options the obturator prosthesis has increasingly gained a temporary function by bridging time to secondary surgical reconstruction of the defect.

New workflows are rising in processing surgical obturators. Several case reports describe production of 3D obturator prostheses[44,45]. 3D knowledge of resection planes provides a better knowledge of the dimensions of the post-resection defect, giving the option of preoperative production of a surgical obturator. With proper tumour visualisation and insight in the remaining anatomic structures, a surgical obturator prosthesis can be digitally designed and printed prior to ablative surgery. A nearby fit can be achieved and only minor per-operative adjustments are needed (Figure 3).

If the defect overextends in size and vertical dimension, obturation of the deffect cannot be adequately addressed with prosthetic management alone[46]. Surgical reconstruction combined with dental rehabilitation is then preferred. Zygomatic implants can, for example , provide a predictable in-defect support for prosthetic rehabilitation of the maxilla if placed at the time of primary surgery[47]. The zygomatic implant perforated flap procedure combines autogenous soft tissue reconstruction with zygomatic implant-supported fixed dental rehabilitation[17,48]. Furthermore, using the Rohner technique in combination with VSP it is possible to reconstruct high level maxillectomy cases with a reliable single-stage approach (Figure 4) in a secondary stage procedure[26,49-51].

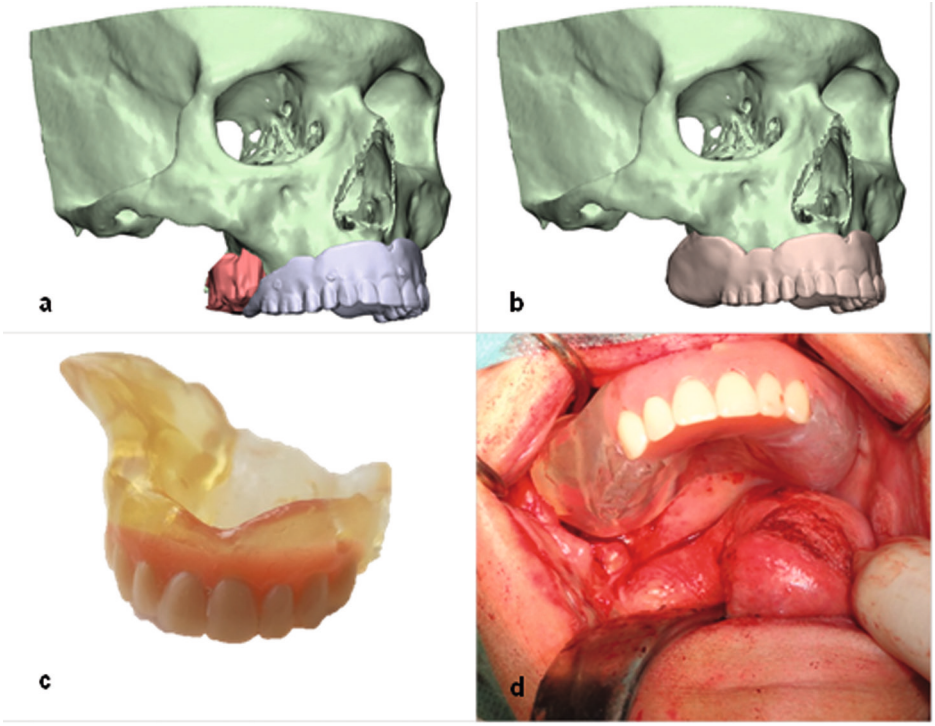


Figure 3. Patient diagnosed with mucoepidermoid carcinoma of the maxilla with prosthetic rehabilitation using a 3D printed obturator prosthesis based on a 3D VSP workflow.

a. Tumour visualization based on CT and MRI data fusion related to position of digitalised conventional prosthesis **b.** Virtual design of surgical obturator **c.** Image showing pre-operative printed surgical obturator **d**. Digital designed and printed obturator prosthesis with nearby fit during ablative surgery.

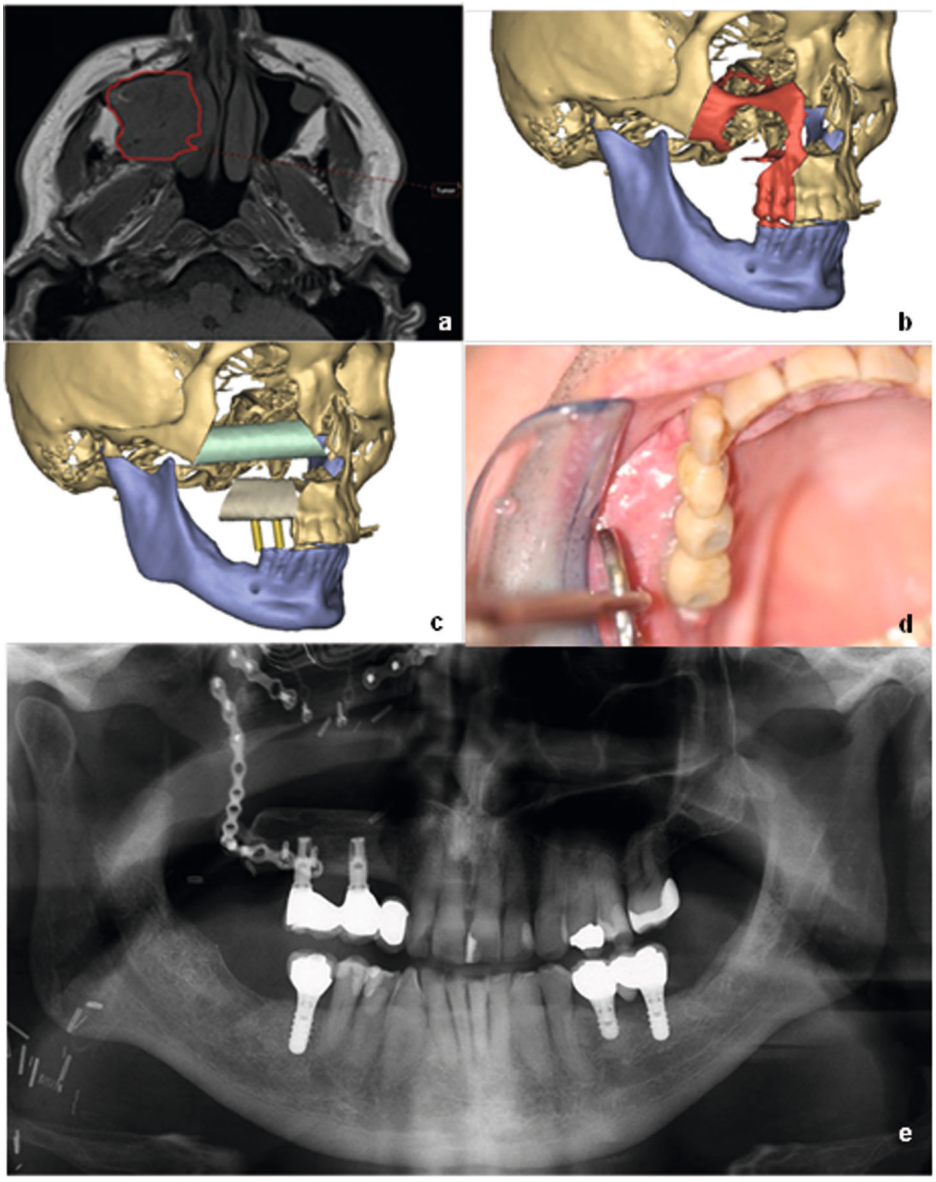


Figure 4. Jaw reconstruction of patient diagnosed with ameloblastoma treated with maxillectomy and reconstruction with fibular free flap.

a. the tumour was delineated on the MRI using radiotherapeutic planning software **b.** 3D VSP for tumour ablation surgery **c.** Virtual surgical planning of the maxilla and orbital floor reconstruction with fibula bone and implant planning. **d.** Suprastructure fixed on 2 endosseous implants placed in the fibula bone segment. **e.** Orthopantomogram four years after reconstructive surgery showing good integration of fibula bone segment and implants.

CONCLUSION

Oral rehabilitation is an encompassing component of the treatment of head and neck cancer patients and is a major contributor to enhance the quality of life of cancer survivors. Involvement in a multidisciplinary team to prepare and excecute the rehabilitation treatment is of utmost importance. Maxillofacial prosthodontists should be involved from the beginning, their role in this process is essential and guiding. The rise of 3D techniques in diagnostics, planning and oral rehabilitation is enormous, and is expected to evolve to the standard of care.

REFERENCES

1. Goon, P. K., Stanley, M. A., Ebmeyer, J., Steinstrasser, L., Upile, T., Jerjes, W., & Sudhoff, H. H. (2009). HPV & head and neck cancer: a descriptive update. *Head & Neck Oncology,* 1(36), 36-3284-1-36. doi:10.1186/1758-3284-1-36
2. Korfage, A., Schoen, P. J., Raghoebar, G. M., Bouma, J., Burlage, F. R., Roodenburg, J. L., Vissink A., & Reintsema, H. (2011). Five-year follow-up of oral functioning and quality of life in patients with oral cancer with implant-retained mandibular overdentures. *Head & Neck, 33*(6), 831-839. doi:10.1002/hed.21544
3. Pace-Balzan, A., Shaw, R. J., & Butterworth, C. (2011). Oral rehabilitation following treatment for oral cancer. Periodontology 2000, 57(1), 102-117. doi:10.1111/j.1600-0757.2011.00384.x
4. Nayar, S. (2019). Current concepts and novel techniques in the prosthodontic management of head and neck cancer patients. British Dental Journal, 226(10), 725-737. doi:10.1038/s41415-019-0318-3
5. Vissink, A., Jansma, J., Spijkervet, F. K., Burlage, F. R., & Coppes, R. P. (2003). Oral sequelae of head and neck radiotherapy. Critical Reviews in Oral Biology and Medicine : An Official Publication of the American Association of Oral Biologists, 14(3), 199-212. doi:14/3/199
6. Bohle, G.,3rd, Rieger, J., Huryn, J., Verbel, D., Hwang, F., & Zlotolow, I. (2005). Efficacy of speech aid prostheses for acquired defects of the soft palate and velopharyngeal inadequacy--clinical assessments and cephalometric analysis: a Memorial Sloan-Kettering Study. Head & Neck, 27(3), 195-207. doi:10.1002/hed.10360
7. Brown, J. S., Rogers, S. N., & Lowe, D. (2006). A comparison of tongue and soft palate squamous cell carcinoma treated by primary surgery in terms of survival and quality of life outcomes. International Journal of Oral and Maxillofacial Surgery, 35(3), 208-214. doi:S0901-5027(05)00324-3
8. Tang, J. A., Rieger, J. M., & Wolfaardt, J. F. (2008). A review of functional outcomes related to prosthetic treatment after maxillary and mandibular reconstruction in patients with head and neck cancer. The International Journal of Prosthodontics, 21(4), 337-354.
9. Rogers, S. N. (2010). Quality of life perspectives in patients with oral cancer. Oral Oncology, 46(6), 445-447. doi:10.1016/j.oraloncology.2010.02.021
10. Kamstra, J. I., Jager-Wittenaar, H., Dijkstra, P. U., Huisman, P. M., van Oort, R. P., van der Laan, B. F., & Roodenburg, J. L. (2011). Oral symptoms and functional outcome related to oral and oropharyngeal cancer. Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer, 19(9), 1327-1333. doi:10.1007/s00520-010-0952-4
11. van Huizen, L. S., Dijkstra, P. U., van der Laan, B. F., Reintsema, H., Ahaus, K. T., Bijl, H. P., & Roodenburg, J. L. (2018). Multidisciplinary first-day consultation accelerates diagnostic procedures and throughput times of patients in a head-and-neck cancer care pathway, a mixed method study. BMC Health Services Research, 18(1), 820-018-3637-1. doi:10.1186/s12913-018-3637-1
12. Spijkervet, F. K., Schuurhuis, J. M., Stokman, M. A., Witjes M. H. J., & Vissink A. (2020). Should oral foci of infection be removed before onset of radiotherapy or chemotherapy? Oral Diseases, 27(1): 7-13. *doi: 10.1111/odi.13329.*
13. Jensen, S. B., Vissink, A., Limesand, K. H., & Reyland, M. E. (2019). Salivary Gland Hypofunction and Xerostomia in Head and Neck Radiation Patients. Journal of the National Cancer Institutes Monographs, Aug 1;2019(53). DOI: 10.1093/jncimonographs/lgz016

14. Spijkervet, F.K., Brennan, M. T., Peterson, D. E., Witjes, M. J., & Vissink A. (2019). Research Frontiers in Oral Toxicities of Cancer Therapies: Osteoradionecrosis of the Jaws. Journal of the National Cancer Institutes Monographs,. 2019(53). pii: lgz006DOI: 10.1093/jncimonographs/lgz006
15. Schuurhuis, J. M., Stokman, M. A., Roodenburg, J. L., Reintsema, H., Langendijk, J. A., Vissink, A., & Spijkervet, F. K. (2011). Efficacy of routine pre-radiation dental screening and dental follow-up in head and neck oncology patients on intermediate and late radiation effects. A retrospective evaluation. Radiotherapy and Oncology : Journal of the European Society for Therapeutic Radiology and Oncology, 101(3), 403-409. doi:10.1016/j.radonc.2011.09.018
16. Alberga J. M., Vosselman N., Korfage A., Witjes M. J. A., Raghoebar G. M., & Vissink A. (2020). What is the optimal timing for implant placement in oral cancer patients? Oral Diseases, 27(1), 94-110. doi: 10.1111/odi.13312.
17. Hackett, S., El-Wasani B., & Butterworth C. (2020). Zygomatic implant based rehabilitation for patients with maxillary and mid-facial oncology defects. Oral Diseases, 27(1): 27-41. doi: 10.1111/odi.13305.
18. Mizbah, K., Dings, J.P., Kaanders, J.H.A.M., van den Hoogen, F.J.A., Koole, R., Meijer G.J. & Merkx, M.A.W. (2013). Inteforaminal implant placement in oral cancer patients: during ablative surgery or delayed? A 5-year retrospective study. International Joural of Oral and Maxillofacillofacial Surgery, 42, 651-655. doi:10.1016/j.ijom.2012/09.013
19. Wetzels J.W.G.H., Meijer G.J., Koole R., Merkx M.A.W. & Speksnijder C.M. (2017). Costs and clinical outcomes of implant placement during ablative surgery and postponed implant placement in curative oral oncology: A five-year retrospective cohort study. Clinical Oral impl ants Research, 28, 1433-1442. doi: 10.1111/clr.13008
20. Chuka, R., Abdullah, W., Rieger, J., Nayar, S., Seikaly, H., Osswald, M., & Wolfaardt J. (2017). Implant utilization and time to prosthetic rehabilitation in conventional and advanced fibular free flap reconstruction of the maxilla and mandible. The International Journal of Prosthodontics, 30: 289–294. doi:10.11607/ijp.5161
21. Nooh N. Dental implant survival in irradiated oral cancer patients: A systematic review of the literature. Int J Oral Maxillofacial Implants. 2013;28, 1233-1242. doi: 10.11607/ jomi.3045
22. Chrcanovic, B.R., Albrektsson T., & Wennerberg A. (2016). Dental implants in irradiated versus nonirradiated patients: A meta-analysis. Head & Neck, 38(3), 448-81. doi: 10.1002/hed.23875. doi:10.1002/HED
23. Witjes, M. J. H., Schepers, R. H., & Kraeima, J. (2018). Impact of 3D virtual planning on reconstruction of mandibular and maxillary surgical defects in head and neck oncology. Current Opinion in Otolaryngology & Head and Neck Surgery, 26(2), 108-114. doi:10.1097/MOO.0000000000000437
24. Kraeima J., Glas H. H., Merema B. J., Vissink A., Spijkervet F. K. L., & Witjes. M. J. H. (2020). Three dimensional virtual surgical planning in the oncologic treatment of the mandible – Current routines and clues for optimization. Oral Diseases, 27: 14-20, doi: 10.1111/odi.13631
25. Davis, B. K. (2010). The role of technology in facial prosthetics. Current Opinion in Otolaryngology & Head and Neck Surgery, 18(4), 332-340. doi:10.1097/MOO.0b013e32833bb38c
26. Seikaly, H., Idris, S., Chuka, R., Jeffery, C., Dzioba, A., Makki, F., Logan H., O'Connell D.A., Harris J., Ansari K., Biron V., Cote D., Osswald M., Nayar S., Wolfaardt, J. (2019). The Alberta Reconstructive Technique: An Occlusion-Driven and Digitally Based Jaw Reconstruction. The Laryngoscope, 129 Suppl 4, S1-S14. doi:10.1002/lary.28064

27. Tarsitano, A., Ricotta, F., Baldino, G., Badiali, G., Pizzigallo, A., Ramieri, V., Cascone P., Marchetti, C. (2017). Navigation-guided resection of maxillary tumours: The accuracy of computer-assisted surgery in terms of control of resection margins - A feasibility study. *Journal of Cranio-Maxillo-Facial Surgery :* Official Publication of the European Association for Cranio-Maxillo-Facial Surgery, 45(12), 2109-2114. doi:S1010-5182(17)30332-3

28. Kraeima, J., Dorgelo, B., Gulbitti, H. A., Steenbakkers, R. J. H. M., Schepman, K. P., Roodenburg, J. L., Spijkervet F.K.L., Witjes, M. J. H. (2018). Multi-modality 3D mandibular resection planning in head and neck cancer using CT and MRI data fusion: A clinical series. Oral Oncology, 81, 22-28. doi:S1368-8375(18)30115-5

29. Vaughan, E. D., Bainton, R., & Martin, I. C. (1992). Improvements in morbidity of mouth cancer using microvascular free flap reconstructions. Journal of Cranio-Maxillo-Facial Surgery : Official Publication of the European Association for Cranio-Maxillo-Facial Surgery, 20(3), 132-134. doi:S1010-5182(05)80095-2

30. Petrovic, I., Ahmed, Z. U., Huryn, J. M., Nelson, J., Allen, R. J.,Jr, Matros, E., & Rosen, E. B. (2019). Oral rehabilitation for patients with marginal and segmental mandibulectomy: A retrospective review of 111 mandibular resection prostheses. The Journal of Prosthetic Dentistry, 122(1), 82-87. doi:S0022-3913(18)30910-7

31. Schoen, P. J., Reintsema, H., Raghoebar, G. M., Vissink, A., & Roodenburg, J. L. (2004). The use of implant retained mandibular prostheses in the oral rehabilitation of head and neck cancer patients. A review and rationale for treatment planning. Oral Oncology, 40(9), 862-871. doi:10.1016/j.oraloncology.2003.08.024

32. Kumar, V. V., & Srinivasan, M. (2018). Masticatory efficiency of implant-supported removable partial dental prostheses in patients with free fibula flap reconstructed mandibles: A split-mouth, observational study. Clinical Oral Implants Research, 29(8), 855-863. doi:10.1111/clr.13304

33. Kansara, S., Wang, T., Koochakzadeh, S., Liou, N. E., Graboyes, E. M., Skoner, J. M., . . . Huang, A. T. (2019). Prognostic factors associated with achieving total oral diet following osteocutaneous microvascular free tissue transfer reconstruction of the oral cavity. Oral Oncology, 98, 1-7. doi:S1368-8375(19)30303-3

34. Barber, A. J., Butterworth, C. J., & Rogers, S. N. (2011). Systematic review of primary osseointegrated dental implants in head and neck oncology. The British Journal of Oral & Maxillofacial Surgery, 49(1), 29-36. doi:10.1016/j.bjoms.2009.12.007

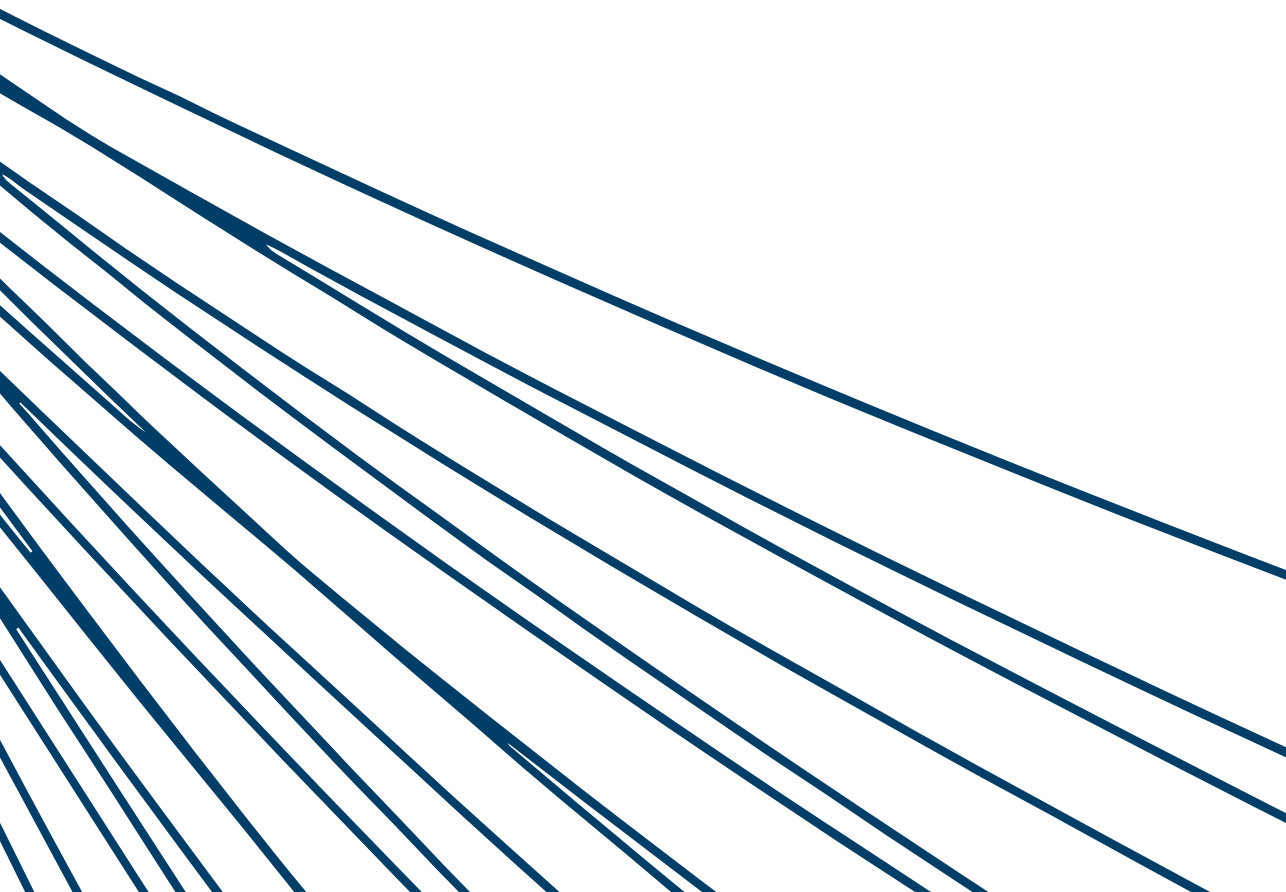
35. Anne-Gaelle, B., Samuel, S., Julie, B., Renaud, L., & Pierre, B. (2011). Dental implant placement after mandibular reconstruction by microvascular free fibula flap: current knowledge and remaining questions. Oral Oncology, 47(12), 1099-1104. doi:10.1016/j.oraloncology.2011.07.016

36. Urken, M. L., Buchbinder, D., Weinberg, H., Vickery, C., Sheiner, A., & Biller, H. F. (1989). Primary placement of osseointegrated implants in microvascular mandibular reconstruction. Otolaryngology--Head and Neck Surgery : Official Journal of American Academy of Otolaryngology-Head and Neck Surgery, 101(1), 56-73. doi:10.1177/019459988910100111

37. Brown, J. S., Rogers, S. N., McNally, D. N., & Boyle, M. (2000). A modified classification for the maxillectomy defect. Head & Neck, 22(1), 17-26. doi:10.1002/(SICI)1097-0347(200001)22:1<17::AID-HED4>3.0.CO;2-2

38. Aramany, M. A. (2001). Basic principles of obturator design for partially edentulous patients. Part II: Design principles. 1978 [classical article. The Journal of Prosthetic Dentistry, 86(6), 562-568. doi:S0022391301307965

39. Desjardins, R. P. (1978). Obturator prosthesis design for acquired maxillary defects. The Journal of Prosthetic Dentistry, 39(4), 424-435. doi:S0022-3913(78)80161-9
40. Andrades, P., Militsakh, O., Hanasono, M. M., Rieger, J., & Rosenthal, E. L. (2011). Current strategies in reconstruction of maxillectomy defects. Archives of Otolaryngology--Head & Neck Surgery, 137(8), 806-812. doi:10.1001/archoto.2011.132
41. Moreno, M. A., Skoracki, R. J., Hanna, E. Y., & Hanasono, M. M. (2010). Microvascular free flap reconstruction versus palatal obturation for maxillectomy defects. Head & Neck, 32(7), 860-868. doi:10.1002/hed.21264
42. Buurman, D.J.M., Speksnijder C.M., B.H.B.T. Engelen, & Kessler, P. (2020). Masticatory performance and oral health-related quality of life in edentulous maxillectomy patients: A cross-sectional study to compare implant-supported obturators and conventional obturators. Clinical Oral Implants Research. 31(5): 405-416. doi: 10.1111/clr.13577 .
43. Rogers, S. N., Lowe, D., McNally, D., Brown, J. S., & Vaughan, E. D. (2003). Health-related quality of life after maxillectomy: a comparison between prosthetic obturation and free flap. Journal of Oral and Maxillofacial Surgery: Official Journal of the American Association of Oral and Maxillofacial Surgeons, 61(2), 174-181. doi:10.1053/joms.2003.50044
44. Rodney, J., & Chicchon, I. (2017). Digital Design and Fabrication of Surgical Obturators Based Only on Preoperative Computed Tomography Data. The International Journal of Prosthodontics, 30(2), 111-112. doi:10.11607/ijp.5066
45. Bartellas, M., Tibbo, J., Angel, D., Rideout, A., & Gillis, J. (2018). Three-Dimensional Printing: A Novel Approach to the Creation of Obturator Prostheses Following Palatal Resection for Malignant Palate Tumors. The Journal of Craniofacial Surgery, 29(1), e12-e15. doi:10.1097/SCS.0000000000003987
46. Urken, M. L., Roche, A. M., Kiplagat, K. J., Dewey, E. H., Lazarus, C., Likhterov, I., Buckbinder D., Okay, D. J. (2018). Comprehensive approach to functional palatomaxillary reconstruction using regional and free tissue transfer: Report of reconstructive and prosthodontic outcomes of 140 patients. Head & Neck, 40(8), 1639-1666. doi:10.1002/hed.25134
47. Butterworth, C. J. (2019). Primary vs secondary zygomatic implant placement in patients with head and neck cancer-A 10-year prospective study. Head & Neck, 41(6), 1687-1695. doi:10.1002/hed.25645
48. Butterworth, C. J., & Rogers, S. N. (2017). The zygomatic implant perforated (ZIP) flap: a new technique for combined surgical reconstruction and rapid fixed dental rehabilitation following low-level maxillectomy. International Journal of Implant Dentistry, 3(1), 37-017-0100-8. doi:10.1186/s40729-017-0100-8
49. Rohner, D., Bucher, P., Kunz, C., Hammer, B., Schenk, R. K., & Prein, J. (2002). Treatment of severe atrophy of the maxilla with the prefabricated free vascularized fibula flap. Clinical Oral Implants Research, 13(1), 44-52. doi:10.1034/j.1600-0501.2002.130105.x chepers, R. H., Raghoebar, G. M., Vissink, A., Lahoda, L. U., Van der Meer, W. J., Roodenburg, J. L., Reintsema H, Witjes, M. J. (2013). Fully 3-dimensional digitally planned reconstruction of a mandible with a free vascularized fibula and immediate placement of an implant-supported prosthetic construction. Head & Neck, 35(4), E109-14. doi:10.1002/hed.21922
50. Runyan, C. M., Sharma, V., Staffenberg, D. A., Levine, J. P., Brecht, L. E., Wexler, L. H., & Hirsch, D. L. (2016). Jaw in a Day: State of the Art in Maxillary Reconstruction. The Journal of Craniofacial Surgery, 27(8), 2101-2104. doi:10.1097/SCS.0000000000003139



CHAPTER 2.2

What is the optimal timing for implant placement in oral cancer patients? A scoping literature review

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This chapter is an edited version of the manuscript: What is the optimal timing for implant placement in oral cancer patients? A scoping literature review

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ABSTRACT

Background

Oral cancer patients can benefit from dental implant placement. Traditionally implants are placed after completing oncologic treatment (secondary implant placement). Implant placement during ablative surgery (primary placement) in oral cancer patients seems beneficial in terms of early start of oral rehabilitation and limiting additional surgical interventions. Guidelines on the ideal timing of implant placement in oral cancer patients are missing.

Objective

To perform a scoping literature review on studies examining the timing of dental implant placement in oral cancer patients and propose a clinical practice recommendations guideline.

Methods

A literature search for studies dealing with primary and/or secondary implant placement in Medline was conducted (last search December 27th, 2019). The primary outcome was 5-year implant survival.

Results

16 out of 808 studies were considered eligible. Both primary and secondary implant placement showed acceptable overall implant survival ratios with a higher pooled 5-year implant survival rate for primary implant placement 92.8% (95% CI: 87.1%-98.5%) than secondary placed implants (86.4%, 95% CI: 77.0%-95.8%). Primary implant placement is accompanied by earlier prosthetic rehabilitation after tumour surgery.

Conclusion

Patients with oral cancer greatly benefit from, preferably primary placed, dental implants in their prosthetic rehabilitation. The combination of tumour surgery with implant placement in native mandibular bone should be provided as standard care.

INTRODUCTION

The general treatment timeline for oral cancer patients consists of diagnostics, surgical treatment followed by postoperative (chemo)radiation therapy depending on the surgical margins and specific tumour properties, or solely (chemo)radiation therapy. Traditionally, oral rehabilitation comes last, i.e., after the oncologic treatment when the oral mucosa is completely healed (Figure 1). Oral function after treatment for a malignancy in the oral cavity is often compromised due to changed anatomy after surgery and/or the oral sequelae of radiotherapy like xerostomia and trismus[1,2]. Sometimes teeth need to be extracted during ablative surgery because of their location in proximity to the tumour or as part of a pre-radiation screening examination[3]. This compromised oral condition also leads to a decrease in oral function and possible a negative effect on nutritional status and quality of life[4]. Fabrication of functional prostheses, frames and conventional partial dentures is often difficult to achieve after oncologic treatment and in some cases even impossible[5,6].

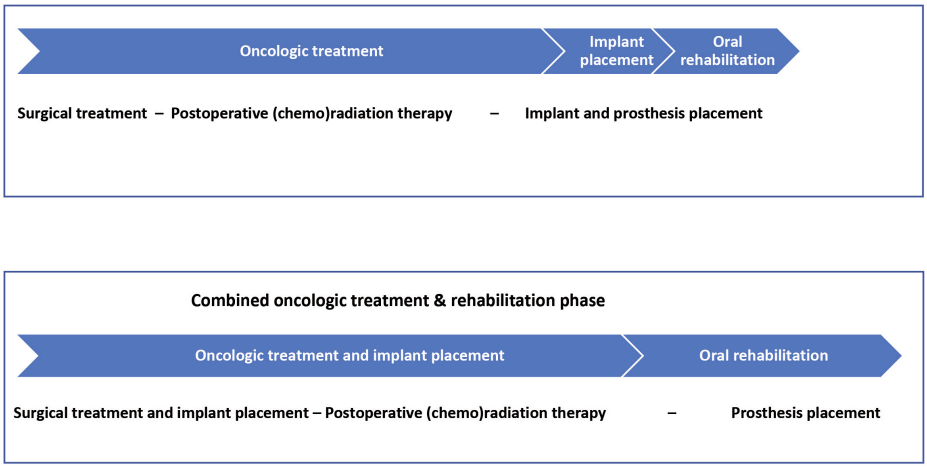


Figure 1. Timing of oncologic treatment and oral rehabilitation.

Dental implants have shown to be a great asset in oral cancer patients and provide good results[7,8]. When dental rehabilitation based on implants first was introduced in oral cancer patients, they were often placed after oncologic treatment (secondary implant placement)[9]. This implies an additional surgery, for irradiated patients under antibiotic prophylaxis, and an additional treatment burden in older patients with often multiple comorbidities. When pre-treatment hyperbaric oxygen treatment is advised, the treatment burden increases even more[10]. When offering implant treatment in a secondary phase, patients are less likely to accept or undergo additional procedures, even when they could benefit from an implant supported prosthesis[7,11].

Implants can also be placed during tumour surgery (primary implant placement)[12]. An advantage of this treatment sequence is that most of the osseointegration takes place during the recovery phase, saving the burden of additional surgery and a considerable amount of time. The patient can function with an implant-supported prosthesis much earlier after completion of oncologic treatment[6]. Disadvantages are possibly improper placement of implants due to the changed anatomy during surgery or the risk of implants not being used because of tumour recurrence or patients passing away before a prosthesis can be made (loss of resources). The effects of radiotherapy on the osseointegration process and implant survival rates are also subject of debate and primary implant placement is not always available in the hospital setting[13-15].

Guidelines when to ideally start oral rehabilitation with dental implants in oral cancer patients are lacking. Several systematic reviews have been published, mainly dealing with timing of secondary implant placement after radiotherapy[16-20]. Claudy et al. (2013) reported that dental implant placement between 6 and 12 months after radiotherapy was associated with a 34 % higher risk of failure and therefore suggest waiting periods over 1 year after radiotherapy[17]. On the contrary, it has been suggested that implant placement just becomes more critical over time because of the ongoing progressive decrease in healing capacity of bone after radiotherapy[21]. Other studies showed no significant relationship between time interval and dental implant survival rates[18,20]. The implant survival rate in patients with a history of radiotherapy seems to be more associated with the location of the implants (more implant loss in the maxilla than in the mandible) than with the of time after radiotherapy[22]. Far less studies on primary implant placement have been published. A systematic review by Barber et al. (2011) on primary implant placement provides an extensive literature overview, but no clear conclusions or recommendations were made[23]. The latter systematic review also included case reports and studies on patients with benign lesions, which could have influenced the outcome. The authors of another systematic review highlighted the importance of timing of implant placement and concluded that they could not extract scientific evidence for the optimal timing of implant placement[15].

Before being able to propose guidelines for optimal timing of implant placement in head and neck cancer patients needing radiotherapy, the following questions have to be answered: (1) what is the optimal timing of dental implant placement in oral cancer patients with regard to implant survival and functional outcomes, and (2) can all oral cancer patients benefit from primary placement or is this method of treatment only suitable for specific patient groups. As implant treatment and techniques have evolved during the last decade, we comprehensively reviewed the literature on the timing of implant placement in oral cancer patients to compose recommendations for clinical practice with regard to optimal timing of implant placement in this category of patients.

METHODS

A search was conducted in MEDLINE (from 1995 through October 16th 2019) on October 16th 2019 according to the syntax rules of the database. Key words and their combinations were used to identify relevant studies (Table 1). The titles and abstracts from all the searches were reviewed.

Inclusion criteria were studies published in English regarding primary or secondary implant placement in oral cancer patients, cohort studies, case-control studies, (randomized) controlled trials. Review articles, animal studies, case reports, case series with less than 10 patients and studies regarding extra-oral craniofacial implants were excluded. When it was not clear from the title and abstract if the paper dealt with implant placement in the upcoming irradiated (primary implant placement) or already irradiated (secondary implant placement) mandible or maxilla, the full text was reviewed and the article was included or excluded. 41 full-text articles were assessed followed by exclusion of 26 articles due to various reasons (Figure 2). Furthermore, hand searches of the references of retrieved articles were carried out. The search was updated on December 27th 2019 and one additional article was included. Eventually 16 studies were included.

Table 1. Search strategy

Database	Search Terms
Medline	("Head and Neck Neoplasms"[Mesh] OR Head and Neck Neoplasm*[tiab] OR Head and Neck cancer*[tiab] OR cancer of head and neck[tiab] OR head and neck oncol*[tiab] OR Head and Neck malignan*[tiab] OR head and neck tum*[tiab] OR Upper Aerodigestive Tract Neoplasm*[tiab] OR mouth neoplasm*[tiab] OR oral cancer*[tiab] OR oral neoplasm*[tiab] OR oropharynx malignan*[tiab] OR oropharynx tum*[tiab]) AND ("Dental Implants"[Mesh] OR "Dental Implantation, Endosseous"[Mesh] OR "Dental Prosthesis, Implant-Supported"[Mesh] OR implant*[tiab] OR denture*[tiab]) AND (Primary placement*[tiab] OR primary insert*[tiab] OR ablation surg*[tiab] OR ablative surg*[tiab] OR "Time"[Mesh] OR time*[tiab] OR timing[tiab] OR delay*[tiab] OR sequence*[tiab])

Data extraction

The following data were collected from the studies: patient demographics (age, oncologic diagnosis, patients' dental status before treatment), type of oncological treatment, timing of endosseous or zygomatic implant placement (primary, secondary), implant system, site of implant placement, type of tissue implants were inserted into (native or augmented bone), time until loading, implant loss, implant survival ratios, complications, perioperative measurements, type of prosthesis and follow-up period (Tables 3.1-3.3). When available, the time span between (implant) surgery and prosthesis placement, and the time between radiotherapy and secondary implant placement was recorded.

Statistical analysis

Quantitative data-synthesis was performed for the studies reporting 5-year dental implant survival rates of primary placed implants and secondary placed implants. Studies which did not report on the 5-year implant survival rate were not included in the quantitative analysis. The pooled 5-year implant survival rates were analyzed using a random effects model. Analyses were performed with Comprehensive Meta-Analysis software, Version 3 (CMA, Biostat, Englewood, NJ 07631, USA).

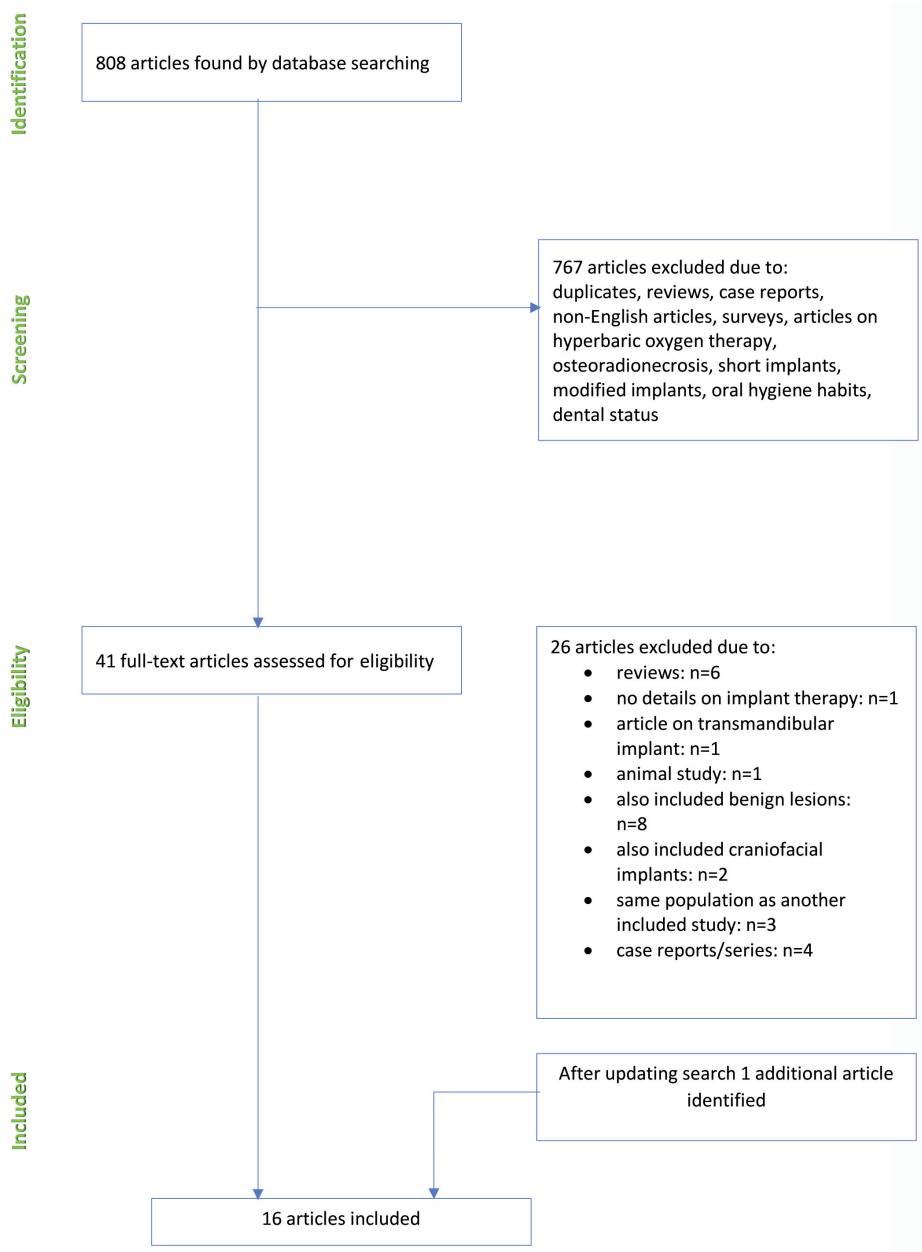


Figure 2. Flowchart of study selection procedure

RESULTS

16 out of 808 papers were considered eligible for our study and one additional article was included after updating the search (Figure 2). These 16 studies provided data on a total of 4449 implants, of which 753 implants were placed in grafted bone (osseous free flaps). The majority of studies (68.8%) had a retrospective design. Preoperative dental status (edentulous or dentate) was not always reported. Patients received an implant supported removable or fixed prosthesis. A variety of malignancies in the head and neck region was reported. Oncologic treatment consisted of tumour surgery in addition to radiotherapy. Three articles reported on including patients who were treated with chemotherapy[11,24,25]. Eight articles reported solely on secondary implant placement[11,24,26-31], two studies described patients with only primary placed implants[32,33,34] and six articles described both primary and secondary implant placement[25,34-38]. In all studies implants were placed in a 2-stage manner. When mentioned, the number of implants per patient ranged between 2 to 4 in the interforaminal region of the mandible[32-34,36]. Only one study reported the number of implants placed in the maxilla (3 to 5)[29]. From the available data, a total of 987 implants were placed in the maxilla and 131 zygomatic implants were placed in the zygomatic bone.

Implant survival

The pooled 5-year survival rate for primary placed implants was 92.8% (95% CI: 87.1%-98.5%) (Figure 3), while the pooled implant survival rate for secondary placed implants was 86.4% (95% CI: 77.0%-95.8%) (Figure 4). The 5-year implant survival rate of primary placed implants tended to be higher compared to secondary placed implants. Survival ratios for dental implants placed in vascularized bone grafts varied between 54 and 93.8% (Table 3.2). The implants in vascularized bone grafts were placed in a secondary procedure. Implant survival ratios in native maxillary bone ranged between 57.1 and 95.3%. One study focused mainly on zygomatic implants (Butterworth 2019) and reported a 5-year implant survival rate of 92%.

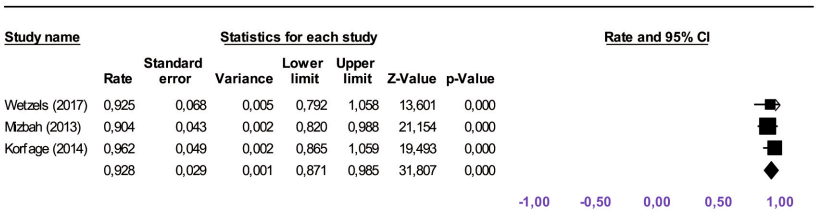


Figure 3. Forest plot for cumulative weighted 5-year implant survival rate for primary implant placement.

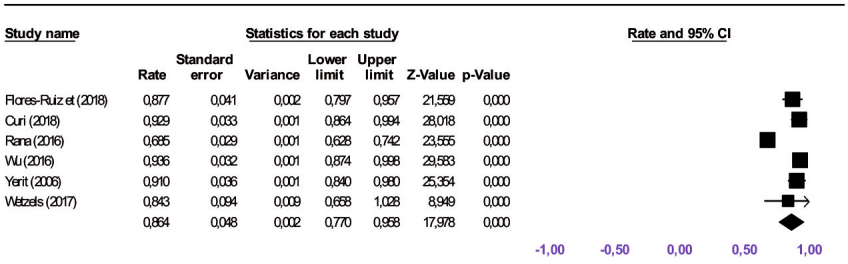


Figure 4. Forest plot for cumulative weighted 5-year implant survival rate for secondary implant placement.

Time between ablative surgery, implant placement, radiotherapy and prosthesis placement

In two studies on primary implant placement, a healing period of 6 months after radiotherapy was applied before second stage surgery[33,38]. In another study a waiting period of 9 months was applied[32]. Time from tumour surgery and implant placement until prosthesis placement from 3 studies varied from 6.3 to 21.4 months[33,36,38].

In the secondary setting there was a preference for waiting at least six months after completing radiotherapy before starting implant treatment. Some studies even preferred to wait at least 1 year[34,36]. Generally, patients had to wait more than one year after oncologic treatment before the oral rehabilitation was started. In the article by Flores-Ruiz et al. (2018) 70% of the patients started with implant therapy even later than 2 years after oncologic therapy[11]. The study of Seikaly et al. (2019) reported a mean time to prosthetic rehabilitation of 73.1 months[38]. For zygomatic implants there was also a difference between primary and secondary placed implants (median time until loading 1.7 months versus 9.3 months)[37].

Functional outcomes

Korfage et al. (2014) described that irradiated patients experience more limitations in oral function than those who were not[33]. Chewing ability decreased over time in irradiated patients, but there was still a better oral function in patients with a prosthesis

than in patients without a prosthesis[33]. A more objective method for measuring oral function was applied in the study by Wetzels et al. (2016) by determining masticatory performance[34]. The authors showed an increased masticatory performance in all patients with implant-supported prostheses, supporting the assumption that implants are beneficial for improved oral function in oral cancer patients.

Complications

Intra- and postoperative complications of dental implant placement were uncommon. The most common reported complication was osteoradionecrosis (ORN) in irradiated patients[25,33-35]. The ORN rate varied between 1.8 and 7.7%. One study reported a pathologic fracture, but it was unclear if the fracture occurred because of implant placement[25]. In the study with zygomatic implants, infection of the overlying skin in secondary placed implants occurred in 2 patients[37]. There were no complications in the group with primary placed zygomatic implants. Other complications like wound infections, wound breakdown and partial fibular skin graft loss were described for implants placed in fibula free flaps[38]. Technical complications in primary and secondary placed implants included incorrect implant positioning. In the study of Korfage et al (2014), 6 out of 164 patients (3.7%) with primary placed implants did not receive an implant supported prosthesis due to incorrect implant positioning[33]. Another study reported 17.7% unused implants after primary placement (17.7%) due to incorrect positioned implants and tumour related factors[36].

DISCUSSION

Timing of dental implant placement in oral cancer patients is a subject of continuing debate. Although most of the studies that were considered to be eligible for the review had retrospective study designs and studied implant placement in heterogeneous patient populations, it can be concluded that dental implant placement, irrespective of the timing of implant placement, is a reliable treatment option for head and neck cancer patients. Both primary and secondary implant placement show an acceptable overall implant survival. Comparison between both groups showed a tendency for a higher 5-year implant survival rate in primary implant placement. This trend, however, did not reach statistical significance. Implants placed in the maxilla tended to have lower survival ratios than implants placed in the mandible. The lower implant survival ratios in maxillary bone might be related to the thinner cortical bone of the maxilla. For zygomatic implants however, 5-year implant survival rates of 92% were reported[37]. An explanation for these favourable outcomes could be that zygomatic implants are inserted in highly cortical bone of the zygoma, leading to a high initial stability. Because of their length, these implants may also be situated outside of the radiated field, therefore avoiding toxic radiation dosages. At this moment, functional results

for zygomatic implants seem good and complication rates low, but guidelines on the optimal workflow are not yet available[39].

A great advantage of primary implant placement is the earlier prosthetic rehabilitation after tumour surgery. The latter is a great asset, also because it is not uncommon that head and neck cancer patients refuse the burden of undergoing the secondary implant placement, notwithstanding the great advantage they could experience from an implant-supported oral rehabilitation[7].

The costs and potential 'loss of resources' from implants not being used is an important issue in primary implant placement. The percentage of incorrect placed implants varied between the studies. We believe that with the help of 3D-technology, implant positioning (especially in difficult cases) can be further improved as has already been demonstrated in small groups for primary implant placement[40]. Placing implants during ablative surgery slightly lengthens the operating time, but the extra costs and burden to the patient of an additional secondary implant procedure under local anesthesia are prevented.

As stated earlier, precision of implant placement can be improved further with 3D-technologies or surgical design and simulation (SDS). In both primary and secondary implant placement 3D-planning software can be used to assess the amount of available bone height and width for dental implants after resection and to assess the ideal location for the implants from a prosthetic point of view[41]. The use of SDS has resulted in a high percentage of implant utilization (96%) for mandibular defects constructed with fibula free flaps[38]. We therefore consider the availability of 3D-planning techniques a necessity in the reconstruction of oral cancer patients with complex (continuity) defects.

Only one study on primary implant placement in osseous free flaps for larger defects was considered eligible for our review[38]. In this prospectively conducted study, dental implants were placed in bone grafts (mainly fibula grafts) during the ablative procedure. This resulted in a significant reduction of time to rehabilitation and percentage of patients rehabilitated. Most reports on implant placement in osseous free flaps include heterogeneous patient populations and show successful treatment outcomes with implant survival ratios between 80 to 100%[42,43]. Jackson et al. (2016) compared primary to secondary implant placement in fibula free flaps and found no difference in implant survival between primary and secondary implantation, and between non-irradiated and irradiated patients[44]. The 1-year results of Sandoval et al. (2019) in 10 patients with primary placed implants in fibula free flaps show that the presence of dental implants in fibula free flaps does not lead to more postoperative complications or an increase of radiotherapy related toxicities[45]. Despite these promising results, correct placement of dental implants in osseous free flaps during ablative surgery is technically challenging as reviewed by Bodard et al. (2011)[46]. One way of partially

reducing these challenges is through the use of occlusion-driven reconstructions aided by 3D-planning, as is demonstrated in the article of Seikaly et al. (2019)[38]. However, the essential difference in tissues covering the grafted bone of the fibula and native mandibular bone remains. The presence of subcutaneous tissue and the absence of keratinized gingiva could affect implant survival and peri-implant health. The patients should be strictly monitored to see whether complications might occur on the long run. Additional thinning or correction of the overlying skin paddle is sometimes necessary during second stage surgery[42,47]. Regarding functional outcomes, Wijbenga et al. (2016) concluded from their systematic review that despite high implant survival ratios, it is not possible to state what the effect of implant-supported dental prostheses is after reconstruction with a fibula free flap, again mainly due to the diversity of methods used to assess functional outcomes[47]. Awad et al. (2019), however, concluded in their systematic review that 61% of patients with a vascularized fibula flap receiving dental rehabilitation reported good oral function and was able to consume a normal diet[48]. The latter authors, however, did not make a statement on the timing of implant placement in vascularized fibula flaps. With respect to timing of implant placement in osseous free flaps, it is generally advised to insert implants primarily only in patients with benign lesions[47,50]. In our clinic we prefer to place dental implants as much as possible in the remaining native mandibular bone (during ablative surgery) in order not to jeopardize the vitality of the vascularized fibula flap. As mechanical stability comes from the more anterior region of the mandible, this approach is successful in lateral and antero-lateral defects.

Limitations of this scoping review include, as stated earlier, the retrospective study designs, heterogeneous patient populations, exclusion of non-English papers, the use of one database and the fact that screening by carried out by assessor. These factors could result in bias. Due to the unavailability of large prospective studies on the timing of implant placement in oral cancer patients, the treatment of choice will mainly depend on surgeon experience and preference. However, based on the findings in the current study and our own experience in treating these patients, we composed treatment recommendations on the timing of implant placement in patients with malignant intraoral tumours (Table 2). We realize that these recommendations may not be applicable to all hospital settings as 3D-planning software and the financial resources for primary implant placement may not be available in every centre.

		Dental status		
		Edentulous mandible	**Edentulous maxilla**	**Suggestions / points of concern**
Extensiveness of oncologic treatment	**Surgery with or without local flap, and with or without (chemo)radiotherapy**	· primary implant placement. · 2 implants in the interforaminal region.	· primary implant placement. · number and type of implants* depends on size of defect, type of reconstruction and prosthetic rehabilitation.	· as an alternative, second stage surgery can be considered after the short-term adverse effects of radiotherapy have subsided.
	Surgery with osseous free flap (e.g., free fibula flap) with or without (chemo) radiotherapy	· primary or secondary implant placement, preferably in remaining native bone or otherwise in osseous free flap. · 2 – 4 implants	· primary or secondary implant placement, preferably in remaining native bone or otherwise in osseous free flap. · number and type of implants* depends on size of defect and type of reconstruction and prosthetic rehabilitation.	· thinning of the overlying soft tissues might be needed as a secondary treatment during second stage surgery. · apply 3D-planning techniques when available for both primary and secondary implant placement. · consider hyperbaric oxygen therapy in cases of treatment in irradiated tissues.

*Includes zygoma implants

Table 2. Recommendations for dental implant placement to support implant-retained overdentures in head and neck cancer patients**.**

CONCLUSION

Based on the studies included in this review, as far as the timing of implant placement is regarded, we propose to routinely combine tumour surgery with implant placement in native mandibular bone as standard care (primary implant placement). The functional benefits of primary implant placement outweigh the risk of leaving (some) implants unused. For more complex reconstructive cases, a personalized treatment approach (aided by 3D-technologies) is necessary and is more often in need of a secondary implant placement. It seems that primary placement of zygomatic implants is accompanied by a high implant survival and good oral rehabilitation although more research is needed on this particular topic.

Conflict of interest

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

Table 3.1 General characteristics of eligible studies.

	First author	Year	Study type	N	Patient age (mean, range)	Oncologic diagnosis	Patients' dental status	Site of implant placement	Implant system	Tissue implants inserted to	RT	Radiation dose in region of implant	Timing of implant placement
1	Flores-Ruiz	2018	Retrospective	17	30-60	Epidermoid carcinoma, osteosarcoma, lymphoepithelioma	Edentulous and partially edentulous	Mandible and maxilla	Unknown	Native and grafted bone	Yes (47%)	Not reported	Secondary
2	Curi	2018	Retrospective cohort study	35	46-94	SCC	Not reported	Mandible and maxilla	Replace Select Tapered; Nobel biocare	Native bone	>50Gy	>50Gy	Secondary
3	Rana	2016	Retrospective	46	60	Oral cancer	Not reported	Mandible and maxilla	Biomet 3i	Native bone	Yes	Not reported	Secondary
4	Wu	2016	Retrospective	34	52.1	SCC, ACC, mucoepidemoid carcinoma, malignant ameloblastoma, nasopharynx tumour, acinic cell carcinoma	Not reported	Mandible and maxilla	Straumann, Nobelbiocare	Native and grafted bone (4 ilium bone, 18 fibula grafts)	Yes <50Gy	Not reported	Secondary
5	Sammartino	2011	Prospective	77	55.8, 28-63	Head and neck cancer	Edentulous and partially edentulous	Mandible and maxilla	Solid screw with microstructured surface	Native bone	Yes all	Not reported	Secondary
6	Nelson	2007	Retrospective	93	59, 26-89	Malignant intraoral tumour	Edentulous and partially edentulous	Mandible and maxilla	CAMLOG, Steri-oss (nobel biocare), Straumann	Native and grafted bone (ilium and fibula bone)	Yes (29/93) patients with up to 72Gy)	Not reported	Secondary
7	Yerit	2006	Retrospective	71	57.8, 16-84.1	Oral cancer (majority SCC T2-T4)	Not reported	Mandible	IMZ (Friadent), Frialit II (Friadent), Xive (Friadent)	Native and grafted bone (iliac bone)	Up to 50Gy	Not reported	Secondary

Table 3.1 General characteristics of eligible studies. *(continued)*

	First author	Year	Study type	N	Patient age (mean, range)	Oncologic diagnosis	Patients' dental status	Site of implant placement	Implant system	Tissue implants inserted to	RT	Radiation dose in region of implant	Timing of implant placement
8	Visch	2002	Prospective	130	62, 34-87	Head and neck cancer	Not reported	Mandible and maxilla	Hydroxy-appatite coated titanium. Dyna, Screw-Vent implants	Native bone	Yes (50-72Gy)	Not reported	Secondary
9	Seikaly	2019	Prospective	30	57	Malignant disease not further specified	Not reported	Mandible and maxilla	Not reported	Grafted bone (fibula free flap)	7/15 primary; 9/15 secondary	Not reported	Primary and Secondary
10	Butterworth	2019	Prospective	49	70, 13-92	SCC, ACC, sarcoma, adenocarcinoma, melanoma, rhabdomyosarcoma, ameloblastoma, pleomorphic adenoma, ORN	Edentulous and dentate	Upper jaw / zygoma	Not reported	Native bone	Yes 16/49	Not reported	Primary and Secondary (2 groups)
11	Wetzels	2017	Retrospective cohort study	97 (79 prim. 18 sec.)	66.25 (prim.), 68.32 (sec.)	SCC, merkel cell carcinoma, salivary gland carcinoma	Edentulous	Mandible and maxilla	Branemark Nobel Biocare (primary), Astra/ Straumann (secondary)	Native bone (both primary and secondary	55% (prim.), 53% (sec.)	Not reported	Primary and Secondary (2 groups)
12	Ch'ng	2016	Retrospective	246	59.0	ACC, adenocarcinoma, ameloblastic carcinoma, desmoid tumour, fibrosarcoma, melanoma, osteosarcoma, SCC, hemangioendothelioma	Unknown	Mandible and maxilla	Astra Tech	Native and grafted bone (67 fibula free flaps)	165/246 (60-72Gy)	Not reported	Primary and secondary

Table 3.1 General characteristics of eligible studies. *(continued)*

	First author	Year	Study type	N	Patient age (mean, range)	Oncologic diagnosis	Patients' dental status	Site of implant placement	Implant system	Tissue implants inserted to	RT	Radiation dose in region of implant	Timing of implant placement
13	Wetzels	2016	Prospective	56	67 - 70	Intraoral malignancies not further specified	Edentulous	Mandible	Branemark (primary), Astra+ Straumann (secondary)	Native and grafted bone. Primary: 2 free vascularized bone flaps.. Secondary: 4 free vascularized bone flaps.	Yes	Not reported	Primary and secondary
14	Mizbah	2013	Retrospective	99	Not reported	Primary SCC	Edentulous	Mandible	Branemark (primary), Frialit (delayed)	Native bone	Primary 47/99. Secondary 17/29.	Not reported	Primary and secondary
15	Korfage	2014	Prospective cohort	164	64.8, 39-88	SCC	Edentulous	Mandible	Branemark (Nobelbiocare)	Native bone	Yes (64)	Not reported	Primary
16	Schepers	2006	Retrospective	48	64.8 (men), 68.1 women)	Primary SCC in oral cavity	Edentulous	Mandible	Branemark	Native bone	Yes (21/48)	10-68Gy	Primary

RT: radiotherapy; SCC: squamous cell carcinoma; ACC: adenoid cystic carcinoma; ORN: osteoradionecrosis, FFF: fibula free flaps; Gy: Gray; prim: primary; sec: secondary,
Studies number 1 – 8: Studies on secondary implant placement
Studies number 9 – 14: Studies on both primary and secondary placed implants
Studies number 15 – 16: Studies on primary implant placement

Table 3.2 Data on implant treatments and implant survival of included studies.

First author	Primary implant placement (N)	Secondary implant placement (N)	Total no. of implants	Time after RT until implant placement	Time until loading	Number of implants per patient	Implant loss	Implant survival rate	Follow-up period
Flores-Ruiz	0	17	106 (15 implants in grafted bone; 43 in the maxilla)	70% >2 years after radiotherapy	Not reported	Not reported	13 failed (9 maxilla, 4 mandible; 9 native bone, 4 grafted bone).	90.1% native bone. 73.3% grafted bone. 79.2% maxilla. 87.7% mandible. Overall 87.7% .	5 yrs
Curi	0	0	169 (79 implants in the maxilla, 90 implants in the mandible)	1-92 mo	6 mo	Not reported	12 implants (3 during healing period and 9 lost after loading)	92.9% 5 yrs	7.43 yrs
Rana	0	46	162 (70 implants in the maxilla)	6-24 mo	Not reported	Not reported	52	65% maxilla 71% mandible	5 yrs
Wu	0	34	187 (63 implants in maxilla; 68 implants in native bone)	6-12 mo	0.8 yrs	Not reported	27	93.2% native bone. 93.8% grafted bone. 87.3% maxilla. 97.5% mandible Overall 93.6%	5 yrs
Sammartino	0	77	188 (42 implants in the maxilla, 146 in the mandible)	At least 6 months. Mean time: 9.4 months.	6 mo (mandible), 8 mo(maxilla)	2 mandible; 3-5 maxilla	2 implants lost in mandible; 18 implants lost in maxilla.	98.4% in mandible; 57.1% in maxilla. 90.5% in <12 mo after RT. 82.2% in >12 mo after RT.	3 yrs
Nelson	0	93	435 (281 implants in the maxilla; 95 implants in grafted bone).	Minimum 6 mo	3 mo mandible, 6 mo maxilla	3 to 8	43 implants	Maxilla 70% after 4 yrs. Overall implant survival 92%, 84%, and 69% after 3.5, 8.5, and 13 years. Implant survival rates for implants in grafted bone unknown.	13 yrs

Table 3.2 Data on implant treatments and implant survival of included studies. *(continued)*

First author	Primary implant placement (N)	Secondary implant placement (N)	Total no. of implants	Time after RT until implant placement	Time until loading	Number of implants per patient	Implant loss	Implant survival rate	Follow-up period
Yerit	0	71	316 (171 in iliac bone)	1.41 yrs after surgery	>6mo	Not reported	44 implants	Overall: 95%, 94%, 91% and 75% after 2,3,5,8 yrs. Irradiated: 93%,90%,84% and 72% after 2,3,5,8 yrs. Grafted bone: 96%,96%,96% and 54% after 2,3,5,8 yrs.	5.4 yrs
Visch	0	130	446 (108 implants in the maxilla, 338 implants in the mandible)	6 mo – 22 yrs	6mo	Not reported	64 implants	Overall: 78% 10yr. Maxilla 60%, mandible 85%. 10 yrs.	10 yrs
Seikaly	15	15	110 (57 implants primary; 53 implants secondary). Number of implants in maxilla / mandible not reported.	Not reported	6mo	Not reported	2 implants lost in both groups	Overall: 96%	1 year
Butterworth	27 patients and 75 zygoma implants + 14 standard	22 patients and 56 implants + 16 standard	131 zygomatic implants. Additionally 30 dental implants in the maxilla.	Not reported	primary 1.7mo, secondary 9.3 mo	NA	9 zygoma implants	12 mo estimated 94%, 60 mo estimated 92%	2-110 mo

Table 3.2 Data on implant treatments and implant survival of included studies. *(continued)*

First author	Primary implant placement (N)	Secondary implant placement (N)	Total no. of implants	Time after RT until implant placement	Time until loading	Number of implants per patient	Implant loss	Implant survival rate	Follow-up period
Wetzels (2017)	79 patients and 207 implants. 52 implants never loaded.	18 patients and 43 implants placed 528 days after surgery	268 (in primary group 18 additional implants were placed post-surgery)	At least 6mo disease free	3 mo (non-irradiated), 6 mo (irradiated)	2 to 4	17 primary implants failed (6.7%), 12 mandible, 5 maxilla. 5/17 due to implant related cause. Secondary group 3 implants lost (7%) due to loss of flap in which implants were placed. In primary group 32% implants failed due to patient death, versus 7% in secondary group due to patient death.	Higher cumulative implant survival rates in secondary group. Primary 60%. Secondary 86%.	5yrs
Ch'ng	115 during ablative surgery. 41 primary RT.	90	1132 (243 implants in fibula free flaps; 618 implants in native mandible, 271 in native maxilla)	Not reported	Not reported	2-9 in fibula free flap.	Overall 42/1132 lost	Mandible 97.4%. Maxilla 95.3%. Fibula free flap 92.6% Overall 96.3% at follow-up. 5 yrs 94.9%.	5 yrs
Wetzels (2016)	18 patients and 40 implants	9 patients and 19 implants placed 568 days after surgery	59	Unknown. (Secondary implants were placed at least 1 year after ablative surgery)	Not reported	2 or 3	In primary group 3/40 implants lost. In secondary group 3/19 implants lost.	Primary 92.5%. Secondary 84.2%.	5 yrs
Mizbah	99	29	163	At least 1 year no recurrence	3 mo (non-irradiated), 6 mo (irradiated)	2 to 4	24 (primary) = 9.6%,. 6 (secondary) = 9.2%.	Primary 90.4%; Secondary 90.8%	5 yrs

Table 3.2 Data on implant treatments and implant survival of included studies. *(continued)*

First author	Primary implant placement (N)	Secondary implant placement (N)	Total no. of implants	Time after RT until implant placement	Time until loading	Number of implants per patient	Implant loss	Implant survival rate	Follow-up period
Korfage	164	0	524	-	3 mo (non-irradiated), 9 mo (irradiated)	2 to 4	31 (irradiated patients), 5 (non-irradiated patients)	93.1%	Up to 14 yrs
Schepers	48	0	139	-	9 mo (irradiated), 4.7 mo (nonirradiated)	2 to 4	2/61 (irradiated) , 0/78 (non-irradiated)	96.7% (irradiated), 100% non-irradiated	29.6mo

RT: radiotherapy; mo: months; yrs: years

Table 3.3 Data on type of prosthetic rehabilitation, functional outcomes and perioperative measurements.

First author	Reported clinical measurements	Peri-implant bone loss	Type of prosthesis	Functional outcomes	Prophylaxis	Complications	Overall conclusion
Flores-Ruiz	None	Not reported	Overdenture, fixed prostheses	None	None	Not reported	There is no consensus as to the time needed to achieve successful survival after placement of implants
Curi	None	Not reported	Overdentures	Patient satisfaction, mastication, speech, aesthetics	Clindamycin 4x300mg 1 week starting 1 day before treatment; HBO (37.1%)	Not reported	Dental implants in head and neck cancer patients with RT is a viable treatment alternative with a high degree of satisfaction. The type of RT may require special consideration. IMRT has less implant failure than conformal RT.
Rana	Not reported	Not reported	Cemented and removable overdentures	None	None	Not reported	Further research is required in this field to improve aesthetics and quality of life.
Wu	BI,GI,PI	1.2 ± 0.4 to 1.6 ± 0.6 mm.	Fixed and removable dentures	None	HBO (14 patients)	65 prosthetic maintenance procedure (abutment/screw loosening). No surgical complications reported.	Dental implants are more successful in the mandible than in the maxilla. No difference in survival rates between patients who received HBO and who did not. The restoration of oral function in radiotherapy patients with tumour resection using implant-supported prostheses is a viable treatment option.
Sammartino	None	Panoramic and periapical	Overdentures, maxillary obturators	None	No HBO	Not reported	Implant therapy can be considered in irradiated patients when from an oncologic standpoint the tumour prognosis is benign and the risk of recurrence is poor. Higher implant success rates in the mandible and in irradiated implant sites with a dosage no more than 40-50Gy.

Table 3.3 Data on type of prosthetic rehabilitation, functional outcomes and perioperative measurements. *(continued)*

First author	Reported clinical measurements	Peri-implant bone loss	Type of prosthesis	Functional outcomes	Prophylaxis	Complications	Overall conclusion
Nelson	None	Not reported	Fixed and removable dentures	None	Irradiated patients clindamycin 300mg 1 day pre- and 3 days postoperatively	Technical complications: Replacement of 11 bar-retained dentures. 2 patients with mucosa ulcers after loss of retention of the removable denture. 3 patients with dehiscence and disturbed wound healing.	The mean 10.3-year survival rate was low, and there was no statistically significant difference in implant survival between irradiated and nonirradiated patients. The increased failure rate was caused by the higher mortality rate of the patients; it was not the result of lack of osseointegration. There was no difference between implant survival in grafted and nongrafted patients.
Yerit	None	Not reported	Removable denture	None	No HBO	1 patient with a pathological fracture of the mandible leading to loss of 3 implants.	Shorter implant survival in irradiated and grafted bone. No difference in survival between implant placed < or > 12mo after RT. Surgical and prosthetic implant rehabilitation of tumour patients offer long-term results with favorable implant survival rates.
Visch	None	Not reported	Not reported	None	AB prophylaxis. No HBO.	Not reported	After a post-irradiation interval of six months, the influence of time on implant survival is not significant. Bone-resection surgery in the jaw where the implant is placed has a significantly negative influence on implant survival. Implant location is the most dominant variable influencing implant survival (more implant loss in maxilla than in the mandible).

Table 3.3 Data on type of prosthetic rehabilitation, functional outcomes and perioperative measurements. *(continued)*

First author	Reported clinical measurements	Peri-implant bone loss	Type of prosthesis	Functional outcomes	Prophylaxis	Complications	Overall conclusion
Seikaly	None	Not reported	Not reported	Not reported	HBO	Primary placement: 2 major complications (hematoma, pulmonary embolism) and 7 minor complications (tachycardia, atelectasis, wound infection/breakdown, partial fibular skin graft loss). Secondary placement: 2 major complications (flap venous congestion and pneumonia) and 5 minor complications (wound infection/breakdown)	Primary implant placement in fibula free flaps reduced the duration of time to complete treatment from 6.1 yrs to 1.8 yrs. The reduction in treatment time was not associated with a statistically significant increase in complications.
Butterworth	None	Not reported	Oral (fixed and removable) and facial prostheses	QOL. No significant problems with swallowing	NA	No significant complications in primary implant group. Secondary implant group: 2 patients with an infection of the skin overlying the zygomatic body. 2 patients with peri-implant bone loss. Small number of patients with screw loosening and screw fracture.	Primary implant placement should be the gold standard. Access for zygomatic implant placement is much improved at primary resective surgery. There is a trend towards worse survival rates in secondary placement.
Wetzels (2017)	None	Not reported	Overdenture	None	6 patients HBO in secondary group	Primary implant group: 52 implants were never loaded. 5 patients with ORN. Secondary implant group: 5 patients with ORN.	1. More functional overdentures in primary group. 2. Prosthetic rehabilitation 484 days earlier in primary implants. 3. Timing of placement does not affect viability of implants.

Table 3.3 Data on type of prosthetic rehabilitation, functional outcomes and perioperative measurements. *(continued)*

First author	Reported clinical measurements	Peri-implant bone loss	Type of prosthesis	Functional outcomes	Prophylaxis	Complications	Overall conclusion
Ch'ng	None	Not reported	Removable denture	None	Not reported		More implant losses in fibula free flaps. RT adversely affects implant survival in FFF but not in the native mandible or maxilla. The sequence of RT in relation to implant placement did not significantly affect the implant survival rate, except in fibula free flaps. Irradiation might be considered a relative contraindication to implant placement in osseous free flaps. No conclusion on timing.
Wetzels (2016)	None	Not reported	Overdenture	Bite force, masticatory performance	HBO in irradiated patients in secondary group	1 patient with ORN (not adjacent to the still functional implants).	There is a strong indication of superior bite force and masticatory performance after 5 years in primary group when compared to postponed placement. It seems that primary placement is superior to secondary placement.
Mizbah	None	Not reported	Overdenture	None	HBO in irradiated patients in secondary group	Not reported	Using primary placement, more patients benefit and receive their overdentures at an earlier stages (20months earlier) compared to secondary placement.
Korfage	Periodontal indices	Panoramic	Overdenture	EORTC QLQ, OHIP.	HBO in 3 patients who developed ORN	5 patients with ORN in proximity to the implants. Pathological mandible fracture in 1 patient with a recurrent tumour and ORN.	More limitations in oral function and less satisfaction in irradiated patients. Better oral function with than without prosthesis. A large number of patients with oral cancer in whom implants are inserted during resection may benefit at an early stage from an overdenture and develop good function, satisfaction. Primary insertion should be routinely incorporated into surgical planning. More implant loss in irradiated patients.

Table 3.3 Data on type of prosthetic rehabilitation, functional outcomes and perioperative measurements. *(continued)*

First author	Reported clinical measurements	Peri-implant bone loss	Type of prosthesis	Functional outcomes	Prophylaxis	Complications	Overall conclusion
Schepers	None	Not reported	Removable denture	None	Not reported	No patients developed ORN. No other complications reported.	Success of prosthetic rehabilitation on implants inserted during ablative surgery is independent of whether postoperative RT is applied. Primary implant placement in edentulous mandibles appears to have advantages over secondary implant placement in patients with oral SCC.

RT: radiotherapy; SCC: squamous cell carcinoma; ACC: adenoid cystic carcinoma; ORN: osteoradionecrosis, FFF: fibula free flaps. PORT: postoperative radiotherapy; IMRT: intensity-modulated radiation therapy, HBO: hyperbaric oxygen; BI: bleeding index; GI: gingiva index; PI: plaque index, Gy: Gray; AB: antibiotic; EORTC QLQ: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; OHIP: Oral Health Impact Profile.

REFERENCES

1. Kamstra, J.I., Jager-Wittenaar H., Dijkstra P.U., Huisman P.M., van Oort R.P., van der Laan B.F.A.M. & Roodenburg J.L.N. (2011). Oral symptoms and functional outcome related to oral and oropharyngeal cancer. Support Care Cancer, 19, 1327–1333. doi: 10.1007/s00520-010-0952-4
2. de Groot R.J., Wetzels J.W., Merkx M.A.W., Rosenberg A.J.W.P., de Haan A.F.J., van der Bilt A., Abbink J.H., Speksnijder C.M. (2019). Masticatory function and related factors after oral oncological treatment: A 5-year prospective study. Head & Neck, 41, 216–224. doi: 10.1002/hed.25445
3. Spijkervet F.K.L., Schuurhuis J.M., Stokman M.A., Witjes M.J.H., Vissink A. (2020). Should oral foci of infection be removed before onset of radiotherapy or chemotherapy? Oral Disease, submitted for publication.
4. Jager-Wittenaar H., Dijkstra P.U., Vissink A., van der Laan B.F., van Oort R.P., Roodenburg J.L.N. (2011). Malnutrition and quality of life in patients treated for oral or oropharyngeal cancer. Head Neck, 33, 490-496.
5. Curtis T.A. & Cantor R. (1974). The forgotten patient in maxillofacial prosthetics. J Prosthet Dent, 31(6), 662-680.
6. Petrovic I., Rosen E.B., Matros E., Huryn J.M. & Shah J.P. (2018). Oral rehabilitation of the cancer patient: A formidable challenge. J Surg Oncol, 117, 1729–1735. doi: 0.1002/jso.25075.
7. Schoen P.J., Reintsema H., Bouma J., Roodenburg J.L.N., Vissink A. & Raghoebar G.M. (2007). Quality of life related to oral function in edentulous head and neck cancer patients posttreatment. Int J Prosthodont, 20, 469-477.
8. Said M.M., Oromaru T., Sumita Y., Leung K.C.M., Khan Z. & Taniguchi H. (2017). Systematic review of literature: functional outcomes of implant-prosthetic treatment in patients with surgical resection for oral cavity tumors. Journal of Investigative and Clinical Dentistry, 8, e12207. doi: 10.1111/jicd.12207.
9. Kim D.D., Ghali G.E. (2011). Dental implants in oral cancer reconstruction. Oral Maxillofacial Surg Clin N Am, 23, 337-345.
10. Spijkervet F.K.L., Brennan M.T., Peterson D.E., Witjes M.J.H. & Vissink A. (2019). Research frontiers in oral toxicities of cancer therapies: Osteoradionecrosis of the jaws. J Natl Cancer Inst Monogr, 53, 86-93. doi: 10.1093/jncimonographs/lgz006.
11. Flores-Ruiz R., Castellanos-Cosano L., Serrea-Figallo M-A., Cano-Diaz E., Torres-Lagares D. & Gutierrez-Perez J-L. (2018). Implant survival in patients with oral cáncer: A 5-year follow-up. J Clin Exp Dent, 10(6), e603-0. doi: 10.4317/jced.54937.
12. Schoen P.J., Reintsema H., Raghoebar G.M., Vissink A., Roodenburg J.L.N. (2004). The use of implant retained mandibular prostheses in the oral rehabilitation of head and neck cancer patients. A review and rationale for treatment planning. Oral Oncology, 40, 862-871.
13. Chrcanovic B.R., Albrektsson T. & Wennerberg A. (2016). Dental implants in irradiated versus nonirradiated patients: A meta-analysis. Head Neck, 38, 448-481.
14. Tanaka T.I., Chan H.L., Tindle D.I. MacEachern M. & Oh T.J. (2013). Updated clinical considerations for dental implant therapy in irradiated head and neck cancer patients. Journal of Prosthodontics, 22, 432-438. doi: 10.11111/jopr.12028.
15. Shugaa-Addin B., Al-Shamiri H-M., Al-Maweri S. & Tarakji B. (2016). The effect of radiotherapy on survival of dental implants in head and neck cancer patients. J Clin Exp Dent, 8(2), e194-200. doi: 10.4317/jced.52346

16. Granström G. (2003). Radiotherapy, osseointegration and hyperbaric oxygen therapy. Periodontology, 33, 145-162.
17. Claudy M.P., Miguens Jr S.A., Celeste R.K., Parente R.C., Hernandez P.A.G. & da Silva Jr A.N. (2013). Time interval after radiotherapy and dental implant failure: Systematic review of observational studies and meta-analysis. Clinical Implant Dentistry and Related Research, 17(2), 402-411. doi: 10.1111/cid.12096
18. Nooh N. (2013). Dental implant survival in irradiated oral cancer patients: A systematic review of the literature. Int J Oral Maxillofax Implants, 28, 1233-1242. doi: 10.11607/jomi.3045
19. Schiegnitz E., Al-Nawas B., Kämmerer P.W. & Grötz K.A. (2014). Oral rehabilitation with dental implants in irradiated patients: A meta-analysis on implant survival. Clin Oral Invest, 18, 687–698. doi: 10.1007/s00784-013-1134-9
20. Filho E.V. Z., de Souza Tolentino E. & Santos P.S.S. (2015). Viability of dental implants in head and neck irradiated patients: A Systematic review. Head Neck, 38, E2229–E2240. doi:10.1002/HED
21. Granström G., Bergström K., Tjellström A., Brånemark P-I. (1994). A detailed analysis of titanium implants lost in irradiated tissues. Int J Oral Maxillofac Implants, 9, 653-662.
22. Buddula A., Assad D.A., Salinas T.J., Garces Y.I., Volz J.E. & Weaver A.L. (2012). Survival of dental implants in irradiated head and neck cancer patients: A retrospective analysis. Clin Implant Dent Relat Res, 14 (5), 716-722. doi: 10.1111/j.1708-8208.2010.00307.x
23. Barber A.J., Butterworth C.J. & Rogers S.N. (2011). Systematic review of primary osseointegrated dental implants in head and neck oncology. British Journal of Oral and Maxillofacial Surgery, 49, 29-36. doi: 10.1016/j.bjoms.2009.12.007
24. Yerit K.C., Posch M., Seemann M., Hainich S., Dörtbudak O., Turhani D., … Ewers R. (2006). Implant survival in mandibles of irradiated oral cancer patients. Clin Oral Impl Res, 17, 337–344. doi: 10.1111/j.1600-0501.2005.01160.x
25. Ch'ng S., Skoracki R.J., Selber J.C., Yu P., Martin J.W., Hofstede T.M. … Hanasono M.M. (2015). Osseointegrated implant-based dental rehabilitation in head and neck reconstruction patients. Head & Neck, 38, E321-327. doi: 10.1002/hed. 23993
26. Curi M.M., Condezo .F.B., Ribeiro K.d.C.B. & Cardoso C.L. (2018). Long-term success of dental implants in patients with head and neck cancer after radiation therapy. Int J Oral Maxillofac Surg, 47, 783-788. doi: 10.1016/j.ijoms.2018.01.012
27. Rana M.C., Solanki S., Pujari S.C., Shaw E., Sharma S., … Singh H.P. (2016). Assessment of the survival of dental implants in irradiated jaws following treatment of oral cancer: A retrospective study. Niger J Surg, 22(2), 81-85. doi: 10.4103/1117-6806.182741
28. Wu Y., Huang W., Zhang Z., Zhang Z. & Zou D. (2016). Long-term success of dental implant-supported dentures in postirradiated patients treated for neoplasms of the maxillofacial skeleton: A retrospective study. Clin Oral Invest, 20, 2457-2465. doi: 10.1007/s00784-016-1753-z
29. Sammartino G., Marenzi G., Cioffi I., Tete S. & Mortellaro C (2011). Implant therapy in irradiated patients. J Craniofac Surg, 22, 443-445. doi: 10.1097/SCS.0b013e318207b59b
30. Nelson K., Heberer S. & Glatzer C. (2007). Survival analysis and clinical evaluation of implant-retained prostheses in oral cancer resection patients over a mean follow-up period of 10 years. J Prosthet Dent, 98, 405-410.
31. Visch L.L. van Waas M.A.J., Schmitz P.I.M. & Levendag P.C. (2002). A clinical evaluation of implant sin irradiated oral cancer patients. J Dent Res, 81(12), 856-859.

32. Schepers R.H. Slagter A.P., Kaanders J.H.A.M., van den Hoogen F.J.A. & Merkx M.A.W. Effect of postoperative radiotherapy on the functional results of implants placed during ablative surgery for oral cancer (2006). Int J Oral Maxillofac Surg, 35: 803-808. doi: 10.1016/j.ijom.2006.03.007
33. Korfage A. Raghoebar G.M. Huddleston Slater J.J.R., Roodenburg J.L.N., Witjes M.J.H., Vissink A. & Reintsema H. (2014). Overdentures on primary mandibular implants in patients with oral cancer: A follow-up study over 14 years. British Journal of Oral and Maxillofacial Surgery, 52, 798-805. doi: 10.1016/j.bjoms.2014.05-013
34. Wetzels J-W.G.H., Koole R., Meijer G.J., de Haan A.F.J., Merkx M.A.W. & Speksnijder C.M. (2016). Functional benefits of implants placed during ablative surgery: A 50year prospective study on the prosthodontics rehabilitation of 56 edentulous oral cancer patients. Head Neck, 38, E2103-E2111. doi: 10.1002/hed.24389
35. Wetzels J-W.G.H., Meijer G.J., Koole R., Merkx M.A.W. & Speksnijder C.M. (2017). Costs and clinical outcomes of implant placement during ablative surgery and postponed implant placement in curative oral oncology: A five-year retrospective cohort study. Clin Oral impl Res, 28, 1433-1442. doi: 10.1111/clr.13008
36. Mizbah K., Dings J.P., Kaanders J.H.A.M., van den Hoogen F.J.A., Koole R., Meijer G.J. & Merkx M.A.W. (2013). Inteforaminal implant placement in oral cancer patients: during ablative surgery or delayed? A 5-year retrospective study. Int J Oral Maxillofac Surg, 42, 651-655. doi: 10.1016/j.ijom.2012/09.013
37. Butterworth C.J. (2019) Primary vs secondary zygomatic implant placement in patients with head and neck cancer – A 10-year prospective study. Head & Neck, 41, 1687–1695. doi: 10.1002/hed.245645
38. Seikaly H., Idris S., Chuka R., Jeffery C., Dzioba A., Makki F., ..., Wolfaardt J. (2019). The Alberta Reconstructive Technique: An occlusion-driven and digitally based jaw reconstruction. Laryngoscope, 129, S1-S14. doi: 10.1002/lary.28064.
39. Hackett S., El Wazani B. & Butterworth C. (2020). Zygomatic implant based rehabilitation for patients with maxillary and mid-facial oncology defects. Oral Disease; submitted for publication.
40. Chuka R., Abdullah W., Rieger J., Nayar S., Seikaly H., Osswald M., Wolfaardt J. (2017). Implant utilization and time to prosthetic rehabilitation in conventional and advanced fibular free flap reconstruction of the maxilla and mandible. Int J Prosthodont, 30, 289-294. doi: 10.11607/ijp.5161
41. Witjes M.J.H., Schepers R.H. & Kraeima J. (2018). Impact of 3D virtual planning on reconstruction of mandibular and maxillary surgical defects in head and neck oncology. Curr Opin Otolaryngol Head Neck Surg, 26, 108-114. doi: 10.1097/MOO.0000000000000437
42. Kumar V.V., Ebenezer S., Kämmerer P.W., Jacob P.C., Kuriakose M.A., Hedne N., Wagner W. & Al-Nawas B. (2016). Implants in free fibula flap supporting dental rehabilitation – Implant and peri-implant related outcomes of a randomized clinical trial. J Craniomaxillofac Surg, 44, 1849-1858. doi: 10.1016/j.jcms.2016.08.023
43. Sozzi D., Novelli G., Silva R., Connely S.T. & Tartaglia G.M. (2017). Implant rehabilitation in fibula-free flap reconstruction: A retrospective study of 1-18 years following surgery. J Craniomaxillofac Surg, 45, 1655-1661. doi: 10.106/j.jcms.2017.06.021
44. Jackson R.S. Price D.L., Arce K. & Moore E.J. (2016). Evaluation of clinical outcomes of osseointegrated dental implantation of fibular free flaps for mandibular reconstruction. JAMA Facial Plast Surg, 18 (3), 201-206. doi: 10.1001/jamafacial.2015.2271

45. Sandoval M., Rosen E.B., Robert A.J., Nelson J.A., Matros E. & Gelblum D.Y. (2019). Immediate dental implants in fibula free flaps to reconstruct the mandible: A pilot study of the short-term effects on radiotherapy for patients with head and neck cancer. Clin Implant Dent Relat Res, 1-5. doi: 10.1111/cid.12870

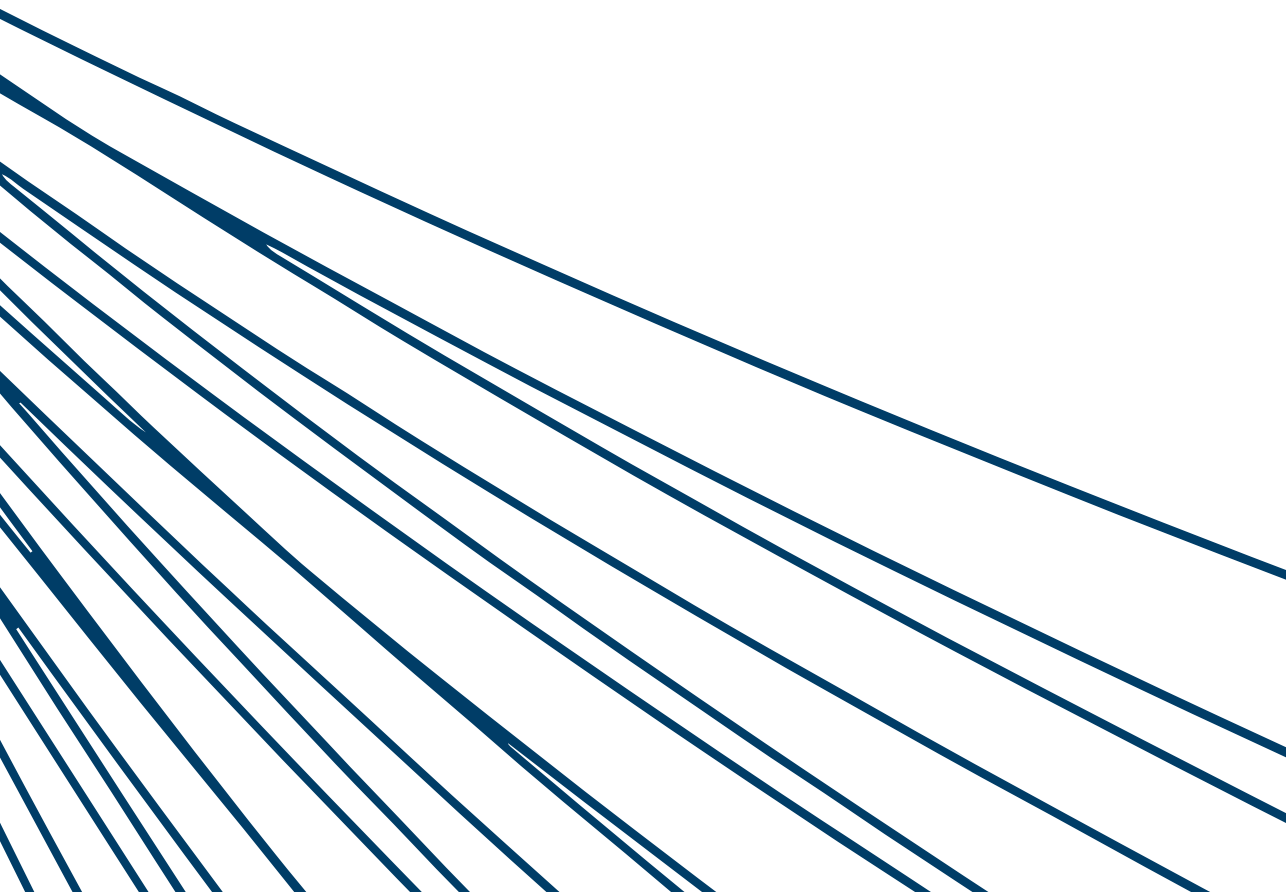
46. Bodard A.G., Salino S., Bemer J., Lucas R. & Breton P. (2011). Dental implant placement after mandibular reconstruction by microvascular free fibula flap: Current knowledge and remaining questions. Oral Oncology, 47, 1099-1104.

47. Patel S.Y., Kim D. & Ghali G.E. (2019). Maxillofacial reconstruction using vascularized fibula free flaps and endosseous implants. Oral Maxillofacial Surg Clin N Am, 31, 259-284. doi: 10.1016/j.coms.2018.12.005

48. Wijbenga J.G., Schepers R.H., Werker P.M.N., Witjes M.J.H. & Dijkstra P.U. (2016). A systematic review of functional outcome and quality of life following reconstruction of maxillofacial defects using vascularized free fibula flaps and dental rehabilitation reveals poor data quality. Journal of Plastic, Reconstructive & Aesthetic Surgery, 69, 1024-1036.

49. Awad M.E., Altman A., Elrefai R., Shipman P., Looney S. & Elsalanty M. (2019). The use of vascularized fibula flap in mandibular reconstruction; A comprehensive systematic review and meta-analysis of the observational studies. J Craniomaxillofac Surg, 47, 629-641.

50. Chang Y.M., Santamaria E., Wei F.C., Chen H.C., Chan C.P., Shen Y.F. & Hou S.P. (1997). Primary insertion of osseointegrated dental implants into fibula osteoseptocutaneous free flap for mandible reconstruction. Plastic and Reconstructive Surgery, 102 (3), 680-688.



CHAPTER 2.3

The use of 3D virtual surgical planning and computer aided design in reconstruction of maxillary surgical defects

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ABSTRACT

Purpose of review

The present review describes the latest development of 3D virtual surgical planning (VSP) and computer aided design (CAD) for reconstruction of maxillary defects with an aim of fully prosthetic rehabilitation. The purpose is to give an overview of different methods that use CAD in maxillary reconstruction in patients with head and neck cancer.

Recent finding

3D VSP enables preoperative planning of resection margins and osteotomies. The current 3D VSP workflow is expanded with multimodal imaging, merging decision supportive information. Development of more personalized implants is possible using CAD, individualized virtual muscle modelling and topology optimization. Meanwhile the translation of the 3D VSP towards surgery is improved by techniques like intraoperative imaging and augmented reality. Recent improvements of preoperative 3D VSP enables surgical reconstruction and/or prosthetic rehabilitation of the surgical defect in one combined procedure.

Summary

With the use of 3D VSP and CAD, ablation surgery, reconstructive surgery, and prosthetic rehabilitation can be planned preoperatively. Many reconstruction possibilities exist and a choice depends on patient characteristics, tumour location and experience of the surgeon. The overall objective in patients with maxillary defects is to follow a prosthetic-driven reconstruction with the aim to restore facial form, oral function, and do so in accordance with the individual needs of the patient.

Keywords

3D VSP, CAD/CAM, maxillary, oral rehabilitation, patient specific, reconstruction

Key points

- Successful dental rehabilitation after maxillary ablative surgery is a complex, multi-disciplinary team effort
- The overall objective in patients with maxillary defects is to follow a dental rehabilitation driven reconstruction with the aim to restore facial form and oral function, in accordance with the individual needs of the patient.
- Integration of multi-modality imaging into a single 3D VSP improves the predictability, accuracy and speed of surgical procedures.
- The design of patient specific implants should be optimised using patient specific finite element analysis and topology optimization.

INTRODUCTION

Surgical treatment of tumours located in the maxilla can be a challenge because of anatomical constraints and impairment of function following treatment. With the introduction of 3D virtual surgical planning (VSP) and guided surgery techniques, complex resections can be planned preoperatively and can be combined with reconstructive solutions. Advantages of using 3D VSP becomes apparent in the operating room as decisions regarding resection margins, location of osteotomies, precise placement of osteosynthesis materials and dental implants are already decided upon before the surgery. Because of the high accuracy of 3D VSP, surgical resections with good tumour margin control can be obtained during ablation[1,-3]. Moreover, it enables the use of bone containing multi-segment composite flaps and/or dental implants in one combined ablative and reconstructive procedure.

Therefore, 3D VSP and guided surgery is the current standard in head and neck oncologic surgery. Another form of computer-assisted surgery (CAS) includes surgical navigation. Surgical navigation is already routinely used during maxillary tumour resections and reduces tumour positive resection margins compared to conventional surgery[4,5]. VSP has been shown to be cost-effective, reproducible, accurate and opens possibilities for creative patient-specific (PS) solutions[6-9].

The aim of this manuscript is to provide an overview of current state of the art routines for using 3D VSP in maxillary ablative surgery, reconstruction and dental rehabilitation. In addition, indications for expected developments in the field of 3D VSP and optimization of patient-specific implants are described.

Resection and reconstruction of maxillary defects

Resection of neoplasms in the maxilla often result in complex defects encompassing soft tissue, bone and dentition. This results in diminished aesthetics and impaired oral functions and thereby lowers the quality of life perceived [1–4]. The aim of reconstruction of maxillary and midfacial defects should be to restore form and function with minimal operative morbidity.

A variety of different single-stage reconstructive techniques in midfacial defects are used. The use of a classification system describing midfacial defects can be helpful in determining reconstructive options [5–10]. The classification of Brown et al. is the most widely recognised classification [5]. Despite these popular classification systems, they describe the defect focusing only on its reconstructive possibilities [11]. Often, defects do not fit in a particular classification, or the classification schemes do not take dental rehabilitation or patient factors in consideration [11].

The reconstructive ladder is a heuristic approach to reconstruction, in which the simplest and safest approach to a problem is often the preferred solution [12]. Taking the reconstructive ladder in consideration is important to manage maxillary and midfacial defects [11]. Small defects can therefore be closed by local flaps such as the buccal fat pad flap or temporalis muscle flap, especially if these are located laterally in the posterior maxilla [6,8,11,13]. If defects limited to the palate are present and retention is possible, obturator prosthesis can be a very good option [11]. These obturators remain a simple, non-surgical and relatively quick approach which offers immediate improvement of oral functions with reasonable outcomes. However, obturator prostheses have several drawbacks regarding oral hygiene, instability, velopharyngeal insufficiency, lack of soft tissue support and they carry a social stigma [13,14]. With larger defects the use of pedicled or free vascularised autologous tissue transfer can offer skin, muscle, fascia and bone and can be used as a foundation for dental implants [7].

Bony reconstruction is not always necessary as retention of a prosthesis can be found on canines and incisors or zygomatic implants can be placed in these defects [7]. The most used autologous reconstruction method of a maxillary defect involving alveolus and maxillary sinus wall, is the radial forearm free flap (RFFF) [5]. The fibular free flap (FFF), Iliac crest or deep circumflex iliac artery (DCIA) and the subscapular system are the most used composite flaps in maxillary reconstruction when bone is required [7,11]. The FFF is the most often used, as it can be reliably harvested and transferred, its bone stock enables reliable placement of implants, has a long vascular pedicle, high success rate, low donor site morbidity and it enables a simultaneous two team approach [7,15]. A DCIA flap offers bigger amounts of muscle and bone that has a contour better suited to reconstruct the most complex defects encompassing loss of all 6 walls of the maxilla [16,17]. Large complex defects that need multiple skin paddles, muscle and bone can be reconstructed by flaps based on the scapular system [18–20].

Dental rehabilitation

Oral functions are not only dependent on reconstruction of the maxillary defect since, after postoperative radiotherapy, stability and retention of a prosthesis are also decreased [15]. Therefore, implants to support prostheses are widely used as part of a standard oral rehabilitation plan [21–24].

Dental rehabilitation is an essential part of the aim of reconstruction and should be planned from the beginning [6,25]. From a prosthodontics perspective CAD assistance benefits the functional outcome. Prosthetic driven reconstruction planning in combination with precise guided placement of dental implants carried out at time of tumour resection ahead of possible radiotherapy is a huge advantage for accelerating the process of oral rehabilitation [26,27].

As an alternative for bone reconstruction with regular dental implants, zygomatic oncology implants can also provide a predictable in-defect support for prosthetic rehabilitation of the maxilla and can be placed at the time of ablative surgery [28–30]. The zygomatic implant perforated flap procedure combines autologous soft tissue reconstruction with zygomatic implant-supported dental rehabilitation [31,32]. However, the limited intraoperative visibility makes accurate placement of the zygoma implants challenging. The use of 3D VSP and guided placement by means of 3D printed drilling and placement guides can possibly improve the success in terms of accuracy. Such 3D VSP workflow is illustrated in Figure 1, where a traditional obturator prosthesis is replaced for zygomatic implants. Sometimes zygoma implants cannot provide satisfactory anchorage due to insufficient bone volume and composite free flaps are not indicated. In those patients, an alternative to achieve oral rehabilitation is to design patient specific subperiosteal implants [33,34]. An example of such 3D VSP workflow including the design of a patient specific implant is seen in Figure 2.

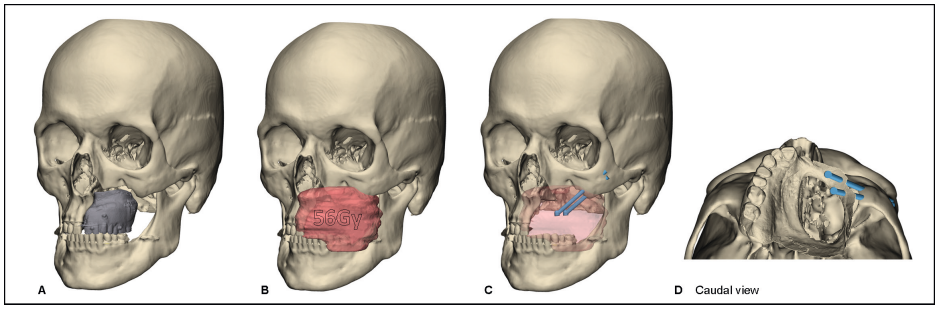


Figure 1. 3D VSP aiming for dental rehabilitation using zygomatic implants. Patient after maxillary resection and radiotherapy rehabilitated with obturator prosthesis resulting in inadequate oral function. With the aim of improving quality of life, zygomatic oncology implants were placed taken into account available bone volume, preferred prosthetic position and previous irradiated volumes**. A.** 3D reconstruction of patient with the primary obturator prosthesis in place **B.** 3D reconstruction of the 56Gy isodosis radiation field. **C.** Planning of the zygomatic implants with respect to the reconstructed radiation field**. D.** 3D reconstruction of intra-oral scan combined with planned implant position to visualise available prosthetic space.

Obturator prostheses maintain their importance in rehabilitation by bridging time to secondary surgical reconstruction of the defect. Preoperative 3D knowledge of resection planes induce new and more efficient workflows in processing surgical obturators. Several case reports describe production of 3D obturator prostheses with the advantage that they can be printed hollow and aligned to the contour of the patients' defect [35–39]. Figure 3 shows an example of a 3D VSP including guided tumour resection and a CAD/CAM manufactured obturator prosthesis.

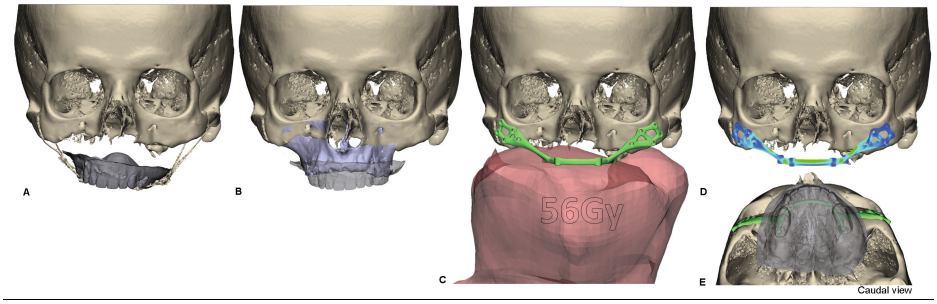


Figure 2. 3D VSP and CAD workflow of a patient specific subperiosteal implant for secondary reconstruction following maxillary resection. Surgical reconstruction with composite flaps or placement of zygomatic oncology implants was not feasible. The aim of the 3D VSP was to obtain an optimal dental rehabilitation using backwards planning, starting with an optimal position of the prosthesis. **A.** Patient after maxillary resection with non-functional obturator prosthesis **(grey),** fixated by zygomatic wires. **B**. 3D VSP of ideal prosthetic position using a 3D reconstruction of the pre-ablative CT scan of the maxilla **(purple). C.** 3D visualisation of sub-periosteal implant (**green)** in relation to 56Gy isodosis radiotherapy field **(red).** The PSI sub-periosteal implant was designed with the position for fixation screws circumventing the irradiated bone. **D.** Implant strength and fatigue resistance was calculated using finite element analysis to withstand reported maximum occlusal loading. **E.** Planned prosthetic outcome **(grey)** and prosthetic driven sub-periosteal implant position **(green).**

Virtual surgical planning and future perspectives

3D VSP and 3D printed cutting guides are used for complex reconstructive surgery including FFF and DCIA transplantations, combined with one stage implant placement for dental rehabilitation. Currently, in most cases 3D VSP and guided surgery is primarily based on computer tomography (CT) data only. 3D VSP enables planning of oncologic resections and reconstructions using computer-aided design and manufacturing (CAD/CAM) of 3D printed anatomical models, surgical guides and patient specific implants [27,33,34,40,41]. Recent improvements in 3D VSP and CAD workflows include the use of multimodal data fusion to increase precision of determining the tumour free resection margin. Data fusion of MRI and CT enables tumour information delineated on the MRI in spatial relation with bone information from CT. The combination of information provided by CT and MRI with regard to localisation, size and shape of the tumour is important for a precise resection [42,43]. An example of such 3D VSP workflow including MRI and CT data fusion is seen in Figure 3. This workflow applied in mandibular tumours provided a tumour free bone resections without per- operative deviation of the 3D VSP [44]. Tumour free resection margins are critical for one stage reconstruction surgery, where the reconstruction is preoperatively planned. An equivalent software pathway can be used for a variety of imaging data, like adding PET data when MRI information is inconclusive about the tumour margin [45–47]. Another recent advancement of data fusion is that of CT and radiotherapy dose. Adding radiation dose as a visual volume in the VSP workflow enables evaluation of prescribed radiation dose on tissue and avoiding areas at risk for osteoradionecrosis in patients which were previously irradiated [48–50]. Both 3D

VSP workflows illustrated in Figures 1 and 2 incorporated data fusion of the radiation dose for implant planning and design, including screw locations.

When a 3D VSP is completed and agreed on by the multidisciplinary surgical team, patient specific 3D cutting and drilling guides and patient specific osteosynthesis are designed and used for translation into the surgical procedure. The design of these patient specific guides is adapted to the contour of the bone to achieve the precise resections and drill holes as intended in the VSP. An alternative method of translating the 3D VSP into the surgical procedure, is intra-operative navigation, especially used in case of maxillary resection [51,52]. Compared to intra-operative navigation, 3D fitted guides lead to the most accurate bone resections [27,53–55]. However, per-operative imaging and navigated surgery enables the surgeon to act on tissue volume changes between preoperative imaging and surgery, in contrary to the 3D fitted premade guides. With the increase of hybrid OR applications (ability of perioperative MRI and CT imaging), one can expect multimodal data fusion real-time in the operating room, updating the preoperatively made 3D VSP with recent per operative imaging data. Intraoperative imaging combined with surgical navigation is reported to be as accurate as the use of 3D printed guides [56].

The main drawback of navigation systems is that the surgeon has to look away from the surgical field in order to receive feedback from the navigation system, this leads to more difficult eye-hand coordination [57]. Augmented reality (AR) could potentially overcome this problem by translating 3D VSP to the actual surgical field with the use of head mounted devices [58]. Preliminary studies report on application of AR for mandibular osteotomies and orthognathic surgery, however the added benefit for maxillary tumour resection and reconstruction has not yet been demonstrated [54,58,59].

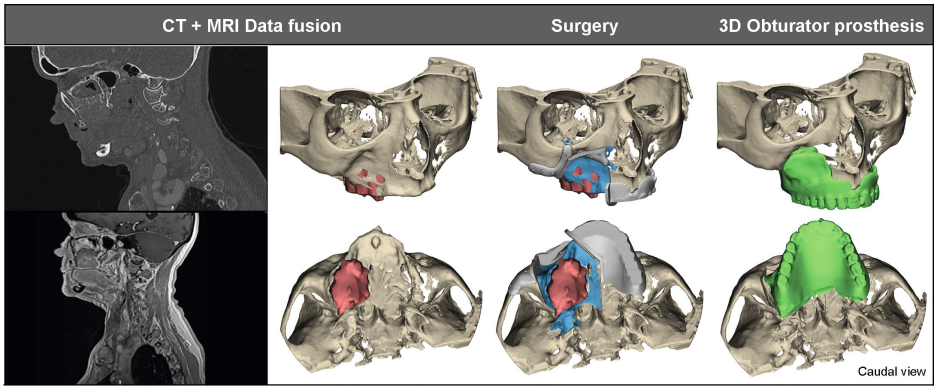


Figure 3. Tumour visualisation based on CT and MRI data fusion. CT images are used for 3D reconstruction of bone tissue, while the MRI enables delineation of the tumour. This enables preoperative planning of the bone resection **(blue)** and thereby guide design **(grey).** Pre-operative CAD/CAM manufactured obturator prosthesis **(green)** designed to obturate the defect following guided resection.

Design and fit of 3D guides and osteosynthesis materials has to be adapted to the patient bony contour to be used in implementing the VSP into the patient. 3D printed patient specific anatomical models have been used for bending of the shelf osteosynthesis materials like titanium meshes and reconstruction plates. While bending a titanium mesh on a PS model can lead to postoperative facial symmetry and successful clinical outcomes in maxillary reconstructions, complications can include exposure of the osteosynthesis material [49,50].

Designing and using patient specific osteosynthesis materials has shown to be a valuable tool in the reconstruction of oncologic defects, enabling planning of adaptation of implant and screw location, based on the thickness of the bone [27,33,34,40,49,60]. Furthermore, possible surgical access can be taken into account. Mostly tailoring of osteosynthesis starts with adapting conventional plate designs and is based on experiences of the involved surgical team and technical physicians. This design process mostly lacks a systematic application of biomechanical analysis on an individual patient basis. It is reported that these osteosynthesis used for mandibular reconstruction can be subject to failure in terms of plate fracture or screw loosening, however comparable complications occur for maxillary reconstructions [61,62]. Although patient specific osteosynthesis have been used regularly, future applications should focus on a more patient tailored approach, using 3D print technology. In this way, nearly every shape of osteosynthesis material can be produced. Therefore an approach of more biomechanically based patient specific designs is the logical next step. Based on individual models including bone morphology, bite forces and anatomy a PSI is designed and manufactured. Pilot-studies have demonstrated validation of virtually modelling the muscles associated with mastication [63]. Those and other models can be used as a foundation for finite element analysis (FEA). Application of finite element models can predict behaviour of osteosynthesis materials with varying inputs of muscle forces, loads, constraints and biomechanical properties of bone. The output of FEA can be used for topology optimisation, whereby the design, structure and layout of patient specific osteosynthesis can be optimized [64]. In addition new materials and surface finishes should be incorporated in the PSI in order to reduce scattering on post-operative imaging and reduce occurrence of infections.

CONCLUSION

Successful rehabilitation after ablative surgery of the maxilla can be achieved through the experience and good collaboration of a multidisciplinary surgical team. The role of a technical physician enabling 3D virtual surgical planning and visualisation of the complex reconstruction of large maxillary defects is of great importance. Preoperative planning enables combined ablation surgery with prosthetic driven reconstruction treatment that benefits the functional outcome. The method of reconstruction is dependent on

many factors like size and location of defect, medical condition, patient factors and previous treatments. In reconstruction of maxillary defects, the use of CAD enables a pre-planned precise, efficient and patient specific treatment with incorporation of dental rehabilitation.

REFERENCES

1. Roumanas ED. Reconstructed mandibular defects: Fibula free flaps and osseointegrated implants. Plastic and Reconstructive Surgery 1997. Doi: 10.1097/00006534-199702000-00008.
2. Schoen PJ., Reintsema H., Raghoebar GM., Vissink A., Roodenburg JLN. The use of implant retained mandibular prostheses in the oral rehabilitation of head and neck cancer patients. A review and rationale for treatment planning. Oral Oncology 2004. Doi: 10.1016/j.oraloncology.2003.08.024.
3. De Graeff A., De Leeuw JRJ., Ros WJG., Hordijk GJ., Blijham GH., Winnubst JAM. Long-term quality of life of patients with head and neck cancer. Laryngoscope 2000. Doi: 10.1097/00005537-200001000-00018.
4. Huryn JM., Zlotolow IM., Piro JD., Lenchewski E. Osseointegrated implants in microvascular fibula free flap reconstructed mandibles. The Journal of Prosthetic Dentistry 1993. Doi: 10.1016/0022-3913(93)90082-Y.
5. Brown JS., Shaw RJ. Reconstruction of the maxilla and midface: Introducing a new classification. The Lancet Oncology 2010. Doi: 10.1016/S1470-2045(10)70113-3.
6. Brown J. Reconstruction of the maxilla and midface. *European Archives of Oto-Rhino-Laryngology* 2012. Doi: 10.1007/s00405-012-1960-4.
7. Lenox ND., Kim DD. Maxillary Reconstruction. Oral and Maxillofacial Surgery Clinics of North America 2013. Doi: 10.1016/j.coms.2013.01.004.
8. Cordeiro PG., Santamaria E. A classification system and algorithm for reconstruction of maxillectomy and midfacial defects. Plastic and Reconstructive Surgery 2000. Doi: 10.1097/00006534-200006000-00004.
9. Okay DJ., Genden E., Buchbinder D., Urken M. Prosthodontic guidelines for surgical reconstruction of the maxilla: A classification system of defects. Journal of Prosthetic Dentistry 2001. Doi: 10.1067/mpr.2001.119524.
10. Yamamoto Y., Kawashima K., Sugihara T., Nohira K., Furuta Y., Fukuda S. Surgical management of maxillectomy defects based on the concept of buttress reconstruction. Head and Neck 2004. Doi: 10.1002/hed.10366.
11. Eskander A., Kang SY., Teknos TN., Old MO. Advances in midface reconstruction: Beyond the reconstructive ladder. Current Opinion in Otolaryngology and Head and Neck Surgery 2017. Doi: 10.1097/MOO.0000000000000396.
12. Ray E. Head and Neck Reconstructive Surgery. Cancer Treatment and Research 2018;174:123–43. Doi: 10.1007/978-3-319-65421-8_8.
13. Dalgorf D., Higgins K. Reconstruction of the midface and maxilla. Current Opinion in Otolaryngology and Head and Neck Surgery 2008. Doi: 10.1097/MOO.0b013e328304b426.
14. Rogers SN., Lowe D., McNally D., Brown JS., Vaughan ED. Health-related quality of life after maxillectomy: A comparison between prosthetic obturation and free flap. Journal of Oral and Maxillofacial Surgery 2003. Doi: 10.1053/joms.2003.50044.
15. Wijbenga JG., Schepers RH., Werker PMN., Witjes MJH., Dijkstra PU. A systematic review of functional outcome and quality of life following reconstruction of maxillofacial defects using vascularized free fibula flaps and dental rehabilitation reveals poor data quality. Journal of Plastic, Reconstructive and Aesthetic Surgery 2016. Doi: 10.1016/j.bjps.2016.05.003.

16. Brown JS. Deep circumflex iliac artery free flap with internal oblique muscle as a new method of immediate reconstruction of maxillectomy defect. Head and Neck 1996. Doi: 10.1002/(sici)1097-0347(199609/10)18:5<412::aid-hed4>3.0.co;2-8.
17. Brown JS., Jones DC., Summerwill A., Rogers SN., Howell RA., Cawood JI., et al. Vascularized iliac crest with internal oblique muscle for immediate reconstruction after maxillectomy. British Journal of Oral and Maxillofacial Surgery 2002. Doi: 10.1054/bjom.2001.0774.
18. Mertens C., Freudlsperger C., Bodem J., Engel M., Hoffmann J., Freier K. Reconstruction of the maxilla following hemimaxillectomy defects with scapular tip grafts and dental implants. Journal of Cranio-Maxillofacial Surgery 2016. Doi: 10.1016/j.jcms.2016.08.010.
19. Miles BA., Gilbert RW. Maxillary reconstruction with the scapular angle osteomyogenous free flap. Archives of Otolaryngology - Head and Neck Surgery 2011. Doi: 10.1001/archoto.2011.187.
20. Granick MS., Ramasastry SS., Newton ED., Solomon MP., Hanna DC., Kaltman S. Reconstruction of complex maxillectomy defects with the scapular-free flap. Head & Neck 1990. Doi: 10.1002/hed.2880120502.
21. Smolka K., Kraehenbuehl M., Eggensperger N., Hallermann W., Thoren H., Iizuka T., et al. Fibula free flap reconstruction of the mandible in cancer patients: Evaluation of a combined surgical and prosthodontic treatment concept. Oral Oncology 2008. Doi: 10.1016/j.oraloncology.2007.07.005.
22. Barber AJ., Butterworth CJ., Rogers SN. Systematic review of primary osseointegrated dental implants in head and neck oncology. British Journal of Oral and Maxillofacial Surgery 2011. Doi: 10.1016/j.bjoms.2009.12.007.
23. Chuka R., Abdullah W., Rieger J., Nayar S., Seikaly H., Osswald M., et al. Implant Utilization and Time to Prosthetic Rehabilitation in Conventional and Advanced Fibular Free Flap Reconstruction of the Maxilla and Mandible. The International Journal of Prosthodontics 2017;**30**(3):289–94. Doi: 10.11607/ijp.5161.
24. Korfage A., Schoen PJ., Raghoebar GM., Roodenburg JLN., Vissink A., Reintsema H. Benefits of dental implants installed during ablative tumour surgery in oral cancer patients: A prospective 5-year clinical trial. Clinical Oral Implants Research 2010. Doi: 10.1111/j.1600-0501.2010.01930.x.
25. Pace-Balzan A., Shaw RJ., Butterworth C. Oral rehabilitation following treatment for oral cancer. Periodontology 2000 2011. Doi: 10.1111/j.1600-0757.2011.00384.x.
26. Chuka R., Abdullah W., Rieger J., Nayar S., Seikaly H., Osswald M., et al. Implant Utilization and Time to Prosthetic Rehabilitation in Conventional and Advanced Fibular Free Flap Reconstruction of the Maxilla and Mandible. The International Journal of Prosthodontics 2017;30(3):289–94. Doi: 10.11607/ijp.5161.
27. Schepers RH., Raghoebar GM., Vissink A., Stenekes MW., Kraeima J., Roodenburg JL., et al. Accuracy of fibula reconstruction using patient-specific CAD/CAM reconstruction plates and dental implants: A new modality for functional reconstruction of mandibular defects. *Journal of Cranio-Maxillofacial Surgery* 2015;43(5):649–57. Doi: 10.1016/j.jcms.2015.03.015.
28. Drobyshev A., Dibirov T., Zhukova N., Yarmolin D., Glushko A., Venter I., et al. Rehabilitation of patients with oncological maxillary defects. *International Journal of Oral and Maxillofacial Surgery* 2017. Doi: 10.1016/j.ijom.2017.02.1016.
29. Butterworth CJ. Primary vs secondary zygomatic implant placement in patients with head and neck cancer—A 10-year prospective study. Head and Neck 2019. Doi: 10.1002/hed.25645.

30. Parel SM., Brånemark PI., Ohrnell LO., Svensson B. Remote implant anchorage for the rehabilitation of maxillary defects. Journal of Prosthetic Dentistry 2001. Doi: 10.1067/mpr.2001.118874.

31. Butterworth CJ., Rogers SN. The zygomatic implant perforated (ZIP) flap: a new technique for combined surgical reconstruction and rapid fixed dental rehabilitation following low-level maxillectomy. International Journal of Implant Dentistry 2017. Doi: 10.1186/s40729-017-0100-8.

32. Araya-Salas C., Brenner C., Bustos F., Valdes F., Pizarro L., Veloso M., et al. Maxillary osteosarcoma and reconstruction with ZIP flap. International Journal of Oral and Maxillofacial Surgery 2019. Doi: 10.1016/j.ijom.2019.03.220.

33. Vosselman N., Merema BJ., Schepman KP., Raghoebar GM. Patient-specific sub-periosteal zygoma implant for prosthetic rehabilitation of large maxillary defects after oncological resection. International Journal of Oral and Maxillofacial Surgery 2019;48(1):115–7. Doi: 10.1016/j.ijom.2018.06.010.

34. Mommaerts MY. Additively manufactured sub-periosteal jaw implants. International Journal of Oral and Maxillofacial Surgery 2017;46(7):938–40. Doi: 10.1016/j.ijom.2017.02.002.

35. Bartellas M., Tibbo J., Angel D., Rideout A., Gillis J. Three-Dimensional Printing: A Novel Approach to the Creation of Obturator Prostheses Following Palatal Resection for Malignant Palate Tumors. Journal of Craniofacial Surgery 2018;29(1):e12–5. Doi: 10.1097/SCS.0000000000003987.

36. Kortes J., Dehnad H., Kotte ANT., Fennis WMM., Rosenberg AJWP. A novel digital workflow to manufacture personalized three-dimensional-printed hollow surgical obturators after maxillectomy. International Journal of Oral and Maxillofacial Surgery 2018;47(9):1214–8. Doi: 10.1016/j.ijom.2018.03.015.

37. Murat S., Gürbüz A., Kamburoğlu K. Fabrication of obturator prosthesis by fusing CBCT and digital impression data. International Journal of Computerized Dentistry 2018;21(4):335—344.

38. Rodney J., Chicchon I. Digital Design and Fabrication of Surgical Obturators Based Only on Preoperative Computed Tomography Data. The International Journal of Prosthodontics 2017;30(2):111–2. Doi: 10.11607/ijp.5066.

39. Tasopoulos T., Chatziemmanouil D., Karaiskou G., Kouveliotis G., Wang J., Zoidis P. Fabrication of a 3D-printed interim obturator prosthesis: A contemporary approach. Journal of Prosthetic Dentistry 2019;121(6):960–3. Doi: 10.1016/j.prosdent.2018.10.004.

40. Rohner D., Guijarro-Martínez R., Bucher P., Hammer B. Importance of patient-specific intraoperative guides in complex maxillofacial reconstruction. Journal of Cranio-Maxillofacial Surgery 2013. Doi: 10.1016/j.jcms.2012.10.021.

41. Witjes MJH., Schepers RH., Kraeima J. Impact of 3D virtual planning on reconstruction of mandibular and maxillary surgical defects in head and neck oncology. Current Opinion in Otolaryngology and Head and Neck Surgery 2018;26(2):108–14. Doi: 10.1097/MOO.0000000000000437.

42. Dai J., Wang X., Dong Y., Yu H., Yang D., Shen G. Two- and three-dimensional models for the visualization of jaw tumors based on CT-MRI image fusion. Journal of Craniofacial Surgery 2012. Doi: 10.1097/SCS.0b013e31824cd433.

43. Blatt S., Ziebart T., Krüger M., Pabst AM. Diagnosing oral squamous cell carcinoma: How much imaging do we really need? A review of the current literature. Journal of Cranio-Maxillofacial Surgery 2016. Doi: 10.1016/j.jcms.2016.02.003.

44. Kraeima J., Dorgelo B., Gulbitti HA., Steenbakkers RJHM., Schepman KP., Roodenburg JLN., et al. Multi-modality 3D mandibular resection planning in head and neck cancer using CT and MRI data fusion: A clinical series. Oral Oncology 2018;81:22–8. Doi: 10.1016/j.oraloncology.2018.03.013.

45. Sarrión Pérez MG., Bagán J V., Jiménez Y., Margaix M., Marzal C. Utility of imaging techniques in the diagnosis of oral cancer. Journal of Cranio-Maxillofacial Surgery 2015;43(9):1880–94. Doi: 10.1016/j.jcms.2015.07.037.

46. Van Cann EM., Rijpkema M., Heerschap A., van der Bilt A., Koole R., Stoelinga PJW. Quantitative dynamic contrast-enhanced MRI for the assessment of mandibular invasion by squamous cell carcinoma. Oral Oncology 2008. Doi: 10.1016/j.oraloncology.2008.02.009.

47. Kolk A., Schuster T., Chlebowski A., Lange P., Scheidhauer K., Kesting M., et al. Combined SPECT/CT improves detection of initial bone invasion and determination of resection margins in squamous cell carcinoma of the head and neck compared to conventional imaging modalities. European Journal of Nuclear Medicine and Molecular Imaging 2014;41(7):1363–74. Doi: 10.1007/s00259-014-2726-6.

48. Kraeima J., Steenbakkers RJHM., Spijkervet FKL., Roodenburg JLN., Witjes MJH. Secondary surgical management of osteoradionecrosis using three-dimensional isodose curve visualization: a report of three cases. International Journal of Oral and Maxillofacial Surgery 2018;47(2):214–9. Doi: 10.1016/j.ijom.2017.08.002.

49. Kraeima J., Glas HH., Witjes MJH., Schepman KP. Patient-specific pre-contouring of osteosynthesis plates for mandibular reconstruction: Using a three-dimensional key printed solution. Journal of Cranio-Maxillofacial Surgery 2018;46(6):1037–40. Doi: 10.1016/j.jcms.2018.03.022.

50. Liu B yao., Cao G., Dong Z., Chen W., Xu J ke., Guo T. The application of 3D-printed titanium mesh in maxillary tumor patients undergoing total maxillectomy. Journal of Materials Science: Materials in Medicine 2019;30(11). Doi: 10.1007/s10856-019-6326-7.

51. Yu H., Wang X., Zhang S., Zhang L., Xin P., Shen SG. Navigation-guided en bloc resection and defect reconstruction of craniomaxillary bony tumours. International Journal of Oral and Maxillofacial Surgery 2013. Doi: 10.1016/j.ijom.2013.05.011.

52. Yu Y., Zhang WB., Liu XJ., Guo C Bin., Yu GY., Peng X. Three-Dimensional Accuracy of Virtual Planning and Surgical Navigation for Mandibular Reconstruction With Free Fibula Flap. Journal of Oral and Maxillofacial Surgery 2016. Doi: 10.1016/j.joms.2016.02.020.

53. Pietruski P., Majak M.,¯wiatek-Najwer E., Popek M., Jaworowski J., Zuk M., et al. Image-guided bone resection as a prospective alternative to cutting templates - A preliminary study. Journal of Cranio-Maxillofacial Surgery 2015;43(7):1021–7. Doi: 10.1016/j.jcms.2015.06.012.

54. Pietruski P., Majak M., Świątek-Najwer E., Żuk M., Popek M., Mazurek M., et al. Supporting mandibular resection with intraoperative navigation utilizing augmented reality technology – A proof of concept study. Journal of Cranio-Maxillofacial Surgery 2019;47(6):854–9. Doi: 10.1016/j.jcms.2019.03.004.

55. Bernstein JM., Daly MJ., Chan H., Qiu J., Goldstein D., Muhanna N., et al. Accuracy and reproducibility of virtual cutting guides and 3D-navigation for osteotomies of the mandible and maxilla. *PLoS ONE* 2017;12(3):1–10. Doi: 10.1371/journal.pone.0173111.

56. Hasan W., Daly MJ., Chan HHL., Qiu J., Irish JC. Intraoperative cone-beam CT-guided osteotomy navigation in mandible and maxilla surgery. Laryngoscope 2019:1–7. Doi: 10.1002/lary.28082.

57. Berger M., Nova I., Kallus S., Ristow O., Freudlsperger C., Eisenmann U., et al. Can electromagnetic-navigated maxillary positioning replace occlusional splints in orthognathic surgery? A clinical pilot study. Journal of Cranio-Maxillofacial Surgery 2017;45(10):1593–9. Doi: 10.1016/j.jcms.2017.08.005.

58. Bosc R., Fitoussi A., Hersant B., Dao TH., Meningaud JP. Intraoperative augmented reality with heads-up displays in maxillofacial surgery: a systematic review of the literature and a classification of relevant technologies. International Journal of Oral and Maxillofacial Surgery 2019;48(1):132–9. Doi: 10.1016/j.ijom.2018.09.010.

59. Ahn J., Choi H., Hong J., Hong J. Tracking Accuracy of a Stereo Camera-Based Augmented Reality Navigation System for Orthognathic Surgery. Journal of Oral and Maxillofacial Surgery 2019;**77**(5):1070.e1-1070.e11. Doi: 10.1016/j.joms.2018.12.032.

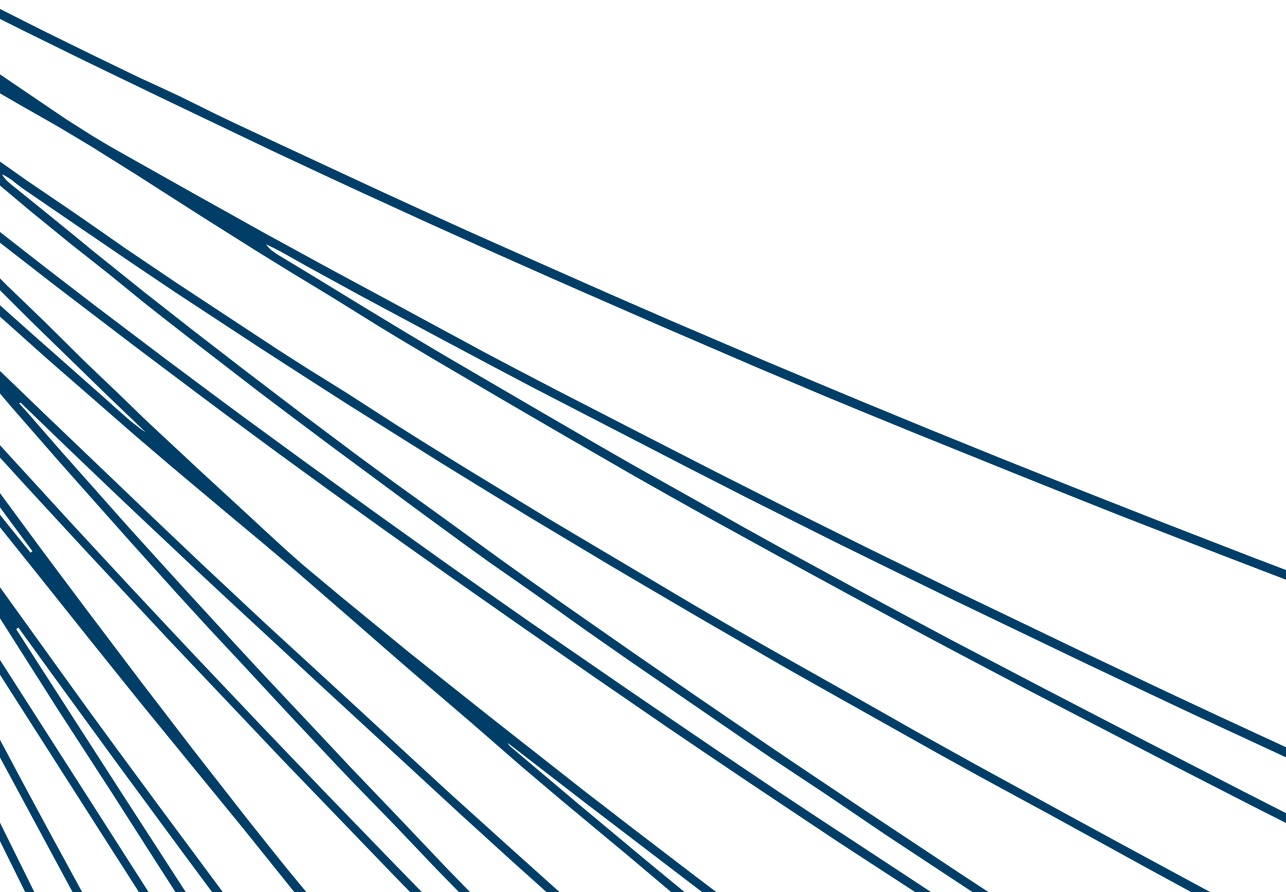
60. Wilde F., Hanken H., Probst F., Schramm A., Heiland M., Cornelius CP. Multicenter study on the use of patient-specific CAD/CAM reconstruction plates for mandibular reconstruction. International Journal of Computer Assisted Radiology and Surgery 2015;10(12):2035–51. Doi: 10.1007/s11548-015-1193-2.

61. Kimura A., Nagasao T., Kaneko T., Tamaki T., Miyamoto J., Nakajima T. Adaquate fixation of plates for stability during mandibular reconstruction. Journal of Cranio-Maxillofacial Surgery 2006. Doi: 10.1016/j.jcms.2006.01.003.

62. Van Gemert JTM., Van Es RJJ., Rosenberg AJWP., Van Der Bilt A., Koole R., Van Cann EM. Free vascularized flaps for reconstruction of the mandible: Complications, success, and dental rehabilitation. Journal of Oral and Maxillofacial Surgery 2012. Doi: 10.1016/j.joms.2011.08.024.

63. Weickenmeier J., Jabareen M., Le Révérend BJD., Ramaioli M., Mazza E. Experimental and Numerical Characterization of the Mechanical Masseter Muscle Response during Biting. Journal of Biomechanical Engineering 2017;139(12):1–10. Doi: 10.1115/1.4037592.

64. Sutradhar A., Park J., Carrau D., Nguyen TH., Miller MJ., Paulino GH. Designing patient-specific 3D printed craniofacial implants using a novel topology optimization method. Medical and Biological Engineering and Computing 2016:1123–35. Doi: 10.1007/s11517-015-1418-0.



CHAPTER 3

Immediate implant-retained prosthetic obturation after maxillectomy based on zygomatic implant placement by 3D guided surgery: a cadaver study

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ABSTRACT

Background

The aim of this study was to introduce a complete 3D workflow for immediate implant retained prosthetic rehabilitation following maxillectomy in cancer surgery. The workflow consists of a 3D virtual surgical planning for tumour resection, zygomatic implant placement, and for an implant-retained prosthetic-obturator to fit the planned outcome situation for immediate loading.

Materials and methods

In this study, 3D virtual surgical planning and resection of the maxilla, followed by guided placement of 10 zygomatic implants, using custom cutting and drill/placement-guides, was performed on 5 fresh frozen human cadavers. A preoperatively digitally designed and printed obturator prosthesis was placed and connected to the zygomatic implants. The accuracy of the implant positioning was obtained using 3D deviation analysis by merging the pre- and post-operative CT scan datasets.

Results

The preoperatively designed and manufactured obturator prostheses matched accurately the per-operative implant positions. All five obturators could be placed and fixated for immediate loading. The mean prosthetic point deviation on the cadavers was 1.03 ± 0.85 mm; the mean entry point deviation was 1.20 ± 0.62 mm; and the 3D angle deviation was 2.97 ± 1.44°.

Conclusions

It is possible to 3D plan and accurately execute the ablative surgery, placement of zygomatic implants, and immediate placement of an implant-retained obturator prosthesis with 3D virtual surgical planning. The next step is to apply the workflow in the operating room in patients planned for maxillectomy.

Keywords

Maxillectomy, 3D VSP, Guided surgery, Zygomatic implants, Prosthetic rehabilitation

INTRODUCTION

Surgical management and oral rehabilitation of patients diagnosed with a maxillary tumour is challenging. The size and extent of the maxillary defect, patient factors, and comorbidities are decisive factors for the choice of surgical, prosthodontic, or combined rehabilitation after a maxillectomy[1,2]. Different treatment modalities have been described in the literature. Primary closure, prosthodontic rehabilitation by an obturator prothesis, or surgical rehabilitation by tissue grafting the maxillary defect, can be considered in order to obtain the best functional outcome for the patient[3].

While the functional results of prosthodontic and surgical rehabilitation of small- to medium-sized maxillary defects are somewhat comparable, reconstruction with free flaps seem to provide better speech and swallowing results for extensive or anterior located defects than conventional prosthetic obturation[4]. Supporting the obturator prostheses with implants improves the results of oral function rehabilitation significantly, as well as being a viable technique to improve the functionality of prosthetic rehabilitation in patients who have undergone a maxillectomy[5]. If conventional (obturator) prostheses are expected to be unsuccessful due to, e.g., lack of retention or load bearing problems of the (irradiated) soft tissues, implant placement to support the prosthesis should be pursued.

Unfortunately, implant survival in irradiated maxillary residual native bone seems less predictable in comparison to placement in the mandible[6] (maxilla or mandible, 59% and 85%, respectively; $p = 0.001$). Remote anchorage in zygomatic bone appears to result in higher survival rates. The anchorage in higher level zygomatic bone, subject to lower or no radiation doses, seems favourable when the maxilla is exposed to post-operative radiotherapy[7,8]. An advantage of the use of zygomatic implants after a maxillectomy is the possibility to obtain immediate prosthetic support. Many studies have reported that immediate prosthodontic rehabilitation after ablative surgery is of benefit for the patient[7-9]. Immediate loading of zygomatic implants is achievable due to a good primary stability in the bicortical plate of the zygoma complex[10,11]. However, accurate free-hand placement of zygomatic implants, taking the preferred prosthodontic positioning into account, is considered difficult. In the absence of guiding anatomic references, it is challenging to place two zygomatic implants at the defect side because of the long drill path.

With the availability of three-dimensional (3D) techniques, head and neck surgery-guided resections and implant placements, based on a preoperative virtual surgical plan (VSP), is becoming a standard of care[12]. 3D VSP enables a combination of ablation and reconstruction due to the knowledge of the pre-operative size of the defect. This permits 3D planned reconstructions with bone-containing free flaps and ideal prosthetic-driven placement of implants in one surgical procedure[12]. For ablative

surgery combined with zygomatic implant placement and prosthetic rehabilitation, 3D virtual planning and computer-aided design have not yet been fully explored.

Although the production of 3D designed implant drill guides is now readily available, the shape and format of zygomatic implants demand a new guide design. The need for a prosthetic angulated implant head to obtain prosthetic support and an ideal screw emergence position on the palatal/occlusal surfaces, together with the implant length, as well as the need for multiple implants and, in oncological cases, the lack of supportive structures, make designing a guide challenging. To the best of our knowledge, a full workflow including tumour surgery, placing of zygomatic implants with 3D printed guides is currently not available. There have been no reports of the design, production, and application of personalized combined bone-supported drill and placement guides for zygomatic implants in order to transfer the virtual planning accurately.

The aim of this study was to develop a workflow that allows one procedure for tumour resection and rehabilitation by immediate placement of zygomatic implants in combination with an implant-retained surgical obturator, as a new treatment modality, using virtual surgical planning. This should lead to optimal placement for immediate loading of the obturator prosthesis as an end result. It is hypothesized that after maxillectomy, the introduction of custom drilling and placement guides for zygomatic implants provides accurate translation of a virtual planning allowing a one procedure workflow for immediate implant-retained prosthetic rehabilitation with a pre-planned obturator prosthesis.

MATERIALS AND METHODS

Cone beam CT-datasets of the skulls of five fresh-frozen edentulous cadavers were obtained (Planmeca, ProMax 3D Max, Stockholm, Finland; 576 slices, voxel size 0.3 mm, FOV: 11 × 16 cm). The settings were in accordance with the clinical settings used for implant planning. A 3D model of the zygomatic bone and maxillae was created using ProPlan CMF 3.0 (Materialise, Leuven, Belgium) software.

Virtual surgical planning

To mimic the clinical problem of a maxillary defect, typical examples of maxillary tumour resection surgeries were planned virtually (Figure 1a, b). 3D VSPs are created that included partial resection of the maxilla, leaving a maxillary defect, based around an assumed tumour volume that would be suitable for obturator prostheses supported by zygoma implants. The defects created in this experiment were classified as low-level Brown Class 2b maxillectomies[13].

Based on the 3D VSP, surgical cutting guides were designed and printed to transfer the resection plan to the cadavers. Next, an obturator prosthesis was designed in the software matching the virtually created defect. Pre-existent dentures were not available for any of the cadavers. The maxillary soft tissues were segmented in order to design digital maxillary dentures as base templates for the final obturator prostheses. Implementing the digital obturator prostheses completed the VSP and enabled the digital planning of the prosthetic implant platform positions.

The position of the zygomatic implants was planned backward from the position of the prostheses. The zygomatic implant heads, to support and fixate the prostheses to the zygomatic implants, were placed in the most ideal prosthodontic positions, slightly palatal from the occlusional plane (Figure 1c, d). In a vertical dimension, enough space for a future bar superstructure and acrylic was taken into account (Figure 1e). Horizontally, the spacing between the prosthetic implant platforms was carefully chosen in order to fit a clip retention system and to enhance any necessary cleaning of the implants (Figure 1f). The positioning of the zygomatic implant was planned with the tip of the implant placed in the lateral cortical bone of the zygomatic complex. The assumption was that placing the apical part of the implant in the cortical bone provides optimal primary stability and will cover the bone on the lateral side of the implant. The preferred apical and abutment positions of the zygomatic implants, implant lengths, and obturator prosthesis were designed virtually. Subsequently, patient specific implant drill and placement guides were designed based on the final virtual set-ups (3Matic Medical, Materialise, Leuven, Belgium) (Figure 1g, h). The drilling/placement guides were developed to fit the following bone structures: alveolar ridge, nasal floor, and zygomatic arch. The guides were printed from polyamide, produced according to the ISO 13485 standards for medical devices, at Oceanz (Ede, the Netherlands). The study ultimately resulted in an advanced implant guide design. The addition of centred channels in the drill-guide enables angled cuts and the length of the channels form an integral depth stop for the drill. The insertion of stainless steel (316 L) milled drill sleeves in the channels should minimize deviation of the drill trajectories. The maxillary bone-supported part included an extension to the nasal aperture to verify good positioning of the guide[14] and was connected with crosslink arms to the zygomatic bone-supported part. In addition, the guide was supplied with holes for temporary fixation with mini screws.

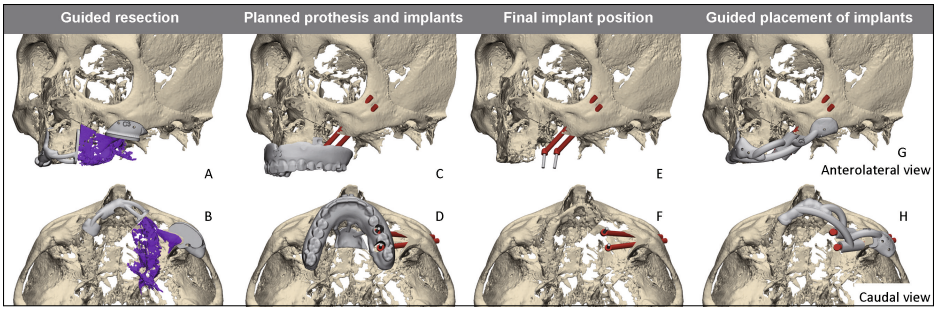


Figure 1. Overview of 3D VSP workflow, including the anterolateral view (upper row) and the matching caudal view (lower row). The 3D VSP starts with planning of the maxillectomy including the design of the cutting guide, with aim is to remove the purple part representing tumour removal (**a, b**). Hereafter the obturator prosthesis position is planned in the defect with the pre-planned screw access holes (**c, d**). The positions of the zygomatic implants are planned backward from this optimal position of the obturator prosthesis (**e, f**). The final step includes the design of the drilling and placement guide of the zygomatic implants (**g, h**)

Surgical procedure

The cadaver surgery was split into two series to evaluate the findings and, if necessary, to adjust the guides and/ or obturator prosthesis before the second test. The surgery was performed by OMF surgeons involved in the planning process, and the supportive visual documentation of the planned guide position was always present in the operating room. Two cadaver heads were thawed before surgery for the first session, and the other three were thawed later for the next session.

To create the Class IIb maxillary defects, the cutting guides were placed on the denuded bone of the maxilla and the zygoma (Figure 2a). The stability and fit of the bone-supported cutting guide was verified. The left-sided maxillectomies were guided by the surgical templates. The resected specimen, mimicking a tumour resection, was removed, resulting in a Class IIb defect. The cutting guides were removed and subsequently the implant drilling guide was fitted and placed.

The precise alignment to the underlying bone structures was verified. The drill-guide was fixed to the bone on two anatomical locations (zygoma and premaxilla) using 2.0 mm cortical locking screws (KLS Martin, Tuttlingen, Germany) (Figures 2c and 3a). After drilling, the implant beds through the guide, according to the drill sequence for oncological zygomatic implants (Southern implants, South Africa), the metal sleeves were removed (Figure 3b). The guide was designed to direct the angle and depth of the implant placement (Figure 3c). The VSP planned implant lengths were placed and the final prosthetic platform position was checked by the maxillofacial prosthodontist and the guide was removed (Figs. 2b and 3d). The obturator prosthesis was then fitted, which provided the surgical team with a visual check as to whether the emergence of

the zygomatic prosthetic platforms was favourable or not, in relation to the pre-planned slots in the obturator prosthesis. The surgical procedure was finalized by fixating the obturator prosthesis. Nonengaging prosthetic cylinders (Southern implants, South Africa) were fixed to the obturator prosthesis with light cured resin to fix the prosthesis firmly on the zygomatic implant abutments (Figure 2d). The obturator prosthesis was checked for balance support on the contralateral side of the residual maxilla. After the surgical procedure, the obturator prostheses were removed and the heads underwent a post-operative cone beam CT scan to analyse implant accuracy.

In preparation for the second cadaver operation session, two alterations were made to the working method. The first alteration was the use of more rigid and solid crosslink arms on the drilling guide, to minimize guide movement due to vibrations during drilling. Secondly, longer mini screws were used to fixate the guides to the bone. The longer 8 mm screws were better for retention in the slightly porous cadaver bone.

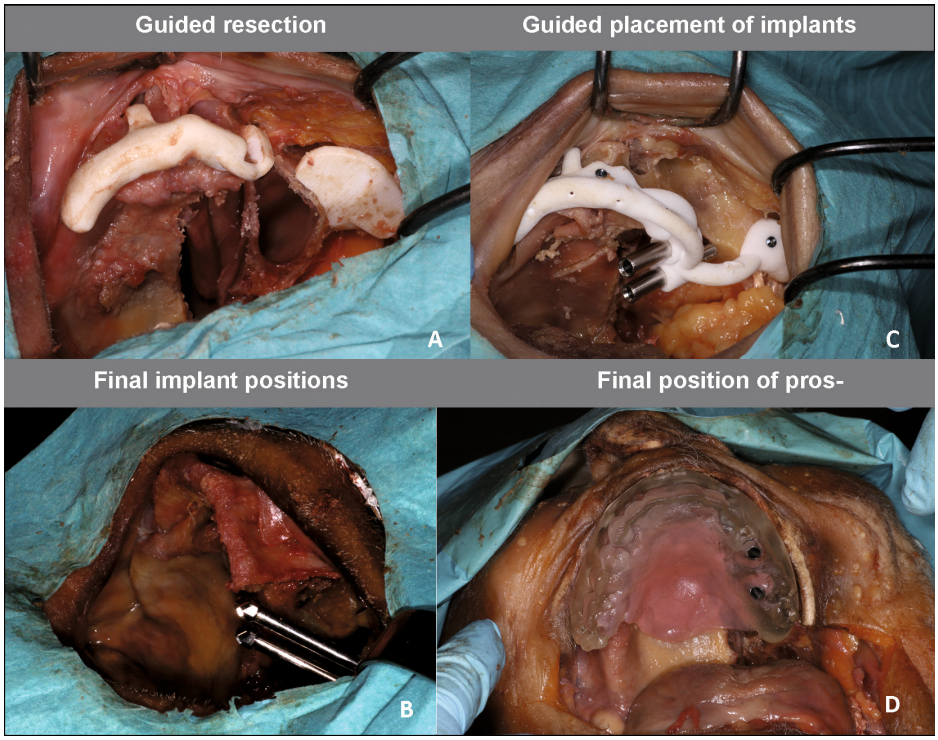


Figure 2. Overview of the surgical procedure. The working method starts with left-sided maxillectomy guided by the surgical template (**a**). Next, the drill-guide was fixed to the bone on two anatomical locations (zygoma and premaxilla) using 2.0 mm cortical locking screws and two zygomatic implants were guided placed in the planned positions (**b**). Finally, prosthetic cylinders were fixated to the obturator prosthesis with light cured resin to fixate the prosthesis firmly on the zygomatic implant abutments (**d**)

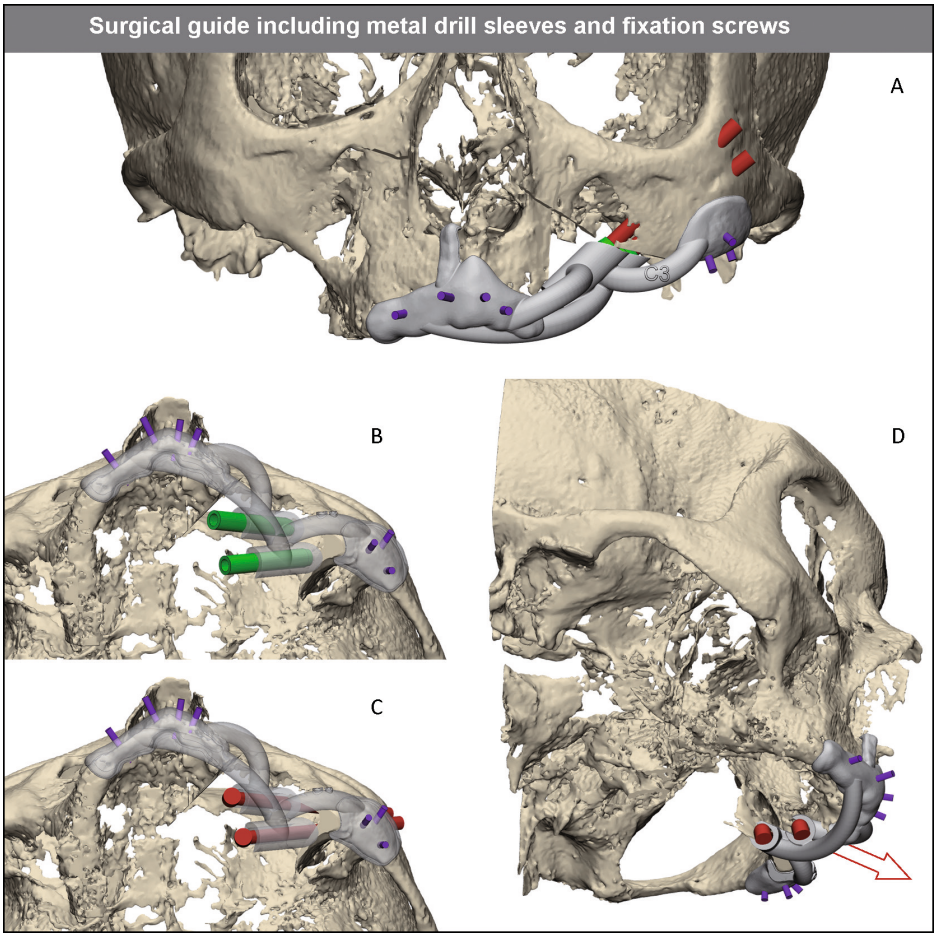


Figure 3. Detailed view of the guide design. In grey the body of the 3D printed polyamide guide **(A)**. In red the planned zygomatic implants. In green the metal inserts used during drilling **(B)**. The metal insert is pushed in the guide by the surgeon during surgery. After drilling the trajectory, the metal insert is removed to accommodate the thicker diameter of the implant. The direction as well as the depth of the implant is set by the design and physical dimensions of the guide **(C)**. After insertion of the implants, the guide is removed by first removing the mini screws (purple) and then removing the guide in the opposite direction of the slots in the implant guide (red arrow) **(D)**.

Outcome measures

The primary outcome of this study was the fit of the prosthetic cylinders connected to the placed zygomatic implants in the preoperative positioned slots of the obturator prostheses. It was noted if the obturator prostheses needed adjusting to fit the cylinders. Both surgical and prosthetic steps were based on one virtual surgical plan and had to tally with the final positions of the prosthetic implant platform above the designed screw access holes in the dental arch of the obturator prosthesis. In all five

cadavers, the support for the obturator prostheses had to be on the remaining maxilla and should match the surgical resection. A placement accuracy of within 3 mm of the prosthetic cylinders in the slots were considered to be successful for a prosthesis, resulting in a passive fit.

A secondary outcome measure for 3D planned series was the zygomatic implant placement accuracy. The post-operative CBCT-data were obtained in a similar fashion as for the pre-operative CBCT. The post-operative maxillae were segmented and, the implant positions were matched with the 3D VSP. The post-operative implant positions are determined by two observers. The most distal part of the long axis of the implant was used as the abutment position (Figure 4a), so that the results were not dependent on a rotation along the long axis. The entry and exit positions in the zygomatic bone were defined by the intersection of this long axis with the virtual maxilla.

Two coordinate systems were defined:

1. The Implant's Coordinate System (ICoS); the z-axis runs along the long axis of each planned implant.
2. The Occlusion Coordinate System (OCoS); congruent with the axial, saggital, and coronal planes, where the axial plane is defined by the occlusion plane of the virtual obturator prostheses.

The planes perpendicular to the z-axis, and running through the planning's abutment point, defined the entry and exit points for the ICoS measurements. The intersections of the implant long-axes with these planes were defined as the corresponding points of the outcome. Then, the distance between the abutment, the entry and exit points, and their corresponding points were defined. Also, the 3D angular deviations between the planning's and the outcome's long axes were determined (Figure 4a– c). Unpaired t-tests were conducted as well as the intraclass correlation (ICC) of the implant reconstruction between the two observers.

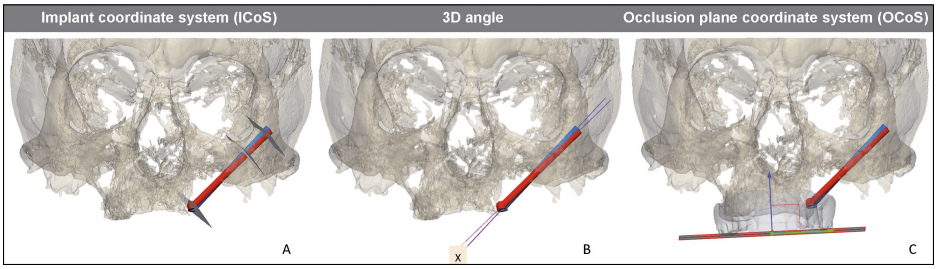


Figure 4. Overview of the several types of measurements and reference planes or coordinate systems for assessing the accuracy of zygomatic implant placement derived from post-op CBCT. In red the planned zygomatic implant position, in blue the postoperative zygomatic implant position. **Left:** the implant coordinate system (ICoS) including the three reproducible reference planes in which the accuracy is measured; the centre of the zygomatic implant head, bone entry point of the implant and bone exit point of the implant. Middle: 3D angular deviation between 3D planned position and postoperative implant position. **Right:** Occlusion plane coordinate system (OCoS). A plane parallel to the prosthetic occlusion plane is defined, perpendicular to this plane is the blue arrow. This arrow indicates the direction in which the abutment height accuracy is calculated.

RESULTS

A total of 10 zygomatic implants were placed in 5 cadaver heads. Some minor alterations were made to the guides between the first and second session. Rigidity was improved by increasing the diameter of the crosslink arms and a window was added to the guide to give the surgeon a direct view of the entry point of the zygoma bone. This enabled minimal movement of the guides due to vibration during drilling. Also, longer cortical osteosynthesis screws were used in the second series for guide fixation to the bone. The longer 8 mm screws allowed better retention in the slightly porous bone. Other than this, the planning and guide design was not essentially changed.

Outcome measure 1: position of the prosthetic implant platform in relation to the obturator screw access hole

Non-engaging prosthetic cylinders were screwed in place and the alignment with the screw access holes was checked. All five obturator prostheses could be placed with high accuracy. The outcome in the horizontal as well as in the vertical dimension was within the 3 mm leeway space for the prostheses. The fit of the pre-planned obturator prosthesis was adequate and well balanced on the remaining maxillary structures in all cases. The prosthetic cylinders were integrated into the obturator prostheses successfully in all cases, without needing any further prosthetic adjustments.

Outcome measure 2: implant placement accuracy

With the aid of the VSP, the drill and placement guides, a total of 10 zygomatic implants were placed. The implant lengths varied between 45 mm and 55 mm and where placed with a mean entry point deviation of 1.20 ± 0.61 mm and a 3D angle deviation of

2.97 ± 1.43° (range 1.0–5.5°). The 3D accuracy of the abutment positions was 1.19 ± 1.31 mm. The accuracy of the abutment position in the occlusional plane was 1.77 ± 1.31 mm, with a height accuracy of 1.03 ± 0.85 mm. The complete accuracy results can be seen in Tables 1 and 2. The intraclass correlations (ICC) between the first and second observer for the positions of the abutment, entry-point, exit-point, and 3D angle were 0.91 mm, 1.00 mm, 0.97 mm, and 0.98°, respectively.

No statistical significant differences were found between the mean values of the ventral and dorsal implants ($P > 0.05$). No statistical differences were found between implants placed in the first session and in the second session.

Table 1. Accuracy data. Result of the post-op analysis of the implant coordinate system (ICoS) measurements.

ICoS measurements	Mean (+/- SD)	Min	Max
Abutment (mm)	1.19 (+/-0.63)	0.1	2.1
Entry-point (mm)	1.20 (+/-0.61)	0.4	2.1
Exit-point (mm)	2.12 (+/-1.24)	0.7	4.1

Table 2. Accuracy data. Result of the post-op analysis. Descriptive statistics of the occlusion coordinate system (OCoS) measurements.

OCoS deviations	Mean (+/- SD)	Min	Max
Abutment in occlusal plane (mm)	1.77 (+/-1.31)	0.8	5.3
Abutment height from occlusal plane (mm)	1.03(+/-0.85)	0.1	3.2
Axial angle (°)	2.07 (+/-2.63)	0.8	5.2
Coronal angle (°)	0.99 (+/-2.32)	0.7	4.2
Sagittal angle (°)	1.48 (+/-3.59)	0.9	7.5
3D angle (°)	2.97 (+/-1.43)	1.0	5.5

DISCUSSION

This study shows that it is possible to accurately apply 3D virtual planning to guided surgery and implant-retained maxillary prosthetic rehabilitation in one procedure. The described treatment protocol merges 3D virtual surgical planning and 3D virtual prosthetic planning into a single overall treatment modality. Full 3D prosthetic planning offers insight into a maxillary defect size, ahead of ablative surgery, and enables highly accurate prosthetic-driven implant planning as well. Primary implant placement at the time of ablative surgery has been shown to be an effective means of accelerating rehabilitation, along with early loading protocols[5,7,15]. Placement of implants in one procedure with ablative surgery is an advantage, especially when the

oncology treatment requires post-operative radiotherapy for disease control because it avoids the issue of secondary surgery in irradiated tissues[5,7,10,16]. The use of virtual planning techniques to enable accurate guided placement of endosseous implants is now a common procedure, and 3D-assisted planning to determine the ideal zygomatic implant position is used regularly. Some case reports mention surgical navigation as a viable technique to transfer planned implant positions[11,17,18]. However, zygomatic implant placement is challenging because of the long drill path and complex anatomic components. The main drawback of current visualization techniques is the difficulty of maintaining the drilling handpiece steady in the right direction, and transferring the surgical view from the navigation display to the operative site[17,18]. A more reliable transferring method for planned zygomatic implant positions seems to be 3D printed drilling/placement templates. This study demonstrates that it is possible to design one zygomatic drilling template to provide an accurate means of translating the virtual 3D plan. It has been reported that immediate loading of zygomatic implants is a viable treatment option. Boyes-Varley et al.[10] described a workflow where the prosthesis was placed immediately after implant placement in close contact with the implants, but not screw-fixed on the prosthetic implant heads. The prosthesis was resting on top of the zygomatic implants and the obturator prosthesis was fixated to the palatal bone with cortical-osteosynthesis screws. In this study, the obturator prosthesis could be fixated rigidly to the implants without the need for any other fixation, due to the accurate 3D planning of the screw holes in the obturator.

The use of an implant-retained surgical obturator may have a positive effect on the primary stability of the zygomatic implants during bone healing. The obturator prostheses used in this study functioned as an external rigid fixation device that splints the implants together. Primary implant stability is provided just with the zygomatic anchorage, while the coronal fixation is provided by the implant fixated obturator prosthesis. Although the obtained stable prosthetic situation is believed to be effective for some months, eventually it is recommended to pursue cross arch splinting of the zygomatic implants in final prosthetics to contribute to implant survival.

It is reasonable to assume that knowledge of the planned resection automatically provides 3D visualization of the necessary obturator outline to restore oral function. In this study, a treatment protocol is described for immediate prosthetic rehabilitation with immediate loading of the zygomatic implants. Restoring oral function immediately after ablative surgery, in one procedure with implant placement, obviates the need for fitting, placing, and adapting the prostheses. After maxillectomy, the frequent necessity of adjuvant radiotherapy limits the possibility of achieving sufficient retention for a conventional obturator prosthesis. An implant-retained obturator prosthesis allows for repeated removal to check the oncological defect visually, or in the event of complications. The addition of subsequently placing a fixed-removable obturator prosthesis during surgery is a major step to shortening the time of prosthetic delivery

and implant utilization. It can be anticipated that the number of prosthetic interventions postoperatively will be less compared to conventional prosthetic planning in which retention is more difficult to obtain. We assume that such patients can recover earlier and better before the often necessary radiotherapy starts and the hospital visits for prosthetic aftercare will be minimized in early postoperative phase.

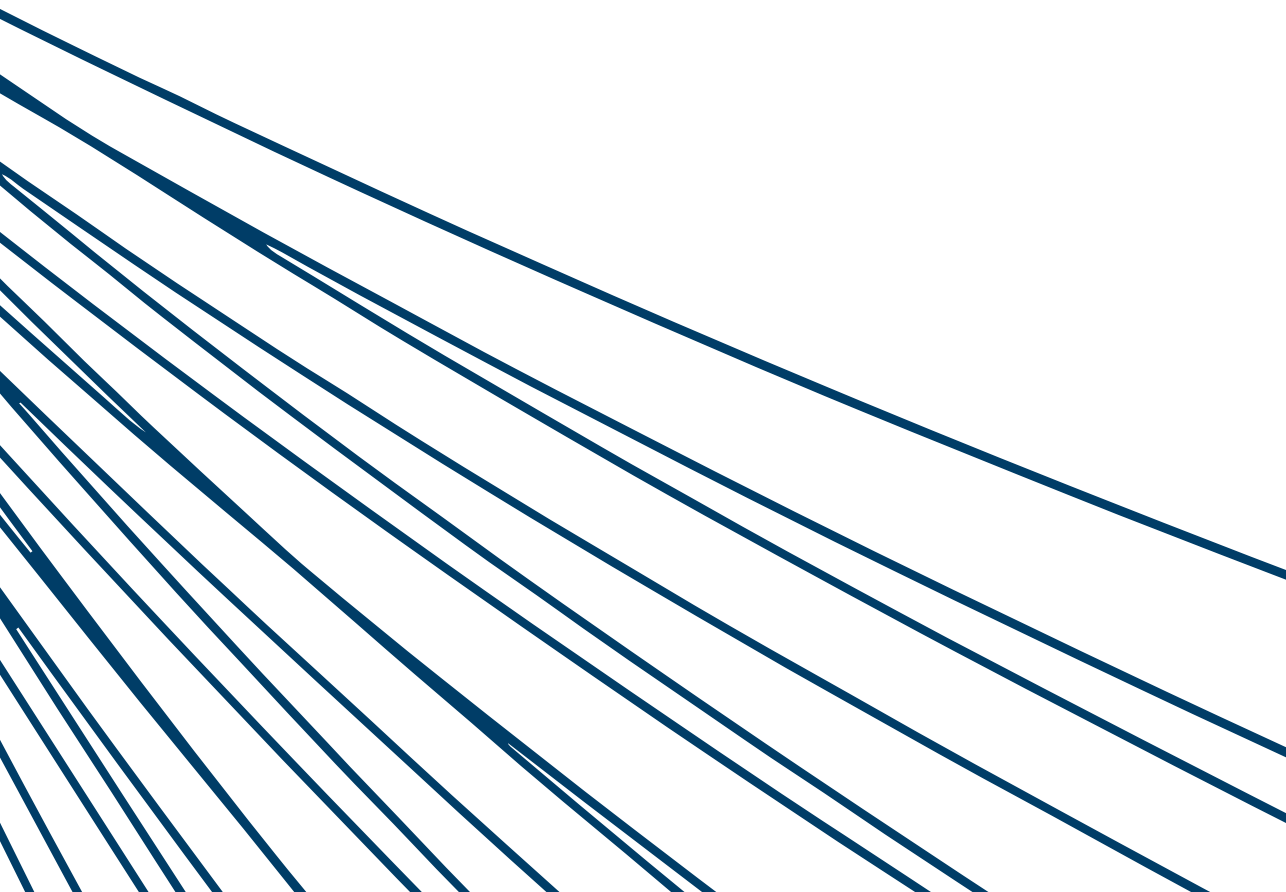
CONCLUSIONS

This report has introduced a full 3D virtual workflow to enable immediate implant retained prosthetic rehabilitation after a maxillectomy. Zygomatic implants should be placed very accurately in the planned positions using the novel designed patient specific drilling and placement guides, allowing screw-retained fixation of an obturator prosthesis. This concept will be verified next in patients with maxillary cancer who have been planned for prosthetic rehabilitation with an obturator prosthesis.

REFERENCES

1. Urken ML, Roche AM, Kiplagat KJ, Dewey EH, Lazarus C, Likhterov I, et al. Comprehensive approach to functional palatomaxillary reconstruction using regional and free tissue transfer: Report of reconstructive and prosthodontic outcomes of 140 patients. Head Neck. 2018;40(8):1639–66. https://doi.org/1 0.1002/hed.25134.
2. Glas HH, Vosselman N, de Visscher SAHJ. The use of 3D virtual surgical planning and computer aided design in reconstruction of maxillary surgical defects. Curr Opin Otolaryngol Head Neck Surg. 2020;28(2):122–8. https:// doi.org/10.1097/MOO.0000000000000618.
3. Andrades P, Militsakh O, Hanasono MM, Rieger J, Rosenthal EL. Current strategies in reconstruction of maxillectomy defects. Arch Otolaryngol Head Neck Surg. 2011;137(8):806–12. https://doi.org/10.1001/archoto.2011.132.
4. Moreno MA, Skoracki RJ, Hanna EY, Hanasono MM. Microvascular free flap reconstruction versus palatal obturation for maxillectomy defects. Head Neck. 2010;32(7):860–8. https://doi.org/10.1002/hed.21264.
5. Buurman DJM, Speksnijder CM, Engelen BHBT, Kessler P. Masticatory performance and oral health-related quality of life in edentulous maxillectomy patients: a cross-sectional study to compare implant-supported obturators and conventional obturators. Clin Oral Implants Res. 2020;31(5):405–16. https://doi.org/10.1111/clr.13577.
6. Visch LL, van Waas MA, Schmitz PI, Levendag PC. A clinical evaluation of implants in irradiated oral cancer patients. J Dent Res. 2002;81(12):856–9. https://doi.org/10.1177/154405910208101212.
7. Alberga JM, Vosselman N, Korfage A, Witjes MJA, Raghoebar GM, Vissink A. What is the optimal timing for implant placement in oral cancer patients? A scoping literature review. Oral Dis. 2021;27(1):94–110. https://doi.org/1 0.1111/odi.13312.
8. Butterworth CJ. Primary vs secondary zygomatic implant placement in patients with head and neck cancer-A 10-year prospective study. Head Neck. 2019;41(6):1687–95. https://doi.org/10.1002/hed.25645.
9. Korfage A, Raghoebar GM, Huddleston Slater JJR, Roodenburg JLN, Witjes MJH, Vissink A, et al. Overdentures on primary mandibular implants in patients with oral cancer: follow-up study over 14 years. Br J Oral Maxillofac Surg. 2014;52(9):798–805. https://doi.org/10.1016/j.bjoms.2014.05.013.
10. Boyes-Varley JG, Howes DG, Davidge-Pitts KD, Brånemark I, McAlpine JA. A protocol for maxillary reconstruction following oncology resection using zygomatic implants. Int J Prosthodont. 2007;20:521–31.
11. Pellegrino G, Tarsitano A, Basile F, Pizzigallo A, Marchetti C. Computer-aided rehabilitation of maxillary oncological defects using zygomatic implants: a defect-based classification. J Oral Maxillofac Surg. 2015;73:2446.e1.
12. Witjes MJH, Schepers RH, Kraeima J. Impact of 3D virtual planning on reconstruction of mandibular and maxillary surgical defects in head and neck oncology. Curr Opin Otolaryngol Head Neck Surg. 2018;26(2):108–14. https://doi.org/10.1097/MOO.0000000000000437.
13. Brown JS, Shaw RJ. Reconstruction of the maxilla and midface: introducing a new classification. Lancet Oncol. 2010;11(10):1001–8. https://doi.org/10.101 6/S1470-2045(10)70113-3.

14. Onclin P, Kraeima J, Merema BBJ, Meijer HJA, Vissink A, Raghoebar GM. Utilising the nasal aperture for template stabilisation for guided surgery in the atrophic maxilla. Int J Implant Dent. 2020;6(1):23. https://doi.org/10.11 86/s40729-020-00221-x.
15. Chuka R, Abdullah W, Rieger J, Nayar S, Seikaly H, Osswald M, et al. Implant utilization and time to prosthetic rehabilitation in conventional and advanced fibular free flap reconstruction of the maxilla and mandible. Int J Prosthodont. 2017;30(3):289–94. https://doi.org/10.11607/ijp.5161.
16. Hackett S, El-Wazani B, Butterworth C. Zygomatic implant-based rehabilitation for patients with maxillary and mid-facial oncology defects: A review. Oral Dis. 2021;27(1):27–41. https://doi.org/10.1111/odi.13305.
17. Wang F, Bornstein MM, Hung K, Fan S, Chen X, Huang W, et al. Application of real-time surgical navigation for zygomatic implant insertion in patients with severely atrophic maxilla. J Oral Maxillofac Surg. 2018;76(1):80–7. https://doi.org/10.1016/j.joms.2017.08.021.
18. Fan S, Hung K, Bornstein MM, Huang W, Wang F, Wu Y. The effect of the configurations of fiducial markers on accuracy of surgical navigation in zygomatic implant placement: an in vitro study. Int J Oral Maxillofac Implants. 2019;34:85–90.



CHAPTER 4

Three-dimensional guided zygomatic implant placement after maxillectomy

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G.M. Raghoebar, M.J.H. Witjes, S.A.H.J. de Visscher

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ABSTRACT

Zygomatic implants are used in patients with maxillary defects to improve the retention and stability of obturator prostheses, thereby securing good oral function. Prosthetic-driven placement of zygomatic implants is even difficult for experienced surgeons, and with a free-hand approach, deviation from the preplanned implant positions is inevitable, thereby impeding immediate implant-retained obturation. A novel, digitalized workflow of surgical planning was used in 10 patients. Maxillectomy was performed with 3D-printed cutting, and drill guides were used for subsequent placement of zygomatic implants with immediate placement of implant-retained obturator prosthesis. The outcome parameters were the accuracy of implant positioning and the prosthetic fit of the obturator prosthesis in this one-stage procedure. Zygomatic implants (n = 28) were placed with good accuracy (mean deviation 1.73 ± 0.57 mm and 2.97 ± 1.38° 3D angle deviation), and in all cases, the obturator prosthesis fitted as pre-operatively planned. The 3D accuracy of the abutment positions was 1.58 ± 1.66 mm. The accuracy of the abutment position in the occlusal plane was 2.21 ± 1.33 mm, with a height accuracy of 1.32 ± 1.57 mm. This feasibility study shows that the application of these novel designed 3D-printed surgical guides results in predictable zygomatic implant placement and provides the possibility of immediate prosthetic rehabilitation in head and neck oncology patients after maxillectomy.

Keywords
3D; 3D VSP; digital; guided surgery; head and neck oncology; maxillary reconstruction; maxillary tumour; maxillectomy; prosthetic rehabilitation; zygomatic implants

INTRODUCTION

Several reconstructive techniques are available for patients with complex defects of the mid-face and maxilla following tumour resection. The size and extent of the maxillary defect, patient factors, and comorbidities are decisive factors for the choice of surgical, prosthodontic, or combined rehabilitation after a maxillectomy. In cases when tumour resection has caused a relatively small maxillary defect, primary closure or surgical reconstruction with a local soft tissue flap alone can lead to excellent functional and aesthetic results. For larger maxillary defects, reconstruction with a vascularized flap or prosthetic rehabilitation with an obturator prosthesis can be used, the latter remaining an important treatment in many institutions[1]. However, conventional obturator prostheses can have their drawbacks, mainly caused by lack of retention of the prostheses. Placement of endosseous implants in the native bone of the maxilla allow for improvement of retention of the obturator prosthesis and thereby increase the success of prosthetic rehabilitation. While there is often not enough bone volume for reliable implant placement, zygomatic implants can be used to improve the retention of the obturator prosthesis[1=3].

The literature reports good zygomatic implant survival rates (78.6 to 100%) after placing maxillary resections[4]. Primary implant placement at the time of ablative surgery along with early loading of implants has been shown to be an effective rehabilitation protocol[1-3]. Although the survival rates are promising, this more complex treatment modality is not a standard implant procedure among many clinicians. Due to drilling with long drills close to critical anatomical structures, compromised visibility, and for oncological cases, also the absence of anatomical landmarks, the oblique drill trajectories for placement of zygomatic implants are challenging[5]. Inaccurate placement could result in uncontrolled bleeding, damage to the orbit and its content, damage to the maxillary sinus, and traumatic fractures to the orbitozygomatic complex[6,7]. Moreover, inaccurate placement and angulation of the implant results in positional errors at the apex and of the prosthetic head. This possibly results in an undesired prosthetic outcome and may even make the use of the zygomatic implant unattainable.

Pre-operative 3D planning and guided placement and drilling according to a virtual surgical plan could solve these problems and result in lower risk of complications compared to the free-hand approach. With the use of virtual implant planning, an optimal inclination, position, and depth of the zygomatic implant can be chosen considering volume and anatomical variation of the malar bone[8]. Moreover, the ideal prosthetic platform positions can be planned, which eliminates the possible need for the intraoperative “guess work” involved with complex zygomatic implant rehabilitation[9].

While there is widespread experience in guided placement of endosseous dental implants and guided resection of tumours, a proper tool for guided placement of

zygomatic implants in maxillectomy patients is not yet available. With the combination of the oblique bone surface, the long drill trajectories and the extent of the defects make designing guided templates a challenge. Any small angular or positional entrance error results in magnification of apical positional error at the tip of the drill[10]. The drill guide for zygomatic implant placement, introduced by Vrielink et al. in 2003, which was solely based on available bone volume, unfortunately had an unfavorable accuracy[11]. A technical note describing guided placement of zygomatic implants in atrophic maxillae lacks implant placement-accuracy analysis[12].

Recently, our group described a novel design of a fully digital 3D surgical planning for accurately executing the ablative surgery, placement of zygomatic implants, and immediate placement of an implant-retained obturator prosthesis in human cadavers[13]. Therefore, the aim of this study was to assess whether this full 3D virtual workflow to guiding zygomatic implants placement and providing the patient with a printed surgical obturator prosthesis in head and neck cancer patients with a maxillary defect would be clinically feasible.

MATERIALS AND METHODS

A total of 10 consecutive patients (7 female, 3 male, mean age of 66.3 years, range 45–73 years) who were treated for oral malignancies at the department of Oral and Maxillofacial Surgery at the University Medical Center Groningen were included. Patients either had a pre-existing defect of the maxilla (n = 3) or were scheduled for a maxillectomy (n = 7) with reconstruction an obturator prosthesis supported by zygomatic implants. All maxillary defects in this study are categorized as a class Brown IIb defect[14]. Patient, tumour, and defect characteristics are described in Table 1. For all patients, a complete 3D virtual surgical planning was made, in which zygomatic implants as well as an implant-retained obturator prosthesis were included.

Table 1. Patient, tumour and defect characteristics.

Patient	Age (years)	Sex	Indication	Laterality	Implants	IMPL length (mm)	Radiotherapy
1	49	F	cT4N0 Adenoid cystic carcinoma maxilla	R	2	42,5; 55	Post-op
2	73	F	cT1N0 Squamous cell carcinoma maxilla	R & L	4	52,5; 45; 52,5; 47,5	Pre-op Post-op
3	64	F	cT4aN1M0 Squamous cell carcinoma maxilla	R	4	55; 50	-
4	74	M	pT4aN0M0 Melanoma cavum nasi	R	2	55; 55	Post-op
5	71	F	cT3N0M0 Oral lentiginous melanoma maxilla	R	4	35; 45; 42,5; 50	Post-op
6	67	M	T4N0 Squamous cell carcinoma maxilla	L	2	47,5; 55	Pre-op
7	60	F	cT4N0 Squamous cell carcinoma maxilla	R	2	47,5; 55	-
8	45	M	Langerhans Histiocytosis	R & L	4	55; 52,5; 55; 52,5	Pre-op
9	66	F	Osteosarcoma maxilla	R	2	45; 50	-
10	71	F	pT4aN0 Squamous cell carcinoma maxilla	R&L	4	55;50;55;47,5	-

Pre-Implant Procedure and 3D Planning

Prior to ablative oncological surgery, each patient underwent a diagnostic work-up consisting of both a CT and MRI of the head and neck region for ablative surgery and implant planning. In dentate patients, the natural dentition of dentulous patients was digitalized through 3D optical surface scanning and could be matched to the 3D patient models. In edentulous cases, additional cone-beam-computed tomography scan (CBCT) datasets of the patients wearing their conventional prostheses were obtained. The patient's prosthesis was prepared before scanning: five radiopaque markers were added and spread over the prosthesis. Immediately after the scanning, a second scan of the prosthesis itself was performed. Through the radiopaque markers, the two CBCT-datasets of the patient and the prosthesis were merged to match the virtual prosthesis to the 3D models of the patient's anatomy.

By using a multi-modality CT and MRI combined workflow for 3D resection margin planning[15], the tumour was delineated on the MRI data, after which this dataset was

fused with the CT bone data in order to construct a 3D bone and tumour model. This model enabled reliable virtual resection planning with oncologic margins[16]. The virtual patient dentition or prosthesis was matched to the virtual planning to allow for digital obturator prosthesis designing, matching the defect, and backwards planning of the zygomatic implants from the position of the obturator prosthesis. The zygomatic implant heads were placed in the most ideal prosthodontic positions. The apical part of the zygomatic implant was planned in the lateral cortical bone of the zygomatic complex with care for maximal bony contact of the implant. The needed length of zygomatic implant was determined. In dentate cases, two zygomatic implants were digitally planned at the maxillary defect site. Four zygomatic implants were planned in edentulous cases.

Guide Design

Translation of the 3D VSP towards the surgical procedure was realized by means of 3D-printed surgical guides (Figure 1). Subsequently, patient-specific implant drill guides were designed based on the preferred apical and abutment positions of the zygomatic implants captured in the final virtual set-ups (3-Matic Medical, Materialise, Leuven, Belgium). In edentulous cases, the drill guides were developed to fit the alveolar ridge, nasal aperture, and zygomatic arch for stable positioning (Figure 2A,B). The maxillary bone-supported part included an extension to the nasal aperture to verify correct positioning of the guide and was connected with crosslink arms to the zygomatic bone-supported part[17]. Centered channels in the drill-guides enable insertion of stainless steel milled drill sleeves, which should minimize deviation of the drill trajectories and prevent polyamide particle formation (Figure 2C,D). The length of the channels functions as an integral depth stop for the zygomatic implants (Figure 2E,F). In addition, the guide was supplied with holes for temporary fixation with mini screws. If natural dentition was remaining after resection, the teeth were used for support of the guides (Figure 3). The guides were printed from polyamide, produced according to the ISO 13485 standards for medical devices, by Oceanz (Ede, The Netherlands).

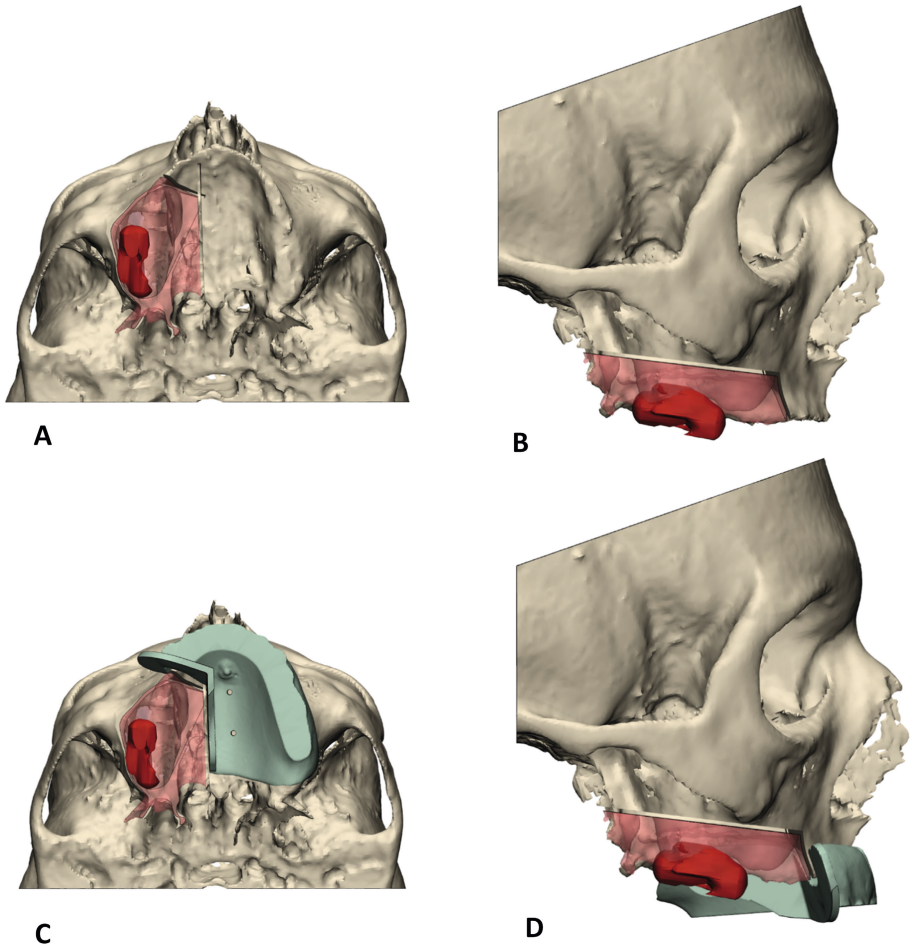


Figure 1. Overview of 3D VSP workflow for virtual resection planning. The working method starts with right-sided maxillectomy. **A**, caudal view and **B**, the matching lateral view guided by the surgical cutting guides **C** & **D**, with which the aim is to remove the red transparent part representing tumour removal with margin.

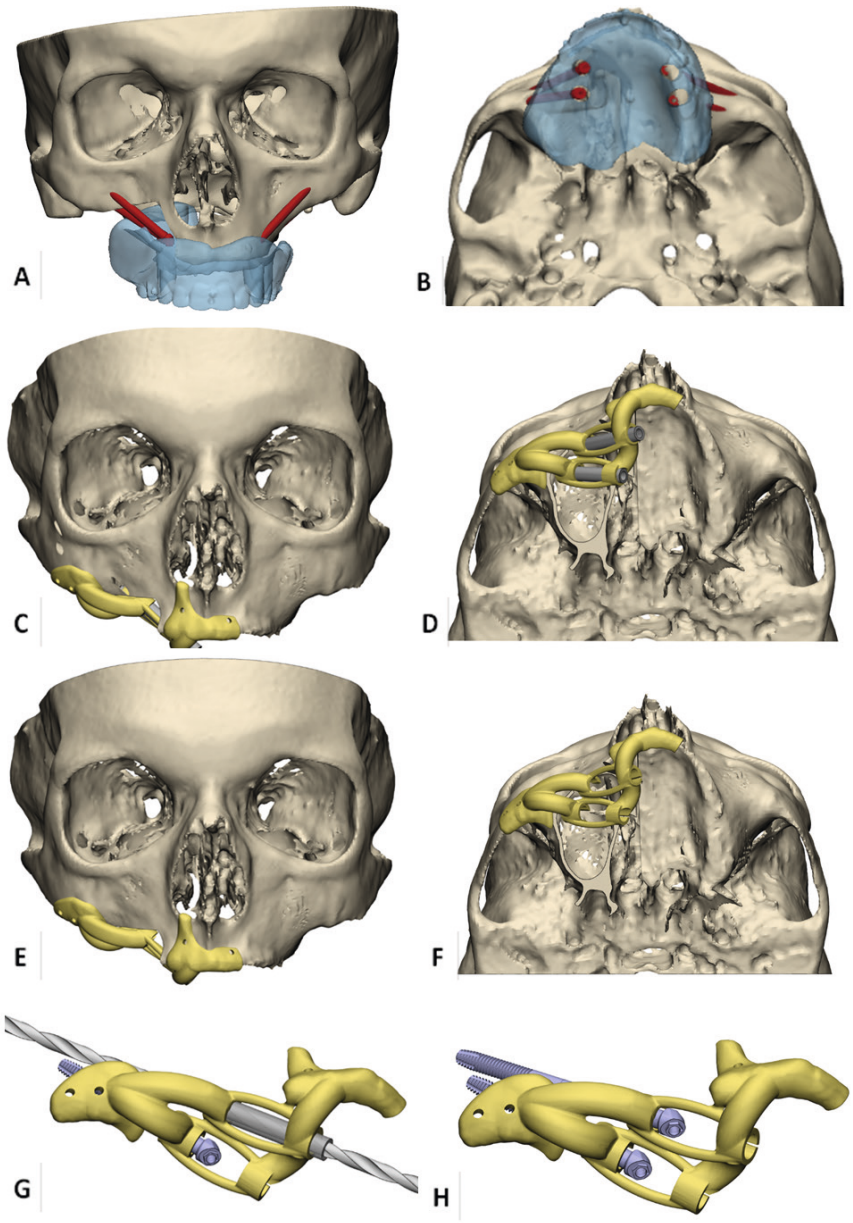


Figure 2. Overview of 3D VSP workflow for virtual zygomatic implant planning. **A**,**B** virtual obturator prosthesis driven zygomatic implant planning in an edentulous patient with right sided maxillary resection planning. **C**,**D** bone supported zygomatic implant drill guide. Support is gained at alveolar ridge, nasal aperture and zygomatic arch for stable positioning and centered channels in the drill-guide enables insertion of stainless steel milled drill sleeves. **E**,**F** the length of the channels forms an integral depth stop for the zygomatic implants. **G**, detailed view of drill guidance. **H**, detailed view of zygomatic implants placed through the guide to enhance correct prosthetic head positions.

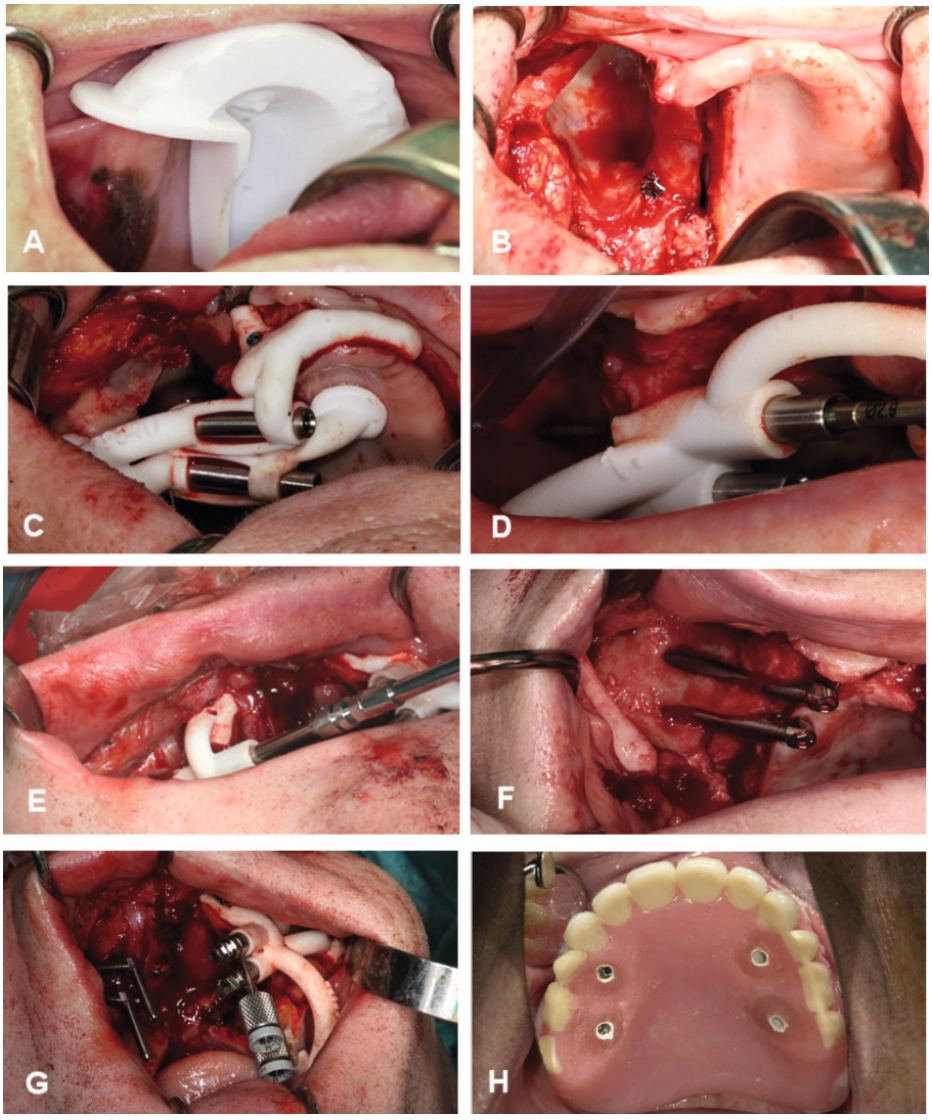


Figure 3. Surgical procedure. **A** & **B**, maxillectomy according to the preplanned, individually-designed cutting guides. **C**, drill guide seated with a tight fit and fixated with osteosynthesis screws. **D**, zygomatic drill inserted in the guide to perform the preplanned drill. **E**, insertion of zygomatic implant into the bone until the fixture mount contact the reference stop on the guide. **F**, view of zygomatic implant positions after removing the guide. **G**, final screw direction of the fixture mounts which correspond exactly with the abutment positions. **H**, implant retained obturator prosthesis immediate fixated with non-engaging prosthetic cylinders mounted into the prepared slots with a light curing denture resin.

Surgical Procedure

First, the tumour was removed by resecting the maxilla (SV) according to the preplanned, individually designed cutting guides (Figure 3A,B). In the two cases in which the maxillectomy already had been performed, a mucoperiosteal flap was raised. Second, the zygomatic implant drill guide was fitted onto the bone. All zygomatic implants were placed by the same surgeons (S.V. and G.R.). During exposure of the maxillary and zygomatic bone, care was taken in order to remove all connective tissue from the guide supporting bone region so that the drill guide could be seated with a tight fit. The guide was fixated with osteosynthesis screws (KLS Martin, Tuttlingen, Germany) (Figure 3C). Third, the first metal sleeves matching the 2.7 mm zygomatic drill with apical lance were inserted in the guide to create the entry point in the malar bone. Subsequently, the preplanned drill trajectories were performed (Figure 3D). The metal sleeve was removed, which transformed the guide into a placing guide for the correct installation angle for the zygomatic implants (Zygex, Southern implants, Gauteng, South Africa). Next, the implants were inserted into the zygomatic bone until the fixture mounts contacted the reference stop on the guide. (Figure 3E). Due to longitudinal slots in the guide, the guide can be removed easily following implant placement by loosening the osteosynthesis screws and unclipping the guide from the implants (Figure 3F). Before removing the guide, the maxillofacial prosthodontist determines the final screw direction of the fixture mount, which corresponds exactly with the abutment position (Figure 3G). The obturator prosthesis with preplanned slots can be used as a reference to ensure a parallel positioning of the prosthetic platforms. In the edentulous cases (n = 5), a second guide was placed on the contralateral side, and the guided implant procedure was repeated. The surgical procedure was finalized by fixating the obturator prosthesis. Non-engaging prosthetic cylinders (Southern implants, Irene) were fixed to the obturator prosthesis with ultraviolet light-curing resin. The obturator prosthesis was checked for balance support and was firmly screw-fixed on the zygomatic implant abutments (Figure 3H). The screw-retained retention allows post-operative removal of the surgical obturator prosthesis and enables replacement as often as necessary.

Analysis of Accuracy

All patients underwent a routine postoperative cone-beam-computed tomography scan (CBCT) within 16 days after surgery, which was used to evaluate the accuracy of the implant placement. The computer-aided design (CAD) files in STL format of the titanium zygomatic implants were superimposed onto the postoperative CT data, and a comparison was made with the planned positions by calculating reproducible reference planes in which the accuracy was measured. The implant coordinate system (ICoS) includes three reproducible reference planes in which the accuracy was measured: the center of the zygomatic implant head, bone entry point of the implant, and bone exit point of the implant (Figure 4A). Furthermore, the 3D angular deviation between 3D-planned position and postoperative implant position was calculated (Figure 4B).

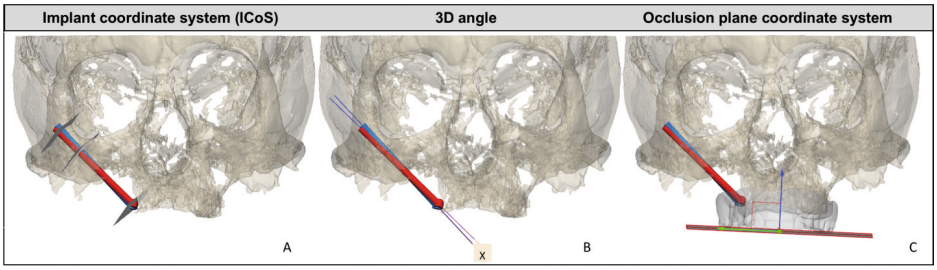


Figure 4. Overview of the different types of measurements and reference planes or coordinate systems for assessing the accuracy of zygomatic implant placement derived from post-op CBCT. In red the planned zygomatic implant position, in blue the postoperative zygomatic implant position. **A**, the implant coordinate system (ICoS) including the three reproducible reference planes in which the accuracy is measured; the centre of the zygomatic implant head, bone entry point of the implant, and bone exit point of the implant. **B**, 3D angular deviation between 3D planned position and postoperative implant position. **C**, Occlusion plane coordinate system. A plane parallel to the prosthetic occlusional plane is defined, perpendicular to this plane is the blue arrow. This arrow indicates the direction in which the abutment height accuracy is calculated. Deviation of the abutment is measured in the occlusional plane (green arrow).

Deviation of abutment position in two dimensions were calculated by defining a plane parallel to the prosthetic occlusional plane as reference: the occlusion plane coordinate system (Figure 4C). If the implant-retained obturator prosthesis on the zygomatic implant abutments was within 3 mm of the prosthetic cylinders in the slots, and a passive fit could be achieved, placement was deemed a success.

RESULTS

Implant Placement Accuracy

The surgical guides fitted well in 9 cases (28 zygomatic implants). In one case, the fit of the surgical guide was not optimal because a larger resection of the tumour than planned was performed. These two implants were placed non-guided and therefore eliminated from the accuracy analysis. The implant lengths varied between 35 mm and 55 mm and were placed with a mean entry point deviation of 1.73 ± 0.57 mm and a 3D angle deviation of 2.97 ± 1.38° (range 0.6–6.1°). The 3D accuracy of the abutment positions was 1.58 ± 1.66 mm. The accuracy of the abutment position in the occlusal plane was 2.21 ± 1.33 mm, with a height accuracy of 1.32 ± 1.57 mm. An overview of the accuracy results can be seen in Table 2 and Table 3. The accuracy was well within tolerance limits.

Table 2. Accuracy data. Result of the post-op analysis of the implant coordinate system (ICoS) measurements and descriptive statistics of the occlusion coordinate system (OCoS) measurements. * SD, standard deviation.

ICoS Measurements *n* = 10	Mean (+/–* SD)	Min	Max
Abutment (mm)	1.58 (+/–1.66)	0.53	3.42
Entry point (mm)	1.73(+/–0.57)	0.43	3.24
Exit point (mm)	2.87 (+/–1.18)	1.11	4.72

Table 3. Accuracy data. Result of the post-operative analysis. Descriptive statistics of the occlusion coordinate system (OCoS) measurements. * SD, standard deviation.

OCoS Deviations *n* = 10	Mean (+/–* SD)	Min	Max
Abutment in occlusal plane (mm)	2.21 (+/–1.33)	0.87	6.04
Abutment height from occlusal plane (mm)	1.32(+/–1.57)	0.01	6.58
Axial angle (°)	2.31 (+/–1.52)	0.19	4.34
Coronal angle (°)	2.43 (+/–1.73)	0.25	7.97
Sagittal angle (°)	2.85 (+/–1.88)	0.27	7.04
3D angle (°)	2,97 (+/–1.38)	0.60	6.13

Fit of the implant retained obturator prosthesis

In nine cases, the obturator prostheses could be fixated with non-engaging prosthetic cylinders (Zygex Southern implants, Gauteng, South Africa) to the zygomatic implants as planned. The prosthetic outcome in the horizontal and vertical dimension was within the 3 mm leeway space. This margin was available in prepared slots of the obturator prostheses needed for fixation. In the case where the zygomatic implants were not guided placed, extensive prosthetic adjustments at the preplanned slots were needed to allow for a proper fit of the obturator prosthesis. Finally, all pre-operatively designed obturator prostheses had an adequate and were well-balanced on the zygomatic implants and remaining maxillary structures.

DISCUSSION

This feasibility study shows that the application of 3D-printed surgical guides results are feasible in predictable zygomatic implant placement and immediate prosthetic rehabilitation in head and neck oncology patients after maxillectomy. Furthermore, application of this reliable method is believed to minimalize the risk of surgical and prosthetic complications.

The literature reports loading of zygomatic implants within a few hours after implant placement[18,19], but to the best of our knowledge, such a CAD workflow involving immediate implant-retained prosthetic rehabilitation in a combined surgical procedure with guided tumour resection and placement of zygomatic implants is not described. Thereby, comparative accuracy data are not available yet. Perioperative prosthetic delivery obviates invasive impression taking in surgical field or shortly after surgery, which is a direct benefit for the patient.

In the literature, an unfavorable zygomatic implant position of the apex or prosthetic head is described as a surgical complication[2,7]. This could indicate that even when executed by experienced surgeons, there is a frequent occurrence of suboptimal zygomatic implant positioning using a free-hand placement. The concept of guided zygomatic implant placement was first tested by our group in a series of human cadavers[12]. The data of this pre-clinical cadaver study and the data presented here are comparable in accuracy. As a consequence, immediate implant support was available for the obturator prosthesis.

This phase I trial shows high clinical potential for this approach of 3D-planned placement of zygoma implants. We think that a larger group of patients is required to confirm our first data on the predictability of placement and subsequent immediate loading of the obturator prosthesis. The lessons learned from this trial are that 3D planning can be accurately used when surgeons and prosthodontists together plan the surgery and prosthetic rehabilitation. 3D visualization of the tumour and planned resection promotes clinical debate and facilitates choices. The execution of the resection is less of a determining factor. Added resections are very well possible since the support for the 3D zygoma guides are chosen outside the expected oncological surgical field. Two factors are critical for accurate placement of the zygomatic implants. The first is the accurate placement of the 3D guide. Surgeons should be aware how the guides should be placed and 3D information should be available in the OR. Time must be taken to place these correctly, as is the case with all 3D-planned surgical guides for another purposes. Second, during placement of the implants, the surgeon should have the possibility of visual inspection of the entry point in the zygoma. Despite accurate 3D planning and well-thought out guide design, the surgeon needs visual feedback on the entry point. Once the entry point is placed accurately, the rigid guide supports the right direction of the implant drill.

Besides guided placement of implants, currently, implant placement using real-time navigation is gaining popularity. Research results are promising, and this most likely accurate and less-invasive surgical technique could be a next step in zygomatic implant placement according to a VSP in the future. To date, the main drawback of current visualization techniques is the difficulty of steadily maintaining the drill handpiece and transferring the surgical view from the navigation display to the operative site, which is

amplified in the long drills used for zygomatic implants[20]. Secondly, it currently involves above-average operating time[9].

It is reasonable to assume that knowledge of the planned resection automatically provides 3D visualization of the necessary obturator outline to restore oral function. In this study, a treatment protocol was used for immediate prosthetic rehabilitation with immediate loading of the zygomatic implants. Restoring oral function immediately after ablative surgery obviates the need for fitting, placing, and adapting the prostheses. After maxillectomy, the frequent necessity of adjuvant radiotherapy limits the possibility of achieving sufficient retention for a conventional obturator prosthesis. An implant-retained obturator prosthesis allows for repeated removal to check the oncological defect visually or in the event of complications. The addition of subsequently placing a fixed, removable obturator prosthesis during surgery is a major step to shortening the time of prosthetic delivery and implant utilization. It can be anticipated that the number of prosthetic interventions post-operatively will be less compared to conventional prosthetic planning, in which retention is more difficult to obtain. We anticipate that oral function in such patients can recover earlier and better before the often necessary radiotherapy starts, and the hospital visits for prosthetic aftercare will be minimized in the early post-operative phase. In case of adjuvant radiotherapy, it is important to provide zygomatic implant-specific information to the radiotherapy team. This enables adjustments of the radiotherapy treatment plan and the dosimetric accuracy in radiotherapy[21,22] .

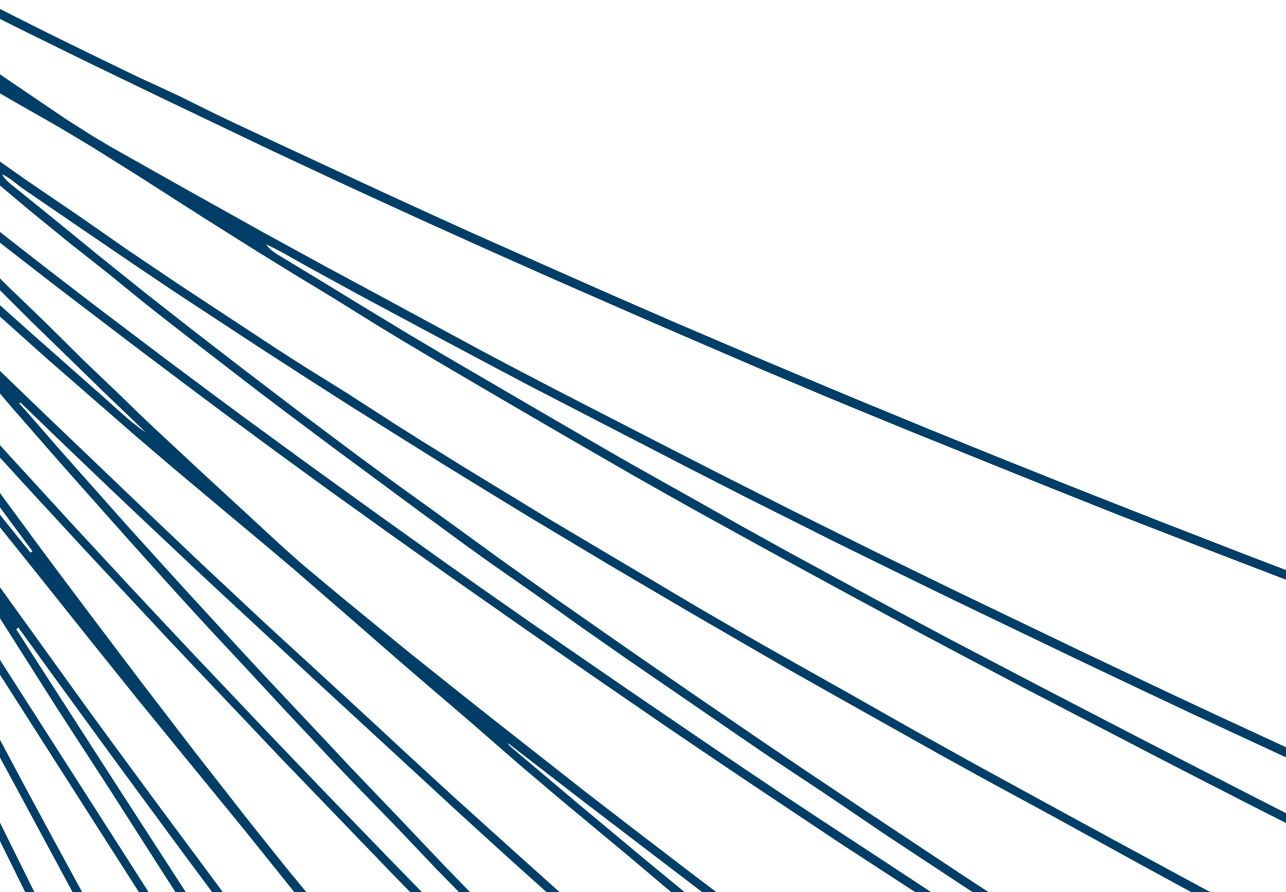
CONCLUSIONS

A fully digitalized workflow for guided resection, zygomatic implant placement, and immediate prosthetic rehabilitation is feasible when planning a zygomatic implant-retained prosthesis. The method presented here is novel and advantageous for head and neck cancer patients because of an immediate implant-based prosthetic rehabilitation after ablative surgery, which otherwise could not have been achieved without delay.

REFERENCES

1. Vosselman N, Alberga J, Witjes MHJ, Raghoebar GM, Reintsema H, Vissink A, Korfage A. Prosthodontic rehabilitation of head and neck cancer patients-Challenges and new developments. Oral Dis. 2021.; 27:64-72. doi: 10.1111/odi.13374.
2. Hackett S, El-Wazani B, Butterworth C. Zygomatic implant-based rehabilitation for patients with maxillary and mid-facial oncology defects: A review. Oral Dis. 2021.; 27:27-41. doi: 10.1111/odi.13305.
3. Boyes-Varley JG, Howes DG, Davidge-Pitts KD, Brånemark I, McAlpine JA. A protocol for maxillary reconstruction following oncology resection using zygomatic implants. Int J Prosthodont. 2007;20:521-31.
4. Butterworth CJ. Primary vs secondary zygomatic implant placement in patients with head and neck cancer-A 10-year prospective study. Head Neck. 2019;41:1687-1695. doi: 10.1002/hed.25645. Epub 2019 Jan 21. PMID: 30664292.
5. Ramezanzade S, Keyhan SO, Tuminelli FJ, Fallahi HR, Yousefi P, Lopez-Lopez J. Dynamic-Assisted Navigational System in Zygomatic Implant Surgery: A Qualitative and Quantitative Systematic Review of Current Clinical and Cadaver Studies. J Oral Maxillofac Surg. 2021;79:799-812. doi: 10.1016/j.joms.2020.10.009. Epub 2020 Oct 14. PMID: 33176128.
6. Chrcanovic BR, Albrektsson T, Wennerberg A. Survival and Complications of Zygomatic Implants: An Updated Systematic Review. J Oral Maxillofac Surg. 2016;74:1949-64. doi: 10.1016/j.joms.2016.06.166. Epub 2016 Jun 18. PMID: 27422530.
7. Aparicio C, López-Piriz R, Albrektsson T. ORIS Criteria of Success for the Zygoma-Related Rehabilitation: The (Revisited) Zygoma Success Code. Int J Oral Maxillofac Implants. 2020;35:366-378. doi: 10.11607/jomi.7488. PMID: 32142574.
8. Bertos Quílez J, Guijarro-Martínez R, Aboul-Hosn Centenero S, Hernández-Alfaro F. Virtual quad zygoma implant placement using cone beam computed tomography: sufficiency of malar bone volume, intraosseous implant length, and relationship to the sinus according to the degree of alveolar bone atrophy. Int J Oral Maxillofac Surg. 2018;47:252-261. doi: 10.1016/j.ijom.2017.07.004. Epub 2017 Aug 18. PMID: 28823906.
9. Ponnusamy S, Miloro M. A Novel Prosthetically Driven Workflow Using Zygomatic Implants: The Restoratively Aimed Zygomatic Implant Routine. J Oral Maxillofac Surg. 2020;78:1518-1528. doi: 10.1016/j.joms.2020.05.030. Epub 2020 May 26. PMID: 32598868.
10. Wu Y, Wang F, Huang W, Fan S. Real-Time Navigation in Zygomatic Implant Placement: Workflow. Oral Maxillofac Surg Clin North Am. 2019;31:357-367. doi: 10.1016/j.coms.2019.03.001. Epub 2019 May 18. PMID: 31113696
11. Vrielinck L, Politis C, Schepers S, Pauwels M, Naert I. Image-based planning and clinical validation of zygoma and pterygoid implant placement in patients with severe bone atrophy using customized drill guides. Preliminary results from a prospective clinical follow-up study. Int J Oral Maxillofac Surg. 2003;32:7-14. doi: 10.1054/ijom.2002.0337. PMID: 12653226
12. Rigo L, Tollardo J, Giammarinaro E, Covani U, Caso G. Fully Guided Zygomatic Implant Surgery. J Craniofac Surg. 2021;32:2867-2872. doi: 10.1097/SCS.0000000000008005. PMID: 34320580.

13. Vosselman N, Glas HH, de Visscher SAHJ, Kraeima J, Merema BJ, Reintsema H, Raghoebar GM, Witjes MJH. Immediate implant-retained prosthetic obturation after maxillectomy based on zygomatic implant placement by 3D-guided surgery: a cadaver study. Int J Implant Dent. 2021 14;7:54. doi: 10.1186/s40729-021-00335-w. PMID: 34121148; PMCID: PMC8200332.
14. Brown, J.S.; Rogers, S.N.; McNally, D.N.; Boyle, M. A modified classification for the maxillectomy defect. Head Neck 2000, 1, 17–26.
15. Kraeima J, Dorgelo B, Gulbitti HA, Steenbakkers RJHM, Schepman KP, Roodenburg JLN, Spijkervet FKL, Schepers RH, Witjes MJH. Multi-modality 3D mandibular resection planning in head and neck cancer using CT and MRI data fusion: A clinical series. Oral Oncol. 2018;81:22-28. doi: 10.1016/j.oraloncology.2018.03.013. Epub 2018 Apr 11. PMID: 29884410.
16. Kraeima, J.; Schepers, R.H.; van Ooijen, P.M. Integration of oncologic margins in three-dimensional virtual planning for head and neck surgery, including a validation of the software pathway. J. Craniomaxillofac. Surg. 2015, 8, 1374–1379.
17. Onclin P, Kraeima J, Merema BBJ, Meijer HJA, Vissink A, Raghoebar GM. Utilising the nasal aperture for template stabilisation for guided surgery in the atrophic maxilla. Int J Implant Dent. 2020;6:23
18. Maló P, Nobre Mde A, Lopes A, Ferro A, Moss S. Five-year outcome of a retrospective cohort study on the rehabilitation of completely edentulous atrophic maxillae with immediately loaded zygomatic implants placed extra-maxillary. Eur J Oral Implantol. 2014;7:267-81. PMID: 25237671.
19. Davó R, Malevez C, Rojas J, Rodríguez J, Regolf J. Clinical outcome of 42 patients treated with 81 immediately loaded zygomatic implants: a 12- to 42-month retrospective study. Eur J Oral Implantol. 2008;9:141-50. PMID: 20467651.
20. Wang F, Bornstein MM, Hung K, Fan S, Chen X, Huang W, Wu Y. Application of Real-Time Surgical Navigation for Zygomatic Implant Insertion in Patients With Severely Atrophic Maxilla. J Oral Maxillofac Surg. 2018;76:80-87. doi: 10.1016/j.joms.2017.08.021. Epub 2017 Aug 24. PMID: 28911958.
21. Puvanasunthararajah, S.; Fontanarosa, D.; Wille, M.L.; Camps, S.M. The application of metal artifact reduction methods on computed tomography scans for radiotherapy applications: A literature review. J. Appl. Clin. Med. Phys. 2021, 6, 198–223.
22. Hansen, C.R.; Christiansen, R.L.; Lorenzen, E.L.; Bertelsen, A.S.; Asmussen, J.T.; Gyldenkerne, N.; Eriksen, J.G.; Johansen, J.; Brink, C. Contouring and dose calculation in head and neck cancer radiotherapy after reduction of metal artifacts in CT images. Acta Oncol. 2017, 6, 874–878.



CHAPTER 5

Guided placement of zygomatic implants in head and neck cancer patients: implant survival and patient outcomes at 1–3 years of follow-up

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ABSTRACT

Zygomatic implants (ZI) are a valuable option for supporting an obturator prosthesis after maxillary resection. This study was performed to assess the clinical outcomes of a digitally validated guided technique for ZI placement, followed by immediate prosthetic obturation. The primary objective was to evaluate implant survival, while the secondary objective was to assess patient-reported quality of life post-rehabilitation. Twelve patients treated for head and neck cancer received a total of 36 ZI after ablative surgery. The mean duration of ZI follow-up was 30.1 months. The survival rate of ZI placed in non-irradiated patients was 100%, while it was 85% in irradiated patients. Patient-reported outcomes were evaluated using the Liverpool Oral Rehabilitation Questionnaire (LORQv3) and the University of Washington Quality of Life Questionnaire (UW-QOL v4). Most patients reported satisfactory outcomes in the oral function domain of the LORQv3 (mean score 17.7 ± 4.5; possible range 12–48, with lower scores indicating better outcomes). Regarding the UW-QOL v4, the swallowing and chewing domains had the highest scores (mean 97.5 ± 8.7 and 95.8 ± 14.4, respectively; maximum possible score of 100). In conclusion, this treatment approach improves function and quality of life after maxillary ablative surgery. However, irradiated patients showed a noticeable trend of higher implant failure, and this was influenced by tumour position and size impacting the radiation dose to the zygomatic bone.

INTRODUCTION

The standard treatment for patients with a maxillary malignancy consists of a (partial) maxillectomy, often in combination with postoperative radiotherapy. The resulting maxillary defect has a profound impact on the patient's functional abilities[1]. The impaired oral functions are often further compromised if post-surgical radiotherapy is needed, due to related radiation-induced sequelae[2].

The repair of maxillary defects after oncological surgery is possible by means of reconstructive surgery or a prosthetic obturator, depending on patient characteristics, the tumour location, and the surgical team[3]. The overall objective in patients with these maxillary defects is to restore oral function by following a prosthetic-driven reconstruction approach[4]. The choice of reconstruction method in cases of extensive maxillary resection involves a comprehensive evaluation of individual patient factors. While free flap reconstruction remains a robust option for many, the patient's age and health status can influence the decision-making process. Zygomatic implants (ZI) with an obturator prosthesis offer a viable alternative that provides adequate closure of the defect and dental rehabilitation in cases where a less invasive approach is preferred or contraindications for extensive bony reconstruction are present.

In cases where an obturator prosthesis is selected as the primary method of reconstruction, enhancing its retention and stability is crucial. One of the options for improving the retention and stability of obturator prostheses is the application of ZI[5]. These implants can significantly enhance the functional and aesthetic outcomes for patients while maintaining a patient-centred approach that prioritizes their overall wellbeing and long-term quality of life. The ablation surgery, reconstructive surgery, and prosthetic rehabilitation can be planned preoperatively with the support of three-dimensional (3D) virtual surgical planning (VSP) and computer-aided design. The accuracy of this approach has been confirmed in cadaver and feasibility studies[6,7]. The question that still needs to be answered through long-term follow-up is whether this advanced technique results in high implant survival and satisfactory patient outcomes in the long term. Therefore, the aim of this study was to assess the ZI survival rate overall and according to post-surgical radiotherapy data, as well as to determine the patients' self-reported quality of life at 1–3 years after the treatment.

METHODS

Study design and patients

The study was designed as an ongoing follow-up study for monitoring ZI survival and patient outcomes over the long term. All included patients who were treated for oral malignancies,underwent guided maxillectomy followed by reconstruction with an

obturator prosthesis, which was supported by immediately placed ZI. The treatment protocol utilizes a novel full 3D workflow. This paper reports the initial phase of the study, at 1–3 years of follow-up after the single-stage treatment procedure.

A VSP was developed for ZI placement and restoration with a screw-retained immediate obturator prosthesis. Before surgery, the patients underwent diagnostic imaging for surgical planning (computed tomography (CT) and magnetic resonance imaging (MRI)). Dentulous patients had their teeth digitally scanned and matched to 3D models, while edentulous patients had additional cone beam computed tomography (CBCT) scans with radiopaque markers on their prostheses. In the constructed 3D models, the ZI were virtually planned based on the occlusion and prosthetic considerations.

The zygomatic oncology implants (Zygex; Southern Implants, Irene, South Africa) were placed by one of two surgeons (G.R. or S.V.). Immediately after guided maxillary resection, the ZI guide was accurately positioned and stabilized, and guided drilling was performed following the manufacturer's recommended drill sequence (Southern Implants protocol). The zygomatic oncology implants were all placed as pairs in the zygomatic bone. Both ZI were placed through the guide into the preferred prosthodontic positions determined before the surgery. Good primary stability was achieved for all of the ZI at the time of insertion. Subsequently, the obturator prosthesis was fitted and the temporary polyether ether ketone (PEEK) abutments were bonded with ultraviolet light curing resin. This enabled stability and retention of the obturator prosthesis and provided the necessary maxillary obturation directly after surgery.

This guided procedure has been described in detail in previous studies[6,7]. All 10 patients from the feasibility study[7] were included in this follow-up study. Following the completion of the feasibility study, two additional patients were treated using this technique and subsequently included in this study. The patients were assessed in the Department of Oral and Maxillofacial Surgery of the University Medical Centre Groningen, the Netherlands. The study was approved by the Medical Ethics Review Board of the University Medical Center Groningen following the guidelines of the Declaration of Helsinki (WMO 202000569).

Assessments

The primary outcome measure was ZI survival. As part of the standard oncological follow-up protocol of the Dutch Cooperative Head and Neck Group, overall disease control is monitored every 3 months. As part of this protocol, a multidisciplinary consultation that included a maxillofacial prosthodontist was conducted to provide the necessary prosthodontic aftercare. All of the patients were monitored closely and had been checked by the maxillofacial prosthodontist (N.V.) within the 3 months prior to the study cut-off date of April 28, 2023.

A CBCT scan was performed and a panoramic radiograph of the implants was obtained directly after surgery. Further panoramic radiographs were obtained after installation of the definitive obturator prosthesis and at 1 year after prosthetic delivery. Regarding the patients who needed postoperative irradiation, the radiotherapy contouring, 3D treatment planning, fractionation, and total dose were reviewed retrospectively. The zygomatic bones of the patients were marked on the CT scan images with specific lines to precisely delineate their size, shape, and location. The implant bed was subsequently verified by imaging until an exact match was found. In this way, accurate radiation doses, including the maximum dose within the ZI implant bed, could be calculated for all of the patients who underwent postoperative radiotherapy.

Patient-reported quality of life after rehabilitation was assessed by administering two questionnaires 4 weeks after the definitive implant-supported obturator prosthesis was placed. In the first questionnaire, the Liverpool Oral Rehabilitation Questionnaire (LORQv3; Dutch version), of the total questionnaire, 27 questions can be divided into four domains consisting of (A) oral function, (B) orofacial appearance, (C) social interaction, and (D) patient/prosthetic satisfaction. The items are rated on a 1–4 Likert scale, with 1 = never, 2 = sometimes, 3 = often, and 4 = always; lower scores indicate better outcomes.

The second questionnaire, the University of Washington Quality of Life Questionnaire version 4 (UW-QOL v4)[8], is a widely used tool for the evaluation of health-related quality of life in patients with head and neck cancer[9]. It consists of 12 questions concerning pain, appearance, activity, recreation, swallowing, chewing, speech, shoulder function, taste, saliva, mood, and anxiety domains. The answers to each question are scored from 0 to 100, with 100 being the best score.

Statistical analysis

The statistical analysis was restricted to descriptive statistics, which were calculated using IBM SPSS Statistics version 28.0.1.0 (IBM Corp., Armonk, NY, USA).

RESULTS

At the data cut-off point (April 28, 2023), 12 patients (seven female, five male), with a median age of 66 years (range 45–87 years), had undergone the procedure and had been followed-up for a minimum of 1 year post-rehabilitation. The maxillary abnormality diagnoses are summarized in Table 1. In total, 36 guided ZI were placed. Among the 12 patients, eight were edentulous when treatment started, of whom six received four ZI, while two received two ZI on the defect side and endosseous implants (Nobel Parallel; Nobel Biocare, Gothenburg, Sweden) were placed in the contralateral native maxilla. The other four patients were dentulous, they all received two ZI on the defect

side. Three of them also received endosseous implants(Nobel parallel, Nobel Biocare, Gothenburg, Sweden) in the shortened contralateral dental arch for further prosthetic retention. All of the patients received a definitive implant-retained obturator prosthesis to replace the fixed surgical obturator prosthesis. Six patients needed postoperative radiation due to the T and N cancer stage. The postoperative radiotherapy dose to the ZI site ranged from 2 Gy to 128 Gy (median dose 40 Gy). An overview of the patient characteristics is shown in Table 2.

Table 1. Maxillary abnormality diagnoses (12 patients).

Diagnoses	Number of patients
Squamous cell carcinoma	8
Melanoma	2
ORN maxilla	1
Osteosarcoma	1

ORN, osteoradionecrosis.

Table 2. Patient characteristics.

Characteristics	
Patients, *n*	12
Sex, *n*	
Female	7
Male	5
Age at start of treatment (years)	
Mean ± SD	64 ± 11.8
Median (range)	66 (45–87)
Therapy, *n*	
Surgery	6
Surgery and postoperative RT	4
Preoperative RT, surgery, and postoperative RT	2
RT dose at the zygomatic implant site (Gy)	
Mean ± SD	40
Median (range)	40 (2–128)
Dentulous maxilla, *n*	4
Edentulous maxilla, *n*	8
Zygomatic oncology implants, *n*	36
Endosseous implants, *n*	7
Obturator prostheses, *n*	12

RT, radiotherapy; SD, standard deviation.

Implant survival

At the data cut-off point, the overall ZI survival rate was 91.7%, with a 100% survival rate in the non-irradiated group of patients and 85% survival rate in the irradiated patient group; the mean ± standard deviation implant follow-up period was 30.1 ± 11.1 months (Table 3).

Table 3. Implant data.

	Number placed	Number lost	Survival rate	Implant follow-up (months), mean ± SD
Zygomatic implants (Zygex)	36	3	91.7%	30.1 ± 11.1
Endosseous implants (Nobel Parallel)	7	0	100%	38.5 ± 8.8

A total of three ZI failed in two irradiated patients: one patient lost one implant and the other patient lost two. One failure was a ZI placed on the dorsal side of the defect, which had received 57.4 Gy post-surgically. Implant mobility was observed during the prosthetic aftercare. The same patient had received a second more ventrally placed ZI during the same surgery. Despite receiving an equal dose of radiotherapy, the implant functioned successfully while loaded with a magnet attachment to achieve prosthetic retention within the defect area. Thus far, no postoperative complications have been observed for this implant. The two other failures were in a patient who received pre- and postoperative radiotherapy. Before the ablative surgery, the zygoma bone was subjected to irradiation, up to a dose of 58 Gy, and unfortunately shortly after surgical treatment a recurrence was observed. An additional dose of 70 Gy was then delivered, bringing the total dose to 128 Gy. The guiding principle is to achieve the desired dose coverage to the target volume while sparing organs at risk (OAR) as much as possible. The dose–volume histograms of both radiotherapy treatment plans were used to evaluate the re-irradiation constraints for the OAR such as the brainstem, spinal cord, larynx, and bone (including the ZI). The boundaries for 'acceptable damage' are therefore different for the re-treatment situation than for the initial treatment, and in this situation maximum doses higher than 100 Gy to the bone are unfortunately not uncommon in head and neck cancer patients, especially when the OAR lies within the target regions[10,11].

Patient-reported outcomes

All of the study patients completed the LORQv3 and UW-QOL v4 questionnaires at 4 weeks after the final obturator prosthesis had been placed. An overview of the questions and domains of the LORQv3, and the mean ± standard deviation scores for the 12 patients, are given in Table 4. The domains of the UWQOL v4 and the mean ± standard deviation scores for the 12 patients are listed in Table 5

Table 4. Liverpool Oral Rehabilitation Questionnaire (LORQv3) scores for the 12 patients with zygomatic oncology implant-supported obturators.

Question number	Question	Score[a] Mean ± SD	Domain/ subtotal scores Mean ± SD (Possible score range)
Chewing			
1	Difficulty with chewing	1.33 ± 0.49	
2	Pain when chewing	1.17 ± 0.39	
16	Chewing ability influences choice of food	1.50 ± 0.67	
Subtotal			4.25 ± 1.36 (3–12)
Swallowing			
3	Difficulty with swallowing solids	1.33 ± 0.65	
4	Difficulty with swallowing liquids	1.00 ± 0.00	
Subtotal			2.33 ± 0.65 (2–8)
Salivation			
5	Food particles collect under tongue	1.33 ± 0.65	
6	Food particles stick to palate	1.58 ± 0.79	
7	Food particles stick inside cheeks	1.33 ± 0.65	
8	Mouth dryness	1.58 ± 0.69	
9	Problems with drooling	1.83 ± 0.72	
Subtotal			7.67 ± 2.53 (5–20)
10	Problems with speech	1.50 ± 0.67	
17	Difficulty with opening the mouth	1.92 ± 0.99	
(A) Oral function			17.67 ± 4.54 (12–48)
11	Upset by your facial appearance	1.17 ± 0.39	
12	Upset by the appearance of your mouth	1.25 ± 0.45	
13	Upset by the appearance of your lips	1.08 ± 0.29	
14	Upset by the appearance of your teeth	1.17 ± 0.39	
(B) Orofacial appearance			4.66 ± 1. 07 (4–16)
15	Chewing ability affects social life	1.50 ± 0.67	
(C) Social interaction			1.50 ± 0.67 (1–4)
Patient satisfaction			
20	Embarrassed about conversing	1.17 ± 0.39	
21	Refuse dinner invitations	1.08 ± 0.29	
22	Feel loss of self-confidence	1.17 ± 0.39	
23	Difficult to open your mouth	1.33 ± 0.65	
Subtotal			5.83 ± 1.47 (4–16)

Table 4. Liverpool Oral Rehabilitation Questionnaire (LORQv3) scores for the 12 patients with zygomatic oncology implant-supported obturators. *(continued)*

Question number	Question	Score[a] Mean ± SD	Domain/ subtotal scores Mean ± SD (Possible score range)
Prosthetic satisfaction			
26	Dissatisfied with your upper implant-retained teeth	1.17 ± 0.39	
27	Teeth cause soreness/ulceration of the gum	1.42 ± 0.51	
28	Food particles collect under your upper implant-retained teeth	2.08 ± 1.00	
29	Have to take out your upper teeth when eating	1.00 ± 0.00	
30	Feel insecure with your upper implant-retained teeth	1.08 ± 0.29	
31	Worried that your teeth might fall out	1.00 ± 0.00	
Subtotal			7.83 ± 1.80 (6–24)
(D) Satisfaction			13.67 ± 2.93 (10–40)

SD, standard deviation.
[a]Score on a 1–4 Likert scale, ranging from 1 'never' to 4 'always'; lower scores indicate better outcomes.

Table 5. Mean scores for the 12 domains of the University of Washington Quality of Life questionnaire (UW-QOL v4), for the 12 patients with zygomatic oncology implant-supported obturators.

Domain	Score[a] Mean ± SD	Total patients scoring 100, *n* (%)
Pain	83.3 ± 22.2	7 (58.3)
Appearance	89.6 ± 16.7	8 (66.7)
Activity	87.5 ± 16.9	7 (58.3)
Recreation	87.5 ± 19.9	8 (66.7)
Swallowing	97.5 ± 8.7	11 (91.7)
Chewing	95.8 ± 14.4	11 (91.7)
Speech	87.5 ± 15.4	7 (58.3)
Shoulder	91.7 ± 21.2	10 (83.3)
Taste	75.8 ± 25.7	5 (41.7)
Saliva	77.5 ± 13.6	3 (25)
Mood	83.3 ± 12.3	4 (33.3)
Anxiety	70 ± 0.0	0 (0)

SD, standard deviation.
[a]Score on a scale of 0–100, with higher scores indicating better outcomes.

The mean overall score for section A of the LORQv3, covering oral function, was 17.7 ± 4.5 (possible range 12–48, with 12 representing the best oral function). This indicates a satisfactory outcome for this domain, and is comparable to the results of other studies[12].

Regarding the UW-QOL v4, the scores for the 12 domains were normally distributed; the mean values are shown in Table 5. Swallowing and chewing were the best scoring domains, with a mean score of 97.5 ± 8.7 and 95.8 ± 14.4, respectively; 11 out of the 12 patients gave responses for these domains with the best possible score of 100. The worst score was for anxiety, with a mean score of 70 ± 0.0; all 12 patients marked the box "I am anxious about my cancer" (score 70). When selecting the three most important domains, activity was considered by the patients to be the most important.

DISCUSSION

This study showed that ZI placed under guidance and immediately loaded with an obturator prosthesis had a high survival rate after a minimum period of 12 months. The overall implant survival rate of 91.7% is consistent with other studies in which ZI have been used to improve prosthetic management in head and neck cancer patients[13]. Compared to the use of ZI for prosthetic rehabilitation in patients with extreme resorption of the maxilla, with a mean survival rate of 96.5%, the rate in the current study is slightly lower[14].

In terms of compromising the soft tissues, the placement of endosseous implants has a less invasive impact when compared to ZI. Endosseous implant placement should be considered when the bone volume in the native maxilla remains sufficient after a maxillectomy. In this study, the residual maxillary bone volume in two of the edentulous patients was good and it was possible to place endosseous implants in the contralateral maxilla instead of ZI. However, the combination of ZI and endosseous implants had drawbacks regarding the time to prosthetic delivery. Compared to the edentulous patients rehabilitated with four ZI, there was a delay of 3 months for installation of the definitive implant-retained obturator prosthesis in these patients. Despite needing additional prosthodontic appointments, as well as interim obturator prostheses, the final prosthetic result was within expectations (Figs. 1 and 2).

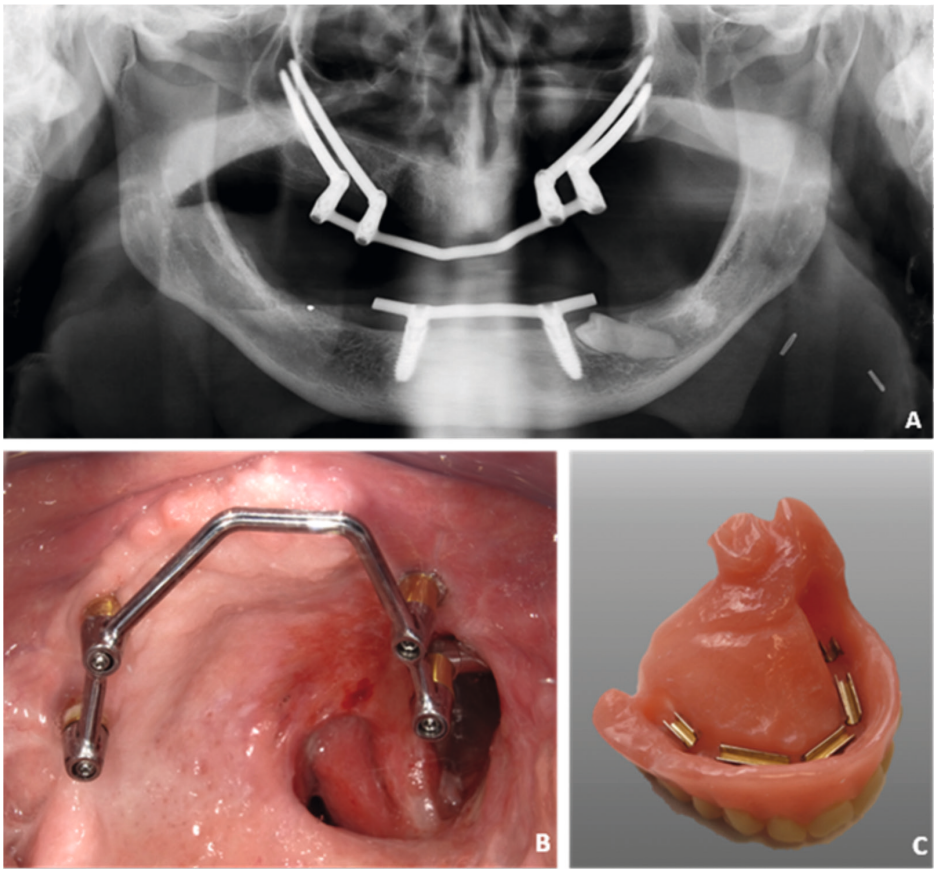


Figure 1. **(A)** Panoramic radiograph and **(B)** intraoral views of a patient with a U-shapedcross-arch suprastructure on four zygomatic oncology implants, two positioned in the defect and two on the contralateral side. **(C)** The matching definitive implant-retained obturator prosthesis.

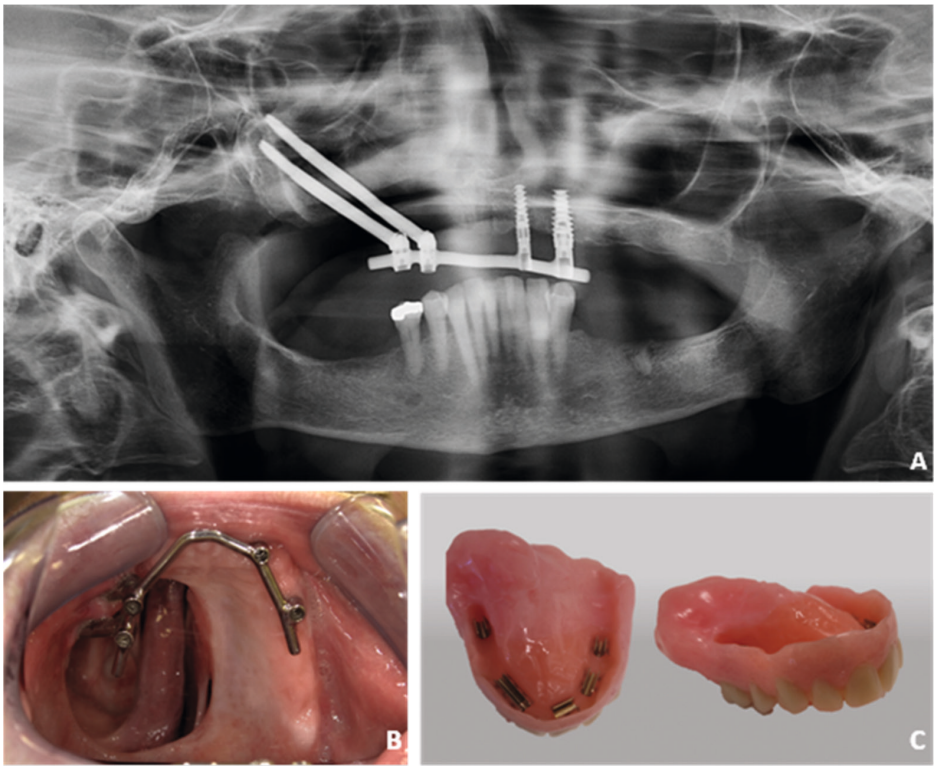


Figure 2. (A) Panoramic radiograph and **(B)** intraoral views of a patient with a U-shaped cross-arch suprastructure on two zygomatic oncology implants positioned in the defect and two endosseous implants in the maxilla on the contralateral side. **(C)** The definitive implant-retained obturator prosthesis.

Implant and prosthetic success are not the only outcomes that should be evaluated in terms of treatment success. The importance of patient quality of life after cancer treatment has become more significant over the past decade[15]. Rehabilitation with the definitive implant-retained obturator prosthesis resulted in favourable patient-reported outcomes, as shown by the results for the UW-QOL v4. Overall quality of life several months after the treatment was good or very good. Regarding the LORQv3, the worst scores were obtained for the domain 'salivation' and for the question on problems with mouth opening. The patients who reported that they often or always experienced problems with these items had all undergone postoperative radiotherapy. Thus irradiation leads to a higher risk of impaired oral function, specifically in relation to mouth dryness and trismus[16].

Caution should be taken with implant placement when radiation is part of the treatment plan[17]. Metallic artefacts, such as in ZI, still pose a major challenge for radiation therapy, as they impact the target volumes, type of radiation, and dose of radiation[18]. In the case of maxillary tumours, the zygomatic bodies are often subjected to irradiation,

which therefore reduces the osseointegration potential. Although several papers have reported significant ZI failure rates of up to 31% in irradiated patients[19–21], it appears that the specific radiotherapy dose to the zygomatic bone in maxillary tumour patients has thus far not been specifically analysed or correlated with ZI failure. In this study, the radiation dose for each ZI was visualized. Implant bed-specific dosages differ significantly depending on the location of the primary tumour[22] (Figure 3), and more than 55 Gy seems to be a risk factor for peri-implant bone resorption and ZI loss.

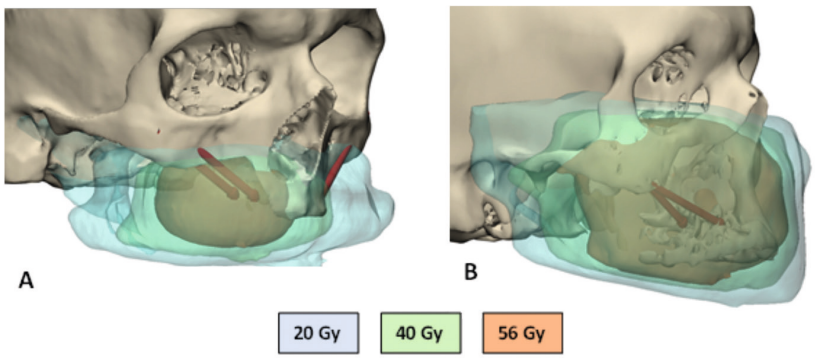


Figure 3. Images **A** and **B** show accurate radiotherapy dose distributions **(orange 56 Gy, green 40 Gy, and blue 20 Gy)** for the primary tumour site, zygomatic bone, and zygomatic implants. Comparison of images A and B shows the significant differences in implant bed-specific dosages based on the location of the primary tumour.

The implant survival rates in this study with follow-up of 1–3 years are favourable, and the patients reported favourable functional outcomes, which suggests that this a worthwhile therapeutic solution. Although the integration of the ZI was successful in the irradiated patients, there was a trend of higher ZI implant failure in the group of patients who underwent postoperative radiotherapy.

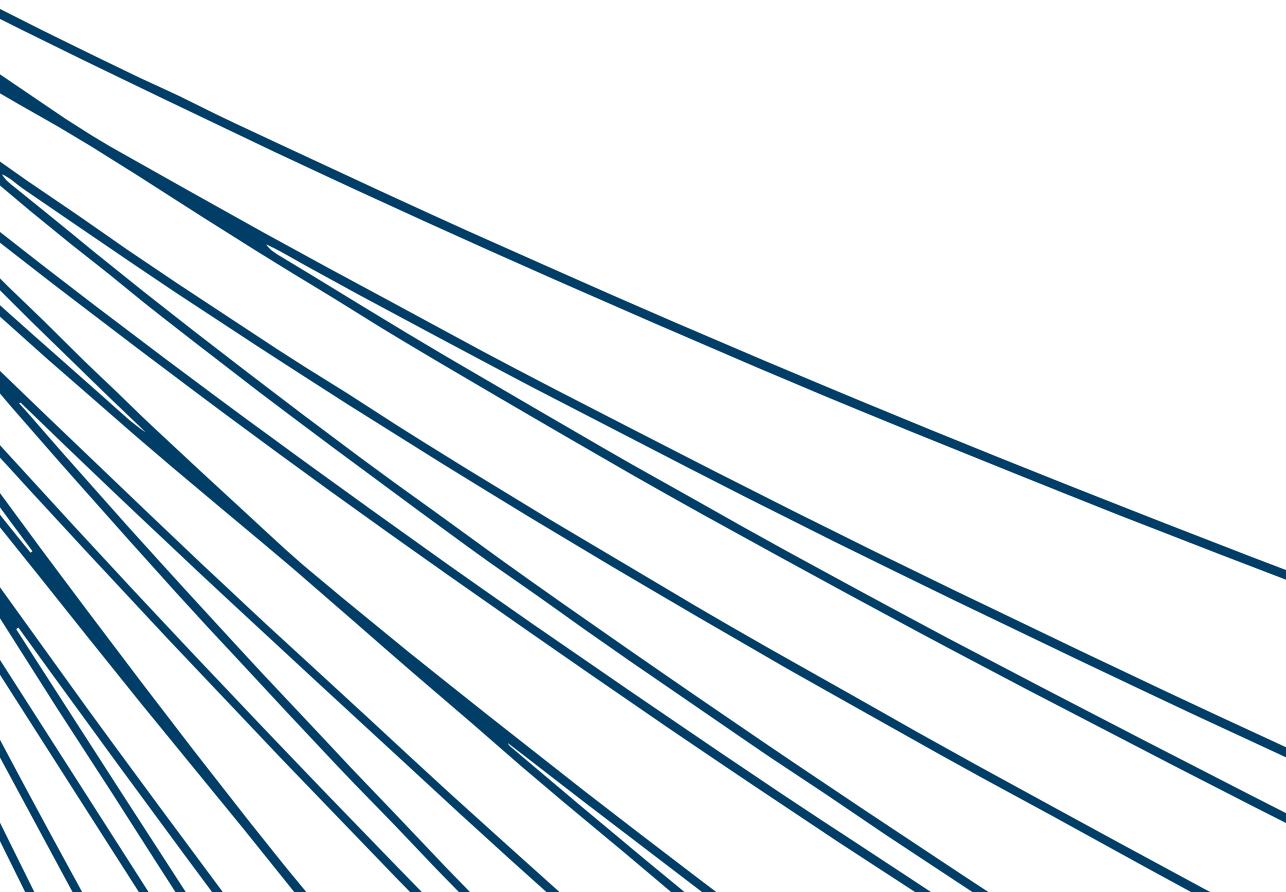
A limitation of this study is the sample size of head and neck cancer patients who received ZI; this may limit the generalizability of the findings. Long-term, prospective, longitudinal research involving a larger cohort of participants is required. Additionally, there is a need for an increased dataset that includes information on radiotherapy fields in relation to ZI.

The position and size of the tumour have a direct impact on the radiation dose to the zygoma bone. Greater insight into these relationships would contribute to a better understanding of the expected survival rate of zygomatic implants in patients who need adjuvant radiotherapy. Good dialogue and exchange of information between the surgical team and radiation oncologists is important and could contribute to the long-term success of zygomatic implant-based rehabilitation in head and neck cancer patients.

REFERENCES

1. Vero N, Mishra N, Singh BP, Singh K, Jurel SK, Kumar V. Assessment of swallowing and masticatory performance in obturator wearers: a clinical study. J Adv Prosthodont 2015: 7: 8–14. doi: 10.4047/jap.2015.7.1.8
2. Vissink A, Jansma J, Spijkervet FKL, Burlage FR, Coppes RP. Oral sequelae of head and neck radiotherapy. Crit Rev Oral Biol Med 2003: 14: 199–212. doi: 10.1177/154411130301400305
3. Glas HH, Vosselman N, de Visscher SAHJ. The use of 3D virtual surgical planning and computer aided design in reconstruction of maxillary surgical defects. Curr Opin Otolaryngol Head Neck Surg 2020: 28: 122–128. doi: 10.1097/MOO.0000000000000618
4. Witjes MJH, Schepers RH, Kraeima J. Impact of 3D virtual planning on reconstruction of mandibular and maxillary surgical defects in head and neck oncology. Curr Opin Otolaryngol Head Neck Surg 2018: 108–114. doi: 10.1097/MOO.0000000000000437
5. Boyes-Varley JG, Howes DG, Davidge-Pitts KD, Brånemark I, McAlpine JA. A protocol for maxillary reconstruction following oncology resection using zygomatic implants. Int J Prosthodont 2007: 20: 521–531.
6. Vosselman N, Glas HH, de Visscher SAHJ, Kraeima J, Merema BJ, Reintsema H, Raghoebar GM, Witjes MJH. Immediate implant-retained prosthetic obturation after maxillectomy based on zygomatic implant placement by 3D-guided surgery: a cadaver study. Int J Implant Dent 2021: 7: 54. doi: 10.1186/s40729-021-00335-w
7. Vosselman N, Glas HH, Merema BJ, Kraeima J, Reintsema H, Raghoebar GM, Witjes MJH, de Visscher SAHJ. Three-dimensional guided zygomatic implant placement after maxillectomy. J Pers Med 2022: 12: 588. doi: 10.3390/jpm12040588
8. Rogers SN, Gwanne S, Lowe D, Humphris G, Yueh B, Weymuller EA. The addition of mood and anxiety domains to the University of Washington quality of life scale. Head Neck 2002: 24: 521–529. doi: 10.1002/hed.10106
9. Laraway DC, Rogers SN. A structured review of journal articles reporting outcomes using the University of Washington Quality of Life Scale. Br J Oral Maxillofac Surg 2012: 50: 122–131. doi: 10.1016/j.bjoms.2010.12.005
10. Eekers DBP, Roelofs E, Jelen U, Kirk M, Granzier M, Ammazzalorso F, Ahn PH, Janssens GORJ, Hoebers FJP, Friedmann T, Solberg T, Walsh S, Troost EGC, Kaanders JHAM, Lambin P. Benefit of particle therapy in re-irradiation of head and neck patients. Results of a multicentric in silico ROCOCO trial. Radiother Oncol 2016: 121: 387–394. doi: 10.1016/j.radonc.2016.08.020
11. Garg S, Kilburn JM, Lucas JT Jr, Randolph D, Urbanic JJ, Hinson WH, Kearns WT, Porosnicu M, Greven K. Reirradiation for second primary or recurrent cancers of the head and neck: dosimetric and outcome analysis. Head Neck 2016: 38(Suppl 1): E961–E969. doi: 10.1002/hed.24136
12. Buurman DJM, Speksnijder CM, Engelen BHBT, Kessler P. Masticatory performance and oral health-related quality of life in edentulous maxillectomy patients: a cross-sectional study to compare implant-supported obturators and conventional obturators. Clin Oral Implants Res 2020: 31: 405–406. doi: 10.1111/clr.13577
13. Butterworth CJ. Primary vs secondary zygomatic implant placement in patients with head and neck cancer—a 10-year prospective study. Head Neck 2019: 41: 1687–1695. doi: 10.1002/hed.25645

14. Moraschini V, de Queiroz TR, Sartoretto SC, de Almeida DCF, Calasans-Maia MD, Louro RS. Survival and complications of zygomatic implants compared to conventional implants reported in longitudinal studies with a follow-up period of at least 5 years: a systematic review and meta-analysis. Clin Implant Dent Relat Res 2023: 25: 177–189. doi: 10.1111/cid.13153
15. Haraldstad K, Wahl A, Andenæs R, Andersen JR, Andersen MH, Beisland E, Borge CR, Engebretsen E, Eisemann M, Halvorsrud L, Hanssen TA, Haugstvedt A, Haugland T, Johansen VA, Larsen MH, Løvereide L, Løyland B, Kvarme LG, Moons P, Norekvål TM, Ribu L, Rohde GE, Urstad KH, Helseth S; LIVSFORSK network. A systematic review of quality of life research in medicine and health sciences. Qual Life Res 2019: 28: 2641–2650. doi: 10.1007/s11136-019-02214-9
16. Carneiro-Neto JN, de-Menezes JD da S, Moura LB, Massucato EMS, de-Andrade CR. Protocols for management of oral complications of chemotherapy and/or radiotherapy for oral cancer: systematic review and meta-analysis current. Med Oral Patol Oral Cir Bucal 2017: 22: e15–e23. doi: 10.4317/MEDORAL.21314
17. Petrovic I, Rosen EB, Matros E, Huryn JM, Shah JP. Oral rehabilitation of the cancer patient: a formidable challenge. J Surg Oncol 2018: 117: 1729–1735. doi: 10.1002/JSO.25075
18. Lommen J, Schorn L, Sproll C, Kerkfeld V, Aksu A, Reinauer F, Kübler NR, Budach W, Rana M, Tamaskovics B. Metallic artifact reduction in midfacial CT scans using patient-specific polymer implants enhances image quality. J Pers Med 2023: 13: 236. doi: 10.3390/jpm13020236
19. Schmidt BL, Pogrel MA, Young CW, Sharma A. Reconstruction of extensive maxillary defects using zygomaticus implants. J Oral Maxillofac Surg 2004: 62(Suppl 2): 82–89. doi: 10.1016/j.joms.2004.06.027
20. Hirsch DL, Howell KL, Levine JP. A novel approach to palatomaxillary reconstruction: use of radial forearm free tissue transfer combined with zygomaticus implants. J Oral Maxillofac Surg 2009: 67: 2466–2472. doi: 10.1016/j.joms.2009.04.062
21. Hackett S, El-Wazani B, Butterworth C. Zygomatic implant-based rehabilitation for patients with maxillary and mid-facial oncology defects: a review. Oral Dis 2021: 27: 27–41. doi: 10.1111/ODI.13305
22. Li J, Feng K, Ye L, Liu Y, Sun Y, Wu Y. Influence of radiotherapy on dental implants placed in individuals before diagnosed with head and neck cancer: focus on implant-bed-specific radiation dosage. Clin Oral Investig 2022: 26: 5915–5922. doi: 10.1007/S00784-022-04549-Z



CHAPTER 6.1

Patient-specific sub-periosteal zygoma implant for prosthetic rehabilitation of large maxillary defects after oncological resection

N. Vosselman, B. J. Merema, K. P. Schepman, G. M. Raghoebar

This chapter is an edited version of the manuscript: Patient-specific sub-periosteal zygoma implant for prosthetic rehabilitation of large maxillary defects after oncological resection

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ABSTRACT

A 74-year-old woman needed a subtotal bilateral maxillectomy due to squamous cell carcinoma of the palate. Immediate and secondary reconstruction of the defect was not feasible, so the defect was closed with an obturator prosthesis wired to the zygoma complex. To improve the patient's severely impaired speech and swallowing, a patient-specific sub-periosteal implant (psSPI) was designed that matched the remnants of the zygoma complex. First, the patient's post-surgical anatomy was visualized through segmentation of the pre- and post-maxillectomy computed tomography data. Next, based on the data, a customized zygoma-supported framework was designed to support the obturator prosthesis. Surgical guides for intraoperative navigation were designed and three-dimensionally printed, along with an obturator prosthesis to fit the planned outcome situation. The preoperatively manufactured psSPI and obturator prosthesis matched the intraoperative conditions. The postoperative results were favourable; within a week after surgery the patient could speak and swallow normally without nasal leakage. No problems occurred during follow-up. These results indicate that a psSPI-retained prosthesis can be considered for the restoration of speech and oral functioning in cases with a largely compromised maxillary bone anatomy, accompanied by impaired oral functioning and no feasible conventional reconstruction options.

INTRODUCTION

The rehabilitation of large maxillary defects resulting from ablative tumour surgery is a reconstructive challenge. To restore oral function and preserve psychological wellbeing, reconstruction can be achieved through conventional approaches, such as closure of the maxillary defect by microvascular free flap surgery or prosthetic obturation[1,2]. In both treatment options, osseointegrated implants can enhance the stability and retention of the prosthesis. Occasionally, zygoma implants cannot provide satisfactory implant anchorage due to insufficient bone volume, but these patients still need an adequate implant-retained obturator prosthesis. Otherwise, oral functions like mastication, swallowing, and speech remain severely impaired. Recently, Mommaerts introduced an innovative concept for an additivemanufactured sub-periosteal jaw implant that uses modern computer-aided design and manufacturing (CAD/CAM) technology[3]. His approach offers an alternative implant option for patients with extreme jaw bone atrophy. He also suggested that this technique could be used for the rehabilitation of extended post-resection defects. However, tissue conditions after oncological resection and postoperative radiotherapy require a specific design due to the lack of sufficient bone to support even a subperiosteal implant.

Case presentation

A 74-year-old female patient was treated with a subtotal bilateral maxillectomy due to squamous cell carcinoma of the palate. Seven years before, the patient had received primary radiotherapy (cumulative dose 60 Gy) for squamous cell carcinoma of the floor of the mouth. To restore speech and swallowing, the resulting maxillary defect was obturated perioperatively with an obturator prosthesis. The obturator was fixed bilaterally with wires around the zygomatic arches. However, the patient developed postoperative swallowing and speech problems due to loosening of the prosthesis. Moreover, the patient experienced increasing problems with cleaning the prosthesis, which resulted in halitosis and a severe negative impact on quality of life. Surgical restoration of the maxillary defect was not feasible due to the patient's poor medical condition, in particular compromised vascularization. As insufficient bone support was present for placement of dental or zygomatic implants to support a prosthesis, a patient-specific sub-periosteal zygoma implant (psSPI) was developed. This psSPI was provided with an implant-supported obturator prosthesis, which was retained to the framework with anchor attachments (the Swiss Dalbo-System) (Figure 1).

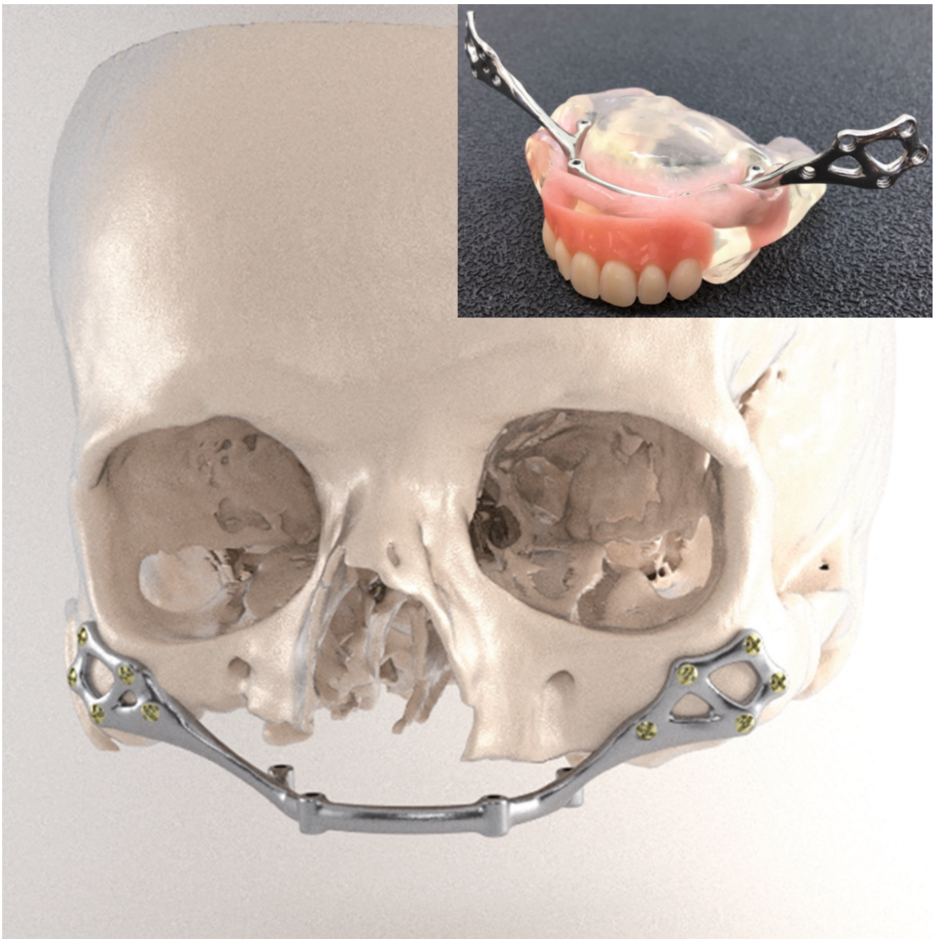


Figure 1. The additive manufactured patient-specific sub-periosteal implant (psSPI).
Rendered three-dimensional model of the patient showing the implant matching the anatomical geometry of the zygoma remnants. Only the extensions of the two connectors on which the U-shaped framework is situated penetrate the oral mucosa, which makes cleaning the psSPI easier. Note the insert showing the additive manufactured psSPI with the implant-retained obturator prosthesis in place.

MATERIALS AND METHODS

Design

Prior to ablative oncological surgery, the patient's functional prosthesis was digitized through three-dimensional (3D) optical surface scanning. This virtual prosthesis model was matched to 3D models of the patient's anatomy – the starting point for the psSPI design. The planned position of the prosthetic dental arch was determinative for the

location of the four anchor attachments. On these attachments, a U-shaped framework was designed to support the obturator prosthesis. After designing the basal structure of the psSPI using CAD techniques, two connectors were designed to fix the psSPI to the zygomatic bone. As part of the design, the preferred screw and retention positions were taken into consideration, thereby circumventing the irradiated areas of the remaining maxillary and zygomatic bone. Only the extensions of the two connectors on which the U-shaped framework was situated penetrated the oral mucosa, making it easier to clean the psSPI. Materialise 3-matic version 11.0 (Materialise, Leuven, Belgium) and SolidWorks Professional 2017 (Dassault Systèmes, SolidWorks Corp., Waltham, MA, USA) software was used to design the psSPI. In addition, a patient-specific surgical drill guide was designed to translate the 3D plan to the surgical procedure. Furthermore, based on the 3D design, a temporary obturator prosthesis with four Dalbo attachments was manufactured prior to the surgical procedure. The psSPI was manufactured by Witec (Witec Fijnmechanische Techniek BV, Ter Apel, the Netherlands) from medical-grade titanium alloy (Ti–6Al– 4V). Threads matching 2.0-mm locking screws (KLS Martin, Tuttlingen, Germany) were added to the screw holes.

Surgical procedure

Under general anaesthesia, a full-thickness flap was raised to expose the remnants of the zygomatic bone. The stability and fit of the bone-supported surgical template was then verified. Guided by the surgical template, the holes for the locking screws were drilled. To align the implant to the drilled holes, the implant was positioned using stainless steel (316L) pins prior to screw insertion. This approach resulted in precise alignment of the psSPI with the underlying zygomatic bone. The psSPI was fixed with the locking screws. Next, the fit of the obturator prosthesis on the U-shaped part of the psSPI was checked, and the mucoperiosteal flap was repositioned and sutured (Vicryl 3–0; Johnson & Johnson, Brunswick, NJ, USA). Finally, the implant-retained obturator prosthesis was placed by the prosthodontist. Only minor adjustments had to be made to the base of the prosthesis to obtain optimal obturation of the defect.

RESULTS

Recovery from the procedure was uneventful. Obturation of the defect was satisfactory. Within 1 week, speech performance was favourable and there was no nasal leakage during swallowing. Two weeks after surgery, the sutures were removed. Oral inspection showed no signs of inflammation or dehiscent bone, and an uncomplicated adaptation of the soft tissues around the arms of the psSPI was apparent. During the next 6 months (final follow-up), the soft tissue remained in a good condition (Figure 2) and the obturator prosthesis functioned well. The patient felt confident with wearing the prosthesis and was very satisfied. She spontaneously reported recovery of her social life as a major achievement.

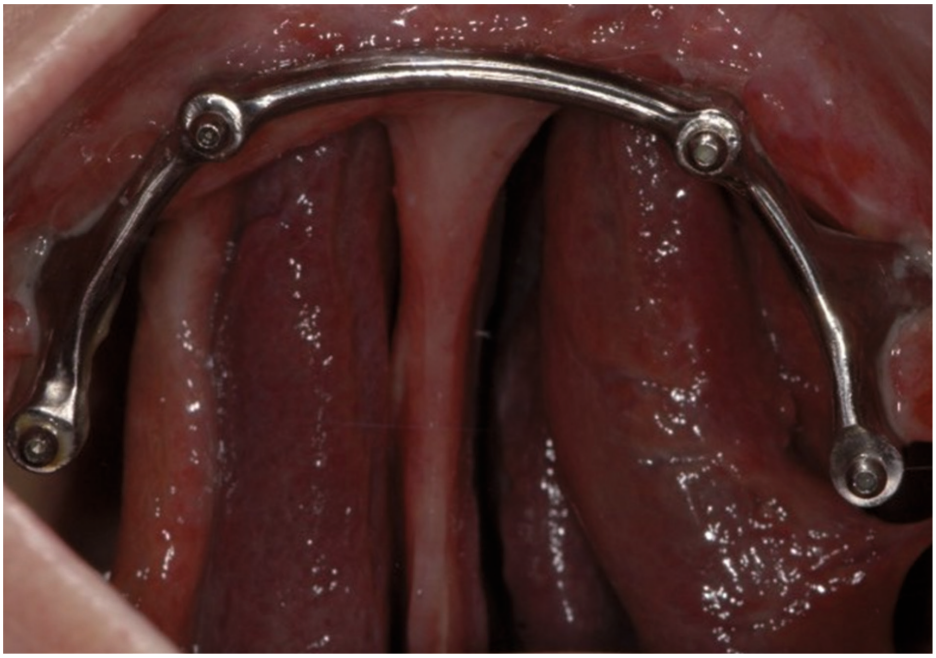


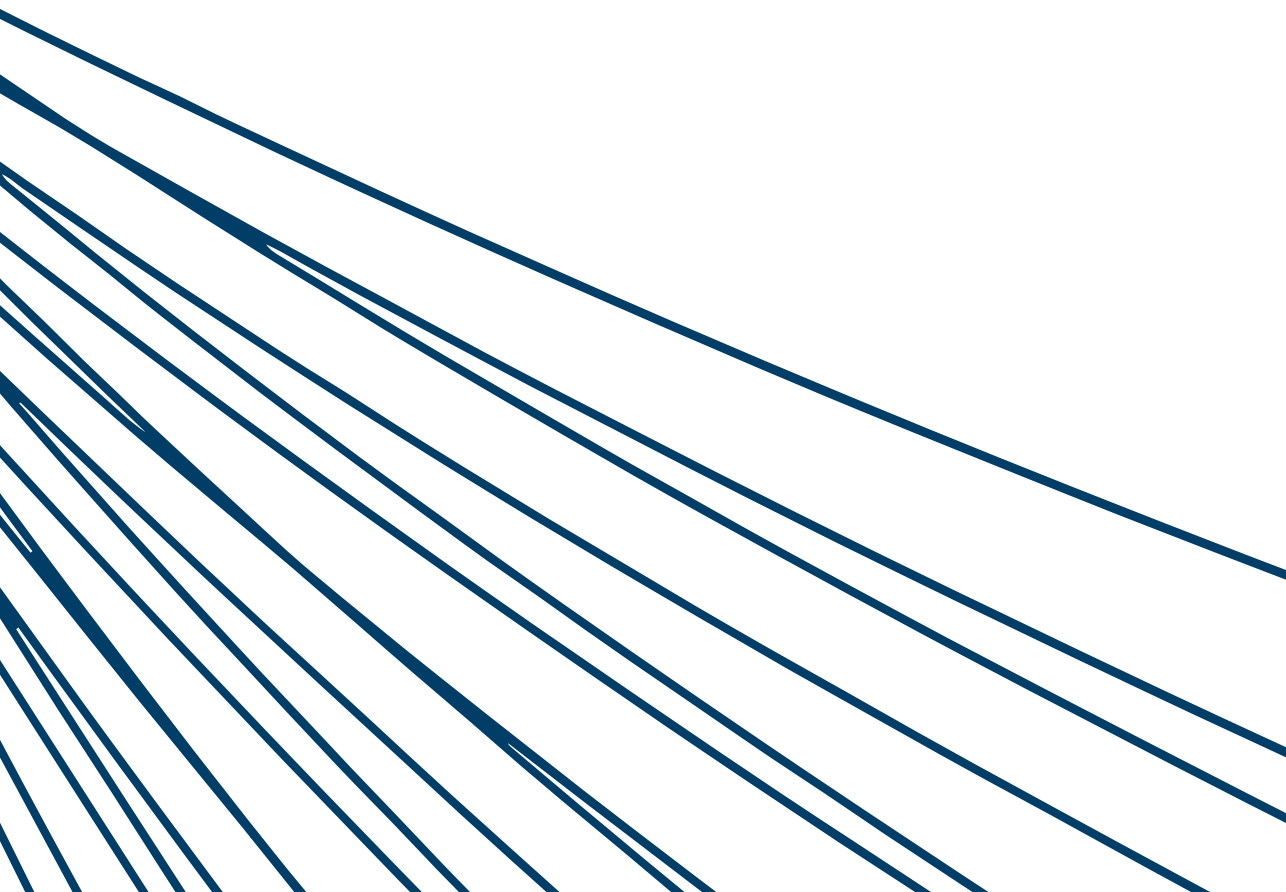
Figure 2. Clinical view of the patient-specific sub-periosteal implant (psSPI). Intraoral view 6 months after surgery showing the large oronasal defect, the psSPI, and healthy peri-implant tissues.

DISCUSSION

This customized, prosthesis-driven implant design offers an alternative approach for the rehabilitation of large maxillary defects in cases where immediate or delayed surgical reconstruction is not feasible and oral functioning and oral cleaning are impaired. The easily removed obturator prosthesis is a major benefit. This allows examination of the tissues and enables patients to maintain and clean the prosthesis and peri-implant tissues themselves. Although sub-periosteal implants have fallen into disuse due to severe inflammation and inappropriate or non-rigid fixation[4], the design used here enabled us to provide a solution for a patient without other treatment options, resolving her poor oral functioning and impaired oral health-related quality of life. Furthermore, titanium is more tissue-friendly than the chrome–cobalt alloys that were used in the previous sub-periosteal implants. As it had to be determined beforehand whether the psSPI would be able to withstand chewing forces, a finite elements analysis was performed to assess implant strength and fatigue resistance (data not shown). This analysis revealed that the psSPI could easily bear occlusal loading. We therefore recommend the digitally planned psSPI to provide effective support for obturation of large maxillary defects in patients for whom a direct or delayed restoration of the defect is not feasible.

REFERENCES

1. Chigurupati R, Aloor N, Salas R, Schmidt BL. Quality of life after maxillectomy and prosthetic obturator rehabilitation. J Oral Maxillofac Surg 2013: 71: 1471–1483.
2. Kornblith AB, Zlotolow IM, Gooen J, Huryn JM, Lerner T, Strong EW, Shah JP, Spiro RH, Holland JC. Quality of life of maxillectomy patients using an obturator prosthesis. Head Neck 1996: 18: 323–334.
3. Mommaerts MY. Additively manufactured sub-periosteal jaw implants. Int J Oral Maxillofac Surg 2017: 7: 938–940.
4. Schou S, Pallesen L, Hjørting-Hansen E, Pedersen CS, Fibaek B. A 41-year history of a mandibular subperiosteal implant. Clin Oral Implants Res 2000: 11: 171–178.



CHAPTER 6.2

Differences in approach for sub-periosteal zygoma implant designs

N. Vosselman, B.J. Merema, G.M.Raghoebar, A. Vissink

This chapter is an edited version of the manuscript: Differences in approach for sub-periosteal zygoma implant designs

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We agree that maximal benefit should be taken from existing anatomical structures. However, in oncology cases such as the one we reported, with an extensive maxillary defect due to ablative surgery, there is a lack of such anatomical structures (Figure 1). Moreover, most patients with large maxillary defects have been subjected to postoperative radiotherapy, which further challenges implant placement because of the inherent risk of developing osteoradionecrosis.

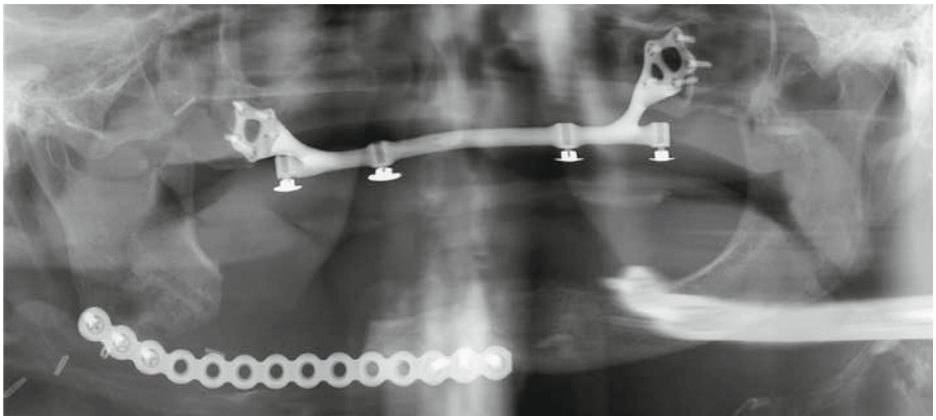


Figure 1. Orthopantomogram showing extensive maxillary defects due to ablative surgery and lack of anatomical structures to allow vertical support. To deal with the lack of anatomical support and compromised tissues, a finite element analysis was performed to design a slim, minimal voluminous sub-periosteal zygoma implant (psSPI) that can be reliably fixed to the remaining zygomatic bone.

In the case presented, the volume, surface, and amount of permucosal connection of the sub-periosteal zygoma implant design was not only prosthetic driven, but also accounted for the minimal available bone remnants after a high resected maxillectomy and the fragility of the irradiated tissues. To deal with such a lack of anatomical support and compromised tissues, as well as our endeavours towards a slimmer and less voluminous single sub-periosteal zygoma implant (psSPI) design, we performed a finite element analysis (FEA) to ensure stable fixation of the psSPI to the available zygomatic bone. In addition, we applied locking screws to obtain en-bloc stabilization. This FEA approach indicated that no failure of the designed implant will occur within 1.75 × 107 loading repetitions, reflecting 25 years in vivo[2] . Matching an 18-month follow-up computed tomography (CT) scan to the CT scan obtained directly postoperative revealed a maximum measured deviation of 0.44 mm (Figure 2). This deviation includes errors of both CT scans (0.4 mm and 0.6 mm thickness), segmentations, and superimposition of the models.

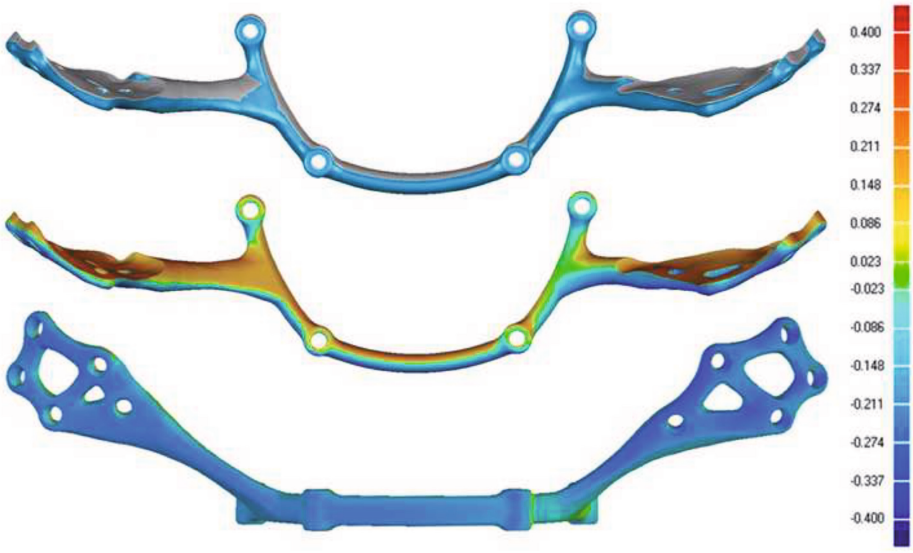


Figure 2. Segmentations of the patient's skull derived from the direct and 18 months postoperative CT scans were aligned using the Best Fit Alignment tool in Geomagic Studio 5 2012 (3D Systems, Rock Hill, SC, USA) software whilst moving along an identical CAD file of the implant. Note the nearly perfect alignment of direct postoperative (grey) and 18 month follow-up (blue) implant position. This nearly perfect alignment indicates good clinical implant stability.

While Mommaerts used sandblasting, acid-etching, and plasma surface activation for the surface of his implant[3] , we opted for high-gloss, polished, milled titanium in order to ease intraoral cleaning. Moreover, as we used locking screws, we did not need osseointegration-promoting surface modifications. With regard to Mommaert's concerns with not using disconnectable posts, it is our opinion that the use of disconnectable posts would be of no added benefit and would even counteract the slim and less voluminous design we prefer for oncological cases. The latter because caution has to be taken in oncology cases when it comes to penetration of the compromised soft tissues due to scarring and/or radiation injury. Therefore, we made the deliberate decision to minimize the amount of permucosal connection and thereby reduce the risk of peri-implant mucositis developing. Furthermore, the FEA showed that there was no need for additional posts to increase vertical support, which is a great achievement in oncology cases in which the implant is placed in highly irradiated tissues. In the event of peri-implantitis occurring, there is a very high risk of developing osteoradionecrosis. The occurrence of osteoradionecrosis in our patient case would result in loss of the implant, with likely substantial bone loss and a maxillary defect that would be very difficult to treat. To safeguard a good result, we have imposed strict hygiene recall appointments. Professional cleaning of the oral cavity and the implant during the recall visits, in addition to strict oral hygiene maintenance by the patient herself, will be of the utmost importance to prevent signs of inflammation and diagnose these early. Our

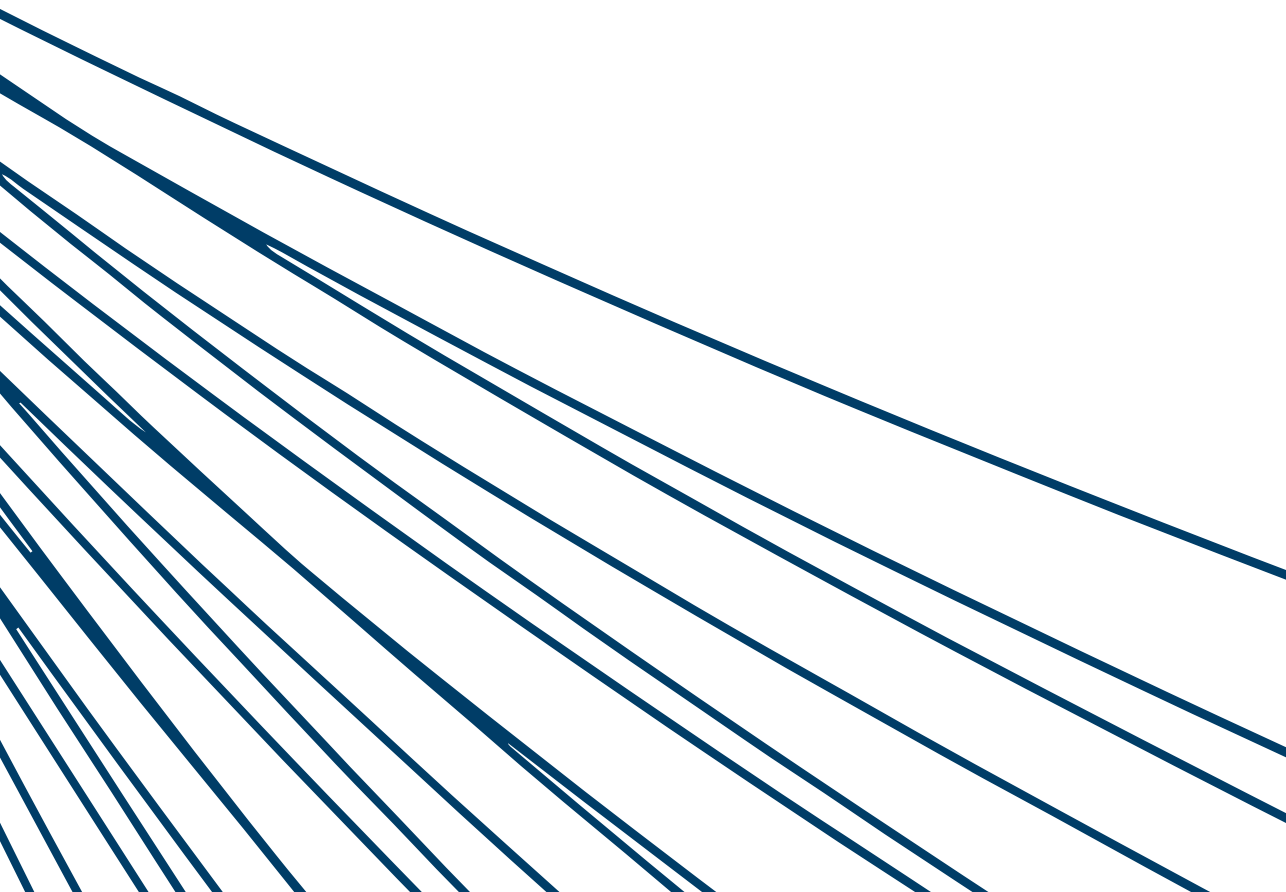
patient has reported no discomfort or pain. No signs of the development of peri-implant mucositis or peri-implantitis have been observed by the dentist or oral hygienists during the 18 months of follow-up to date since placement of the psSPI. The additively manufactured sub-periosteal jaw implant – AMSJI – developed by Mommaerts is a valid treatment option for excessive maxillary bone loss, poor bone quality, and maxillary pneumatization[3] . However for oncology cases, such as our case, an unmodified Mommaerts approach is not applicable, as that approach relies on vertical support and fixture on maxillary and palatal bone structures that are often no longer present.

REFERENCES

1 Vosselman N, Merema BJ, Schepman KP, Raghoebar GM. Patient-specific sub-periosteal zygoma implant for prosthetic rehabilitation of large maxillary defects after oncological resection. Int J Oral Maxillofac Surg 2019;48:115–7.

2 Gibbs CH, Lundeen HC. Jaw movements and forces during chewing and swallowing and their clinical significance. In: Lundeen HC, Gibbs CH, editors. Advances in occlusion. Boston: John Wright PSG Inc.; 1982 .p. 2–32.

3 Mommaerts MY. Evolutionary steps in the design and biofunctionalization of the additively manufactured sub-periosteal jaw implant 'AMSJI' for the maxilla. Int J Oral Maxillofac Surg 2019;48:108–14.



CHAPTER 7

General discussion

GENERAL DISCUSSION

This thesis demonstrates the need for integrating 3D VSP and computer-aided design (CAD) in complex prosthodontic rehabilitation. In chapter 2, the current challenges and new developments in literature on prosthodontic management of head and neck cancer patients is described. A synergy of various digital workflows regarding treatment and rehabilitation contribute to a better prosthodontic outcome and thereby enhance the well-being and comfort of patients undergoing maxillary resections. By obtaining a three-dimensional understanding of resection planes prior to surgery[1,2], valuable insights into the expected dimensions of the post-resection defects is gain. This, in turn, enables to digitally design and fabricate a surgical obturator prosthesis (figure 1A-F) before the ablative surgery, ensuring a precise fit with only minimal per-operative adjustments required. In the literature a limited number of case reports and series on this subject is reported[3-6]. Although studies comparing digital and conventional workflows are still lacking, the utilization of CAD-CAM obturator prostheses has shown promising outcomes in terms of improved prosthetic base and obturator part fit. Additionally, these prostheses, whether printed or milled, offer the advantage of reduced weight due to differences in material characteristics, thereby enhancing the effectiveness and comfort of head and neck cancer patients, especially during postoperative radiotherapy when dealing with radiotherapy-induced mucositis. It should be noted that the 2017 amendment to the Medical Device Regulations (MDR) in the European Union allows in-house 3D printing of custom medical devices like obturators, but strict adherence to guidelines is required[7]. This necessitates expertise in regulatory compliance and thorough documentation of processes. Continuous training is essential to stay updated on regulations. In-house 3D printing offers possibilities, but strict compliance with regulations is vital for patient safety and MDR adherence.

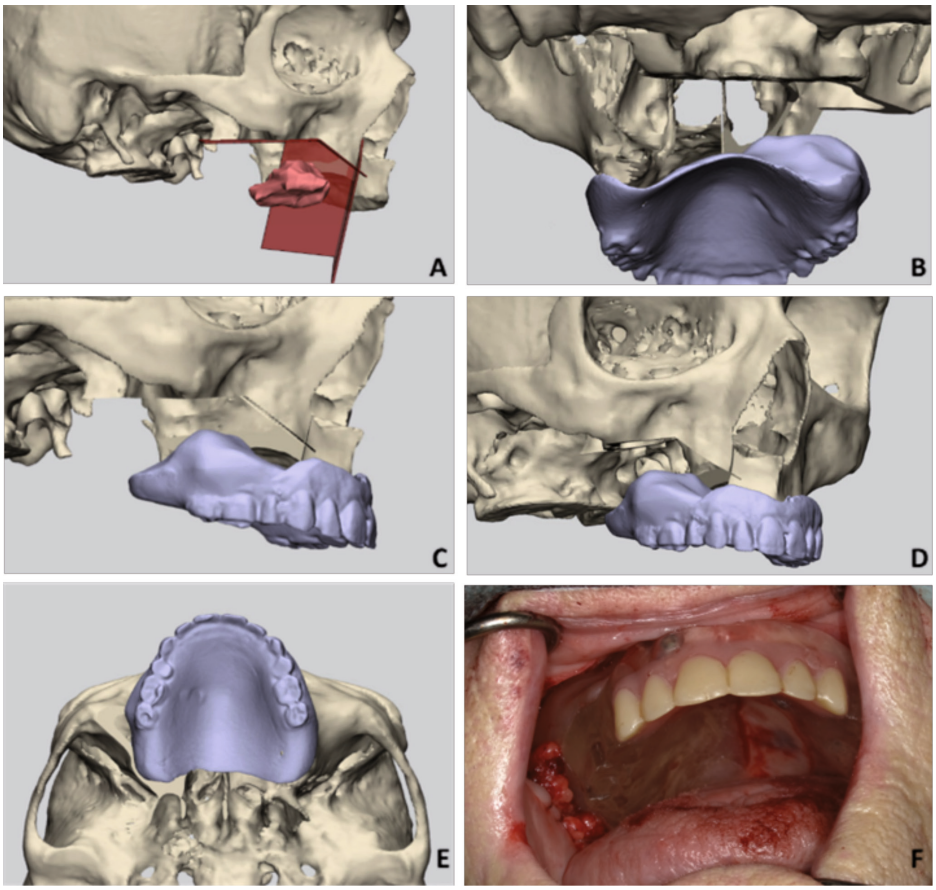


Figure 1A-F. Digital workflow for an obturator prosthesis. **A**. osteotomy planes and tumour visualisation. **B-E**. obturator design based on planned maxillary resection. **E**. peroperative view of obturator prosthesis.

Dental implants have shown to be a great asset to support maxillary prosthodontic rehabilitation in head and neck cancer patients[8-10], particularly in edentulous cases with an extensive maxillary defect involved implant support for prosthetic rehabilitation is desirable. The larger the defect, the more pronounced the benefit of implants is for the patients in terms of treatment outcome. Based on the scoping review on the optimal timing of implant placement in head and neck cancer patients (chapter 2), it was determined that the timing of implant placement had no impact on implant survival rates, regardless of whether they were placed during ablative surgery or after the completion of oncologic surgery. This finding aligns with our institution's standard practice, which favors implant placement during ablative surgery. As a result, the majority of implants are inserted at this stage, providing the advantages of avoiding the need for an additional surgery for the patient and potentially expediting the process of receiving their prosthesis[11]. Secondary placement is only performed

under specific circumstances, such as when patients were initially managed elsewhere without implants or when the loss of prior implant(s) compromises the retention of the prosthesis.

While there is often not enough bone volume for reliable implant placement, zygomatic implants can be used to improve the retention of the obturator prosthesis. However, placement of these implants after maxillectomy is challenging and is noted for its risk at implant failure, poor placement or positioning and mucosal complications[12-14]. The guided zygomatic implant placement technique introduced in this thesis (chapters 3,4 and 5) uses patient specific drill guides to transfer the preplanned implant positions towards the patients. This novel 3D workflow ensures safe and predictable zygomatic implant placement. However, from a prosthodontic standpoint, the transcendental step in the 3D workflow is the ability to safeguard optimal positioning of the implant heads and create a matching 3D-designed and milled obturator prosthesis (figure 2 A-D). The ability to immediately fixate the obturator to the guided placed zygomatic implants in one procedure with ablative surgery is a game changer in terms of immediate prosthodontic rehabilitation and is currently a proven method. Chapter 5 shows for this technique favorable implant survival rates up to three years post-treatment. However, irradiated patients showed a noticeable trend of higher implant failure (non-radiated patients 100%, while in irradiated patients 85%), influenced by tumour location and size, impacting radiation dose on the zygomatic bone.

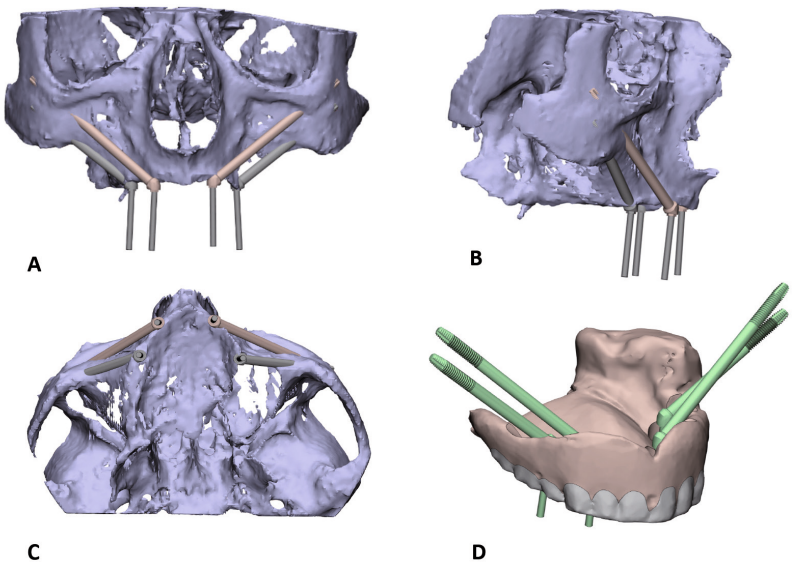


Figure 2A-D. A-C. prosthetically driven virtual implant planning of zygomatic oncology implants that places the implant heads in a parallel and prosthodontic favorable position. **D**. the matching digital designed obturtor prosthesis.

Multidisciplinary team

In such combined surgical and prosthodontic 3D workflows, effective multidisciplinary collaboration is essential in order to meet the constraints in lead-time set by Dutch oncological regulations, which determine the timeframe between oncological diagnosis and treatment. 3D virtual prosthodontic planning is the final step of the preoperative planning and manufacturing process of guides. Customized prostheses tailored to the patient's specific virtual maxillary resection can pose challenges in terms of time constraints. It is necessary to thoroughly review and reach a consensus on the oncological surgical planning before initiating the virtual prosthetic planning, followed by the 3D printing of surgical guides and the milling of the prosthesis, all of which must be completed prior to the surgical procedure. While time pressure can be demanding for the team during the preoperative phase, in the long run, the utilization of 3D surgical and prosthodontic planning facilitates a reduction in the overall treatment duration and is believed to minimize the burden on patients compared to analogue prosthodontic rehabilitation techniques. It is to be expected that in the near future virtual techniques can reduce the lead-time of the aids and parts needed. A new wave of advancements like virtual, augmented reality and robotic surgery show promising results in accuracy[15-18]. Therefore, a possible next step towards an accurate surgical outcome might involve replacing printed guides by virtual techniques that allow the omission of physical 3D printed guides regarding the surgical procedure.

The implementation of our digital prosthodontic pathways for maxillary defect rehabilitation represents a significant advancement in head and neck cancer treatment. By leveraging 3D technology and personalized treatment planning, we aim to enhance the quality of life for patients undergoing maxillary resection. However, the patient still relies on the clinical skills of the maxillofacial prosthodontist within the context of modern healthcare. To implement 3D workflows in maxillary prosthetic rehabilitation for head and neck oncology patients, teams must be willing to work multidisciplinary and discuss and plan surgical treatment in alignment with potential prosthetic rehabilitation. The head and neck oncology team in Groningen has the privilege to collaborate with highly experienced technical physician specialists and design specialists from the 3D lab at the UMCG. Optimizing and initiating 3D workflows, and thus the completion of this thesis, could not be accomplished without this collaboration. At present, the ability to directly place implants as a team during oncological surgeries and/or to have a maxillofacial prosthodontist present during the surgical procedure for prosthodontic treatment is not yet implemented in all head and neck oncology centers. There is a general consensus about the importance of accessible innovative medical care for all patients, mandating medical institutions to exchange information and adopt new treatment methods as presented in this thesis. Uniform collaboration with a widely diversified surgical team in other clinics is indispensable to obtain data for further research and clinical studies to assess the long-term outcomes and efficacy of this approach. Consequently, the Department of Oral and Maxillofacial Surgery in

Groningen has already initiated courses for guided placement of zygomatic implants for multidisciplinary head and neck cancer teams.

Radiotherapy

As mentioned earlier, dental implants have the potential to enhance oral function recovery through the use of implant retained fixed or removable prostheses. With the increasing life expectancy of patients, it is crucial to prevent treatment-related harm that can significantly impact the quality of life and daily functioning of head and neck cancer (HNC) patients. The Normal Tissue Complication Probability (NTCP) model is widely employed in radiotherapy to predict the risk of complications in healthy tissues and organs resulting from radiation exposure[19]. This model aids in assessing potential side effects of radiotherapy and allows radiation therapists to plan treatments that optimize the dose to the target area while minimizing damage to surrounding healthy tissue. Organs at Risk (OARs) refers to healthy organs and tissues near the treatment area that are susceptible to radiation-induced damage. In the case of head and neck cancer patients, OARs encompass organs such as the brain, salivary glands, and thyroid glands, which are associated with various toxicities and symptoms including swallowing difficulties, salivary dysfunction, mucosal changes, speech impairments, pain, and general complaints. Although oral function-related complications are considered in the NTCP model, the dental implant site in the bone necessary for restoring oral function are not recognized as OARs. In our care path implant placement during the ablative surgery, aims to ease the prosthodontic rehabilitation after oncological treatment. The loss of dental implants in irradiated patients results significant consequences to wearability of a prosthesis and thereby impacting speech, chewing abilities, pain and significantly compromising quality of life. Placement of implants in second stage surgery after radiotherapy is usually not feasible in this high dose radiated patient group. Therefore, it is recommended to include dental implant sites as prioritized organs for sparing in relation to high-impact symptoms.

Future perspectives

The successful implementation of 3D workflows in maxillary prosthetic rehabilitation of head and neck oncology patients represents a notable achievement. However, the journey does not end here. Future research should focus on refining these workflows, prioritizing patient-centered care and fostering multidisciplinary collaboration. By doing so, we can continue to improve the quality of life and treatment outcomes for the head and neck cancer patient population.

1. The focus of next phase research in this field should be on resolving the issues of time constraints in the planning of head and neck oncology patients. In the Netherlands guidelines state that patients should be treated within 30 days after the primary visit. Therefore, studies should be initiated assessing whether replacing the printed guides by virtual techniques is an accurate and safe method that allows

the omission of physical medical guides regarding the surgical procedure. This most likely will reduce lead-time and thus reduce pressure on the planning. More time will be available to design an fabricate the obturator prosthesis, since this is the only medical device that needs to be brought to the operating theatre.

2. The data in this thesis is promising but is just phase I data. It is needed to both provide the long term data of this small cohort as well as to join with other centers to be able to perform multi center studies proving that indeed zygomatic implants placed at primary surgery with immediate loading with an obturator prosthesis is a favourable treatment option.
3. Multidisciplinary collaboration with radiotherapists during the preoperative virtual planning phase is needed to gain further insight into adapting radiation fields to implant reconstruction when feasible. A fully coordinated surgical, radiotherapeutic and prosthodontic plan is a future goal as this approach could greatly improve the quality of life for these patients.

Based on the studies in this thesis, the following conclusions can be drawn;

- Patients with maxillary cancer benefit from 3D workflows and this should be provided as standard care. In addition, it lowers the physical burden of patients due to a more efficient procedure and thereby reduces the necessary time for functional prosthodontic rehabilitation.
- Based on very promising treatment outcomes, guided placement of zygomatic implants for prosthodontic rehabilitation should be considered as a reliable rehabilitation treatment plan in case of large maxillary resections.
- Multidisciplinary collaboration should be further expanded, in particular aimed to incorporate radiotherapy planning prior to surgery. This approach can lead to significant improvement in rehabilitation outcomes and thus the quality of life for head and neck cancer patients.

REFERENCES

1. Kraeima J, Dorgelo B, Gulbitti HA, Steenbakkers RJHM, Schepman KP, Roodenburg JLN, Spijkervet FKL, Schepers RH, Witjes MJH. Multi-modality 3D mandibular resection planning in head and neck cancer using CT and MRI data fusion: A clinical series. Oral Oncol. 2018;81:22-28. doi: 10.1016/j.oraloncology.2018.03.013. Epub 2018 Apr 11. PMID: 29884410.
2. Kraeima, J.; Schepers, R.H.; van Ooijen, P.M. Integration of oncologic margins in three-dimensional virtual planning for head and neck surgery, including a validation of the software pathway. J. Craniomaxillofac. Surg. 2015, 8, 1374–1379.Kortes J., Dehnad H., Kotte ANT., Fennis WMM., Rosenberg AJWP. A novel digital workflow to manufacture personalized three-dimensional-printed hollow surgical obturators after maxillectomy. *Int J Oral Maxillofac Surg* 2018;**47**(9):1214–8. Doi: 10.1016/j.ijom.2018.03.015.
3. Rodney, J., & Chicchon, I. (2017). Digital Design and Fabrication of Surgical Obturators Based Only on Preoperative Computed Tomography Data. The International Journal of Prosthodontics, 30(2), 111-112. doi:10.11607/ijp.5066
4. Murat S., Gürbüz A., Kamburoğlu K. Fabrication of obturator prosthesis by fusing CBCT and digital impression data. *International Journal of Computerized Dentistry* 2018;**21**(4):335—344.
5. Tasopoulos T., Chatziemmanouil D., Karaiskou G., Kouveliotis G., Wang J., Zoidis P. Fabrication of a 3D-printed interim obturator prosthesis: A contemporary approach. *Journal of Prosthetic Dentistry* 2019;**121**(6):960–3. Doi: 10.1016/j.prosdent.2018.10.004.
6. Bartellas, M., Tibbo, J., Angel, D., Rideout, A., & Gillis, J. (2018). Three-Dimensional Printing: A Novel Approach to the Creation of Obturator Prostheses Following Palatal Resection for Malignant Palate Tumors. *The Journal of Craniofacial Surgery, 29*(1), e12-e15. doi:10.1097/SCS.0000000000003987
7. Goetze E., Zeller AN., Pabst A. Approaching 3D printing in oral and maxillofacial surgery - suggestions for structured clinical standards. *Oral Maxillofac Surg* 2024. Doi: 10.1007/S10006-024-01208-3.
8. Schoen PJ., Reintsema H., Bouma J., Roodenburg JLN., Vissink A., Raghoebar GM. Quality of life related to oral function in edentulous head and neck cancer patients posttreatment. *Int J Prosthodont* 2007;**20**(5):469–77.
9. Korfage A., Schoen PJ., Raghoebar GM., Roodenburg JLN., Vissink A., Reintsema H. Benefits of dental implants installed during ablative tumour surgery in oral cancer patients: A prospective 5-year clinical trial. *Clinical Oral Implants Research* 2010. Doi: 10.1111/j.1600-0501.2010.01930.x.
10. Said MM., Otomaru T., Sumita Y., Leung KCM., Khan Z., Taniguchi H. Systematic review of literature: functional outcomes of implant-prosthetic treatment in patients with surgical resection for oral cavity tumors. *J Investig Clin Dent* 2017;**8**(2). Doi: 10.1111/jicd.12207.
11. Chuka R., Abdullah W., Rieger J., Nayar S., Seikaly H., Osswald M., et al. Implant Utilization and Time to Prosthetic Rehabilitation in Conventional and Advanced Fibular Free Flap Reconstruction of the Maxilla and Mandible. *The International Journal of Prosthodontics* 2017;**30**(3):289–94. Doi: 10.11607/ijp.5161.
12. Hackett S., El-Wazani B., Butterworth C. Zygomatic implant-based rehabilitation for patients with maxillary and mid-facial oncology defects: A review. *Oral Dis* 2021;**27**(1):27–41. Doi: 10.1111/ODI.13305.

13. Kämmerer PW., Fan S., Aparicio C., Bedrossian E., Davó R., Morton D., et al. Evaluation of surgical techniques in survival rate and complications of zygomatic implants for the rehabilitation of the atrophic edentulous maxilla: a systematic review. *Int J Implant Dent* 2023;**9**(1):11. Doi: 10.1186/s40729-023-00478-y.

14. Al-Nawas B., Aghaloo T., Aparicio C., Bedrossian E., Brecht L., Brennand-Roper M., et al. ITI consensus report on zygomatic implants: indications, evaluation of surgical techniques and long-term treatment outcomes. *Int J Implant Dent* 2023;**9**(1):28. Doi: 10.1186/s40729-023-00489-9.

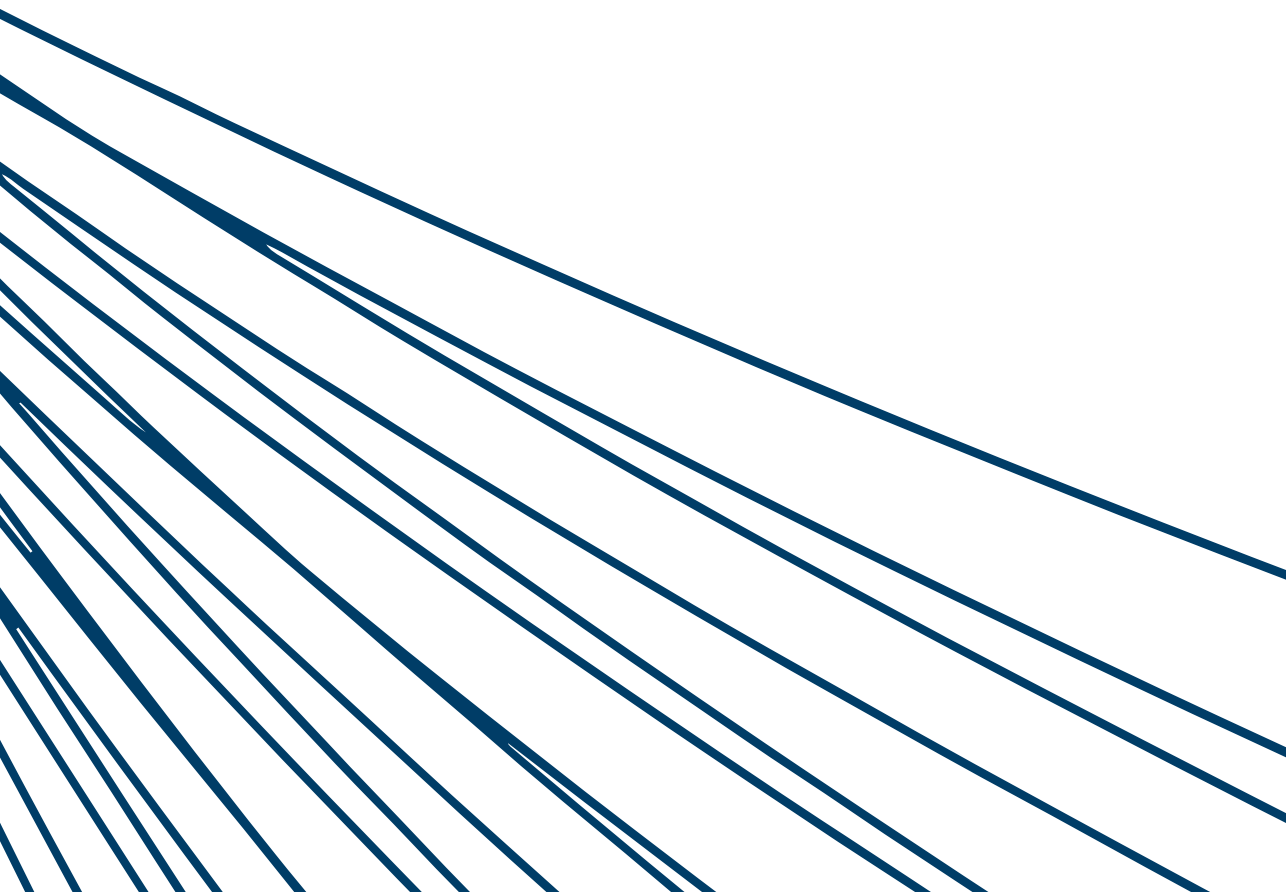
15. González Rueda JR., García Ávila I., de Paz Hermoso VM., Riad Deglow E., Zubizarreta-Macho Á., Pato Mourelo J., et al. Accuracy of a Computer-Aided Dynamic Navigation System in the Placement of Zygomatic Dental Implants: An In Vitro Study. *J Clin Med* 2022;**11**(5). Doi: 10.3390/jcm11051436.

16. Hung K-F., Wang F., Wang H-W., Zhou W-J., Huang W., Wu Y-Q. Accuracy of a real-time surgical navigation system for the placement of quad zygomatic implants in the severe atrophic maxilla: A pilot clinical study. *Clin Implant Dent Relat Res* 2017;**19**(3):458–65. Doi: 10.1111/cid.12475.

17. Hung K., Huang W., Wang F., Wu Y. Real-Time Surgical Navigation System for the Placement of Zygomatic Implants with Severe Bone Deficiency. *Int J Oral Maxillofac Implants* 2016;**31**(6):1444–9. Doi: 10.11607/jomi.5526.

18. Pellegrino G., Lizio G., Basile F., Stefanelli LV., Marchetti C., Felice P. Dynamic Navigation for Zygomatic Implants: A Case Report about a Protocol with Intraoral Anchored Reference Tool and an Up-To-Date Review of the Available Protocols. *Methods Protoc* 2020;**3**(4). Doi: 10.3390/mps3040075.

19. Van den Bosch L., van der Schaaf A., van der Laan HP., Hoebers FJP., Wijers OB., van den Hoek JGM., et al. Comprehensive toxicity risk profiling in radiation therapy for head and neck cancer: A new concept for individually optimised treatment. *Radiother Oncol* 2021;**157**:147–54. Doi: 10.1016/J.RADONC.2021.01.024.



CHAPTER 8
APPENDICES

Summary
Samenvatting
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SUMMARY

Treatment of tumours in the upper jaw requires multidisciplinary involvement due to their effects on oral functions, aesthetics, and psychological aspects. Choosing the appropriate rehabilitation for a maxillary defect depends on factors such as tumour characteristics, the size and position of the defect, the patient's health, and any associated conditions.

Prosthetic rehabilitation with an obturator prosthesis has historically been a good option for restoring defects in the upper jaw, but often suffers from insufficient retention. In case of insufficient bone in the upper jaw, zygomatic implants can be placed to improve retention of the obturator prosthesis in addition to using endosseus implants. However, an accurate placement of these long implants is challenging, and deviation from the desired implant position can negatively impact the quality and outcome of the prosthodontic rehabilitation.

Advanced digital planning techniques, such as three-dimensional virtual surgical planning (3D VSP), can help to improve the accuracy and predictability of surgical outcomes for head and neck oncology patients. The research compiled in this thesis contributes to the development and optimization of 3D workflows by combining the surgical planning of maxillary resections with complex prosthodontic rehabilitations in a 3D virtual surgical plan. This contributes to personalized and optimized prosthodontic care for head and neck cancer patients with a tumour in the upper jaw.

Early involvement of the maxillofacial prosthodontist (MFP) in the head and neck oncology care pathway ensures that the patient receives an early understanding of the prosthetic possibilities and the various treatments required. The importance of the MFP and the benefits of 3D technology for planning and prosthetic treatment are described in **Chapter 2.1.** It is expected that with the help of 3D technology, the prosthetic outcome and thus the quality of life of head and neck oncology patients can be improved.

One of the factors influencing the rehabilitation of head and neck oncology patients is the timing of implant placement. **Chapter 2.2** presents the outcome of a literature review on primary and secondary placement of implants. The primary outcome measure was 5-year implant survival. Sixteen studies were included. Based on the quantitative analysis, a higher 5-year implant survival rate was found for primary placed implants (92.8% (95% CI: 87.1%–98.5%)) compared to secondary placed implants (86.4% (95% CI: 77.0%–95.8%)). Not only because of the increased implant survival but also due to other advantages of primary implant placement (earlier prosthetic rehabilitation and, increased quality of life), it is advised to standardly combine resection surgery with implant placement in edentulous situation.

Chapter 2.3 provides an overview of the latest developments of 3D VSP and computer-aided design (CAD) for the (prosthetic) reconstruction of maxillary defects. 3D VSP allows preoperative planning of resection margins and osteotomies, and recent advancements in multimodal imaging and personalized implant development using CAD have improved the translation of 3D VSP into surgery. Additionally, techniques such as intraoperative imaging and augmented reality have improved the accuracy and precision of the procedure. With the use of 3D VSP and CAD, ablation surgery, reconstructive surgery and prosthetic rehabilitation can be planned preoperatively. The goal of maxillary defect rehabilitation is to restore facial form and oral function in accordance with the individual needs of the patient.

Chapter 3 introduces a complete 3D workflow for immediate implant-fixed prosthetic rehabilitation after maxillary resection. This approach includes several steps, starting with 3D virtual surgical planning for tumour removal, followed by the placement of zygomatic implants and the fabrication of an obturator prosthesis that fits the planned situation and can be immediately fixed to the zygomatic implants. It is hypothesized that when specially designed guides are used, implants can be placed with such precision that they are suitable for immediate loading with an obturator prosthesis.

To test the feasibility of this approach, 3D virtual surgical planning was performed on five fresh frozen human cadavers for the resection of the maxilla and guided placement of ten zygomatic implants using custom cutting and drill/placement guides. A preoperatively designed and printed obturator prosthesis was placed and connected to the zygomatic implants. Accuracy of implant positioning was assessed by merging pre- and post-operative designed obturator prostheses matched the per-operative implant positions accurately, allowing for immediate loading. The mean prosthetic point deviation on the cadavers was 1.03 ± 0.85 mm, the mean entry point deviation was 1.20 ± 0.62 mm, and the 3D angular deviation was 2.97 ± 1.44°. These results demonstrate the feasibility of 3D virtual surgical planning for accurate execution of ablative maxillary surgery, zygomatic implant placement, and placement of an immediate implant-retained obturator prosthesis. The next step is to apply this workflow in the operating room for patients undergoing maxillectomy.

Chapter 4 evaluates the 3D VSP method for placing zygomatic implants from Chapter 3 in patients. In ten patients, partial maxillary resection was performed, followed by the placement of zygomatic implants using 3D VSP and 3D-printed patient-specific guides. The study aims to assess the accuracy of zygomatic implant placement and the fit of the obturator prostheses in this one-stage procedure. The results showed that zygomatic implants (n = 28) were placed with good accuracy (mean deviation 1.73 ± 0.57 mm and 2.97 ± 1.38° 3D angular deviation. The 3D accuracy of the prosthetic platform position was 1.58 ± 1.66 mm, with an accuracy of 2.21 ± 1.33 mm in the occlusal plane, and a height accuracy of 1.32 ± 1.57 mm. Additionally, in all cases the obturator prothesis

fitted as pre- operatively planned. This feasibility study shows that this novel application of 3D-printed surgical drill guides results in predictable zygomatic implant placement and provides the possibility of immediate prosthetic rehabilitation in head and neck oncology patients after maxillectomy.

Chapter 5 describes the immediate loading of guided placed zygomatic implants and its impact on implant survival rates after at least 12 months. The study shows good survival rates for zygomatic implants up to three years post-treatment. There was a trend of higher implant loss in irradiated patients (100% without radiation; 85% in irradiated patients). The study emphasized the importance of evaluating not only the success of implant placement and the fit of the obturator prosthesis but also the quality of life (QoL) of patients post-treatment. Patients reported favourable outcomes regarding QoL, although some reported issues with xerostomia and limited mouth opening, especially those who had undergone radiation therapy. The study highlighted that the radiation dose to the zygomatic bone significantly impacts implant survival rates, and the tumour's position and size directly affected the radiation doses to the zygomatic bone. Further research is necessary, and closer collaboration between surgical teams and radiotherapists during the virtual surgical planning phase of treatment and rehabilitation is crucial to improve the survival rates of zygomatic implants in patients undergoing postoperative radiotherapy.

An important development in the reconstruction of the upper jaw is the possibility of designing patient-specific implant (PSI) to retain prostheses. In **Chapter 6**, we demonstrate the use of an implant for the rehabilitation of large maxillary defects in cases where direct or delayed surgical reconstruction is not feasible. The benefits of an easily removable obturator prosthesis are emphasized, allowing for tissue inspection and cleaning of the oral cavity and defect by the patient.

3D techniques enable the creation of a patient-specific design, as demonstrated in this study. It provides a solution for patients when more conventional treatment options are not possible. The possibility of adequate prosthetic rehabilitation has a direct positive impact on oral functions and quality of life of the patient. We performed a finite element analysis (FEA) to ensure rigidity of the implant design. We achieved a maximum deviation of 0.44 mm compared to preoperative scans, indicating accurate placement. Despite the success reported in this case, several unanswered questions remain regarding optimal technical principles. It is anticipated that guidelines will be developed to support the design of patient-specific implants.

In the general discussion (**Chapter 7**), the results of the previous studies are further discussed. Based on the findings of the research, several recommendations and perspectives for future studies are given.

SAMENVATTING

Behandeling van tumoren in de bovenkaak vereisen een multidisciplinaire aanpak vanwege het effect op mondfuncties, esthetiek en psychologische aspecten. Het kiezen van de juiste rehabilitatie van een defect in de bovenkaak hangt af van meerdere factoren, zoals tumor eigenschappen, de grootte en positie van het defect, de gezondheid van de patiënt en eventuele bijkomende aandoeningen.

Prothetische rehabilitatie met een obturator prothese is historisch gezien een goede optie voor het herstellen van defecten in de bovenkaak, maar hebben als nadeel dat vaak de houvast van de prothese onvoldoende is. Naast het gebruik van klassieke implantaten kunnen, indien er te weinig bot is in de bovenkaak, zygoma implantaten worden geplaatst ter ondersteuning van de obturator prothese. Echter, het nauwkeurig plaatsen van deze lange implantaten is een uitdaging waarbij een afwijkende implantaat positie ten opzichte van de gewenste situatie een negatieve invloed kan hebben op de kwaliteit en uitkomst van de prothetische eindsituatie.

Geavanceerde digitale planningstechnieken zoals driedimensionale virtuele chirurgische planning (3D VSP) kunnen helpen bij het verbeteren van de nauwkeurigheid en het voorspelbaar maken van chirurgische uitkomsten bij hoofd-hals oncologie patiënten. Het onderzoek gebundeld in dit proefschrift draagt bij aan de ontwikkeling en het optimaliseren van 3D workflows, door het combineren van de chirurgische planning van bovenkaaksresecties met de complexe prothetische rehabilitaties in een 3D virtueel chirurgisch plan. Dit draagt bij aan gepersonaliseerde behandelkeuzes met optimalisatie van prothetische zorg voor patiënten met een tumor in de bovenkaak.

Vroege betrokkenheid van de tandarts maxillofaciale prothetiek (MFP) in het hoofd hals oncologie zorgpad zorgt ervoor dat de patiënt al tijdig in het behandeltraject een beeld krijgt van de prothetische (on)mogelijkheden en de diverse behandelingen die benodigd zijn. Het belang van de tandarts MFP en de voordelen van 3D technologie voor de planning en prothetische behandeling worden beschreven in **hoofdstuk 2.1**. De verwachting is dat met behulp van 3D technologie de prothetische uitkomsten en daarmee de kwaliteit van leven van hoofdhals oncologie patiënten kunnen verbeteren.

Eén van de factoren die van invloed is op de rehabilitatie van hoofd-hals oncologie patiënten is de timing van het plaatsen van implantaten. In **hoofdstuk 2.2** wordt de uitkomst van een literatuuroverzicht gepresenteerd over primair en secundair geplaatste implantaten beschreven. De primaire uitkomstmaat was 5-jaars implantaatoverleving. 16 studies werden geïncludeerd. Op basis van de kwantitatieve analyse werd een hogere 5-jaars implantaatoverleving gevonden voor primair geplaatste implantaten (92.8% (95% CI: 87.1%–98.5%)) dan voor secundair geplaatste implantaten (86.4% (95% CI: 77.0%–95.8%)). Niet alleen vanwege de verhoogde implantaatoverleving, maar ook

vanwege de andere voordelen van primaire implantaat plaatsing (snellere prothetische rehabilitatie, toegenomen kwaliteit van leven) wordt geadviseerd om resectie chirurgie standaard te combineren met het plaatsen van implantaten in edentate kaken.

In **hoofdstuk 2.3** wordt een overzicht gegeven van recente ontwikkelingen van 3D VSP en computerondersteund ontwerp (CAD) voor de (prothetische) reconstructie van defecten in de bovenkaak. 3D VCP maakt preoperatieve planning van resectiemarges en zaagvlakken mogelijk. Recente ontwikkelingen in multimodale beeldvorming en gepersonaliseerde implantaat ontwikkeling met behulp van CAD hebben de vertaling van 3D VSP naar de chirurgie verbeterd. Bovendien hebben technieken zoals intra-operatieve beeldvorming en augmented reality de nauwkeurigheid en precisie van de procedure verbeterd. Het doel van reconstructie van de bovenkaak is om het profiel van het gelaat en mondfuncties zo goed mogelijk te herstellen, in overeenstemming met de individuele behoeften van de patiënt.

In **hoofdstuk 3** wordt een volledige 3D-workflow geïntroduceerd voor direct implantaat gefixeerde prothetische rehabilitatie na resectie van de bovenkaak. De aanpak omvat verschillende stappen, beginnend met 3D-virtuele chirurgische planning voor het verwijderen van tumoren, gevolgd door het plaatsen van zygoma-implantaten en het vervaardigen van een obturator prothese die past bij de geplande situatie en direct gefixeerd kan worden op de zygoma implantaten.

Om de haalbaarheid van deze aanpak te onderzoeken, werden de procedures uitgevoerd op vijf kadavers. Met behulp van op maat gemaakte zaag- en boormallen werd eerst de resectie van de maxilla uitgevoerd en vervolgens geleid de zygoma-implantaten geplaatst. Hierna werd een preoperatief ontworpen en geprinte obturator prothese geplaatst en verbonden met de geplaatste zygoma implantaten. Nauwkeurigheid was van cruciaal belang en om de positie van de implantaten te controleren werden 3D-afwijkinganalyse uitgevoerd door de pre- en postoperatieve CT-scans te combineren. De resultaten waren veelbelovend: de preoperatief ontworpen obturator protheses pasten nauwkeurig bij de peroperatieve implantaatposities en konden allen worden geplaatst en gefixeerd voor onmiddellijke belasting.

De gemiddelde afwijkingen waren minimaal: de afwijking van het prothetische punt bedroeg 1,03 ± 0,85 mm, de afwijking van het ingangspunt was 1,20 ± 0,62 mm, en de 3D-hoekafwijking was 2,97 ± 1,44°. Deze resultaten tonen aan dat het mogelijk is om met behulp van 3D VSP nauwkeurig de chirurgische resectie, implantatie van zygoma implantaten en een preoperatief vervaardigde obturator prothese direct te fixeren en het maxillaire defect goed af te sluiten. De volgende stap is het toepassen van deze workflow in de operatiekamer bij patiënten die een maxillectomie moeten ondergaan.

In **hoofdstuk 4** wordt de daadwerkelijke uitvoering van de 3D VCP methode omtrent de plaatsing van zygoma implantaten uit hoofdstuk 3 geëvalueerd bij patiënten. Bij tien patiënten is er een gedeeltelijke resectie van de bovenkaak uitgevoerd en werden vervolgens zygoma implantaten geplaatst met behulp van 3D VSP en 3D geprinte patiënt specifieke mallen. Het doel van de studie is om de nauwkeurigheid van de plaatsing van de zygoma implantaten en de pasvorm van de obturator protheses bij deze een fase procedure te beoordelen. Zygoma implantaten (n = 28) werden geplaatst met goede nauwkeurigheid (gemiddelde afwijking 1,73 ± 0,57 mm en 2,97 ± 1,38° 3D-hoekafwijking) en in alle gevallen paste de obturator prothese zoals vooraf gepland. De 3D-nauwkeurigheid van de positie van het prothetisch platform was 1,58 ± 1,66 mm, waarbij de nauwkeurigheid ter hoogte van het occlusale vlak 2,21 ± 1,33 mm was , met een hoogte nauwkeurigheid van 1,32 ± 1,57 mm. Deze haalbaarheidsstudie toont aan dat de toepassing van deze nieuw ontworpen 3D-geprinte chirurgische boormallen resulteert in voorspelbare plaatsing van zygoma implantaten en de mogelijkheid biedt van directe prothetische rehabilitatie bij patiënten die een bovenkaaksresectie moeten ondergaan.

De directe belasting van op geleide geplaatste zygoma implantaten en de impact ervan op het overlevingspercentage van implantaten na minimaal 12 maanden wordt in **hoofdstuk 5** beschreven. De studie laat gunstige overlevingspercentages zien van de zygoma implantaten tot drie jaar na de behandeling, maar er was een trend van meer implantaatverlies bij bestraalde patiënten (100% zonder bestraling; 85% bij bestraalde patiënten). De studie benadrukt het belang van het evalueren van niet alleen het succes van de implantaat plaatsing en de obturator prothese, maar ook van de kwaliteit van leven (QoL) van patiënten na behandeling. Patiënten meldden gunstige resultaten wat betreft hun QoL, hoewel sommigen problemen meldden betreffende xerostomie en een beperkte mondopening, vooral degenen die bestralingstherapie hadden ondergaan. De studie benadrukte dat de bestralingsdosis op het zygoma bot een significante invloed heeft op de overlevingspercentages van implantaten. De positie en grootte van de tumor beïnvloedden rechtstreeks die bestralingsdoses op het zygoma bot. De noodzaak van verder onderzoek werd benadrukt en een nauwere samenwerking tussen chirurgische teams en radiotherapeuten in de planningsfase van behandeling en rehabilitatie wordt cruciaal geacht om de overlevingspercentages van ZI te verbeteren bij patiënten die postoperatieve radiotherapie ondergaan.

Een belangrijke ontwikkeling in de reconstructie van de bovenkaak is de mogelijkheid van het patiënt specifiek ontwerpen van implantaten (PSI's) voor verbetering van het houvast voor obturator protheses. In **hoofdstuk 6** demonstreren we het gebruik van een implantaat voor de rehabilitatie van grote maxillaire defecten in gevallen waarin directe of uitgestelde chirurgische reconstructie niet haalbaar is. De voordelen van een gemakkelijk verwijderbare obturator prothese worden benadrukt, waardoor weefselonderzoek en reiniging van de mondholte en defect door de patiënt mogelijk zijn.

3D technieken maken het mogelijk om een patiënt specifiek ontwerp te maken zoals is aangetoond in deze studie. Het biedt een oplossing voor patiënten als de meer reguliere behandelopties niet mogelijk zijn. De mogelijkheid tot een adequate prothetische rehabilitatie heeft direct een positieve invloed op de mondfuncties en kwaliteit van leven. Er werd een eindig-elementanalyse (FEA) uitgevoerd om de sterkte van het implantaatontwerp te waarborgen. We bereikten een maximale afwijking van 0,44 mm in vergelijking met preoperatieve scans, wat wijst op nauwkeurige plaatsing. Ondanks het succes dat in dit geval wordt gemeld, blijven er verschillende onbeantwoorde vragen bestaan over optimale technische principes. Het is te verwachten dat richtlijnen zullen worden ontwikkeld ter ondersteuning voor het ontwerpen van patiënt specifieke implantaten.

In de algemene discussie (**hoofdstuk 7**) worden de resultaten van voorgaande studies verder bediscussieerd. Op basis van de bevindingen uit de onderzoeken worden enkele aanbevelingen en perspectieven voor toekomstige studies gegeven.

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ABOUT THE AUTHOR

Nathalie Vosselman was born on 7th of Januari,1979, in Rotterdam, The Netherlands. After finishing secondary school in 1998 she studied dentistry at the University of Amsterdam and graduated in 2003. She started her private dental practice in Haarlem were she mainly provided complex restorative and prosthetic dental care for 17 years. Following completion of her training in Maxillofacial Prosthodontics in 2018 Nathalie works as fulltime staffmember at the department of Oral and Maxillofacial Surgery in the UMCG. As maxillofacial prosthodontist of the Head and Neck Oncology Centre she primarily focuses on oral and facial rehabilitation, in particular 3D workflows in prosthodontic rehabilitation of Head and Neck cancer patients. In 2023 Nathalie was appointed Head of the Centre for Special Dental Care at the Department of Oral and Maxillofacial Surgery, University Medical Center Groningen (UMCG). In this capacity, she oversees a team dedicated to providing specialized dental care to patients with complex needs.

Nathalie lives together with Danny Beenen and they joyfully share their home with multiple pets, in the serene countryside of Engelbert, Groningen.

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