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groningen

3D planning in the reconstruction of maxillofacial defects

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Introduction and aim of the study

Introduction

The reconstructive challenge

Rehabilitation of patients affected by continuity defects of the mandible and/or maxilla after resection of a tumor has been a reconstructive challenge throughout time. Resection of a tumor can result in significant facial deformities, impaired oral function such as chewing, swallowing and speech, and concomitant psychosocial problems. Before 1950 large bony defects left after oral cancer resection typically were not reconstructed. Primary apposition with soft tissue closure was performed without a bony reconstruction or the bone stumps were connected by a metal plate (osteosynthesis plate) leaving patients with a poor oral function (Fig. 1).[1]

The use of autologous bone in reconstruction

Autologous bone grafts, either free flaps or non-vascularized grafts, have meanwhile evolved to a valuable means for the rehabilitation of maxillofacial defects resulting from head and neck cancer as it allows for restoration of both hard and soft tissues. Small bony defects can be bridged with free bone grafts, e.g., free iliac crest grafts when there is postoperatively no need for radiotherapy (Fig. 2). For large bony defects (> 5 to 8 cm), when sufficient soft tissue coverage is lacking or when post operative radiotherapy is indicated, such an approach is not feasible. The first step to bridge large defects was the introduction of free vascularized osseous flaps, either with or without adjoining soft tissues.[2-4] The technique of transfer of soft tissue from a different part of the body as a free flap to close a defect was introduced in 1959.[5] The first free vascularized bone graft transplantation was documented in 1975.[6] The concept where bone and soft tissue (osteocutaneous or osteomuscular flap) are harvested from a donor area and the vessels (artery and vene) are reconnected for immediate recirculation in the recipient area to bridge a bony gap opened a field of reconstructive techniques. In the upcoming years, mandibular defects were reconstructed with, amongst others, iliac crest flaps and fibula flaps.[1,7]

Figure 1 Reconstruction plate on the mandible after tumor resection.

Figure 2 Mandibular resection of the left mandibular angle for the treatment of a ameloblastoma. Reconstruction with a free bone graft of the iliac crest and a reconstruction plate.

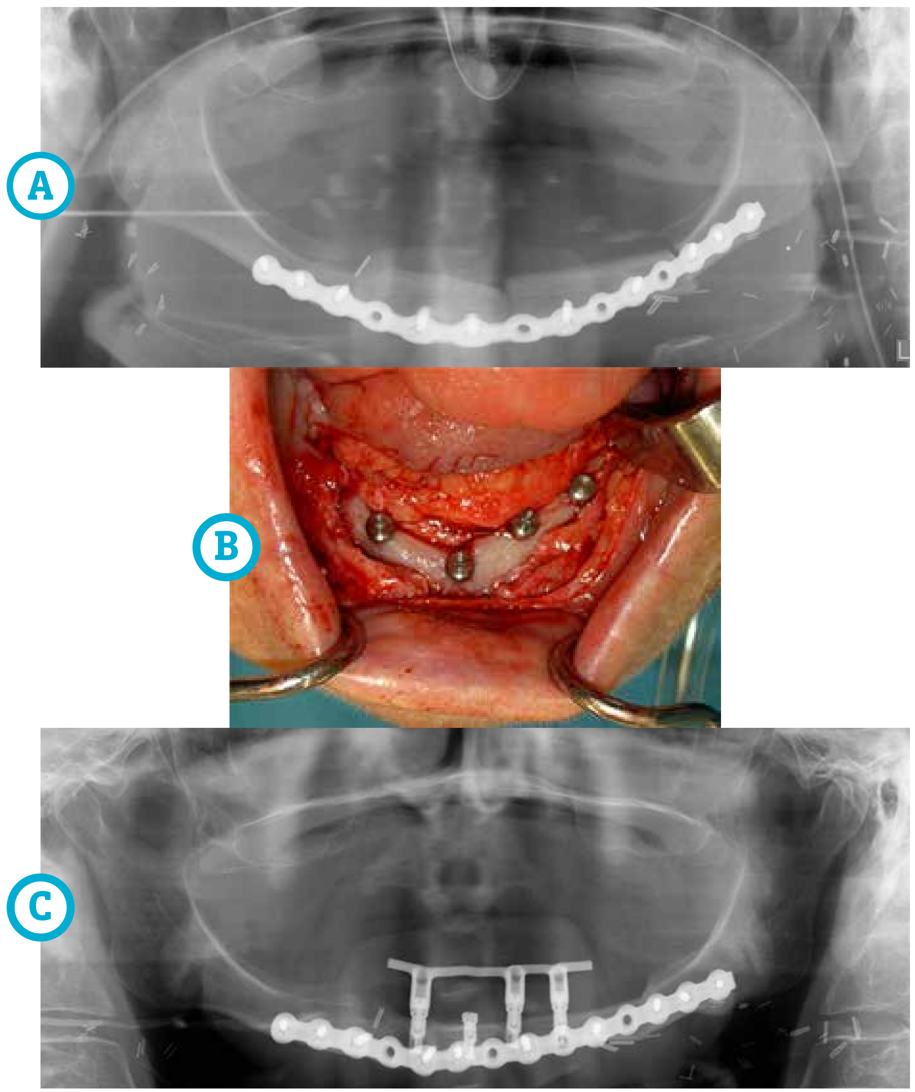

Figure 3 Mandible reconstruction with a free vascularized fibula flap and implants.
A: orthopantomogram of a mandibular reconstruction using a two-segment fibula graft after tumor resection of the mental segment. The graft is fixated with a reconstruction plate.
B: intra oral image of 4 implants placed in the fibula graft 6 months after the graft was inserted.
C: orthopantomogram one year after the reconstruction showing a bar on three of the four implants. The most ventral implant was left as a sleeping implant, because it was angulated too much buccal and because of a local insufficient vestibule.

The free vascularized fibula flap

For mandible reconstruction, the fibula is currently the most used osteocutaneous flap.[8,9] The bone of the free flap is fixed in the defect, in contact with the bone of the remaining mandible or maxilla with osteosynthesis plates made of medical grade titanium (Fig. 3A). Tumor removal and reconstruction of the mandibular defect can be performed in one operation. Maxillary defects are often closed by use of an iliac crest free flap or fibula.[10-12] Reconstruction of craniofacial defects with osseous free flaps often provide excellent anatomical recontouring, however, it does not always offer restoration of oral function. Especially obtaining a proper masticatory function is a common problem since overlying soft tissue is often mobile and fragile, and there can be lack of a buccal sulcus. A mucosa-bearing denture that offers function can therefore be difficult or sometimes impossible to produce, even though the continuity of the jaw is restored with a free vascularized flap.

Dental implants in the reconstructed mandible or maxilla

Quite early after the introduction of the osteocutaneous and osteomuscular free flaps, inserting dental implants in transplanted bone was recognized as a possibility to provide patients with a dental prosthesis.[13] Generally the concept of implant-retained prostheses completing mandibular reconstructions was explored for defects reconstructed with non-vascularized bone grafts as well as all kinds of free vascularized flaps (Figs. 3B, 3C).[14,15] From the moment the concept of placement of dental implants in grafted areas was introduced, a variety of issues was raised that need to be addressed before combining grafted areas with implants can be considered a successful strategy for routine application. These issues include timing of implant placement, soft tissue management, and inserting implants before or after radiotherapy. Initially, most authors placed implants in a graft secondarily to healing of that graft and, when applied, after radiotherapy. A variety of papers reported on the beneficial outcome of placing implants in osseous grafts.[14,16-18] However, despite these optimistic reports several authors also reported that a relatively low percentage of reconstructed patients eventually received implants and completed the prosthetic rehabilitation.[19-22] Major causes of not completing the prosthetic treatment are the difficulties that surgeons and prosthodontists encounter in the technical aspects accompanying implant placement and implant-retained prosthodontics. Optimal planning of the position of the graft and implants is one of these aspects.

Planning of reconstruction to increase chances of achieving a functional outcome

Due to limited options, reconstructive surgeons have been using various types of free flaps for reconstructing the mandible without incorporating a prosthetic plan.[8] Without a pre-operative prosthodontic rehabilitation plan the bone is cut (osteotomy) and positioned according to the best fit in the mandibular defect at that moment during surgery.[26] In general flap position is important to support prosthetic rehabilitation. When dental implants are considered to be a part of the treatment plan, correct positioning of the osseous component of the free flap is even more important to allow for implant placement at the preferred anatomical locations from a prosthodontic perspective. When the bone transplant is suboptimal positioned, implants often are or have to be placed in a suboptimal position for prosthodontic rehabilitation. It is not uncommon that some implants may not be used to support the prosthesis rendering a suboptimal basis for retaining a prosthesis.[27] As a result, a prosthesis cannot be made or the post operative function and esthetics of the implant-retained prosthesis can be impaired, thereby negatively affecting the patient's quality of life.[28] Therefore, a precise pre-operative planning may help to improve chances of a functional implant position.

In general, implants are not inserted primarily in free vascularized flaps, even though there are advantages in primarily placement.[16,27,29,30] Insertion of the implants at the time of resection and reconstruction means that osseointegration can take place prior to radiotherapy, which accelerates oral rehabilitation and improves overall functional outcome.[31] Overall, primary insertion (at the time of tumor resection) of implants reduces functional rehabilitation time and has at least the same rate of success of osseointegration as secondary inserted implants.[23,31-33] As a result, reconstructive surgeons have stratified the approach to craniofacial defects into immediate reconstruction and delayed or secondary reconstruction.

In the immediate approach, the time for optimizing the free flap is limited, due to for instance the time pressure of cancer growth or severe trauma. Secondary reconstructive approach does allow for preparation of the graft for optimal prosthetic rehabilitation.

Backward planning in secondary reconstruction using the "Rohner" method

To gain control of the implant and graft position in complex rehabilitation of mandibular and maxillary defects, a planning method was developed designing a reversed workflow of treatment, beginning with the prospective endpoint of the reconstruction.[34,35] Vinzenz et al[36] showed the idea of prefabrication not only addressed the problem of peri-implant tissues, but also the new occlusion and implant bearing tissues (Fig. 3). Thus, the dental prosthetics that is strived for play a leading role in the planning and executing of the fibula reconstruction and the dental implant placement in fibula grafts.

Rohner's technique is essential a two-step approach with two surgeries that completes the reconstruction. The Rohner technique can be used for secondary reconstructions and ensures functional positioning of the implants and graft. The first surgery involves preparation of the fibula with implants and a skin graft for mucosal lining (Fig. 4D). After a healing period of at least six weeks allowing for osseointegration of the implants and revascularization of the skin graft, the transplant can be transferred to the defect during the second surgery. For this purpose, a provisional prosthesis is made to fit on the implants of the transplant and guides the position of the flap in the defect determined by the occlusion (Fig. 4F). Through this top down planning starting with the prosthesis, a functional positioning of the implants and flap is better warranted.

Backward planning starts with a stereolithographic (stl) model of the maxillofacial region including the maxilla, mandible and the bony defect. Dental casts are positioned in the stl-model using a facebow registration to create an accurate fusion model of bone and dentition (Fig. 4A). Next a solid model of the patients' fibula is tailored and inserted into the defect in a position that is favorable for implant placement meanwhile reestablishing the external contour. The number and position of osteotomies and implants

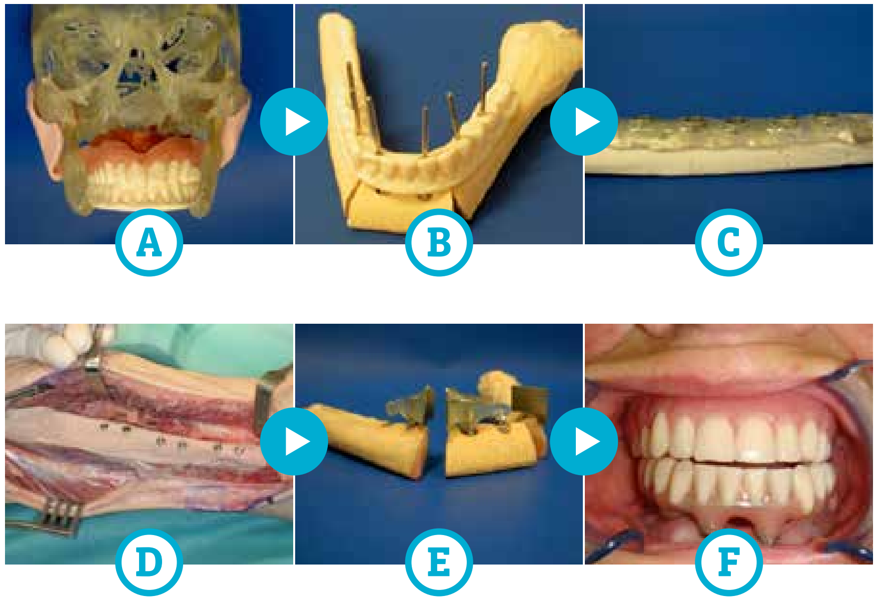

Figure 4 The "Rohner" method. A: stereolithographic model of the mandibular anterior defect including the cast of the upper and lower dental model, B: implant planning in the preferred locations in the 3 parts of the fibula, C: drilling guide for implant placement in the uncut fibula, D: fibula prefabricated with dental implants and split skin graft, E: implant abutted saw guides to guide the cutting of the fibula parts, F: prosthesis (which is made before the surgery) in occlusion screwed on the implants of the fibula reconstruction.

are determined this way (Fig. 4B). Based on this information the technician fabricates a template that serves as a drilling template for the implants during the first surgery (Fig. 4C). During the second surgery this template is used as a guide for the osteotomies.

A limitation of the Rohner technique is that it relies on extinctive laborious work to facilitate the planning and guided execution. Therefore, this two-step technique for secondary reconstruction is restricted to departments who have a highly specialized dental technician in their team; unfortunately most departments worldwide lack this support. Technical progress might provide the technicians and surgeons with new tools to reduce the laborious work. First signs are that nowadays, virtual 3D surgical planning using CT (computed tomography) or CBCT (cone-beam computed tomography) is commonly available and has shown to be useful in effective and efficient planning of reconstructions.[37,38,39] 3D surgical planning gives great anatomical insight in the recipient and donor anatomy facilitating optimal anatomic rehabilitation of the defect.[26,37] Furthermore, 3D guided implant surgery has evolved to a common place for guided implant placement.[40] This allows for more anatomical insight and the planning of more complex reconstructions.[41] This virtual planning software might facilitate virtual planning of fibula graft based reconstruction of mandibular and maxillary defects together with dental implants. Added with virtually planned surgical guides this might provide virtualizing of the technique according to Rohner, bringing it within reach of treatment centers who are not facilitated with a specialized dental technician.

Virtual planning of immediate fibula reconstructions

It is known that for primary reconstruction of mandibular and maxillary defects, 3D virtual planning can be performed with a reasonably high level of accuracy using fibula grafts.[38,42] It is noted that the ability to correctly contour the plate by hand to replicate the plate template is limited, indicating that the precision of the surgery is hampered by the lack of a precisely fitting osteosynthesis plate.[38] Virtual planning of a CAD-CAM made reconstruction plate in the 3D plan of the fibula graft has the potential to overcome this accuracy issue. Moreover, the reconstruction plate can serve as a tool to translate the virtual planning of a mandibular reconstruction to the surgery by guided drilling of the screw holes. When dental implants are also a part of the virtual plan it might be possible to immediate reconstruct a patient after tumor resection with a fee vascularized fibula graft and dental implants with sufficient accuracy and high predictability to facilitate implant supported prosthetics.

Assessment of bone invasion by oral squamous cell carcinoma

A potential drawback of the 3D planning of immediate reconstructions is the difficulty of adapting to situations in which the surgical resection plane has to be adapted due to tumor presence or recurrence. Incorrect resection causes substantial clinical problems. The decision to extend the resection margins during the surgical procedure bears even the hazard that the prefabricated surgical guides and/or CAD-CAM made reconstruction plate can no longer be used. Therefore, it is of key importance that tumor margins can be visualized well and can be fused accurately with the virtual treatment planning. To include free surgical mandibular bone margins in the treatment planning, the extension of the tumor has to be accurately assessed prior to surgery. Magnetic Resonance Imaging (MRI) currently provides the best soft tissue-, tumour expansion and invasion information (tumour delineation).[10] When combining tumor expansion and invasion information obtained with MRI with the corresponding bone anatomy obtained with (CB)CT more precise bone and soft tissue resection margins can be determined. To be able to combine both imaging modalities, an image fusion algorithm has to be developed to facilitate optimal planning of resection of tumors.

Aim of the study

The overall aim of this PhD study was to develop and to assess the accuracy of digital planning methods for mandibular and maxillary reconstructions of craniofacial defects resulting from tumor surgery with free vascularized fibula flaps combined with dental implants.

The specific aims were:

1. To systematically review the literature regarding the impact of oral rehabilitation of large mandibular and maxillary defects with free vascularized fibula flap with or without dental implants on functional outcome and quality of life (QoL) (chapter 2);
2. To develop a virtual planning method for the backwards planning technique according to “Rohner” (chapters 3.1 and 3.2);
3. To assess the accuracy of the developed digital planning method in reconstructive surgery (chapter 4);
4. To assess the accuracy of reconstructive surgery of the mandible using the free vascularized fibula flap and dental implants in the combination with the CAD-CAM reconstruction plate (chapter 5);
5. To develop and validate a software pathway to combine tumor margins determined on MRI with the CB(CT) based virtual treatment planning of maxillary and mandibular reconstructions (chapter 6).

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2

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

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Submitted

Abstract

Background

Reconstruction and oral rehabilitation of segmental maxillofacial defects resulting from ablative surgery is commonly achieved by osteocutaneous vascularized free fibula (FFF) transplantation combined with implant-supported dental prostheses. We systematically reviewed the literature regarding the impact of oral rehabilitation with or without dental implants on functional outcome and quality of life (Qol) following reconstruction of such segmental maxillofacial defects with FFF.

Methods

A literature search was conducted using the databases of Cochrane, MEDLINE and EMBASE. Relevant search terms for maxilla or mandible, reconstruction with FFF, and oral rehabilitation were used. Two reviewers independently assessed the publications using eligibility and research quality criteria (MINORS).

Results

In total, 557 unique publications were found; after scrutinization two prospective studies and 8 retrospective-case-series-studies without comparison were left for ultimate analysis. Quality ranged from 44% to 88% of the maximum score. Overall survival rate of the FFF was 99% and the survival rate of dental implants was 95%. Speech intelligibility was excellent or good in most patients. Overall aesthetic outcome rated by both patients and physicians was good to excellent. No statistically significant changes in QoL were found. Methods to measure functional outcome varied strongly, making pooling impossible.

Conclusion

Oral rehabilitation with implant-supported dental prostheses after reconstruction of segmental maxillofacial defects with FFF results in good to excellent speech intelligibility and aesthetics. Results are probably positively biased by the retrospective nature of the studies. In future prospective research, functional outcome measures should be addressed using standardized questionnaires and validated objective tests with adequate follow-up.

Introduction

Segmental resection of the maxilla and/or the mandible for the treatment of neoplasms often results in complex maxillofacial defects, involving soft tissue, bone and dentition. These defects can be debilitating since they impair oral functions and disturb aesthetic contours, and may lead to social isolation and poor quality of life (QoL).[1-4] Since its introduction, the transplantation of a vascularized free fibula flap (FFF) has evolved into the standard procedure for reconstruction of complex segmental maxillofacial defects.[5-13] The FFF can be reliably harvested and transferred, with a flap survival rate up to 95%, and low donor site morbidity.[6,14-19]

Restoration of oral functions requires not only reconstruction of the maxillofacial defect, but also dental rehabilitation.[20-22] Due to the surgical ablation and reconstruction, the options to obtain sufficient prosthesis retention and stability are reduced. When radiotherapy has been applied and/or the mobility of the tongue and overlying soft tissues is reduced, chances of successful dental rehabilitation decrease further due to the changed anatomical conditions and the intolerance of the denture-bearing mucosa to mechanical loading.[1-4,23-26]

The bicortical fibular bone of FFF has an excellent ability to accept dental implants to support dental prostheses, and implant survival rates are reported to be high (93-96%).[27-30] Implant-supported prostheses contribute significantly to oral functions such as speech, swallowing and mastication, and there seems to be a tendency to use implants as (a part of) the standard rehabilitation plan.[1,2,5-8,10-13,20-22,25,26,31-47]

Systematic evaluation of the literature regarding functional outcomes related to prosthetic treatment after maxillofacial reconstruction in patients treated for head and neck cancer has been performed previously, but did not focus specifically on reconstruction with FFF, and QoL assessment was not performed.[48] The aim of this study was to systematically review the literature regarding the impact of oral rehabilitation with or without dental implants on functional outcome and quality of life following reconstruction of a segmental maxillofacial defect with FFF.

Table 1 Search strategy

Pubmed and Cochrane search	EMBASE search
#1 "Face"[MeSH] OR "Jaw"[MeSH] OR "Mouth"[MeSH] OR Head and Neck OR Jaw OR Mouth OR Oral OR Mandib* OR Maxill* OR Palat* OR Midfac* OR Alveolar bone* OR Alveolar process* OR Dental OR Dentition OR Tooth OR Teeth OR Periodont* OR Lip OR Lips OR Gingiv* OR Tongue* OR (Mouth AND Floor) OR (Mouth AND Mucos*) OR (Oral mucosa) OR Chin OR Cheek* OR Salivary gland* OR Parotid gland* OR Sublingual gland* OR Submandibular gland* OR Oropharyn* OR Hypopharyn*	#1 'Face'/exp OR 'Skull'/exp OR 'Mouth and Teeth'/exp OR 'Head and Neck' OR Jaw OR Mouth OR Oral OR Mandib* OR Maxill* OR Palat* OR Midfac* OR 'Alveolar bone' OR 'Alveolar bones' OR 'Alveolar process' OR 'Alveolar processes' OR Dental OR Dentition OR Tooth OR Teeth OR Periodont* OR Lip OR Lips OR Gingiv* OR Tongue* OR (Mouth AND Floor) OR (Mouth AND Mucos*) OR 'Oral mucosa' OR Chin OR Cheek* OR 'Salivary gland' OR 'Salivary glands' OR 'Parotid gland' OR 'Parotid glands' OR 'Sublingual gland' OR 'Sublingual glands' OR 'Submandibular gland' OR 'Submandibular glands' OR Oropharyn* OR Hypopharyn* AND [embase]/lim
#2 "Fibula"[MeSH] OR Fibul*	#2 'Fibula'/exp OR Fibul* AND [embase]/lim
#3 "Dentistry"[MeSH] OR "Prosthodontics"[MeSH] OR "Dental Prosthesis"[MeSH] OR "Dental Implants"[MeSH] OR ((Mouth OR Oral OR Dental) AND (Rehabilitation OR Implant OR Implants OR Prosthes*)) OR Prosthodontic* OR Denture	#3 'Reparative dentistry'/exp OR ((Mouth OR Oral OR Dental) AND (Rehabilitation OR Implant OR Implants OR Prosthes*)) OR Prosthodontic* OR Denture AND [embase]/lim
#4 ((#1 AND #2) AND #3) NOT Review	#4 #1 AND #2 AND #3

Materials and methods

Information sources and search strategy

An initial literature search was conducted on May 31, 2013 and updated until April 10, 2015 using the electronic databases of Cochrane Library, MEDLINE by means of PubMed, and the search was adapted for EMBASE. Relevant search terms for the head and neck area involving the maxilla or mandible, reconstruction with FFF, and oral rehabilitation were used. These search terms were matched to relevant MeSH (MEDLINE, Cochrane) and EMTREE terms (EMBASE) and exploded or searched as keywords (Table 1). (Systematic) reviews were not included in the study but were used to identify potentially relevant studies missed in the search.

Selection and assessment of relevant studies

Results of the search were imported into a RefWorks® database. Duplicate publications were removed. Publications were assessed for inclusion in two selection rounds according to inclusion criteria (Table 2). Publications were excluded if they were published in a language other than English, German or Dutch. In case of overlapping study populations in publications from the same authors, these publications were considered as one study, or the most recent publication with the longest follow-up was used.

In the first selection round, two reviewers (JW, RS) independently assessed titles and abstracts for inclusion and exclusion criteria. If an abstract was not available, the full text of the article was assessed in the second round. Both reviewers allocated titles and abstracts as 'included', 'excluded', or 'indecisive'. In the second round, full text assessment of the 'included' and 'indecisive' publications was performed according to the same criteria. After each selection round, discrepancies between the two reviewers were resolved in a consensus meeting. If no consensus could be reached, a third reviewer (PD) gave a binding verdict. Inter-reviewer agreement was determined by Cohen's κ.[49,50] Reference lists of the included studies were searched for relevant studies missed in the database searches.

Table 2 Inclusion and exclusion criteria

Studies were included in case of:

Population

1. ≥10 human subjects
2. Segmental maxillary or mandibular defect
3. Reconstruction with vascularized free fibula flap

Intervention

4. Oral rehabilitation with conventional or implant-supported prosthesis

Outcome measures

A. Survival of the free fibula flap
B. Success rate of dental implants
C. Mastication
D. Mouth opening/trismus
E. Speech
F. Swallowing
G. Oral diet
H. Quality of life
I. Aesthetic outcome
J. Donor site morbidity
K. Complications

Studies were excluded in case of:

- Follow-up <4 months or mean follow-up <1 year
- Language other than English, Dutch or German
- (Systematic) reviews
- Cadaveric studies
- Animal studies

Quality assessment of included studies

The Methodological Index of Nonrandomized Studies (MINORS), a valid and reliable instrument to assess methodological quality and potential bias in nonrandomized studies, was applied.[51] The MINORS scoring list consists of 12 items, eight apply to non-comparative studies and the remaining four items apply to comparative studies. Items are scored as 0 (not reported), 1 (reported but inadequate) and 2 (reported and adequate). JW and RS independently assessed the quality of the included studies. Disagreement was resolved in a consensus meeting.

Data extraction and analysis

JW and RS independently performed data extraction using a pre-designed electronic database form (Microsoft Excel; Microsoft Corp., Redmond, WA, USA). Agreement on data collection was reached by consensus. Data was collected and analyzed regarding study characteristics, patient characteristics, information on the treatment modality (FFF with conventional or implant-supported prosthesis), and outcome measures regarding functional outcome and QoL (speech, mastication, deglutition, dietary intake, oral continence, mouth opening/trismus, QoL, aesthetic outcome, and donor site morbidity).

Results

Study selection

The data base search and updated searches (629 articles) together with the reference check (105 publications) yielded 734 publications (Fig. 1, see p. 39). Removing duplicate publications (177) yielded a total of 557 unique publications. Assessment of the titles and abstracts resulted in 180 unique publications that were eligible for further assessment. In the second selection round, a further 168 publications were excluded. Three publications were excluded because they revealed extensive overlap of data (same study population) with a more recent paper.[52-54]. One study was excluded because no full text was available.[55] Of the 12 remaining studies, three studies addressed the same population using the same study design and were considered as

Table 3 MINORS score and summary of study characteristics

Reference	MINORS Score	Study design	Subjects with VFFF (*n*)	Defect Maxilla/ Mandible (*n*)	Mean age (range, years)	Gender (Male/Female)	Mean follow-up (range, month)	Pre-operatieve dental status	Radiotherapy pre-implant or post-implant	Number of subjects with implants	Number of implants (in VFFF/ in native jaw)	Type of prothesis (*n*)
*Garrett et al., 2006[56] *Roumanas et al., 2006[57] *Fueki et al., 2014[58]	88% (14/16)	P	46	-/46	60.0 (19-83)	22/24	19.7 (15-31)	7 E, 39 PD	NR	17	58 (NR)	13 NP, 18 CP, 15 IP
Ferrari et al., 2013[59]	75% (12/16)	R	14	-/14	50.8 (15-65)	8/6	110.4 (12-120)	NR	7 pre-implant	14	62 (57/5)	14 IP
Wang et al., 2013[60]	75% (12/16)	R	12	-/12	42.9 (28-55)	7/5	42.1 (36-47)	3 E, 9 PD	0	12	37 (35/2)	12 IP
Dholam et al., 2011[61]	75% (12/16)	P	12	10/2	NR	NR	18.0 (18-18)	5 E, 7 PD	8 pre-implant	12	35 (NR)	12 IP
Sun et al., 2011[62]	63% (10/16)	R	20	20/-	42.6 (23-63)	14/6	34.7 (9-83)	NR	15, pre or post not specified	1	3/-	9 CP, 1 IP
Katsuragi et al., 2011[63]	63% (10/16)	R	12	-/12	56.3 (14-80)	8/9	15.8 (6-33)	NR	2 post-VFFF (no implants)	1	NR	107 CP, 1 IP
Raoul et al., 2009[28]	63% (10/16)	R	30	25/6	46.0 (19-72)	18/12	74.9 (7-155)	2 E, 28 PD	14 pre-implant	30	105/0	31 IP
Bodard et al., 2015[65]	56% (9/16)	R	26	-/26	54.1 (19-72)	17/9	75.3 (9-156)	NR	NR	26	80 (NR)	26 IP
Hundepool et al., 2008[64]	56% (9/16)	R	14	-/14	58.0 (19-77)	8/6	39.5 (6-89)	NR	NR for this subgroup	24	90 (69/21)	18 IP
Fang et al., 2015[66]	44% (7/16)	R	74	-/74	47.0 (19-75)	61/13	153.0 (41-267)	NR	9 pre-implant	74	192 (NR)	74 IP

MINORS, Methodological Index of Nonrandomized Studies; VFFF, vascularized free fibula flap; n, number;
*, three articles describing different outcome measurements in the same study population; P, prospective study;
R, retrospective study; E, edentulous; PD, partially dentate; NR, not reported; NP, no prosthesis;
CP, conventional prosthesis; IP, implant-supported prosthesis.

Table 4 Functional outcome measures

Reference	FFF survival rate	Implant survival rate	Mastication (*n*)	Deglution (*n*))	Dietary intake (*n*)	Speech (*n*)	Quality of Life	Aesthetic outcome (*n*)	Complications (*n*)	Donor site morbidity (*n*)
*Garrett et al., 2006[56] *Roumanas et al., 2006[57] *Fueki et al., 2014[58]	100%	98% performance	Masticatory with the IP similar to presurgical levels may be achieved with both CP and IP	SwT performance was similar to that of an average denture wearer	NR	NR severe	Moderate to limitations in food choices increased from 61% to 78%	NR	NR	NR
Ferrari et al., 2013[59]	100%	92%	NR	NR	12 normal 1 soft 1 tube	11 intelligible 2 intelligible with effort 1 unintelligible	NR	10 good 2 moderate 2 poor	1 flap necrosis, 1 plate loss, 1 implant loss	1 difficult wound healing, 2 impaired foot motility
Wang et al., 2013[60]	100%	100%	NR	NR	NR	7 fully satisfied 5 partially satisfied	NR	10 fully satisfied 2 partially satisfied 0 unsatisfied	2 granulation around implants	NR
Dholam et al., 2011[61]	100%	80%	No improvement	No improvement	6 normal 3 soft 3 NR	Speech intelligibility was improved in 80%	Scores remained unchanged after 18 months	NR	2 food pocketing, 4 xerostomia, 4 hypersensitive to food temperature	NR
Sun et al., 2011[62]	95%	100%	Post operative occlusal force 61 of preoperative	NR	All patients regular or soft	Mean speech intelligibility score of 97% at 6 months postoperative	NR	15 excellent 4 good 1 fair	1 partial fibular ORN, 1 necrotic FFF, 3 fistulas	NR
Katsuragi et al., 2011[63]	100%	100%	NR	NR	12 normal 5 soft diet 0 tube feeding	All patients exhibited excellent speech patterns	NR	12 excellent 2 good 2 fair 1 poor	2 salivary fistulae, 1 abscess, 1 partial necrosis of skin flap, 1 late fracture 1 hammer toe	
Raoul et al., 2009[28]	100%	96%	22 excellent 7 good 1 bad	NR	NR	21 excellent 9 good 0 bad	NR	25 excellent 4 good 1 bad	NR	NR
Bodard et al., 2015[65]	100%	98%	NR	NR	20 regular, 6 soft; Dietary improvement in 9/20 (35%)	Improvement in speech in 6/26 (23%)	NR	Aesthetic improvement in 20/26 (77%)	NR	NR
Hundepool et al., 2008[64]	100%	97%	Improvement after prosthetic rehabilitation (p > 0.01)	Improvement after prosthetic rehabilitation (p > 0.01)	NR	Improvement after prosthetic rehabilitation (p > 0.01)	No improvement except for social aspect	Aesthetic satisfaction score of 3.3 on a 10-point	NR	NR
Fang et al., 2015[66]	98%	90% (5 y)§ 83% (10 y) 69% (20 y)	NR	NR	Diet unsatisfactory: N: 26%, HE: 33%, OC: 21%, FO: 9%, VO: 11%	ĐTrouble pronouncing: N: 32%, HE: 23%, OC: 21%, FO: 16%, VO: 9%	ĐLife less satisfying: N: 11%, HE: 33%, OC: 28%, FO 15%, VO: 13%	NR	6 recipient site problems	3 impaired ankle function

FFF, vascularized free fibula flap; n, number; *, three articles describing different outcome measurements in the same study population; CP, conventional prosthesis; IP, implant-supported prosthesis; cumulative survival rate of implants; Đ, OHIP questionnaire outcome: N: normal, HE: hardly ever, OC: occasionally, FO: fairly often, VO: very often.

SwT, swallowing threshold; NR, not reported; ORN, osteoradionecrosis; y, years; §, 5-year survival used for cumulative survival rate of implants; Đ, OHIP questionnaire outcome: N: normal, HE: hardly ever, OC: occasionally, FO: fairly often, VO: very often.

one study.[56-58] Thus, ten unique studies were included in this systematic review.[28,56-66] During the selection process, the inter-reviewer agreement (Cohen's K and percentage of agreement) for the first round the second round, and quality assessment was 0.76 (87%), 0.55 (82%), and 0.53 (60%), respectively.

Characteristics and quality of included studies

Of the ten included studies, two were non-randomized prospective cohort studies[56-58,61], the others were retrospective case series.[28,59,60,62-66] One prospective case series was used in three publications, each described different functional outcomes of conventional and implant supported dental prosthesis in patients requiring segmental mandibulectomy and reconstruction with FFF.[56-58] The other prospective study assessed treatment outcomes and impact on QoL in patients rehabilitated with implant-retained prosthesis after segmental resection and reconstruction.[61] None of the retrospective studies were comparative.

In the ten included studies, 260 patients were described who underwent reconstruction using 261 FFF's following segmental resection of the maxilla (55 FFF's) or mandible (206 FFF's). The number of patients per study ranged from 12[61] to 74 patients[66] (mean: 26 patients), in the age range of 14-83 years (weighted mean, 50.9 years). Preoperative dental status was reported in four studies.[28,56-58,60,61] The time interval between reconstruction with FFF and placement of dental implants ranged from 0 to 75 months. The follow-up period after dental rehabilitation ranged from 6 to 267 months (weighted mean, 58.3 months)(Table 3). The median MINORS score was 50% (inter quartile range 25-75) (Table 3).[56-58]

Survival of the FFF and success rate of dental implants

In only two of the included studies, loss of the FFF was reported,[62,66] resulting in an overall survival rate of 99% (Table 4). Nine studies reported a total of 662 osseointegrated dental implants inserted in 210 patients, with a cumulative survival rate of 95% in a follow-up period of 0 to 155 months (Table 4). In five studies, the number of implants placed was specified to the implant site, being FFF or native jaw[28,59,60,62,64] (Table 3). All patients received dental implants secondarily after healing of the FFF, except for five patients who received dental implants at the time of reconstruction.[62,64] Four studies described that radiotherapy was administered before implant placement in 38 patients.[28,59,61,66] Two of these studies reported late (>17 months) loss of seven implants in two patients who had received radiotherapy,[61] and a reduction in survival rate from 84% to 97%.[59] Another study reported loss of one implant in an irradiated FFF[28] (Table 4).

Mastication, deglutition, and dietary intake

Five studies reported on mastication.[28,56-58,61,62,64] One prospective study used a standardized masticatory performance test, using peanuts as test food.[56-58] Furthermore, three questionnaires were applied in this study, of which two regarded chewing and food preference. The outcomes of the study showed that patients with implant retained dentures performed better than patients rehabilitated without implants.[56-58] One study found excellent or good chewing ability in 29 of 30 patients.[28] Another study found a reduced occlusal force of 61±10% of the pre-ablative occlusal force irrespective of the dental status.[62] Two studies found no significant improvement in mastication performance (Table 4).[61,64]

Speech

Speech outcome was assessed in nine studies, but methods to assess speech varied between studies. One study reported both objective evaluation of speech using speech software and subjective evaluation using standardized questionnaires.[61] In a Chinese study a standardized speech intelligibility test was performed,[62] and in a Japanese study a standard classification was used.[63] In the other studies, speech intelligibility was assessed using a questionnaire[64-66] or a 3-point Likert scale.[28,59,60] Overall, speech intelligibility was excellent or good in most patients, and moderate or poor in a minority of patients (Table 4).

Quality of Life

Only two studies used a Quality of Life Questionnaire (EORTC QLQ-H&N35, EORTC QLQ-C30).[61,64] They found no statistically significant changes in quality of life after dental rehabilitation except for the social aspect. In another study, an Oral Health Impact Profile (OHIP) questionnaire showed that most of the subjects rarely reported to have had problems at one year postoperatively.[66] In one study a visual analogue scale (VAS) was used (Anchored 0: best outcome,10: worst outcome) to assess oral functioning (mean VAS 4.2), aesthetic outcome (mean VAS 3.3), and overall satisfaction (mean VAS 3.6).[64] One study reported that social life and satisfaction were not altered grossly. However, the percentage of subjects experiencing moderate to severe limitations in food choices after the ablative and reconstructive surgery, but before oral rehabilitation increased from 61% to 78% ($P<0.05$) (Table 4).[56-58]

Aesthetic outcome

Seven studies reported on aesthetic outcome. None of these studies used a standardized questionnaire or objective test. In most studies, aesthetic outcome was scored either by a physician and/or through self-assessment, on a 3-point or 4-point Likert scale. The overall outcome of these rating of both patients and physicians was 'good' to 'excellent', only one study described a mean aesthetic satisfaction score of 3.3 on a 10-point VAS-score (Table 4).

Complications and donor site morbidity

Overall, complications rarely occurred. Five studies reported on complications such as flap necrosis, peri-implant soft tissue hyperplasia, fracture or exposure of osteosynthesis, abscesses, and saliva- or oronasal fistula development.[59-63] Wound healing disturbance of the donor site was observed in just one case. Five patients complained of difficulties in foot motility[59] or impaired ankle function[66] after surgery (Table 4).

Discussion

The aim of this study was to systematically review the literature regarding effects of oral rehabilitation with or without dental implants on functional outcome and quality of life following reconstruction of a segmental maxillofacial defect with FFF. We found that most studies report high patient satisfaction and favorable oral function after implant supported dental rehabilitation, but generally there is a great diversity in methods used to assess functional outcomes and QoL. We cannot draw firm conclusions about dental rehabilitation following FFF because all studies presented relative small sample sizes, with a substantial heterogeneity in sample characteristics, based on inclusion and exclusion criteria for further rehabilitation with dental implants, number of implants and/or prosthesis, heterogeneity in tests for oral functions and patient satisfaction, and time of follow-up (several months to a few years). This heterogeneity made data pooling impossible.[67]

Comparing functional outcome of patients who received a FFF for the reconstruction of a jaw defect is generally hampered by diversity in the bone and soft tissue defects patients have. Large defects requiring multisegment reconstructions cause more loss of function compared to small sized defects with single segment FFF.[31,42] Next to that, resection of the symphysis area has a more profound effect on function than lateral mandibular defects. In the included studies other essentials such as the size of the soft tissue defect or details of radiotherapy treatment were poorly described, hampering adequate comparison of outcomes between studies.

Ten studies met our inclusion criteria and were included in this review, and only two of these studies were prospective.[56-58,61] It must be noted that in most of the included studies patients had already been successfully reconstructed with FFF at the beginning of the study and had received dental implants and/or prosthesis. Due to this selection bias, the survival rate of the fibula grafts in these studies is probably overestimated as compared to the survival rate of the FFF in the total population of patients receiving a FFF for reconstruction of a maxillofacial defect.

Many objective methods exist to evaluate masticatory function, such as measuring color change in chewing gum or paraffin wax, measuring the degree of breakdown of a food by sieving the comminuted food, or measuring occlusal force.[68] In most studies included in this review, mastication was described in general terms, such as "satisfaction with mastication" or related to "type of diet" used. Only one study reported the outcome of standardized masticatory performance tests, which showed a favorable performance after implant supported dental rehabilitation.[56-58] Overall mastication performance after dental rehabilitation was generally compared to the performance immediately after the jaw defect was conceived or after FFF and not to the performance before both of these events. These relative changes were always measured in retrospect, and therefore could have been subject to recall bias.

Swallowing was reported in only a few studies using dietary intake as outcome measure. Only one study used a validated swallowing threshold test.[56-58] In future research, prospective and objective assessment of deglutition should be performed, such as a swallowing threshold test, with baseline measurements before ablative surgery. Furthermore, subjective problems that patients experience regarding mastication and deglutition after reconstruction with FFF and oral rehabilitation should be assessed using validated questionnaires specifically designed for head and neck cancer patients, for example the EORTC QLQ-H&N35 or the University of Washington Quality of Life Questionnaire for patients with head and neck cancer (UW-QOL). Unfortunately, the EORTC QLQ-H&N35 questionnaire was only used in two studies included in this review.[61,64]

Seven studies reported on speech outcome, and in these studies the majority of patients performed well, while in some patients speech was slightly impaired but generally not unintelligible. In most of these studies, speech was rated for intelligibility using non-standardized rating systems (3-pount or 4-point Likert scales), or for understandability of patients to hospital personnel or patients' relatives. It would have been better to use a standardized rating system for speech, which is observer-independent, and preferably the baseline speech outcome should be measured before surgery.

In general, the aesthetic outcome was rated by the surgeon and the patient and was reported to be satisfactory. Observer bias was likely because observers who were involved in the treatment of these patients rated the aesthetic outcome. Future research would benefit if independent observers would rate esthetic outcome at pre-ablative and post reconstructive intervals using standardized patient (stereo) photographs or video. A validated scoring system for aesthetic outcome after head and neck reconstructive surgery is lacking. However, a more comprehensive patient-reporting outcome instrument for patients with head and neck cancer including assessment of facial appearance is under development, the FACE-Q Oncology.[69]

Since we found no randomized studies, the validated MINORS tool was used to assess methodological quality and potential bias in the nonrandomized studies included in our review. Use of this tool made it clear that most of the current studies on functional outcome and quality of life after reconstruction of maxillofacial defects with FFF and oral rehabilitation are lacking methodological quality (median score of 50%). In none of the included studies 'unbiased assessment of the study endpoint' was performed, scoring no points on this item of the MINORS tool. All but two studies[56-58,61] did not score points on 'prospective collection of data', and only one study performed prospective calculation of study size.[56,57,59]

Our search strategy was performed in the databases of the Cochrane Library, MEDLINE by means of PubMed, and EMBASE. By limiting our search to these three databases, additional publications not indexed for these databases may have been missed. We therefore searched the references of included studies for additional studies missed in the search. Furthermore, publications were excluded if they were published in a language other than English, German, or Dutch. Due to this limitation, publications in other languages were not included, despite the fact that these publications might have met all the other inclusion criteria.

Case studies and case series with less than 10 subjects were not included in this review because these studies are susceptible to sample variation, and lack power. Kappa values for inter-reviewer agreement for the first selection round were 'substantial', and 'moderate' for the second selection round and quality assessment.[70] This result illustrates the need of the consensus meetings.

Conclusion

Based on this review it can be concluded that the evidence is not robust to determine how many patients requiring reconstruction of a maxillofacial defect with FFF may benefit from an implant-retained prosthesis. Nor is it clear on what criteria patients can be selected for oral rehabilitation with implant-retained prostheses and what the overall benefit of implant-retained prostheses for patients can be. Future studies should be prospectively designed describing in more detail the inclusion and exclusion criteria for post-reconstructive oral rehabilitation. Consensus should be obtained on standardization of assessing oral functions, using questionnaires and validated objective tests, before and after oral rehabilitation.

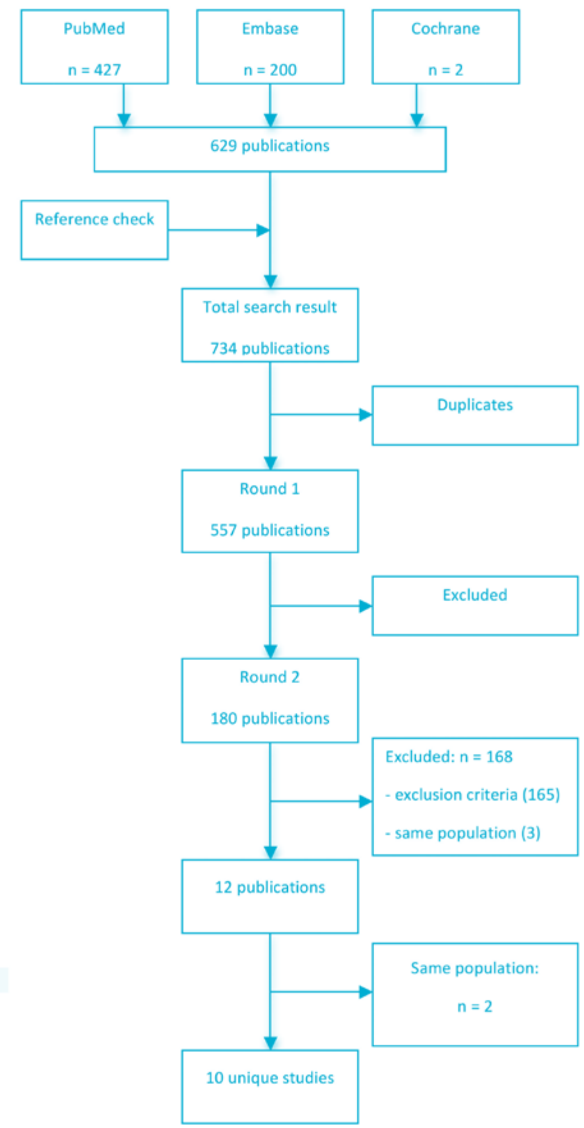

Figure 1 Flowchart of study selection procedure.

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3

Application of full 3D digital planning of free vascularized flaps for maxillofacial reconstructions

Currently, 3D planning of primary and secondary reconstructions of defects resulting from head neck tumor surgery can be performed fully digitally. In this chapter the development of a 3D planning method, including dental implants, according to the two-step approach introduced by Rohner (see chapter 1 for details) is illustrated. It is also shown that this method is not only applicable for free vascularized fibula flaps, but also for a variety of other free vascularized bony flaps used in reconstructive maxillofacial surgery.

In **chapter 3.1**, a case report of a 54 year old male who developed osteoradionecrosis of the mandible is described in whom a fully 3D digitally planned reconstruction of the mandible and immediate prosthetic loading using a fibula graft in a two-step surgical approach was performed.

In **chapter 3.2**, a case is described of a full 3D digital planning of implant-supported bridge in secondarily mandibular reconstruction with prefabricated fibula free flap. To illustrate the versatility of 3D planning of other free vascularized bony grafts in **chapter 3.3** two cases are described using 3D planning of such other flaps. One case describes the planning of a deep circumflex iliac artery flap for the reconstruction of a midface defect combined with secondary implant placement and a second case describes a prefabricated free vascularized scapula flap to reconstruct a mandibular defect.

3.1

Fully 3D digital planned reconstruction of a mandible with a free vascularized fibula and immediate placement of an implant-supported prosthetic construction

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Abstract

Background

Reconstruction of craniofacial defects becomes complex when dental implants are included for functional rehabilitation. The first case is described of a fully 3D digitally planned reconstruction of a mandible and immediate prosthetic loading using a fibula graft in a two-step surgical approach.

Methods

A 54-year-old male developed osteoradionecrosis of the mandible. The resection, cutting and implant placement in the fibula were virtually planned. Cutting/drilling guides were 3D printed and the superstructure was CAD-CAM milled.

Results

First operation: the implants were inserted in the fibula and the position registered by an optical scanning technique, which defined the final planning of the superstructure.
Second operation: the osteoradionecrosis was resected, the fibula was harvested and, with the denture fixed on the pre-inserted implants, placed in the mandibula guided by the occlusion.

Conclusion

It was possible to plan a mandibular reconstruction with immediate prosthetic loading completely by 3D virtual techniques.

Background

The use of vascularized osseous free flaps in the reconstruction of large maxillofacial defects has evolved to a standard treatment modality during the last two decades.[1,2] For optimal prosthodontic rehabilitation it is commonly accepted that dental implants are part of the treatment planning as implant supported dentures enhance the masticatory and speech function in edentulous patients.[3]

However, when dental implants are considered to be a part of the treatment plan, a precise preoperative planning of the reconstruction is required since a correct positioning of the bone is eminent to allow for implant placement at the from a prosthodontic perspective preferred anatomical locations. When the bone is incorrectly positioned, the implants are often located in a suboptimal position for prosthodontic rehabilitation. As a result, the post operative function and esthetics of the implant-retained prosthesis are often disappointing in such cases thereby affecting the patient's quality of life.[3]

Amongst the vascularised osseous free flaps, particularly the free vascularised fibula is often used in reconstruction of large maxillofacial defects.[1,4,5] To achieve optimal support of the denture and a stable peri-implant soft tissue layer, the free vascularised fibula can be prefabricated as described by Rohner.[6,7] This prefabrication includes the pre-operative planning of implant insertion, osteotomies of the fibula as well as the planning of a skin graft on the fibula for a thin lined soft tissue reconstruction.[6,7] This technique essentially is a two-step approach.
The first step starts with planning of the implants in the fibula using stereolithographic models of the maxillo-mandibular complex and the fibula. Next, a backward planning for the placement of the dental implants is made based on the desired dental occlusion, which yields a drilling guide for the dental implants in the fibula. The first step is completed by insertion of the implants at the exact pre-defined position in the fibula followed by taking impressions. The second step encompasses of preparing the cutting guide and the dentures during the 5 weeks osseointegration time of the implants, after which the fibula is harvested and placed in the maxillo-mandibular complex. The disadvantage of this technique is the extensive and difficult planning

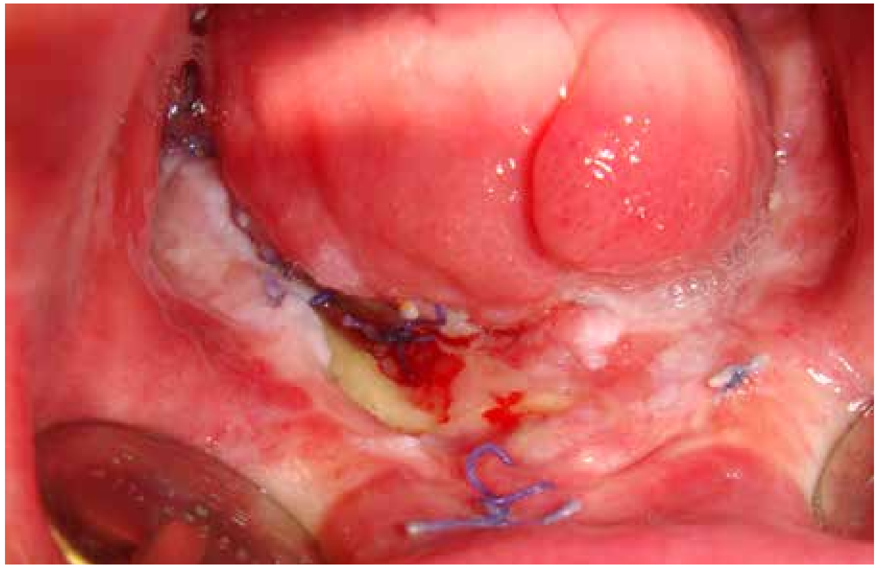

Figure 1 Intra oral image showing oral dehiscence and necrotic mandibular bone. The dehiscence developed one year after receiving radiotherapy (cumulative dose 66 Gy) to the mandible. Primary surgery comprised resection of a squamous cell carcinoma of the floor of the mouth and reconstruction with a radial forearm flap.

Figure 2 Panoramic radiograph. Showing osteolysis due to osteoradionecrosis of the right corpus of the mandible. In the upper jaw a full arch bridge and periradiculair healthy bone is present.

procedure, which requires a lot of laboratory work by an experienced technician, especially in the manufacturing of the drilling and cutting guides. For instance, Rohner utilizes laser welding techniques in the preparation of his drilling and cutting guides.[6,7] Therefore, the applicability of this procedure may prove to be difficult in the average hospital setting when these necessary skills and equipment are lacking. Recent developments in 3-dimensional (3D) digital planning and rapid prototype printing may provide a solution to overcome the difficult laboratory steps.

3D virtual treatment planning is becoming increasingly popular in implant surgery and reconstructive surgery of the maxillo-mandibular complex. Virtual treatment planning of implants and implant supported prosthesis has been reported for several years as well as the virtual planning of free fibula grafts for rehabilitation of maxillofacial defects.[8-12] The main advantage of virtual planning compared to the conventional planning is that it reduces the laborious manual steps significantly. To date it has been possible to plan the placement of a free fibula-transplant in the maxillo-mandibular complex by the use of several commercial software packages provided a digitally planned and printed cutting guide. Separately, planning software is available for dental implants placement yielding digitally planned and printed drilling guides. There are no reports on the combining of these software systems. We report a case combining digital planning methods and software, to create a full digital workflow for the prefabricated reconstruction of maxillofacial defects with free fibula grafts. In a virtual environment, otherwise complex laboratory steps can be easily performed without extensive training. These advantages provide accessibility of these reconstructive procedures for almost every reconstructive surgeon. In this paper we describe the first case of a fully digitally planned secondary reconstruction of a mandible in a patient with osteoradionecrosis.

Case report

A 54-year-old patient was diagnosed with a squamous cell carcinoma of the anterior floor of the mouth in 2007. Treatment consisted of tumor resection, and adjuvant radiotherapy to a cumulative dose of 66 Gy. He developed osteoradionecrosis of the right side of the corpus of the mandible in 2008 (Fig. 1 and 2). Despite removal of bone sequesters and primary closure by

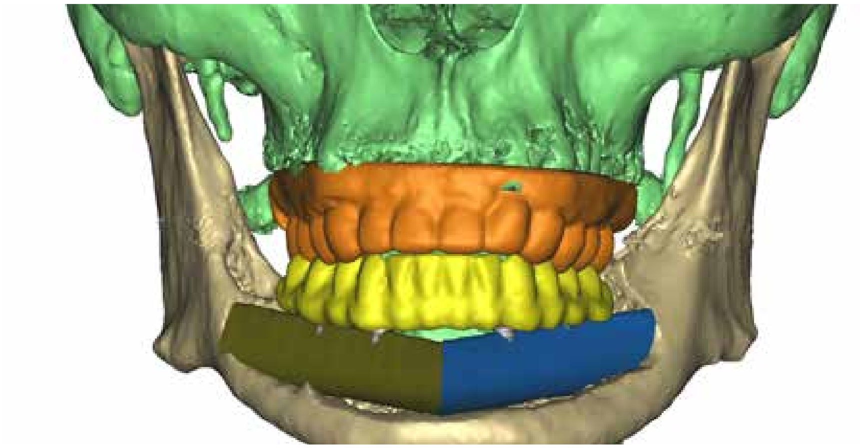

Figure 3 Virtual planning using SurgiCase CMF software (Materialize NV, Leuven, Belgium) and Simplant Crystal (Materialize Dental, Leuven, Belgium) showing reconstruction of the mandible with fibula bone and optimal planned position of the implants supporting the lower prosthesis. The augmented skull model is completed with a detailed scan of the upper dentition.

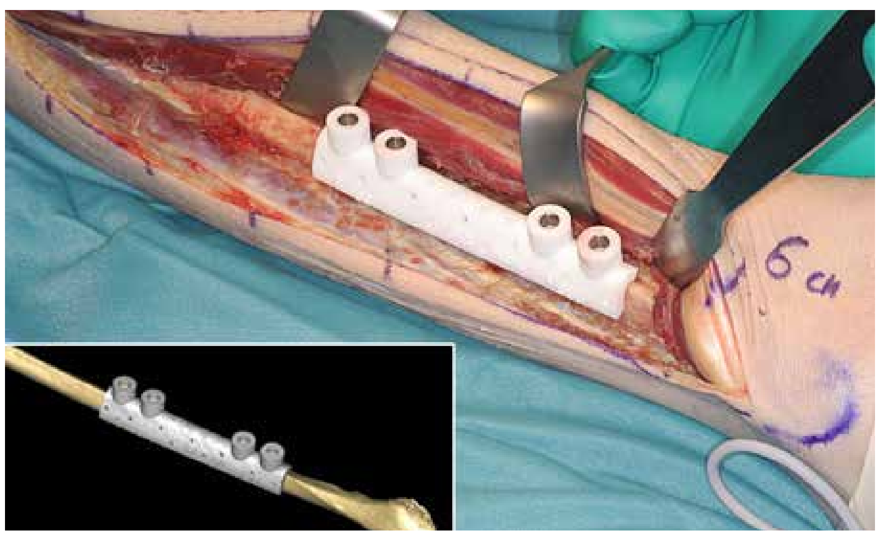

Figure 4 Virtual drilling guide (lower left) and stereolithographic drilling guide on the right fibula (upper right). After the osteotomies the middle segment can be removed and the two-implant pairs become positioned closer together (as can be seen in figure 7).

the use of a nasolabial regional flap healing was impaired due to lack of sufficient healing capacity of the irradiated tissues. The patient was offered a reconstruction with a free fasciocutaneous flap or a reconstruction with a free osseous flap with the planning of an implant based prosthesis. The patient preferred the latter.

Virtual pre planning

In the planning of the resection of necrotic bone the lower border of the mandible could be left in situ allowing an onlay bone graft on the mandible (Fig. 3). Functional reconstruction was chosen to be done with a prefabricated free fibula graft. The reconstruction was planned digitally using SurgiCase CMF software (Materialize NV, Leuven, Belgium) and Simplant Crystal (Materialize Dental, Leuven, Belgium). A back up planning following the conventional planning method according to Rohner was performed as an escape and to check every digital step of the process before surgery.[6,7]

The maxillofacial region and the mandible were scanned with a CBCT (i-CAT, Imaging Sciences International, Hatfield, USA). The right fibula was scanned using a CT scanner (Siemens AG Somatom Definition Dual Source, Forchheim, Germany). The maxillofacial scan was imported into Simplant Crystal, and a 3D model was created using volume rendering. In the upper jaw the natural dentition was present, the periodontal chart revealed no pockets or bleeding on probing. The central incisors and the lateral incisor at the right side were missing (Fig. 2). Because he had a full arch bridge, on this level there was substantial scattering on the scan. To retrieve a detailed scan of the bridge an optical scan was made with the Lava™ Chairside Oral Scanner C.O.S. (3M™ ESPE™, St. Paul, USA). The surface scan was imported into the Simplant software at the correct anatomical location. The necrotic bone of the mandible was virtually resected using the CT-slides. After this virtual resection the planning of the reconstruction was performed.

The lower prosthesis of the patient was scanned with the CBCT and also imported in the Simplant software in the proper occlusion of the denture with the pre-existing maxillary dentition (Fig. 3). On ideal positions under the lower prosthesis 4 implants (Nobel Speedy; Nobel Biocare AB, Götenborg, Sweden) were planned digitally. The file was converted and loaded into SurgiCase CMF together with the fibula CT-scan. The fibula reconstruction and

Figure 5 Virtual cutting guide (upper right) and Stereolithographic model of the cutting guide fixed on the implants with Nobel guide fixation screws in the right fibula (lower left).

Figure 6 To fabricate a prosthesis, the position of the digital bar and upper dentition had to be translated to the articulator. Therefore an intermediate occlusal guide between the virtual bar and upper dentition was designed (left). This guide was 3D printed and used to position the upper cast and the CAD-CAM milled titanium bar in the correct relation in the articulator (middle). The occlusal guide is replaced by the prefabricated implant supported lower prosthesis (right). The prosthesis could be made on the bar in the correct occlusion.

cutting planes were virtually planned onto the lower border of the mandible, following the anatomic border of the mandible and correctly supporting the implants. The planning was then converted and loaded into Simplant for optimalisation of the implant position. The reconstruction data were used to produce a drilling template for guided implant placement in the fibula (Fig. 4). Sterilization of the guide was performed using gamma irradiation.

Prefabrication of the fibula

The first surgical phase included placement of the dental implants in the fibula, registration of the exact location of the implants in the fibula and covering the bone with a split thickness skin graft. After exposure of the ventral rim as for a free fibula transfer, the drilling guide was placed and fixed on the bone with miniscrews (KLS Martin Group, Tuttlingen, Germany). Even though the axial position of the drilling guide was determined using the lateral malleolus as an anatomical landmark, it was difficult to localize the planned position in this axis. However, the drilling guide fitted well on the fibula and provided adequate guidance of the implant placement. Since guided implant placement always has a small error in implant position compared to the planned position,[10,13] an intra operative optical scan of the implants with scan abutments (E.S. Healthcare, Dentsply International INC.) was made with the Lava™ Oral Scanner to register the exact position and angulations. To check whether the accuracy of the oral scan was accurate for the fabrication of a titanium bar and as a fail-safe, the position of the implants was registered too by taking conventional dental impressions. Hereafter, the fibula was covered with a split thickness skin graft and a Gore-Tex patch (W.L. Gore and Associates, Flagstaff, Ariz). The wound was closed primarily and the implants and split skin graft was left to heal for 5 weeks.

Intermediate virtual planning

The optical scan was imported in the Simplant software and manually matched with the original fibula reconstruction planning creating a superimposed fusion model with the accurate position of the implants. The cutting guide of the fibula was planned and printed (Fig. 5). The digital design of the titanium bar on the scanned position of the implants was converted to a STL file from which a digital bar was fabricated out of titanium (E.S.

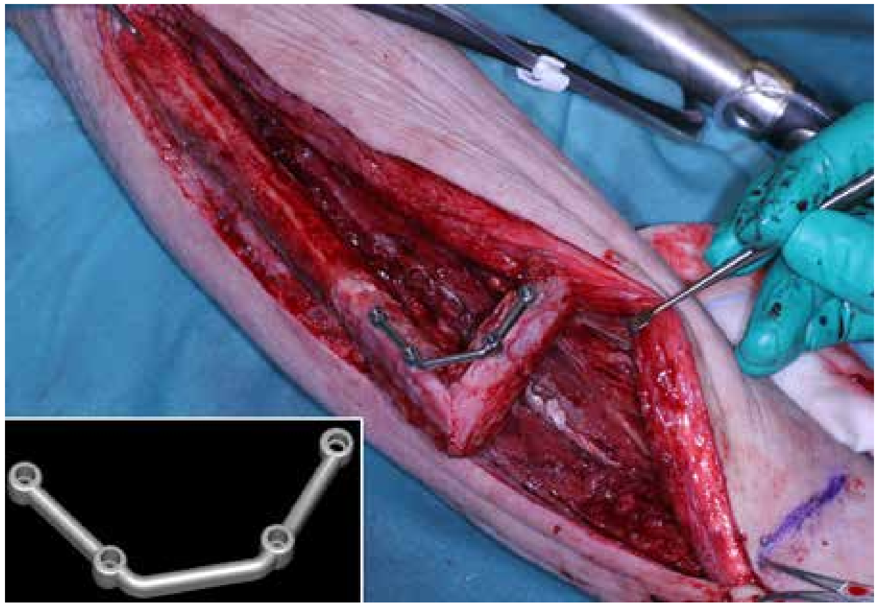

Figure 7 Virtual design of the bar (lower left) and the titanium bar fixated on the implants in the osteotomized fibula (upper right).

Figure 8 Lower denture fixated with clips on the bar attached to the implants placed in the osteotomized fibula. The blood circulation of the graft is still in tact to minimize ischemia time.

Healthcare). The titanium bar was tested on the cast retrieved from the conventional imprint and fitted without tension. To position the implant and bar supported fibula in the correct dimension to the upper dental arch bridge an intermediate occlusal guide was virtually planned in Simplant and printed in a stl model (Fig. 6). The occlusal guide functioned as an upper cast positioner in the articulator to plan the prosthesis; also during reconstruction it functioned as a positioner of the bar-supported fibula. The reconstruction was planned 5 weeks after the prefabrication procedure.

Reconstruction surgery

The second surgical phase included the harvesting of the fibula and, while the vascular support of the fibula was kept intact, performing the osteotomies using the implant supported cutting guide. The cutting guide fitted excellent on the implants and could be used according to the virtual planning. After the osteotomies were performed, the titanium bar connecting the implants was placed and fitted perfectly without any strain on the metal (Fig. 7). Subsequently, the dental prosthesis was fixed onto the titanium bar. Following, the prefabricated fibula with the dental prosthesis in place (Fig. 8) was harvested and placed into the mandible. The graft was situated intra orally using the occlusal guide. Due to volume created by the arterial and venous vessel formation of the fibular graft a change in treatment plan was needed. Fibula blood supply would be compromised too much due to compression of the transplant pedicle and the remaining lower border of the mandible, so a full resection of the anterior mandible was performed. The lower prosthesis was placed, showing a good fit and acceptable occlusion (Fig. 9). Superimposition of the pre- and post operative CBCT showed a near-exact alignment of the fibula graft compared to the planned position (Fig. 10).

Discussion

This case report demonstrates that it is possible to completely plan and perform the secondary reconstruction with immediate prosthetic loading of a maxillo-mandibulair defect by 3D virtual techniques. In contrary to

Figure 9 Intra oral image of the fibula reconstruction and bar retained implant supported lower prosthesis (upper). Occlusion of the prosthesis showing an acceptable interdigitation and good midline alignment (lower).

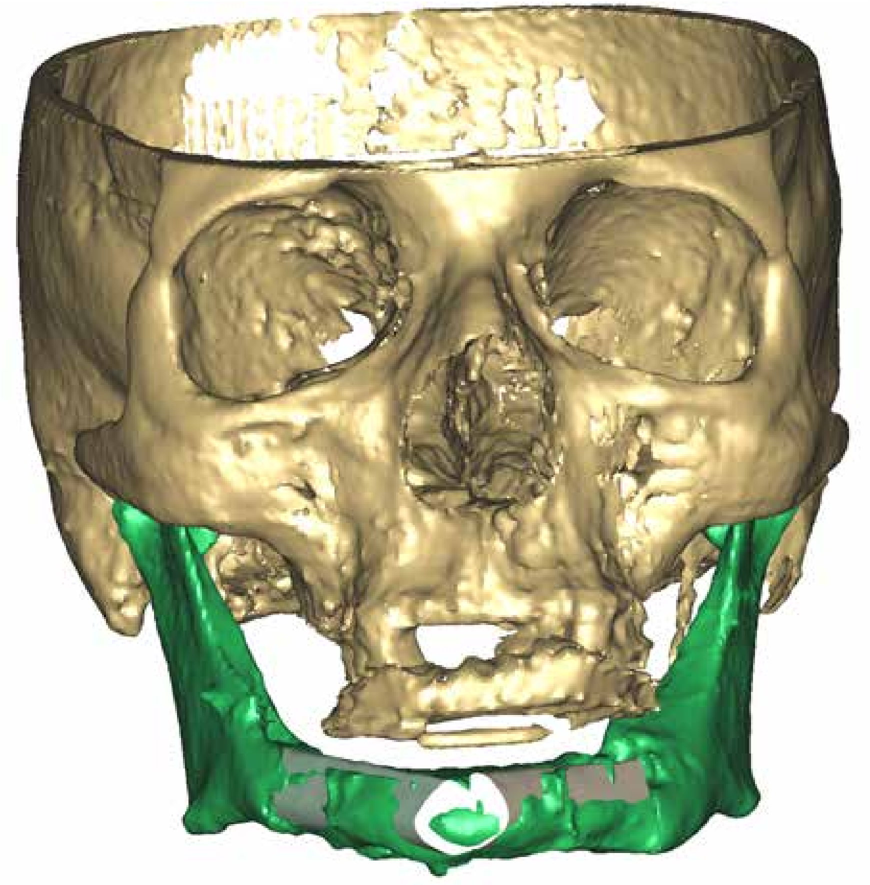

Figure 10 Superimposition of the postoperative CBCT scan and the planned fibula graft position. Alignment was done on the scull and maxilla complex. In grey the planned fibula parts are shown, in green the postoperative mandible and fibula reconstruction are shown. A high similarity in planned and postoperative position of the fibula grafts can be seen corresponding with the position of the denture in figure 9.

conventional planning, no laboratory steps were involved in the virtual planning and the 3D printed guides and occlusal guide showed to be accurate and were easy to use during the various surgical steps. The technical difficulties that had to be overcome included: digitalization of the exact location of the implant position in the fibula, the conversion of data between the software systems, positioning the guide along the axis of the fibula and exact planning of the fibula vessels.

The Lava™ is an intraoral scanner used in impression taking for conventional crown and bridgework. The use of the scanner for the fabrication of an implant supported titanium bar had not been adopted before. The fit of the bar proved very well and tensionless on the cast retrieved from the conventional impression of the implants and fibula, showing the high accuracy of this scanner. Implant supported titanium frameworks made with the CAD-CAM technology, have been reported to fit significantly better than frameworks made with the conventional lost wax technique.[14] The high strength of these bars milled out of a titanium block makes them ideal for fixation of the fibula osteotomized parts.

The second difficulty that had to be solved was the conversion of data between the different software systems. STL file format was chosen as a communication file format and proved to be accurate in the 3 dimensional shape and position throughout the conversions. Van der Meer et al.[13] combined 2 software packages for planning implants in the mastoid region and successfully uses STL file format as a communication file format. This is a critical step in the process, which makes it possible to combine a drilling guide and a sawing/cutting guide fixated on the implants. There are no previous publications on combining planning software systems in this type of reconstructive surgical procedures. Some authors report the use of digitized techniques in implant planning in the jaw. A first step in using an intraoral scanner in planning of implant position on CBCT data was made by Bindl et al.[15] They combined an intra oral scan with the Cerec Bleucam camera and a 3D CBCT dataset to plan implant position. The virtual planning of reconstruction of large maxillomandibular defects with free fibula grafts using 3D printed sawing guides has been reported to be accurate.[9] However, this is the first report of a technique that utilizes 3D virtual planning for

occlusion guided reconstruction of a mandibular defect in which the planning of implants was included.

During surgery it proved to be difficult to find the intended axial positioning of the implant drilling guide on the fibula. By sliding along the axis of the fibula the anatomical shape at positioning of the guide was different compared to the planned position. This resulted in an implant insertion, which was 2 cm more caudally in the fibula than planned. Because the second planning step started from the implant position derived from the optical scan, this difference in position could be incorporated easily in the planning and it did not significantly influenced the end result. The long size of the fibula allowed for these adjustments without compromising the functional outcome. Another problem that had to be overcome was the planning of the exact position of the supporting vessels of the fibula, since the bone was planned to be used as an onlay graft (Fig. 3). When designing a reconstructive plan in which a fibula is used as the only graft with the dental implants already in position, the flexibility of adjusting the position of the fibula in the defect is limited. The position of the vessel proved to be difficult to plan, although it was given ample attention in the pre-operative design. Nevertheless, after harvesting it became clear that the vessel would be trapped between the fibula and the mandible. For this patient this resulted in a change of treatment plan during surgery. Instead of using the fibula as an onlay graft it was used to replace a part of the mandible. In the future a CT based angiogram, combining the 3D position of the bone and vessels might help to plan the vessel configuration of the fibula more precise. However, this change of surgical plan did not alter the outcome of the possibility of the 3D backward planning of a reconstruction in occlusion. Given the exciting new developments in 3D printing and CAD-CAM techniques, in the near future it will probably be possible to virtually plan and fabricate dental prostheses without the need for laboratory articulator steps.[16]

In conclusion, this paper demonstrates the applicability of a full 3D digital workflow in secondary reconstruction of large craniofacial defects and it is shown that this approach provided a digital workflow that is relatively easy to use for any reconstructive surgeon.

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3.2

Full 3D digital planning of implant supported bridges in secondarily mandibular reconstruction with prefabricated fibula free flaps

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Abstract

Objective

In the reconstruction of maxillary or mandibular continuity-defects of (dentate) patients, the most favourable treatment goal is placement of implant retained crowns or bridges in a bone graft that reconstructs the defect. Proper implant positioning is often impaired by suboptimal placement of the bone graft. This case describes a new technique of a full digitally planned, immediate restoration, two step surgical approach for reconstruction of a mandibular defect using a free vascularized fibula graft with implants and a bridge.

Procedure

A 68-year old male developed osteoradionecrosis of the mandible. The resection, cutting and implant placement in the fibula were virtually planned. Cutting/drilling guides were 3D printed and the bridge was CAD-CAM milled. During the first surgery, 2 implants were placed in the fibula according the digital planning and the position of the implants was scanned using an intra oral optical scanner. During the second surgery, a bridge was placed on the implants and the fibula was harvested and fixed in the mandibular defect guided by the occlusion of the bridge.

Conclusion

3D planning allowed for positioning of a fibula bone graft by means of an implant-supported bridge which resulted in a functional position of the graft and bridge.

Introduction

Large maxillary and mandibular bone defects have been a reconstructive challenge throughout time. A free bone transplant to restore a mandibular bone defect was first used in 1900. As reconstructions of larger bone defects with free bone transplants are accompanied by a high risk to dehisce, free vascularized osseous flaps have become increasingly popular since the mid-seventies of the previous century.[1] Large mandibular bone defects can be restored using free vascularized osseous flaps, though masticatory function often remains unfavorable because of problems with retention and stabilization of a mandibular prosthesis. This problem can be solved by placing dental implants in these osseous flaps to retain a mandibular denture; thus improving mastication and speech.[2] However, when placement of dental implants is considered part of the treatment plan, correct positioning of the osseous component of the free flap is eminent to allow for implant placement in the preferred anatomical locations from a prosthodontic perspective. When the bone is incorrectly positioned, implants often have to be placed in a suboptimal position. As a result, post operative function and esthetics with an implant-retained prosthesis are often impaired thereby negatively affecting the patient's quality of life.[2]

The vascularized fibula is often used in the reconstruction of large maxillary and mandibular defects.[3,4] Furthermore, implant survival in the vascularised fibula is shown to be high, which might be due to the presence of dense cortical bone contributing to adequate initial implant stability.[5,6] Rohner et al[7] described a method to prefabricate a free vascularised fibula graft to obtain optimal support of the superstructure and to create a stable peri-implant soft tissue layer as well. Prefabrication includes pre-operative planning of implant insertion, osteotomies of the fibula and planning of a skin graft on the fibula for a thin lined soft tissue reconstruction. The technique by Rohner et al[7] essentially is a two-step approach. The first surgical step starts with planning of the implants in the fibula using stereolithographic models of the maxillo-mandibular complex and the fibula. Next, a backward planning for the placement of the dental implants is made based on the desired dental occlusion, which yields a drilling guide for inserting the dental implants at the exact pre-defined position in the

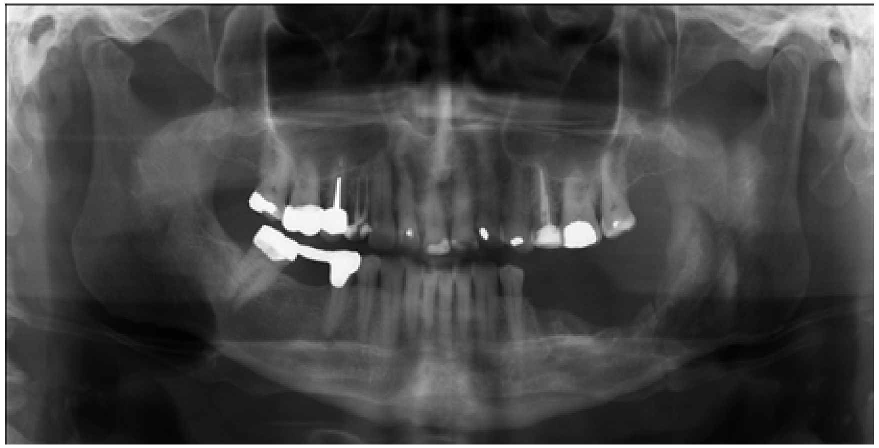

Figure 1 Panoramic radiograph showing osteolysis due to osteoradionecrosis of the left corpus of the mandible and a pathologic fracture. In the upper and lower jaw a natural dentition is present with a bridge in the mandible from the second premolar to the second molar and absence of the second premolar and all molars on the left side. Periradiculair healthy bone is present and the periodontal chart revealed no pockets or bleeding on probing of the remaining dentition.

fibula. The first step is completed by taking impressions of the implants in the fibula. The second step encompasses of preparing the cutting guide for segmentation of the fibula and fabrication of the superstructure for completing the prosthodontic rehabilitation. The superstructure also acts as a guide for correctly positioning the fibula segments in the mandibular or maxillary defect that has to be reconstructed. A disadvantage of this technique is the extensive and demanding planning procedure, which requires a lot of laboratory work by an experienced technician, especially in the manufacturing of the drilling and cutting guides.

Recent developments in 3-dimensional (3D) digital planning and additive manufacturing printing allow for entirely digitizing this procedure for edentulous jaws[8], but never has been described for dentate patients. In this paper we describe the next step towards functional reconstruction of mandibular or maxillary defects in dentate patients, viz. full 3D digital planning of a functional reconstruction with rehabilitation of all missing teeth. The main advantage of virtual planning compared to the conventional planning is that it significantly reduces the laborious manual steps.

Full digital planned secondary mandibular reconstruction

A 68-year-old patient was diagnosed with a squamous cell carcinoma (T3N0M0) of the left tonsil in 2005. Treatment had consisted of accelerated radiotherapy of the oropharynx and neck at the left side with a cumulative dose of 70 Gy on the tonsil area and 50 Gy on the corpus of the left mandible. He developed osteoradionecrosis of the latter area in 2010. Despite hyperbaric oxygen therapy, combined with surgical removal of the second molar and bone sequesters, including local decorticalisation, osteoradionecrosis progressed and resulted in a pathologic fracture of the mandible in the left molar region with a persisting submandibular fistula in 2011 (Fig. 1).

The patient was offered a local resection of the diseased bone combined with a conventional reconstruction with a free vascularized osseous flap or a reconstruction with a free vascularized osseous flap with the subsequent planning of an implant supported bridge. The patient preferred the latter. Written informed consent was obtained from the patient for this treatment. The treatment was divided into 4 phases. The first phase was the 3D pre-

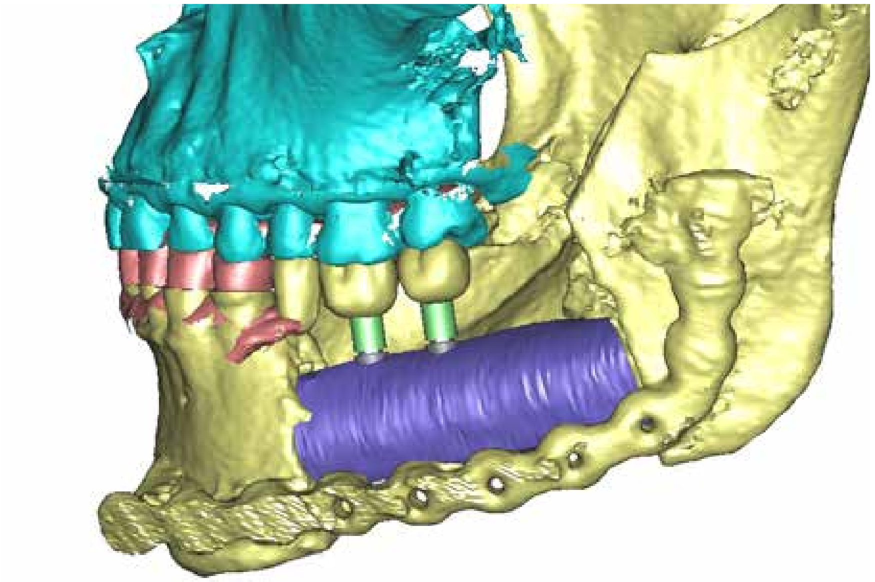

Figure 2 Virtual planning of a fibula segment derived from a CT scan of the lower leg (Siemens AG Somatom Definition Dual Source, Forchheim, Germany). The fibula was positioned in the 3D model of the CBCT of the maxillofacial region and the mandible after the resection. A virtual set up of the missing molars en premolar was performed in Symplant Crystal. Two Implants (Nobel Speedy; Nobel Biocare AB, Götenborg, Sweden) were planned in an ideal position in the fibula supporting the missing dentition in the optimal prosthetic position for the bridge.

planning of the fibula resection and implant positioning related to the needed reconstruction of the mandibular defect (Fig. 2). The second phase comprised of prefabrication of the fibula by guided implant insertion, digital implant registration, applying a skin graft around the implants and resection of the necrotic bone of the mandible. In the third phase the implant supported bridge and the fibula cutting guide were manufactured. The fourth and final phase included the reconstructive surgery of the bony mandibular defect with the free vascularized fibula flap and the bridge in the proper occlusion and position in the mandible.

1. Virtual pre-planning of the fibula resection and implant position related to the jaw defect

For virtual pre-planning, the maxillofacial region and the mandible were scanned with a cone beam CT (CBCT) (i-CAT, Imaging Sciences International, Hatfield, USA) and the fibula of choice (right or left) was scanned using a CT scanner. The maxillofacial scan was imported into ProPlan CMF (Synthes, Solothurn, Switserland and Materialise, Leuven, Belgium), whereafter a 3D model was created by volume rendering. The upper and lower dentition was optically scanned using the Lava™ Chairside Oral Scanner C.O.S. (3M™ ESPE™, St. Paul, USA) to retrieve a detailed surface model of the dentition. The surface scan was imported into ProPlan CMF at the correct anatomical location. The first surgical procedure started with the virtual planning and visualization of the jaw defect. For functional reconstruction a prefabricated free fibula graft was chosen. The fibula graft has ideal aspects for mandibular reconstruction as it has a substantial cortical layer assisting in excellent implant stability, a good shape for jaw reconstruction, and a vessel with sufficient length to reach the neck vessels for recirculation connection.[3] The reconstruction was planned digitally using ProPlan CMF and Simplant Crystal (Materialise Dental, Leuven, Belgium). The virtual reconstruction started with the CBCT of the maxillofacial region and the mandible. The file was converted and loaded into ProPlan together with the CT scan of the fibula. The fibula segmentation was planned following the jaw defect. A virtual set up of the missing dentition was performed. Implants were planned in the fibula supporting the missing dentition in the optimal prosthetic position (Fig. 2). The planning was used to produce a drilling template for guided implant placement in the fibula. The

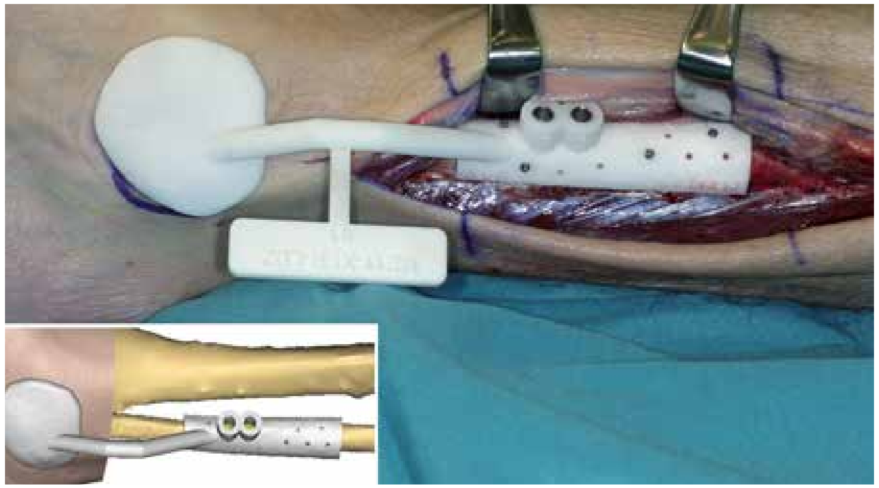

Figure 3 The 3D printed drilling guide (Synthes, Solothurn, Switzerland and Materialise, Leuven, Belgium) is positioned on the ventral rim of the fibula bone in the left lower leg. The guide was fixated with miniscrews (KLS Martin Group, Tuttlingen, Germany). The implants were placed guided through the drilling guide. The insert shows the virtual planning of the guide (ProPlan CMF).

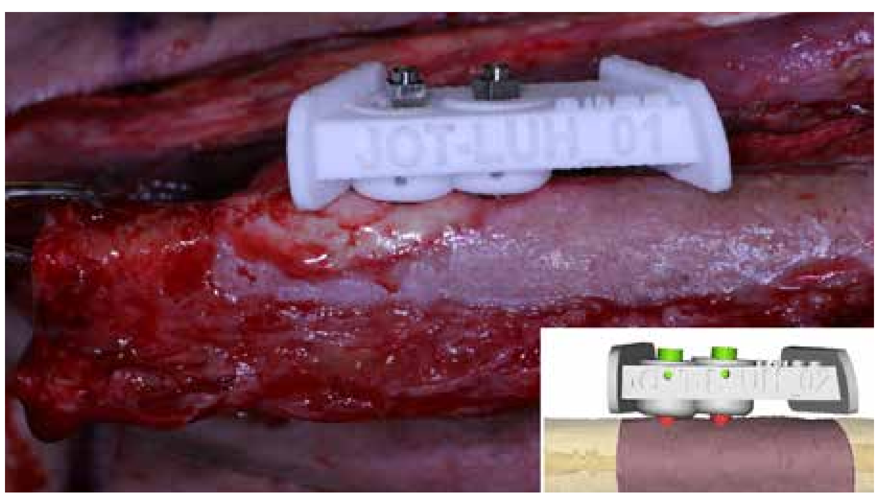

Figure 4 Selective laser sintering model of the cutting guide (Synthes, Solothurn, Switzerland and Materialise, Leuven, Belgium) fixed on the implants with Nobel guide fixation screws in the left fibula. The insert shows the virtual cutting guide (ProPlan CMF).

drilling guide was planned on the level of the periostium of the fibula with an extension to the skin of the lateral malleolus for optimal support of the exact planned position. The drilling and cutting guides were sterilized using gamma irradiation.

2. Prefabrication of the fibula

The first surgical step included placement of the dental implants in the fibula by using the drilling guide and digital registration of the implant position. After surgical approach of the fibula, comparable to the standard technique used for free-vascularised fibula transfer, the ventral rim of the fibula was exposed. The drilling guide was placed in position, with the lateral malleolus as reference, and fixed on the bone with miniscrews (KLS Martin Group, Tuttlingen, Germany; Fig. 3). After placement of the implants the guide was removed. Since guided implant placement always has a small error in implant position compared to the planned position,[9,10] an intra operative optical scan of the implants with scan abutments (E.S. Healthcare, Dentsply International INC) was made with the Lava™ Chairside Oral Scanner to register the exact position and angulations. The Lava scanner is an intraoral optical scanner developed for scanning crown preparations. The scanner has a very high accuracy, which makes it useful for digitizing implant positions and replacing the conventional impression in this process. For research purposes we registered the position of the implants also by taking a conventional dental impression. Hereafter, the periostium around the implants was covered with a split skin graft, to create a stable attached peri-implant soft tissue layer and covered this with a Gore-Tex patch (W.L. Gore and Associates, Flagstaff, Ariz). The wound in the lower leg was closed primarily.

3. Virtual planning of the bridge and cutting guide preceding the second surgical step

The data of the optical scan using the Lava™ Chairside Oral Scanner of the implant positions in the fibula was imported in the Simplant software and manually matched with the original fibula planning creating a superimposed fusion model with the accurate position of the implants. The resection margins of the fibula were optimized according to the post operative CBCT scan of the head. An implant supported cutting guide of the fibula was

Figure 5 At the left an intermediate positioning wafer is shown which is designed virtually in between the upper and lower dentition and the implant position (left panel). The purpose of this wafer is to translate the implant position and virtual planning of the fibula to the articulator. The occlusal guide printed (Synthes, Solothurn, Switserland and Materialise, Leuven, Belgium) in a STL model in the articulator (middle panel). The implant supported bridge in the correct dimension to the upper and lower dentition with a partial splint in between to position the bridge out of occlusion to prohibit transmission of occlusal forces on the fibula graft during consolidation (right panel).

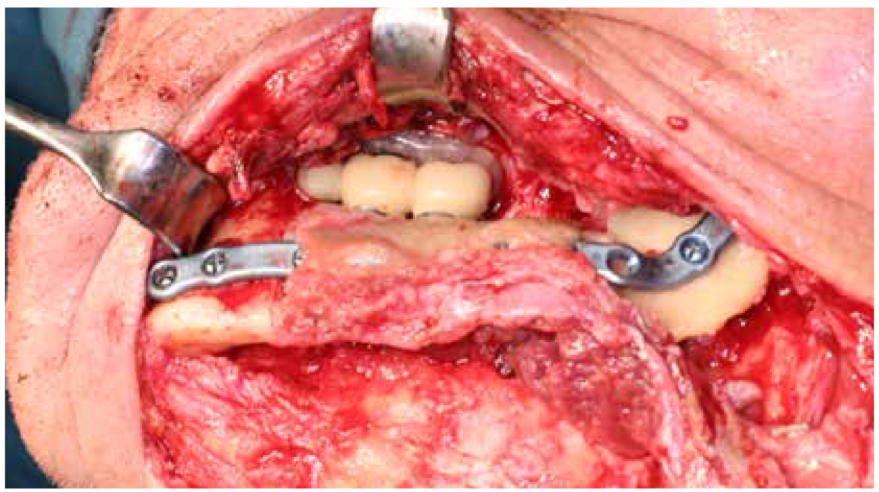

Figure 6 Fixation of the fibula was performed with 2.4 mm reconstruction plates (Synthes, Solothurn, Switserland). The positioning splint was used to position the bridge and graft out of occlusion.

then planned and printed (Fig. 4). A digital design of the custom bridge abutment was virtually planned on the scanned position of the implants and subsequently converted to a STL-file from which the bridge abutment was milled out of titanium (E.S. Healthcare). The titanium structure was tested on the cast retrieved from the conventional impression and fitted without tension. To position the implant supported bridge in the correct dimension to the upper and lower dentition an intermediate occlusal guide with an extension to the implants was virtually planned in Simplant and printed in a STL model (Fig. 5). The occlusal guide functioned as an implant positioner in the articulator to finish the bridge with composite. The bridge was planned out of occlusion to avoid occlusal forces to interfere with bone healing of the fibula.

4. Reconstructive surgery of the jaw

The second surgical step was planned 5 weeks after the prefabrication procedure to give the implants sufficient time to osseointegrate. The fibula with the implants was harvested while the vascular supply of the fibula stays intact, the osteotomies were performed using the implant supported cutting guide. After the osteotomies were performed, the bridge connecting the implants was screwed into place. The defect edges can be optimized to fit the reconstructive planning exactly using cutting guides. The prefabricated fibula with the bridge in place was detached from the blood vessels and placed into the mandibular defect (Fig. 6). The graft was situated intra orally using a positioning wafer, which was made out of occlusion to prohibit occlusal forces in the consolidation time of the fibula graft to the jaw (Fig. 7). The skin graft was sutured to the oral mucosa. The patient was discharged from the hospital one week after surgery. A post operative panoramic radiograph shows the favorable fit of the bridge on the implants (Fig. 8).

Discussion

With this new technique it is possible to fully plan and perform the secondary reconstruction, using optical scanning of the implant position with an intra

Figure 7 The insert left shows the positioning of the bridge, which is deliberately made out of occlusion in the consolidation period of the fibula bone to the mandible. The bridge is finished with composite. The insert right shows the bridge after the healing period, the composite was corrected to a better occlusion and crown shape. In the future the bridge will be finished with ceramic in a more ideal shape. Three months post operative the peri-implant soft tissue created by the split skin graft shows a favorable attached lining.

Figure 8 The post operative orthopantomogram shows a favorable fit of the bridge on the implants. It also shows the well-planned segmentation of the fibula and resection of the mandible

oral scanner and manufacturing a bridge by CAD-CAM techniques. In contrary to conventional planning, no laboratory steps were needed in the virtual planning and the 3D printed guides and occlusal guide showed to be accurate and were easy to use during the various surgical step.

Secondary reconstruction of maxilla-mandibular defects using a prefabricated fibula always implies that the patient must be willing to undergo at least two surgical procedures. It is possible to reconstruct such defects without pre-planning and insert implants directly or separately in a later stage. As Schmelzeisen et al.[11] have shown that without pre-planning a major problem is the positioning of the implants as in only two of the nine patients in whom implants were inserted in the fibula before fixating the fibula in the defect, these implants could be used without placement of more implants. This observation showed that direct implant placement in a graft without planning is prone for suboptimal placement of the implants. Proper planning and guided placement can prohibit this.

There are three major benefits of using pre-fabricated fibulas instead of conventional planning. First, occlusion guided implant planning ensures a functional implant position and thus a functional graft position. Therefore implant placement and prosthetic rehabilitation are not impaired by wrong placement of implants and bone. Secondly, the skin graft provides an excellent thin soft tissue cover around the implants of the fibula bone (Fig. 7).[12] Skin pedicles that come with a free graft are much more bulky and less appropriate for lining implants. In large maxillofacial defects there is usually not only a lack of bone but also a lack of soft tissue, a problem that can be resolved by the proposed technique. Third, the ischemia time of the flap is limited because segmentation of the fibula and fixation of the bridge on the implants is done in the lower leg with the vascularization still being intact. This reduces the time needed to fixate the bone transplant in the jaw defect thus promoting the chances for flap survival.[13]

Planning backward from the preferred occlusion towards surgical reconstructive surgery may result in placement of the bone at a different position than would have been the case in conventional reconstructive surgery. In the case we described to illustrate our new technique, this resulted in placement of the fibula in a higher position in the midline of the mandibular bone instead of aligning it with the lower border of the mandible.

This position was chosen to provide optimal support of the fibula under the bridge without compromising oral hygiene. The results were good intra oral peri implant conditions of the soft tissues without creating a facial aesthetic problem for the patient (Fig. 7).

Titanium abutment bridge structures can be planned digitally and milled highly accurately.[14] However, to date it is not possible to finish the bridge with ceramic or composite in a digitized procedure. To be able to finish the titanium bridge structure with composite, the bridge has to be positioned in an articulator together with a cast of the upper and lower dentition. To support this step in the proposed process an occlusal guide was designed. The purpose of this guide was to translate the digital implant position to the articulator for finishing the bridge with composite. Every step back from a digital situation to plaster models in an articulator is a step back in accuracy and therefore unwanted. In an ideal digital process a total CAD-CAM manufactured ceramic bridge in the appropriate color should overcome this unwanted extra step of conversion.

The accuracy of the 3D images produced by intra oral scanners has not yet been assessed. There is still lack of clinical evidence pointing towards the limits of these scanners. Intra oral scanners offer the possibility to digitize preparations of crowns, bridges and single implant positions relative to adjacent teeth. In this case the scanned area of the fibula is much larger than when applying the scanner for an intra oral scan. The tensionless fit of this bridge on two implants, as was shown in the case presented, points out how powerful these scanners in combination with CAD-CAM superstructures can be. Future research should aim at determining the accuracy of these intra oral scanners for their use in larger implant supported constructions.

From this study it can be concluded that 3D virtual planning provides an essential, powerful tool for complex reconstruction of mandibular defects. All necessary guides for this type of surgery can be designed by computer and printed by additive manufacturing. We foresee that for complex reconstructions 3D virtual planning combined with additive manufacturing might evolve to the standard approach instead the use of conventional dental laboratory procedures.

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3.3

Is virtual planning and guided surgery applicable to other osseous free vascularized flaps?

Introduction

Composite full thickness resection of the mandible or maxilla as a part of the oncologic treatment plan can result in a large defect of the jaw. These resections are in general followed by immediate reconstruction with an osseous free vascularized flap shaped and placed free hand.[1,2] For mandibular reconstructions the free vascularized fibula flap (FFF) is considered to be the golden standard.[3-5] Other osseous free vascularized flaps, like the deep circumflex iliac artery flap (DCIA) and the free vascularized scapula flap (FSF), are considered as proper alternative options.[6,7,8] The DCIA flap offers a large volume of bone and a suitable contour to reconstruct the maxilla.[9] The internal oblique muscle that accompanies this flap offers a good opportunity to seal the oral cavity from the nasal cavity.[10] The lateral border of the FSF offers less bone volume, but the availability of extended soft tissue components on the same vascular pedicle together with the option to segment the inferior angle and tip makes the FSF to a versatile flap too.[10,11] The available bone volume of especially the DCIA and in lesser extent the FSF offer, like the FFF, a sufficient bone volume and bone quality to enable rehabilitation with dental implants, although the FFF provides the surgeon with more cortical bone than the DCIA and FSF so that primary implant stability is easier to achieve.[12,13] Moreover, both the DCIA and FSF can be used to reconstruct defects of the mandible and maxilla. Virtual planning of the DCIA and FSF seems possible and adheres the same principles as planning of the FFF.[14] However, placement of the guides to facilitate the resection of the lateral scapular rim segment is more complex, because of anatomical differences. The DCIA flap offers bony support of the cutting guide on the lateral and caudal rim to a certain extent, but the central part of the flap offers less sight and possibilities to facilitate guided sawing of the bone. The FSF offers limited bony support of the cutting guide on the graft due to the origo of the muscle cuff existing of the m. infraspinatus, m. teres minor/major and m. subscapularis portions that must be preserved around the lateral rim to facilitate blood supply.[15] Large bony support of the cutting guide on the FSF graft is therefore compromised, but on the other hand the dorsal spine and caudal tip of the scapula can be used to facilitate guide support. Precise planning of DCIA and FSF grafts offer great advantages because the

precise size and shaping of both flaps is not easy to determine for the surgeon when harvesting the graft. Besides, the FSF is known to be more prone of pseudoartrosis between bone segments in reconstruction of the mandible when the contact between the segments is suboptimal. Guided segmentation is known to offer high accuracy and therefore good chances of bony contact between the bone segments and might therefore be a step forward in the use of FSF in the reconstruction of maxillofacial defects.[16] The aim of the cases described in this chapter is to highlight the possibilities of 3D planning of the DCIA flap and the FSF.

Case 1: 3D planning of a DCIA flap and dental implants for maxillary reconstruction

A 43-year-old male was diagnosed with a T1N0M0 chondroblastic osteosarcoma of the left maxilla. Treatment comprised chemotherapy and tumor resection including a hemimaxillectomy. Due to the extent of the defect that results from the resection, immediate reconstruction using a DCIA flap was chosen as the preferable treatment. The patient had a full dentition at the time of surgery. The iliac graft was planned virtual to reconstruct the shape of the midface and adhere a functional position to facilitate implant placement. Three implants were planned to be inserted in the immediate reconstruction, after fixating the DCIA flap in the maxilla region. The implants were to be inserted guided using a guide supported on the remaining upper dentition.

Virtual planning of the iliac crest graft

The reconstruction was planned digitally using ProPlan CMF (Synthes, Solothurn, Switzerland and Materialise, Leuven, Belgium; Fig. 2). The maxillofacial region and mandible were scanned with a CBCT (i-CAT, Imaging Sciences International, Hatfield, USA) at 0.3 voxel size. The pelvis was scanned using a CT scanner (Siemens AG Somatom Definition Dual Source, Forchheim, Germany). The CBCT of the maxillofacial scan and the CT of the pelvis were imported into ProPlan CMF, and 3D models were created by volume rendering (Fig. 1 and 2). To facilitate dental rehabilitation 3 dental implants were planned in the iliac crest graft for the fabrication of a bridge (Fig. 2). A 3D print of the guide to facilitate implant placement and a 3D print of the DCIA graft was made (Fig. 3). The cutting guide to harvest the DCIA was designed to fit the periosteum

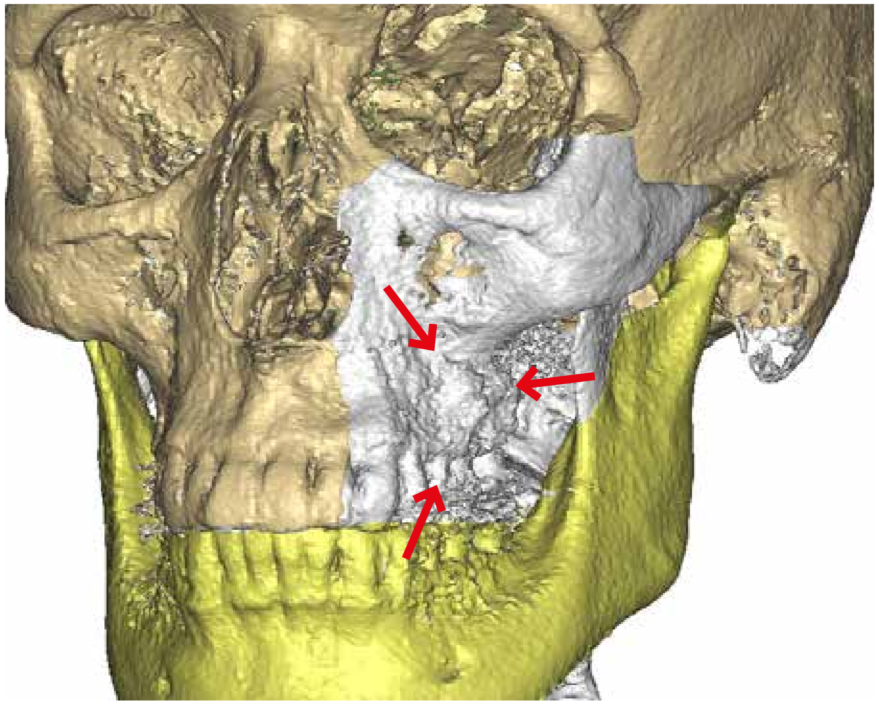

Figure 1 3D bone model of a CBCT showing the tumor in the left maxillary molar region (red arrows). The planned resection area of the maxilla is shown (grey).

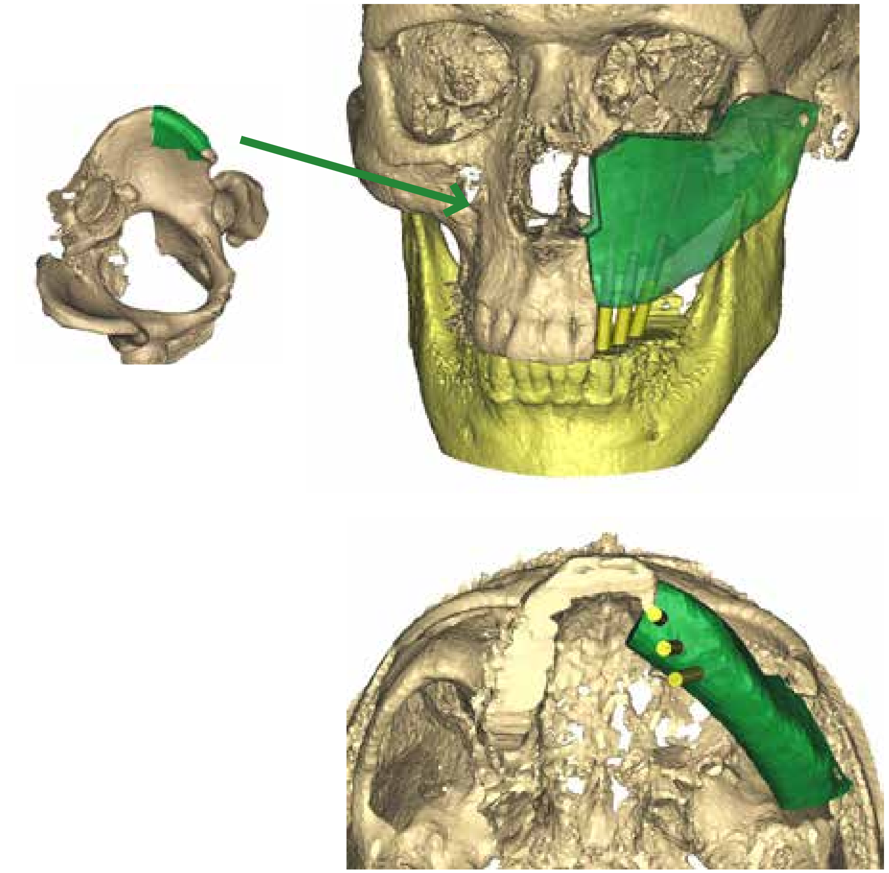

Figure 2 3D bone model of a CT of the pelvis with the planned graft segment DCIA flap indicated (left). The planned DCIA is positioned in the maxillary defect (right and lower). The latter 2 show also the three implants that are planned in the DCIA. In yellow 3 tubes are shown on the implants to help plan the implants in the direction opposite to the antagonistic dentition.

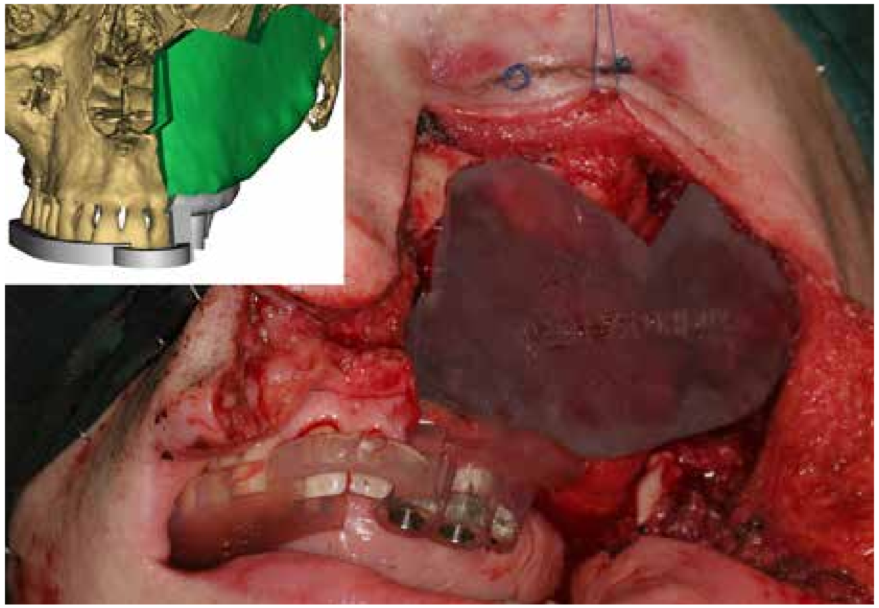

Figure 3 The insert on the left upper side shows the 3D planning of the DCIA flap and the implant guide. The central clinical picture shows the maxillairy defect after resection of the tumor. In the defect the 3D print of the DCIA graft is show. This print is used to check the match between the graft and the recipient area. After this check the harvesting and guided sawing of the DCIA flap can be performed. The dentition supported drilling guide to facilitate guided implant placement in the graft is also shown.

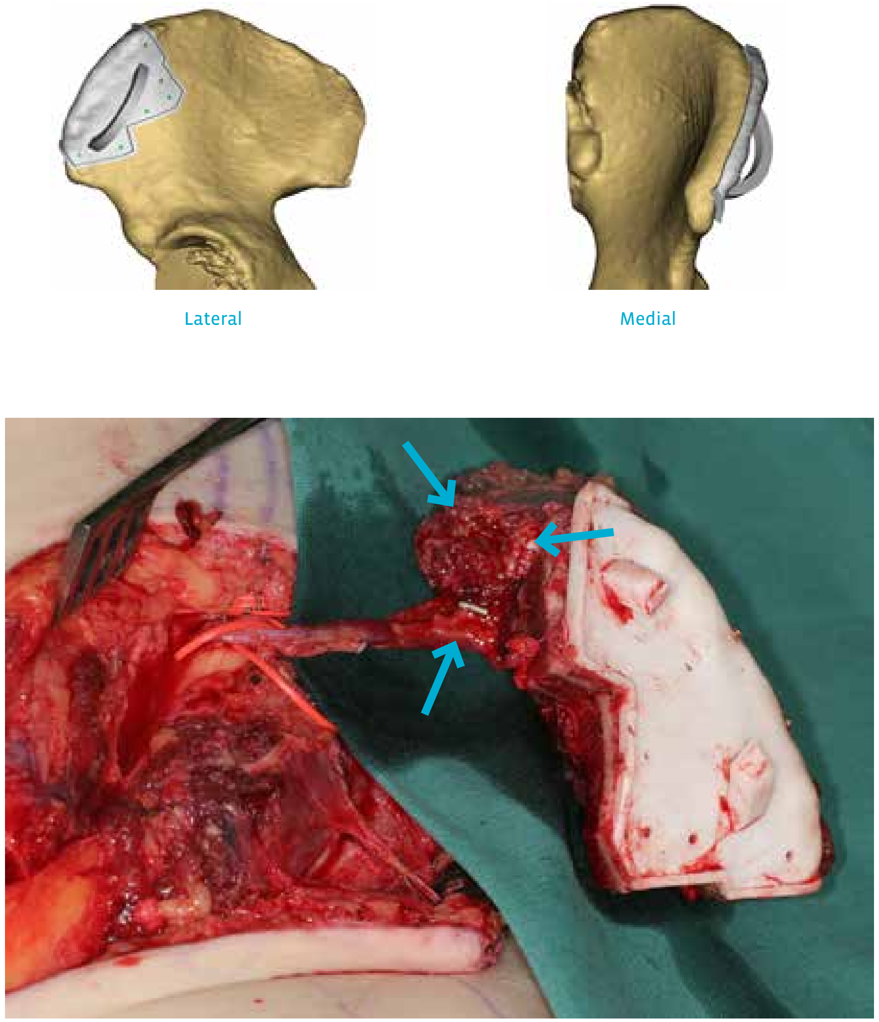

Figure 4 In the upper part the cutting guide placed on the lateral/caudal anterior iliac crest rim to facilitate cutting of the graft in the planned contour is shown. Holes for temporary screw fixation are planned in green.

In the lower part the intra operative image showing the DCIA flap after harvesting according to the cutting guide, but still attached to its native blood supplying artery and vene. Note how well the shape of the flap is following the cutting guide and also the muscle soft tissue bulk (arrows).

of the lateral rim of the left anterior iliac crest, extending to the caudal lateral side (Fig. 4).

The tumor resection and reconstruction surgery

The resection of the tumor is performed first and a 3D printed outcome model of the planned iliac graft was tried in the resection gap. It turned out that the edges had to be grinded only slightly to facilitate good seating of the 3D printed outcome model (Fig. 3). Knowing this, the iliac graft was harvested using the 3D printed resection guide. The edges of the graft were prepared to exactly match the resection guide while the blood supply of the graft was still intact (Fig. 4). Even though the bony edges of the graft resembled the planning well, proper seating was prohibited due to the soft tissue bulkiness of the flap in the region of the arterial and venous blood supplying vessels. After grinding the zygomatic bone in the region of the infratemporal fossa the graft could be inserted into the defect. The graft was fixated with three 2.0 mm titanium osteosynthesis plates (2.0 system, KLS Martin Group, Tuttlingen, Germany). Even though the printed outcome model of the DCIA graft could be seated well, the flap itself could not, because of the soft tissue bulk in the vessel region; bony contact of the graft was adequate. The implant guide could therefore not be seated well. Immediate implant placement was postponed for this reason. Post operative the accuracy measurements of the DCIA graft position was done and a adjusted planning of the implants was made. Post operative the position of the reconstruction was evaluated using a CBCT. The post operative CBCT was compared to the virtual plan and the graft deviated 9.2 mm. The deviation was most prominent in the dorsal region where the soft tissue bulk of the muscle and vascular feeders was located. The graft consolidated well in the post operative period.

Implant planning and placement in the iliac graft

In a secondary surgery three implants were planned on congruent positions like the implant plan that was already made as a part of the reconstructive plan primarily. It turned out that the primary implant plan was still viable but to adhere to the definite graft position the implants were shifted 4,3 mm on average. The shift was mainly in the axial direction of the implants. The placement of three implants (Nobel Speedy, Nobel Biocare AB, Götenborg,

Sweden) was performed guided two years after the tumor resection and iliac graft reconstruction was carried out. After three months, a three-segment bridge and a crown were made on three implants (Fig. 5). To evaluate the implant position, post operative a CBCT was made and The DCIA flap and the post operative CBCT was compared to the virtual plan. The implants deviated 1.2mm from the virtual plan ((range:1.09-1.33mm) measured at the center of the implant). The implant-supported bridge and crown function well (follow-up two year after implant placement).

Case 2: 3D planning of a free vascularized scapula flap, prefabricated with dental implants and a split skin graft, in a secondary reconstruction

A 64-year-old patient had a continuity defect of the lateral mandible on the left side and mental part due to resection of a squamous cell carcinoma (Fig. 6.). The patient was tumor free for three years and presented with the wish to improve his chewing ability. Because there was substantial arteriosclerosis of the blood vessels of the lower legs the free vascularized scapula flap was chosen to reconstruct the defect. A two-segment reconstruction was planned using the lateral border of the right scapula. A total of five implants were planned. Because of the lack of soft tissues in the planned implant region, it was decided to reconstruct the defect with a prefabricated graft according to the digital Rohner method described in chapters 3.1 and 3.2.

Virtual scapula planning

The reconstruction was digitally planned using ProPlan CMF software. The maxillofacial region and mandible were scanned with a CBCT. The scapula region was scanned using a CT scanner. The maxillofacial scan and scapula scan were imported into ProPlan CMF, and 3D models were created by volume rendering. In the upper and lower jaw the patient was edentulous. The upper and lower dentures were scanned using the CBCT (0.2 voxel). The scans were imported into the ProPlan CMF software and 3D models were created of the lower and upper denture and positioned at the correct location. The scapula reconstruction was planned in two segments onto the lower border of the mandible, following the anatomic contour of the mandible and matching

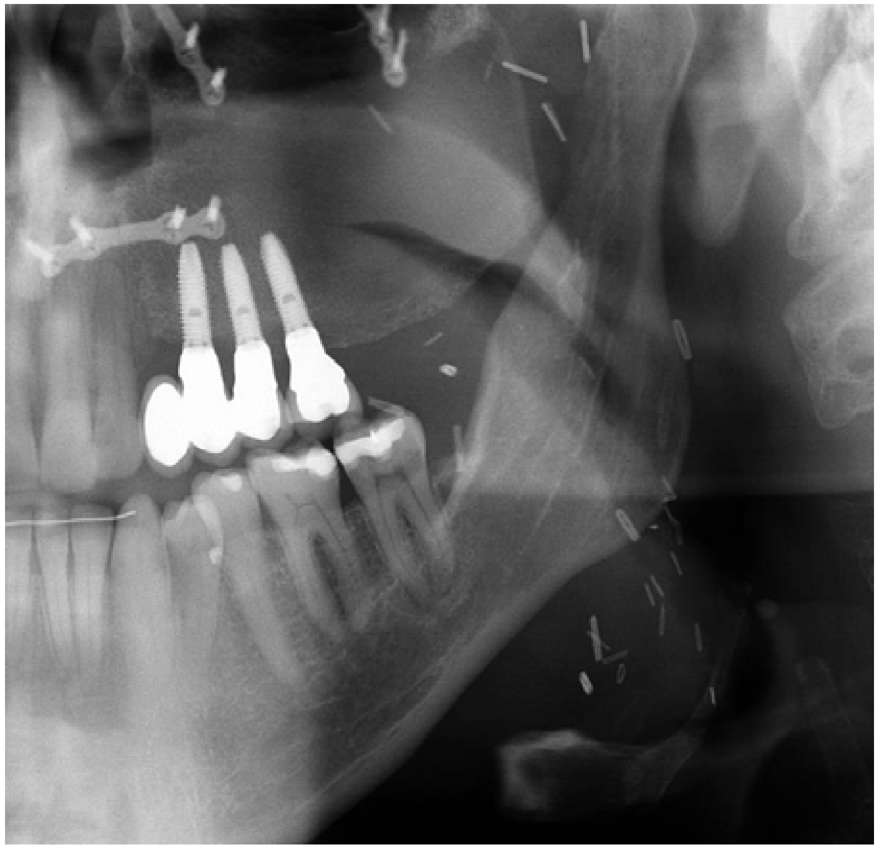

Figure 5 Orthopantomogram showing the DCIA flap with the three implants (Nobel Speedy, Nobel Biocare AB, Gotenborg, Sweden), the implant-supported bridge and the implant-supported crown. A granuloma around the 37 is seen as well.

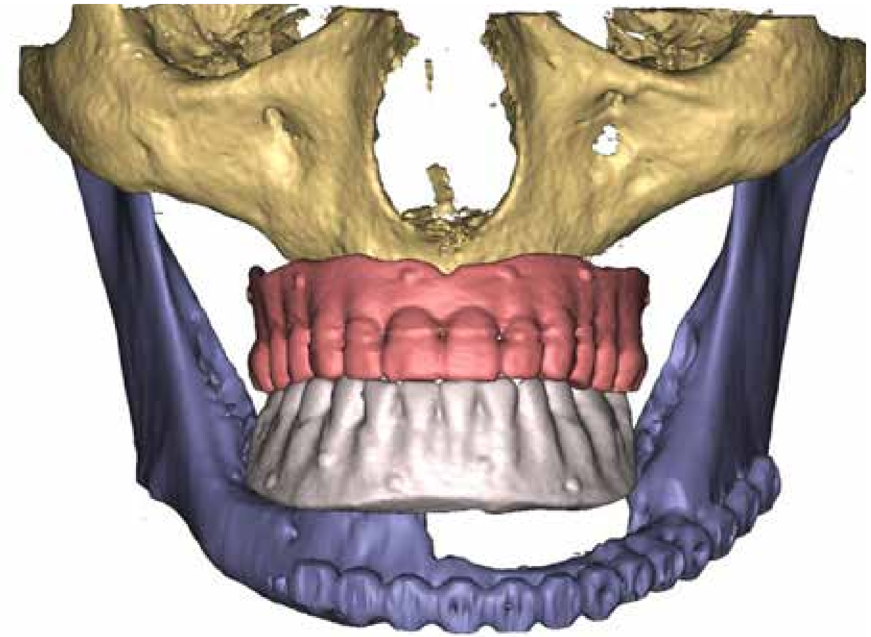

Figure 6 Visualization of 3D models extracted out of a CBCT of the upper and lower jaw of the patient. The upper and lower denture were scanned using glass markers and positioned into the CBCT and matched with the corresponding glass markers in the CBCT. A reconstruction plate is shown on the mandible bridging the gap of the tumor resection in the left corpus.

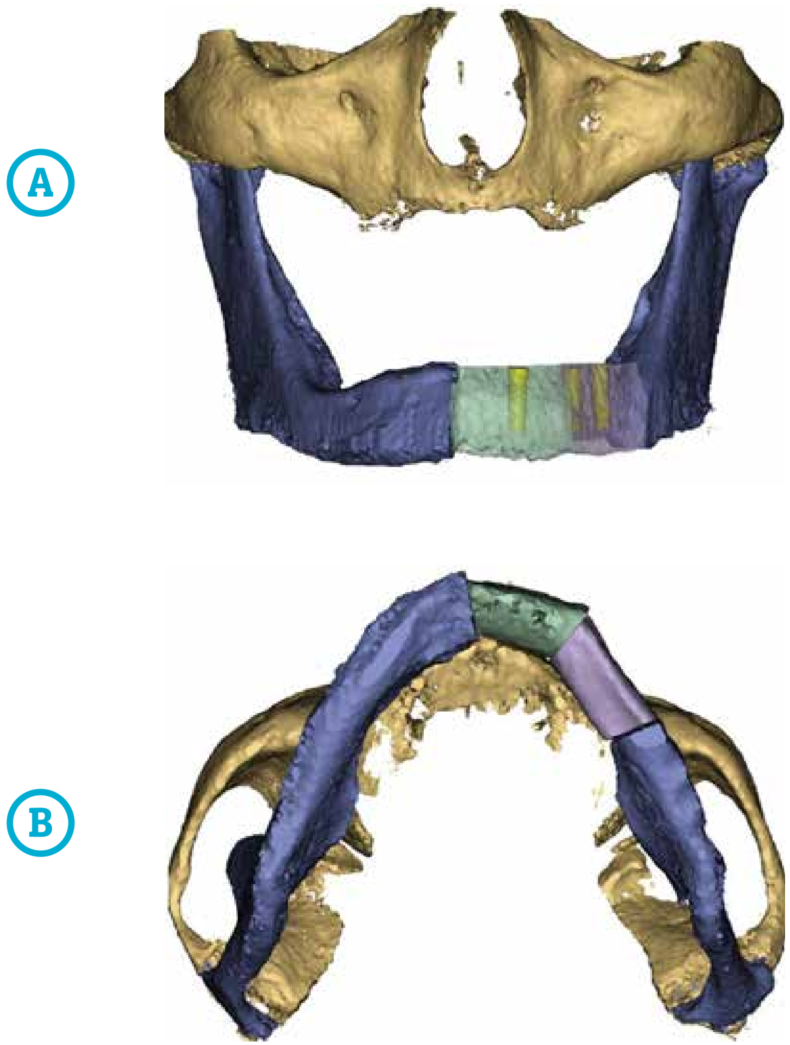

Figure 7 Showing a two-segment scapula reconstruction (green and purple segment) in the frontal (A) and caudal view (B). The height and contour of the original mandible is maintained in the planning of the reconstruction segments. Three implants are planned in the scapula segments. One in the ventral segment (green) and one in the dorsal segment (purple).

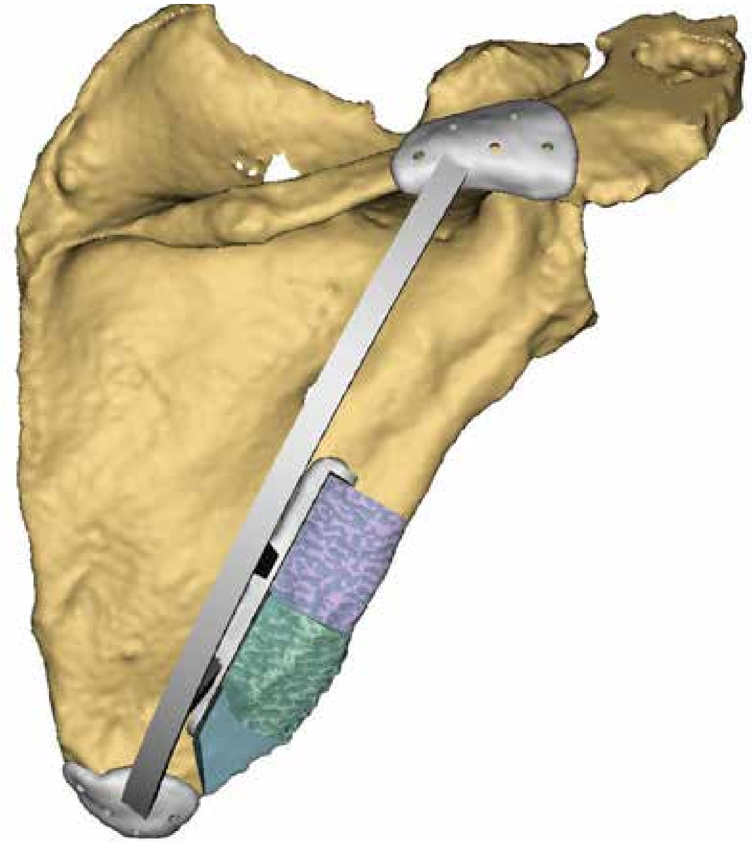

Figure 8 CT-scan of the scapula (3D model), planning of the scapula resection guide and two scapula graft segments (purple and green). The graft that is primarily resected to facilitate implant planning is blue and includes the purple and green segment. The cutting guide is used to resect the blue segment, which can be rotated to visualize the cutting plane and facilitate implant placement between the cortical layers in the cutting plane. The inferior angle tip was not included in the two-segment scapula graft planning and could therefore serve as a support location for the guide together with the spine.

the height of the mandible (Figs. 7 and 8). Five implants (Nobel Active; Nobel Biocare AB, Götenborg, Sweden) were planned digitally to support the implant-retained mandibular denture, viz., three in the scapula graft and two in the remaining mandible segment on the right side. The implants were planned in the medial side of the lateral scapular rim (osteotomy side of the rim) because the vascular bundle is situated on the lateral rim side, implant placement on the lateral rim can jeopardize the vascularity of the graft (Figs. 7, 8 and 10). Through 3D printing a drilling template for guided implant placement in the scapula was fabricated. Sterilization of the guide was performed using gamma irradiation.

Prefabrication of the scapula

In the first surgery the implants are placed into the scapula and the split skin graft and Gore-Tex patch (W.L. Gore and Associates, Flagstaff, Ariz) are placed to facilitate a fixed peri-implant soft tissue layer. The implants can only be placed after resecting the scapula rim and rotating it outward dorsal, to facilitate this guided a resection guide is printed in 3D as well. The dorsal spine of the scapula was exposed; the cutting guide was placed and fixed on the scapula bone with miniscrews (Synthes, Solothurn, Switzerland). The lateral border was cut guided until the inferior tip, and rotated outward dorsal (Figs. 8 and 10). The drilling guide was placed on the bicortical medial side of the resection plane on the lateral border segment and three Nobel Active implants Nobel (Biocare AB, Götenborg, Sweden) were inserted. An intra operative optical scan of the implants with scan abutments (E.S. Healthcare, Dentsply International INC.) was made with the Lava™ Oral Scanner to register the exact position and angulations. Hereafter, the peri-implant region of the scapula graft was covered with a split thickness skin graft and a Gore-Tex patch, rotated back inward and fixated with 3 osteosynthesis plates (Synthes, Solothurn, Switzerland). The wound was closed primarily and the implants and split skin graft were left to heal for 5 weeks. In the mandible two Nobel Active implants were inserted according to the guide and also their position was registered using the oral scanner (Fig. 9).

Intermediate virtual planning

The Lava™ Oral Scan was imported in the ProPlan CMF software and manually matched with the original scapula reconstruction planning, creating a superimposed fusion model with the accurate position of the implants. A cutting guide to facilitate the segmentation osteotomies of the scapula was planned and printed. The digital design of the superstructure (titanium base for a fixed denture; Fig. 11) on the scanned position of the implants was converted to a STL file from which a digital superstructure was fabricated out of titanium (E.S. Healthcare, Hasselt, Belgium). An occlusal guide was printed to function as an upper cast positioner in the articulator to plan the fixed prosthesis on the implants (Fig. 12). The reconstruction was planned 5 weeks after the prefabrication procedure.

Reconstruction surgery

In the second surgery, the scapula graft is harvested and the mandible is reconstructed. The scapula is exposed surgical and the osteotomies in the lateral scapula segment were performed using the implant-supported cutting guide (Fig. 13). After the osteotomies were performed, the fixed prosthesis was placed on the implants (Fig. 14). Next, the prefabricated scapula with the dental prosthesis in place was harvested and fitted into the mandible, where the prosthesis was screw retained on the two implants in the mandible (Fig. 15). The prosthesis had a good occlusion and in the follow-up of three months post operative the patient recovered well and the reconstruction was stable. Unfortunately, the patient died four months post operative of a cardiac arrest.

Discussion

The two cases described above illustrate that 3D reconstructive planning of defects of the jaw is not restricted to planning of FFFs, but is more versatile and can also be used for planning of other osseous flaps like FSF and DCIA flap. Compared to the FFF, guided harvesting of FSF and DCIA flaps is more challenging as in both flaps there is more of the muscular cuff and vascular feeders that need to be preserved and therefore less anatomical landmarks

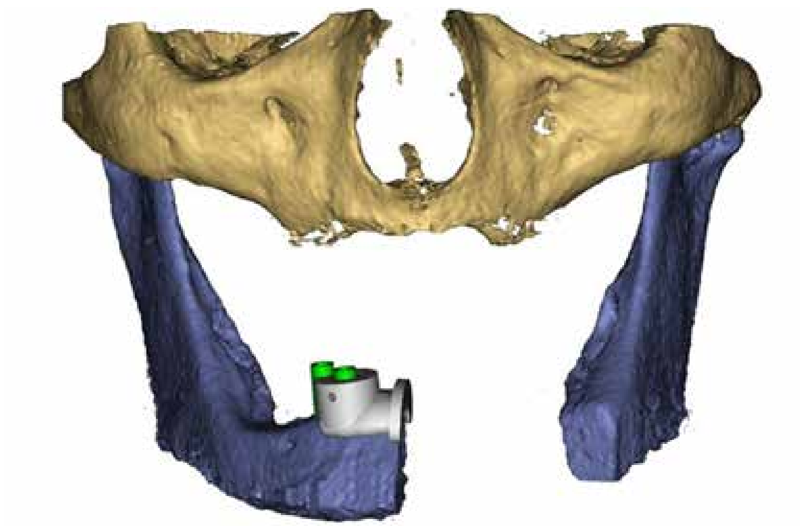

Figure 9 Shows the lower jaw segments after digitally removing the reconstruction plate. Two implants are placed virtual in the right mandible. In green tubes are visualized that align the center axis of the implant to illustrate the implant angulation, in light grey an implant drilling guide is visualized for guided drilling of the implants and guided placement.

Figure 10 Drilling template design for the placement of 3 dental implants in the scapula graft after rotating the graft segment to the lateral outward. The segment that was resected guided is colored bleu (Fig. 9). In light grey the guide is shown which is supported on the resection side of the scapula transplant after the transplant is rotated towards the operator. In the center the scapula is shown from the caudal side and in bleu the graft is shown with its rotation dorsal to facilitate the placement of the implants. On the left side (transparent yellow) the scapula is shown as a whole to visualize the orientation of the graft and planning of the guide virtual. After placement of the implants the graft is rotated back inward almost to its original position to facilitate osseointegration of the implants.

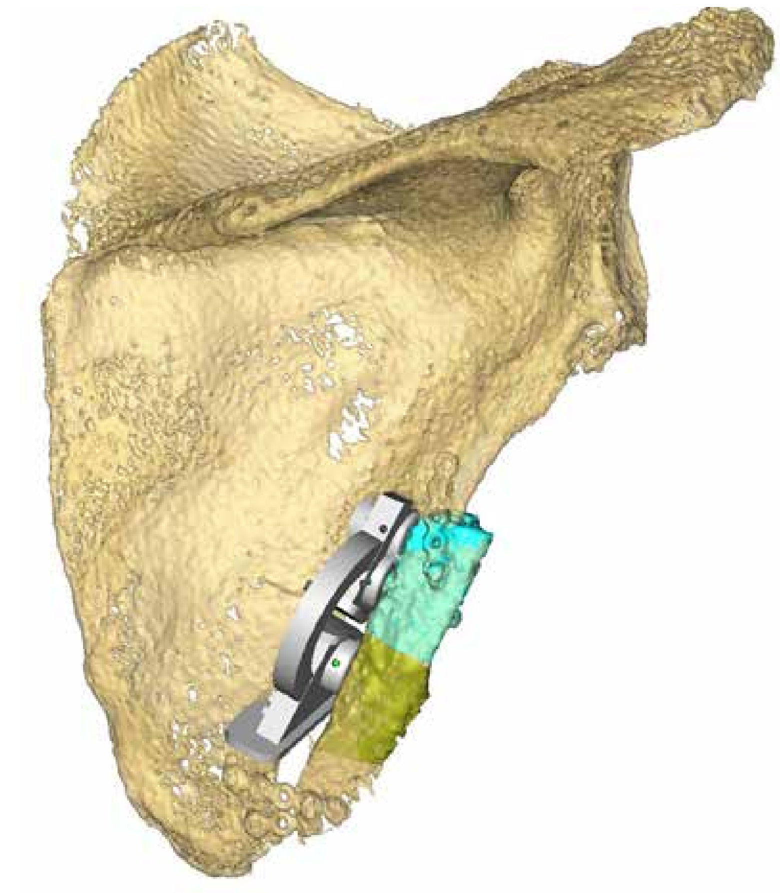

Figure 11 CT-scan of the right scapula after implants were inserted in the graft, and the graft was rotated back inward almost to its native position. This native position is not reached because there is a split skin graft and a Gore-Tex patch overlying the resection side of the graft in the peri-implant region. The graft segment is fixated with three miniplates to the remaining scapula, and left there for 6 weeks, in this time the implants can osseointegrate and the skin graft can heal in the peri-implant region to facilitate a fixed peri-implant soft tissue layer around the implants. The segmentation sawing guide is virtual planned on the graft segment of the scapula (the lateral border) and is shown here virtual in light grey.

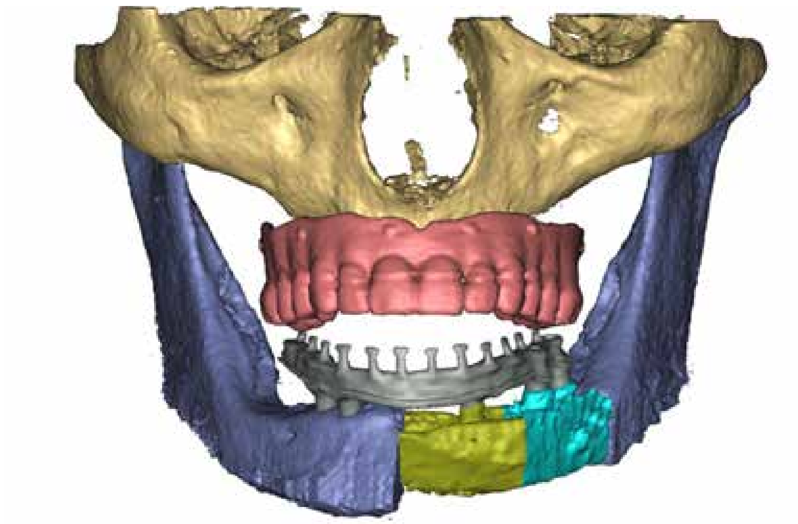

Figure 12 Base superstructure of the fixed lower denture planned on the 5 implants (three in the two segments of the scapula and two in the right mandible).

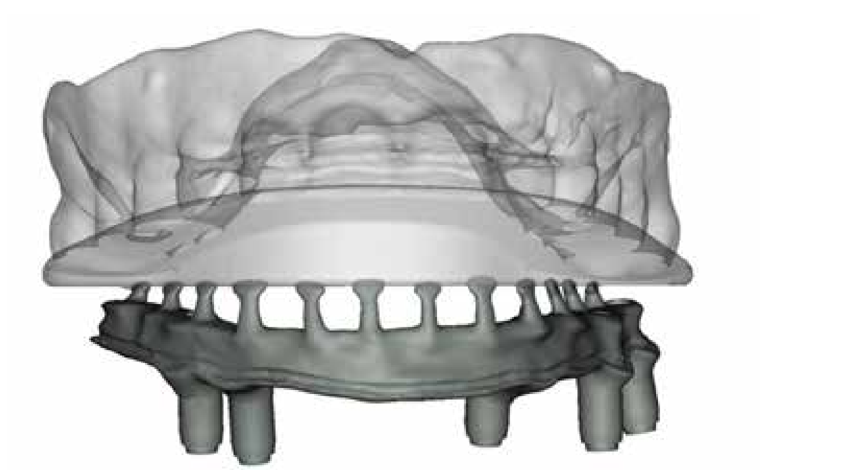

Figure 13 Three 3D objects visualized; the upper prosthesis and the lower base structure of the lower fixed prosthesis. In between a wafer is designed. This wafer is used to cast the base structure in the articulator against the upper denture in the right position. The lower denture can be finished on the base structure.

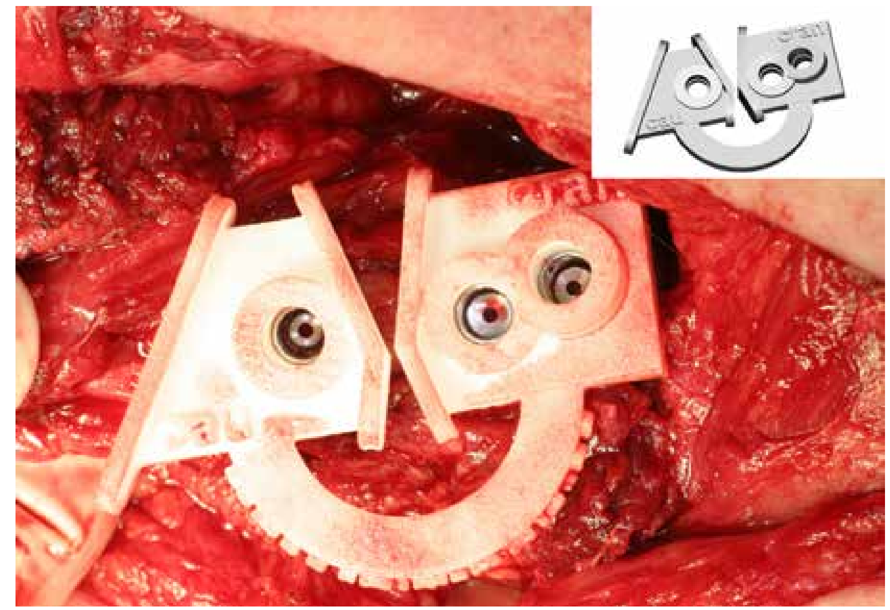

Figure 14 The insert on the upper right shows the digital design of the cutting guide to segment the scapula graft. The central picture shows the guide printed out of polyamide in the patient fixated on the implants in the scapula graft. The graft is segmented using piëzo sawing to protect the muscular cuff and perforator vessels as much as possible. The graft is still attached to its native blood supply in the scapular region.

are available to orientate and support guides during the resection of these grafts. Less landmark support can result in less accuracy of the resection and segmentation and a less accurate reconstruction. In our case the accuracy of the DCIA flap was 9.2 mm. Accurate positioning of the flap may also be impaired by the presence of the soft tissue bulk (Fig. 4). More guidance in placing the graft may improve the accuracy and predictability of the reconstruction using these flaps. Thomas et al. did not report about accuracy but do show that adding a CAD CAM osteosynthesis plate to facilitate planned positioning and fixating might help to achieve more predictable outcomes.[14] Both the FSF and the DCIA flap have a shorter pedicle compared to the FFF. Especially in reconstructing the midface where the DCIA flap has the advantage of the use of the internal oblique muscle to close the palate this short pedicle length can be a problem.

The idea of prefabricating a scapula with dental implants originates from 1996.[17] Rohner was inspired by this idea of Vinzenz to start prefabricating the FFF.[17] Prefabrication of the scapula is not as straightforward as prefabrication of the FFF. The scapula has to be osteotomized fist in order to rotate the lateral rim outward and provide implant insertion on the osteotomy side. There has been only one report of the prefabricated scapula flap since 1996, which was in 2008, again by Vinzenz.[18] He described 9 scapula reconstructions prefabricated with implants to reconstruct the midface in noma patients. An advantage of digital planning over the conventional planning by Vinzenz[18] is the use of printed outcome models of the reconstruction and the defect/graft anatomy. The use of these models allows for preparing of the defect edges and try-in of the graft 3D print without the use of the flap itself. This minimizes damage to the vulnerable flap and minimizes ischemia time as the flap is bound to fit in the defect more readily after harvesting.

Prefabrication of a FSF with implants is more risky than the prefabrication of a FFF due to the varying bone stock of the FSF.[19,20] The lateral scapula rim is twisting towards the inferior angle and is thinning out towards inferior with less chance of finding enough bone volume for the implants to be inserted in. In our case the width of the scapula was sufficient for implant placement, probably because only three implants were planned. A second less predictable challenge of inserting implants in the scapula flap

is the retrograde implant placement in the medial side of the lateral border. The implants have to be placed between the cortical outer and inner layer, which is probably more unpredictable in resorption than the thick cortical layer of the fibula.[19] Harvesting the scapula flap is a time consuming process, a two-team approach is hardly possible due to the rotation of the patient that is needed in the majority of the cases and the redraping of the patient, which takes time.[20] This reserves a place for the scapula flap behind the fibula flap in the ranking of choice for flaps to use in the reconstruction. The FSF and the DCIA flap are, however, good alternatives when the fibula cannot be used due to arteriosclerosis, virtual planning and guided resection may ease the harvesting of these flaps.

Conclusion

The virtual planning software developed to plan the FFF is versatile and can also be used to plan the FSF and the DCIA flap. Guided surgery can be performed using 3D printed guides to facilitate the harvesting of the flap and the placement of dental implants in these flaps.

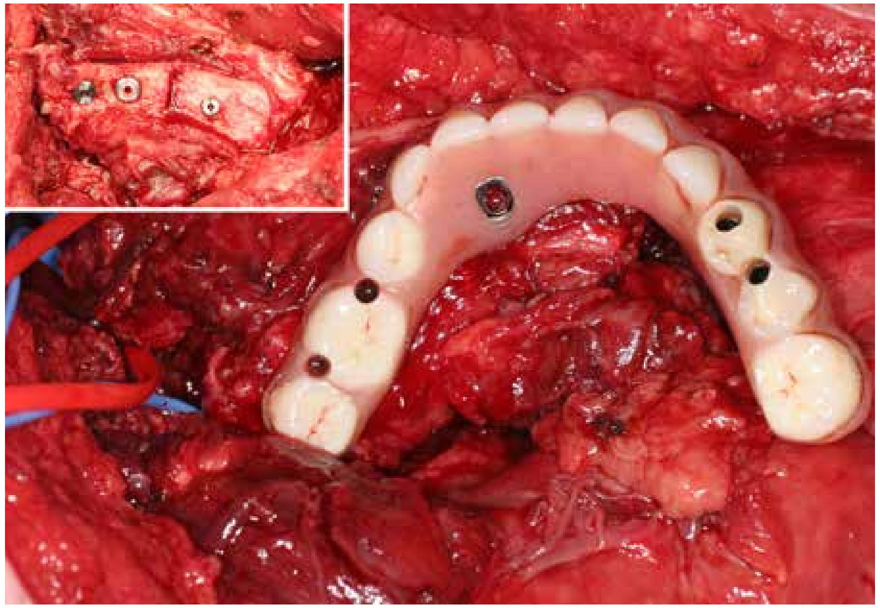

Figure 15 The insert on the left upper side shows the scapula graft after segmentation with the three implants and the healed peri-implant fixed split skin graft. The central picture shows the fixed prosthesis screw retained on the implants in the scapula graft while the native blood supply of the scapula graft is still in tact.

Figure 16 Fixed lower prosthesis intra orally situated screw retained on the two implants in the mandible and on the three implants in the scapula transplant. The position shows a good occlusion resembling an accurate planning and execution.

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4

Accuracy of secondary maxillofacial reconstruction with prefabricated fibula grafts using 3D planning and guided reconstruction

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Abstract

Background

We compared the pre-operative 3D-surgical plan with the surgical outcome of complex two-stage secondary reconstruction of maxillofacial defects using inserted implants in the prefabricated fibula graft.

Methods

Eleven reconstructions of maxillofacial defects with prefabricated fibulas were performed using a 3D virtual planning. Accuracy of placement of the fibula grafts and dental implants was compared to pre-operative 3D virtual plans by superimposing pre-operative and post operative CT-scans: we first superimposed the CT-scans on the antagonist jaw, to represent the outcome of occlusion, and then superimposed on the planned fibula segments.

Results

Superimposing the CT scans on the antagonist jaws revealed a median deviation of the fibula segments and implants of 4.7mm (IQR:3-6.5mm) and 5.5mm (IQR:2.8-7 mm) from the planned position, respectively. Superimposing of the CT scans on the fibula segments revealed a median difference of fibula and implant placement of 0.3mm (IQR:0-1.6mm) and 2.2mm (IQR:1.5-2.9mm), respectively.

Conclusion

The final position of the fibula graft is determined by the occlusion of the denture, which is designed from the 3D plan. From a prosthodontic perspective, the accuracy of 3D-surgical planning of reconstruction of maxillofacial defects with a fibula graft and the implants allows for a favorable functional position of the implants and fibula graft.

Introduction

Functional reconstruction of large maxillofacial defects has long been a surgical challenge. In the past decade, the free vascularized fibula flap (FFF) has become the most popular choice for reconstruction of defects.[1] Moreover, for optimal prosthodontic rehabilitation it is widely accepted that dental implants are part of the treatment planning, as implant-supported prosthetics enhance the masticatory and speech function in patients.[2] Fibula bone has favorable conditions for inserting dental implants due to its high quality of cortical bone.[3]

Correct positioning of the FFF and the implants to support an implant-retained prosthesis is often difficult.[4] If implants are positioned in an unfavorable position, post operative function and esthetics may be impaired, thereby negatively affecting the patient’s quality of life.[2] In planning these complex reconstructions it is therefore important to not only plan the fibula bone in the preferred anatomical location to optimally reconstruct the defect, but also to ‘topographically’ plan the position of the implants in the fibula for optimal support of the superstructure.

Rohner described a method to prefabricate a FFF using dental implants and split skin grafts for complex rehabilitations.[5] This approach can provide optimal support of the prosthesis and can create stable peri-implant soft tissues. Prefabrication of a FFF enables functional placement of bone in a defect by using backward prosthetic planning. The Rohner technique essentially is a two-step approach. The first surgical step starts with planning the desired prosthetics (position of the teeth) in the jaw defect using stereolithographic models of the maxillo-mandibular complex. Next, backward planning for the placement of the fibula bone graft and the desired location of the dental implants is done based on the prosthetic design. Based on this planning, a drilling guide for inserting the dental implants at the preferred position location in the fibula can be produced. This drilling guide is sterilized and used in the first surgical procedure for placing the dental implants in the fibula bone after exposing the anterior side of the fibula. The first surgical step is completed by taking impressions of the implants inserted into the fibula to register their position in the lower leg, followed by a split thickness skin graft covering the part of the fibula to be implanted. This impression is used to finalize the design of the superstructure and dental prosthesis before the second surgical step of harvesting of the fibula. Also, because the position of the dental implants is known, cutting guides fitted on the implants can be produced for the subsequent fibular osteotomies. During the second surgical step, usually 6-8 weeks after the first one, the superstructure and/or dental prosthesis fixed to the inserted dental implants acts as a guide for correctly positioning the fibula segments in the craniofacial defect. Thus, during the second surgical step, the prosthetics and fibula graft are placed as one complete entity. The prosthesis is placed in occlusion and as a result the bone is automatically placed in a functional position.

A disadvantage of the conventional Rohner technique is the extensive planning procedure, which requires extensive vast laboratory work by experienced dental technicians, especially in manufacturing the drilling and cutting guides. For instance, Rohner utilized laser-welding techniques in the preparation of his drilling and cutting guides.[5] To facilitate the laborious work and to use the advantage of detailed anatomical insight, a method using 3D-software and 3D-printing techniques was developed.[6,7] 3D planning also allows for mathematically evaluating the surgical result when a post operative (Cone beam) CT is superimposed over the 3D plan. Several publications provide data on the mathematical accuracy of fibula-based craniofacial reconstructions using 3D-printed cutting guides and pre-bend plates or CAD-CAM reconstruction plates.[8-10] For instance, it was shown that 3D-virtual planning could be performed within 4 mm of accuracy.[11,12] In prefabrication, however, the occlusion of the prosthesis determines the placement of the complete graft during surgery, which is not included in the 3D plan. Dentures are made based on the information of the 3D plan fixed in the articulator. However, the denture is traditionally made in central occlusion and through articulation can maintain occlusion in the articulation movement. This allows for slight freedom of positioning of the graft without causing occlusion problems. Theoretically, this could lead to a different level of accuracy regarding the surgical outcome, because the fibula graft and denture are fixed and then placed in the defect guided by the occlusion. Therefore, the aim of this study was to determine the accuracy of the surgical outcome of the fibula graft and the implants inserted in a two-stage reconstruction of secondary maxillofacial defects, compared to the pre-operative 3D-surgical plan.

Materials and methods

Patients

We assessed the accuracy of the fibula segments, and implants inserted in these segments of 11 consecutive patients who received reconstruction of a maxillofacial defect, including the maxilla or mandible with a free vascularized fibula flap. The reconstructions were carried out between January 2011 and May 2015 at the University Medical Center Groningen, University of Groningen, the Netherlands. The inclusion criteria were (1) secondary reconstruction of the maxilla or mandible using a free vascularized fibula graft, (2) use of a prefabricated fibula with dental implants, and (3) positioning of the graft into the defect using a bar retained denture or fixed superstructure supported by the implants in the graft. The patients needed a reconstruction due to a preexisting craniofacial defect resulting from tumor surgery (N=8) or osteoradionecrosis (N=3). Two to four weeks after reconstruction, conebeam CT (CBCT) scans to check the position of the transplanted fibula segments provided with dental implants were made.

The institutional review board (IRB) of our university hospital approved the study design and requirements for patient anonymity under reference number M15.176617.

Virtual planning

The 3D virtual treatment plan started with a CBCT scan of the maxillofacial region and mandible (i-CAT, Imaging Sciences International, Hatfield, USA). The patients were seated in an upright position using a chin rest and headband for fixation. Upper and lower dentition were in maximal occlusion, and in case of an edentulous or partially dentulous jaw, the denture was worn. Scanning settings used were: 120KV, 5mA, 0.4 voxel with a field of view of 23 x 16 cm to capture the maxillofacial region. A high-resolution CT angiography scan from the lower legs was acquired (Siemens AG Somatom Definition Dual Source, Forchheim, Germany). A digital subtraction arteriogram (DSA) of the lower leg was made with a 0.6 mm collimation and a 30f kernel (medium smooth). Images were stored in an uncompressed DICOM format. Both scans were imported into ProPlan CMF 1.3 (Synthes, Solothurn, Switzerland and Materialise, Leuven, Belgium) to plan the reconstruction of the jaw defect in

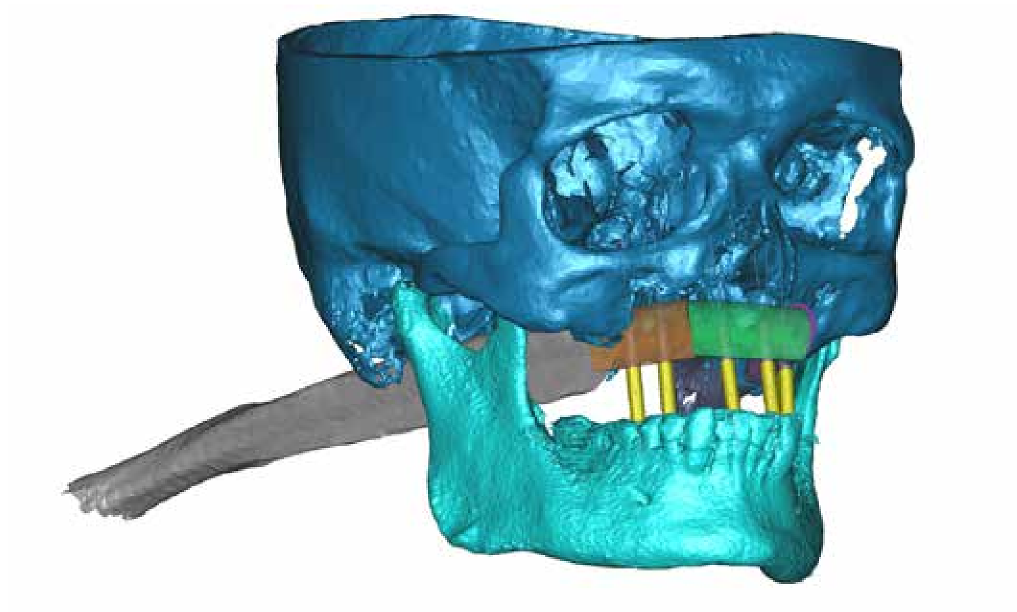


Figure 1 Planning of implants in a segmented fibula to reconstruct a bony defect of nearly the entire maxilla. In yellow, virtual implant direction tubes are visualized that help to plan the implant angulation.

a virtual environment. The 3D-models of the jaw-defect and the fibula were created and the fibula was virtually cut and planned in the defect.

To plan the antagonist dentition and the implants, the virtual reconstruction file was converted to Simplant Pro 2011 (Materialise Dental, Leuven, Belgium), virtually the antagonist dentition was added in the proper occlusion. This was done in two ways: the first was to scan the antagonist denture separately (if present) using the CBCT (120KV, 5mA, 0,3 voxel) and create a 3D model of the dentition in Simplant pro 2011. If there was no denture or setup, the second possibility to determine the best implant position was to use the virtual teeth in Simplant Pro 2011. Next, virtual implants (Nobel Speedy, Ø: 4.0 mm, length: 10-13 mm; Nobel Biocare AB, Götenborg, Sweden) were planned in the optimal position supporting the virtual antagonist dentition, thus creating a total reconstructive plan of fibula graft and implants (Fig. 1). Then a multidisciplinary team judged the reconstructive plan to be clinically feasible. The file was then converted to ProPlan CMF 1.3 to optimize the position of the fibula parts and have the guides designed. The implants were locked to the fibula cuts. These pieces were virtually relocated to their original position before virtual cutting. On the original fibula a drilling guide was designed virtually using 3-matic 7.0 (Materialise, Leuven, Belgium) to facilitate guided drilling and guided tapping of the implants in the fibula (Nobel guide; Nobel Biocare AB, Götenborg, Sweden). Finally, the implant positioning guide for placement was a 3D print of Polyamide and sterilized with gamma irradiation to be used intra operatively (Fig. 2).

Prefabrication of the fibula

In the first surgical step, the fibula was prefabricated using implants and a skin graft. This included guided implant placement (Nobel guide, Nobel Biocare AB, Götenborg, Sweden), registration of the exact topographic location of the implants within the fibula, and covering the exposed bone with a split-thickness skin graft creating a neo-mucosa. The anterior plane of the fibula was exposed and in case of a sharp edge, which becomes apparent during planning, it was trimmed until a flat surface was created to insert the implants surrounded a solid bony margin. The surgical template was positioned and fixed onto the periosteum of the bone with miniscrews (KLS

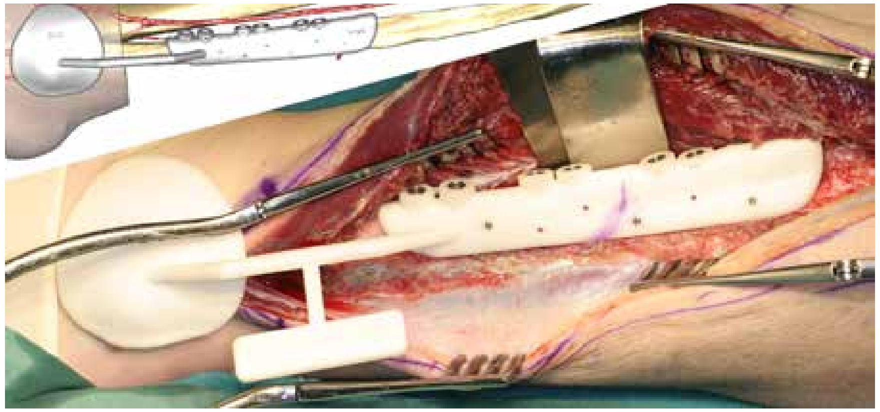


Figure 2 The insert shows the virtual drilling guide (ProPlan CMF). The drilling guide is situated on the periosteum of the fibula graft and is skin-supported on the lateral malleolus to prohibit axial sliding. The guide was printed through selective laser sintering of polyamide and sterilized using gamma irradiation. The guide is fixated with 3 miniscrews (KLS Martin Group, Tuttlingen, Germany).

Figure 3 3D model of the upper jaw reconstruction (left). A 3D print of the positioning wafer was made. The CAD-CAM milled titanium bar was positioned in the articulator to facilitate fabrication of the denture (middle). Next, the prosthesis was fabricated (right).

Martin Group, Tuttlingen, Germany; Fig. 2). The surgical template contained metal cylinders holding removable sleeves of different diameters, to fit the drill diameters used to prepare the implant sites. Drills with increasing diameters were used to prepare the implant site as suggested by the manufacturer. The surgical template was removed and screw tapping of the implant sites was performed. All implants were inserted with a minimum torque of 35 N/cm and a maximum of 50 N/cm, which indicates whether the implants were placed on the level of the bone crest.

It is reported that guided implant placement can result in an apical deviation up to 4.5 mm.[13] Therefore, an intraoperative optical scan of the implants with scan abutments (E.S. Healthcare, Dentsply International, York, PA) was obtained with the Lava™ Chairside Oral Scanner C.O.S. (3M™ ESPE™, St. Paul, USA) to register the exact position and angulations. To check whether the accuracy of the oral scan was accurate for the fabrication of a titanium bar and as a fail-safe, the position of the implants was also registered by taking impressions, using impression posts and conventional dental impression paste (Impregum™ soft polyether impression, 3M™ ESPE™, St. Paul, USA). The fibula was then covered with a split-thickness skin graft and the skin graft subsequently covered by a matching Gore-Tex patch (W.L. Gore and Associates, Flagstaff, AZ). The wound was closed primarily, and the implants and split skin were left to heal for 6-8 weeks.

Intermediate virtual planning

The optical scan of the scan abutments and of the final implant positions was imported in ProPlan CMF 1.3 software and manually matched with the original fibula reconstruction planning, creating a superimposed fusion model showing the accurate position of the implants. In case of an existing denture or total loss of dentition, a denture was made and a virtual bar was designed on the implants to support the denture. In case of a partial dentate jaw, a screw retained fixed bridge was made. The digital design of the custom bridge abutment was virtually planned on the implants. The bar or bridge abutment was subsequently converted to an STL file format and milled out of titanium (E.S. Healthcare, Dentsply International).

To create the denture or finish the bridge, a laboratory phase still is needed. A 3D planned wafer is then designed to translate the position of the

Figure 4 Selective laser sintering polyamide model of the cutting guide (Synthes, Solothurn, Switzerland and Materialise, Leuven, Belgium) fixed on the implants with Nobel guide fixation screws in the left fibula (upper). The virtual cutting guide is shown on the fibula (ProPlan CMF; below).

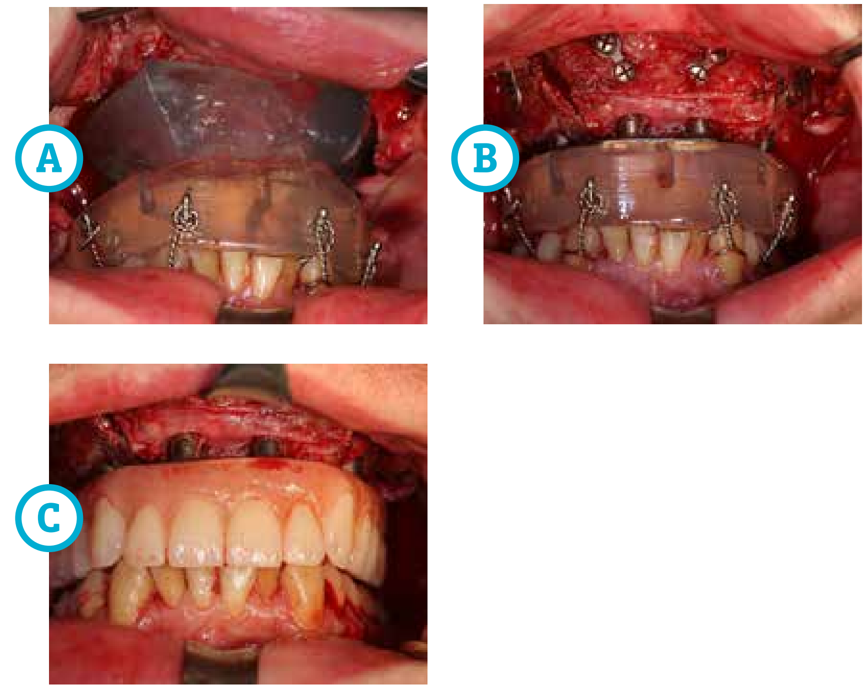


Figure 5 A 3D-printed surgical planned outcome model of the fibula segments and bar was used together with the positioning wafer (see also fig 3) intra orally to resect the defect edges until they properly match the graft dimensions (A). Fibula graft seated intra oral and fixated with miniplates and monocortical screws (Synthes, Solothurn, Switzerland; B). Intra operative immediate placement of the denture (C).

implants to the antagonist dentition of the patient. This wafer resembles the space that the prosthesis or bridge fills up after the reconstruction, therefore this wafer can be printed and function as a cast positioner (Fig. 3). This wafer is needed to translate the digital plan to a plaster model to fabricate the denture or finish the bridge with porcelain in a conventional manner. The final step in preparation for the reconstruction was designing the cutting guides of the fibula; these guides were planned according to the virtual treatment plan, printed and sterilized using gamma irradiation.

Reconstructive surgery of the jaw

The second surgical step was planned at least 6 weeks after the prefabrication procedure to give the implants time to osseointegrate. The fibula with the implants was exposed while the vascular supply of the fibula stayed intact. The cutting guide was fixed on the implants. The osteotomies were performed using a reciprocating saw with a 35 mm blade (Aesculap microspeed uni, Aesculap inc, Center Valley, USA). After the osteotomies were performed, the cutting guide was removed and the superstructure was screwed on the implants. After this, the fibula was raised as a free graft. To ensure a highly accurate fit of the graft in the oral defect, the intra oral defect edges were optimized using a planned outcome model and cutting guides (Fig. 5). After preparation of the recipient site, the prefabricated fibula with the denture or bridge in place was then transplanted into the defect of the maxilla or mandible (Fig. 5). The graft with the denture/bridge was situated intra orally in occlusion, and fixed using osteosynthesis plates (2.0 or 2.3 system) and monocortical screws (KLS Martin Group, Tuttlingen, Germany). The fibular skin graft was sutured to the oral mucosa. 7 to 10 days after surgery the patients were discharged from the hospital.

Analysis of the results

A CBCT scan of the mandible was made routinely two to four weeks post operatively to judge the position of the graft and implants in the defect. The planned 3D-fibula objects were imported into the post operative scan file in ProPlan CMF 1.3 and matched on the outline of the post operative fibula segments. The fibula segments and the implants of the pre- and post operative ProPlan file were exported as STL files and imported in Geomagic Studio 2012 (Geomagic Gmbh). Surface-based superpositioning of the post operative CBCT scan onto the pre operative 3D-plan was carried out. Because the graft was placed according to the dental occlusion of the superstructure, the antagonist jaw was taken as a reference for superpositioning. A best-fit match, using an iterative closest point registration algorithm, was performed on the antagonistic jaw outline. To perform measurements, the software auto-generated virtual cylinders around the fibula segments and implants (Fig. 6). These cylinders have a diameter corresponding with the maximum diameter of the fibula segment/implant and are aligned with the segment/implant. Subsequently, the centerpoints and centerlines of these cylinders were determined automatically. To determine the deviation of the surgical outcome of the fibula reconstruction, linear measurements were made between the centerpoints of the fibula segments and the implants. The angle between the centerlines of the fibula segments and implants was also measured. This indicates the accuracy of the fibula reconstruction. To investigate the accuracy of the implant insertion, fibula shaping as well as topographic positioning of its segments, the post operative scan was also matched using the fibula segments of the planning as a reference. To evaluate the matching of the planned fibula segments on the fibula outline of the post operative scan, two independent observers (RS and JK) performed the matching of these files manually to provide the inter-observer correlation. The deviation of the centerpoints of the fibula segments were compared and expressed as average Euclidean distance of the centerpoints.

Results

Patients

In the period between January 2011 and May 2015, 11 consecutive patients who received a reconstruction with a prefabricated fibula graft were included in this study. The patients (seven males and four females, mean age of 48.3 years, range 21 to 68 years), were offered reconstruction of the mandible (6) or maxilla (5). All patients were treated for a malignant-, benign tumor or osteoradionecrosis. Five patients received radiotherapy (Table 1).

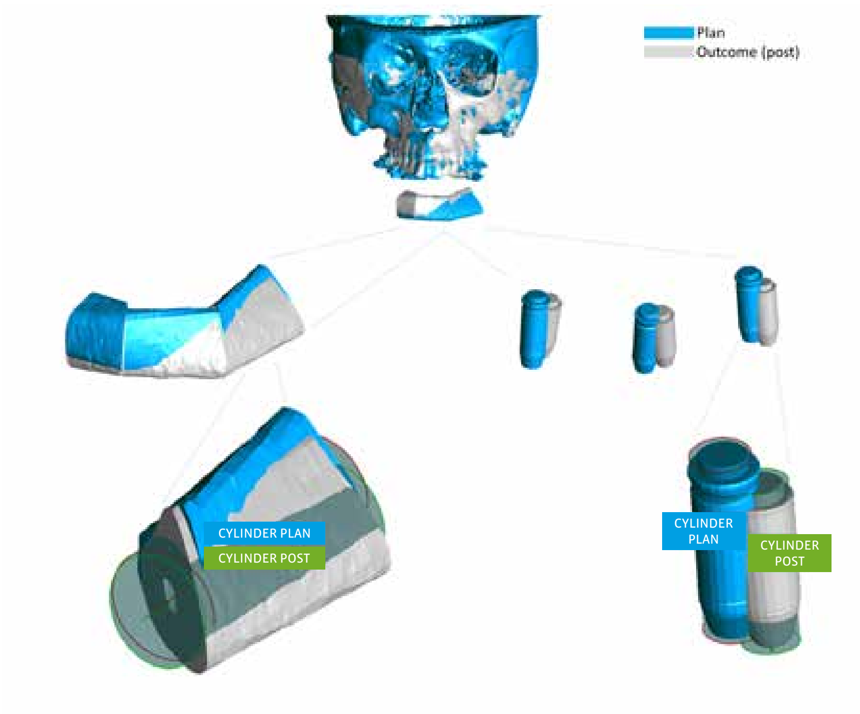
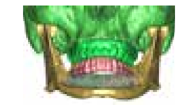
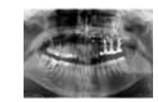
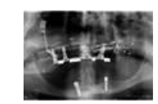


Figure 6 Superimposition of virtual reconstruction planning (blue) and post operative CBCT of reconstruction (grey) of an anterior mandible segment (upper). The alignment was performed on the maxilla and scull base using an iterative closest-point algorithm Geomagic Studio 2012 (Geomagic Gmbh). The deviation of the post operative fibula segments and implants (grey) and virtual plan (blue) is shown (middle). Automated cylinders are situated on the fibula segments and implants by the software to determine the center-point distances and axis deviations of the fibula and implants (lower).

Table 1

no.	Age	Sex M/F	primary diagnosis	primary treatment	3D plan	post op OPG	superstructure
1	54	M	scc ventral floor mouth	mandibular resection and RTX (ORN)			bar retained prosthesis
2	68	M	oropharynx carcinoma left tonsil	primary RTX (ORN)			fixed bridge
3	43	M	osteosarcoma anterior maxilla	partial maxillectomy			bar-retained prosthesis
4	35	F	osteosarcoma left maxilla	partial maxillectomy			fixed bridge
5	67	M	scc right maxilla and RTX	partial maxillectomy			bar-retained prosthesis
6	58	F	adenoid cystic carcinoma right maxilla	partial maxillectomy			bar-retained prosthesis
7	45	M	n.olfactorius neuroblastoma left mandible	primary RTX (ORN)			bar retained prosthesis
8	21	F	ameloblastoma right mandible	segmental mandibular resection			fixed bridge
9	44	F	ameloblastoma anterior mandible	segmental mandibular resection			impl fixated prosthesis
10	46	M	ameloblastoma right mandible	segmental mandibular resection			bar-retained prosthesis
11	55	M	scc anterior floor mouth	segmental mandibula resection			bar-retained prosthesis

No. = reconstruction plan number, M = male, F = female, RTX = radiotherapy before the reconstruction, ORN = osteoradionecrosis, present before the reconstruction, SCC = squamous cell carcinoma.

Accuracy

When using occlusion as reference, superimposing of the post operative CBCT scan on the virtual treatment plan revealed that the median centerpoint distance between the planned fibula segments and the post operative fibula segments was 4.7mm (Inter Quartile range[IQR]:3-6.5mm) and the mean angulation was 6.6° (IQR:4.9-7.8°) (Table 2). The mean centerpoint distance between the planned implants and the position of the post operative implants was 5.5mm (IQR:2.8-7 mm) and the mean difference in angulation was 6.1° (IQR:4.5-9.3°) (Fig. 7).

When superimposing the fibula segments of the post operative CBCT and the pre operative virtual plan, the mean center-point deviation between the planned fibula segments and the post operative fibula segments was 0.3mm (IQR:0-1.6mm), and the mean angulation was 0.6° (IQR:0.1-4°). The mean centerpoint distance between the planned implants and the post operative implants was 2.2mm (IQR:1.5-2.9mm), and the mean angulation was 4.6° (IQR:1.3-8.2°; Fig. 7). The inter-observer correlation was expressed as average Euclidean distance of the centerpoints, which were 0.8mm (SD 0.5mm) for the implants and 1.7mm (SD 1mm) for the fibula segments (Fig. 8).

Discussion

This study shows that virtual planning and executing reconstruction of a maxillary or mandibular defect with prefabricated fibular grafts containing dental implants, relying on a prefabricated superstructure (denture or bridge) to guide the positioning of the graft in the defect, corresponds with a favorable prosthodontic rehabilitation. The accuracy measured by superimposition onto the antagonist jaw is clinically very feasible because the denture is placed in occlusion and the positioning of the graft follows and they are fixed as one entity. Thus, the relatively large deviation of the graft and implants compared to the virtual planned position has no negative impact with regard to functioning of the prosthodontic rehabilitation. The procedure described is a result of combining a 3D virtual technique with an analogue procedure (designing of the prosthesis and positioning the graft using this prosthesis). The plan relies on functional occlusion, and we found that minimal manipulation of the graft in the defect leads to good FFF and acceptor site alignment, while occlusion remains proper. Precise 3D planning of the implants, graft and occlusion even creates a relative freedom of movement of the transplant without resulting in an improper occlusion. Most probably without occlusion guided positioning it would be questionable whether the implants could have been used for a well-functioning prosthodontic rehabilitation. The planning method described is essentially a backwards planning and is based upon the desired functional result, being a dental superstructure in proper occlusion.[5] Because the denture is placed in occlusion at the end of surgery, the virtual planned sectioning of the graft allows for direct placement of the implant-retained denture in occlusion.

When analyzing the accuracy of reconstruction by superimposing the fibula segments of the post operative CBCT and the pre operative virtual plan at the level of the fibula segments or the implant position onto the fibula including the implants, the average deviation was low: 0.8mm and 2.7mm, respectively. We consider this to be the actual accuracy of the 3D virtual planning, since this deviation is a direct result of the design of the drilling and cutting guides. In the literature, only sparse data are available on the accuracy of prefabricated fibula reconstruction with dental implants. We recently reported the use of a CAD-CAM reconstruction plate to position dental implants into fibular grafts.[9] That procedure showed a mean accuracy of 3.0mm (SD:1.8 mm) for the fibula and 3.3mm (SD:1.3 mm) for the implants. Roser et al.[8] reported a 90.93±18.03% overlap of the planned fibula graft. Hanken et al.[10] reported a very small mean deviation of the fibula segment length of -0.12mm. The positive and negative deviations in his study had a range up to 10 mm, respectively. Therefore, the very small mean deviation reported has to be interpreted with caution.

Besides accuracy, the most important factors adding value in fibula reconstruction are functional outcome and cost. Currently, functional outcome has only been reported by Avram et al.[14] They compared virtually planned reconstructions to conventionally planned reconstructions and found increased complexity of flap design in the virtual group and achieved unprecedented rates of dental rehabilitation along with reduced operative

Table 2 Outcome measurements after superimposing the post operative CBCT scan over the pre operative 3D virtual plan. Matching was performed using the antagonist jaw (iterative closest point algorithm) as a reference and secondarily using the fibula surface of the segments as a reference. The deviation of the implants (impl) and fibula (fib) segments is displayed for each of the 11 patients.

nr plan		mandibula match		fibula match	
		centerpoint	angulation	centerpoint	angulation
1	impl 1	9.1	9.84	4.66	2.63
	impl 2	6.97	11.59	4.44	6.57
	impl 3	6.19	7.82	2.21	0.81
	impl 4	8.83	10.48	2.5	1.28
	fib 1	6.87	7.04	0.04	0
	fib 2	8.01	6.52	0.09	0.5
2	impl 1	3.73	2.43	2.07	2.36
	impl 2	2.59	0.81	1.4	0.56
	fib1	2.56	7.06	0	0
3	impl 1	3.86	7.13	0.57	1.27
	impl 2	2.78	6.04	0.28	1.28
	impl 3	2.04	5.31	0.64	0.37
	impl 4	1.52	4.72	1.18	0.35
	impl 5	2.67	5.92	1.19	1.35
	impl 6	3.47	5.85	1.34	3.14
	fib 1	3.03	3.62	0.83	0.82
	fib 2	1.34	1.81	0.59	0.14
	fib 3	3.03	5.88	0.94	0.55
4	impl 1	2.06	5.18	5.79	2.42
	impl 2	3.54	19.65	1.94	13.81
	impl 3	2.7	14.39	2.23	19.75
	fib 1	3.26	8.16	0	0
	fib 2	4.22	10.1	2.82	6.02
5	impl 1	5.29	4.83	1.95	4.42
	impl 2	4.66	4.97	2.86	3.87
	impl 3	5.66	6.14	4.52	9.48
	impl 4	5.51	6.4	4.37	9.06
	fib 1	4.66	6.23	0.82	14.15
	fib 2	6.12	6.58	0.32	0.79
6	impl 1	7.58	4.48	0.59	2.81
	impl 2	7.35	2.98	1.79	7.99
	impl 3	7.93	9.6	1.34	0.56
	impl 4	7.85	6.93	2.56	4.65
	fib 1	6.9	2.09	1.35	0.74
	fib 2	8.53	6.32	2.42	6.33
7	impl 1	6.5	0.65	2.03	0.57
	impl 2	6.7	0.21	1.52	0.45
	impl 3	5.66	0.57	1.88	0.13
	fib 1	7.75	11.26	0	0
8	impl 1	5.03	11.89	2.52	13.06
	impl 2	6.35	11.35	1.9	16.85
	impl 3	5.57	9.32	2.78	13.98
	fib 1	4.92	2.26	0	0
9	impl 1	4.57	13.81	2.25	2.9
	impl 2	1.98	8.03	2.31	4.83
	impl 3	5.9	6.2	1.6	9.65
	fib 1	3.44	6.21	2.5	6.05
	fib 2	3.54	4.54	0.4	1.49
	fib 3	3.91	2.64	1.32	5.96
10	impl 1	5.66	1.91	2.92	8.2
	impl 2	4.93	2.06	2.29	7.12
	impl 3	4.7	0.98	1.69	7.74
	fib 1	4.82	8.74	2.98	14.11
	fib 2	5.8	7.51	0.18	1.05
11	impl 1	8.02	9.88	3.07	6.6
	impl 2	7.1	7.16	4.51	8.58
	impl 3	6.36	7.74	2.9	11.13
	impl 4	8.17	8.57	2.51	5.88
	fib 1	4.4	5.81	2.02	1.9
	fib 2	6.07	17.08	1.88	6.41

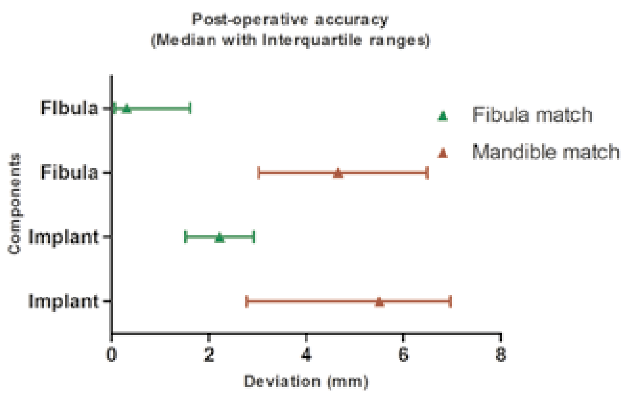


Figure 7 Plot showing the post operative accuracy of the fibula segments and implants (centerpoints) compared to the virtual planning. The vertical axis shows the implants and the fibula segments, either matched on the level of the mandible or with the fibula segments as a reference. The horizontal axis shows the median and interquartile ranges.

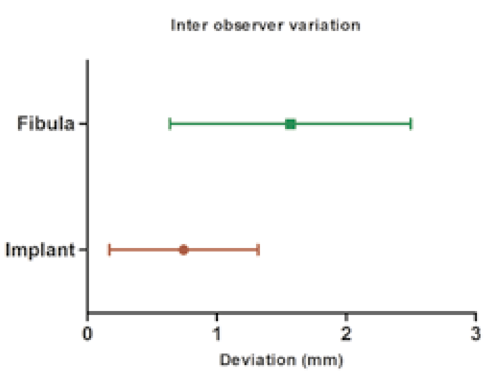


Figure 8 Plot showing the inter-observer variation. The vertical axis shows the implants and fibula segments in dimension x, y and z between both observers. The horizontal axis shows the average implants and fibula segments centerpoints of deviation in mm and the 95% confidence interval. The inter-observer deviation is the highest on the z-axis.

times in the virtual planning group. Guided surgery results in additional costs for planning and creating cutting guides, including milled plates. These currently relatively high costs probably will reduce in the future, e.g., by savings in operating time reduction, by preventing additional surgery (for example, placing implants during reconstruction) and reduced costs of hard- and software. In line with this assumption, Zweifel et al.[15] reported that even in capped health care systems, virtual planning and guided surgery, including pre-bent or milled plates, are financially viable.

Three major advantages of 3D-planning in prefabricated fibula reconstructions are the anatomical insight into the bony defect at the recipient site, the option of cutting and designing the fibula as preferred, and the restoration of dental occlusion. Additionally, most of the laborious steps needed in former prefabrication described by Rohner et al.[5] can be overcome with 3D planning. Another benefit is the use of a 3D-printed planned outcome of the fibula graft. Thus, the recipient site can be prepared before releasing the graft from the lower leg, which can therefore save ischemia time and will safeguard the pedicle from any damage due to manipulation of the graft into and out of the defect more often. Furthermore, the stable peri-implant soft tissue layer that is created around the implants using a split skin graft in the first surgical step is favorable to obtain good peri-implant health.[16] Among other benefits, the skin graft creates a buccal and lingual sulcus of the implants, thus reducing unfavorable traction from surrounding tissues, as well as allowing for proper oral hygiene.

Conclusion

The use of digital planning and 3D printing to virtually plan and execute reconstruction of maxillofacial defects with prefabricated fibula grafts provided with dental implants is accurate. The procedure relies on prefabricated superstructures (denture or bridge) to guide the positioning of the graft in the defect according to the occlusion to reach favorable clinical outcome.

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5

Accuracy of fibula reconstruction using patient-specific CAD-CAM reconstruction plates and dental implants: a new modality for functional reconstruction of mandibular defects

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Abstract

Background

The purpose of this study was to analyze the accuracy of mandibular reconstruction using patient-specific computer-aided designed and computer-aided manufactured (CAD-CAM) reconstruction plates as a guide to place fibula grafts and dental implants in a one-stage procedure using pre-operative 3D virtual planning.

Methods

Seven consecutive patients were analyzed retrospectively; the 3D accuracy of placement of the fibula grafts and dental implants was compared to the virtual plan.

Results

Six out of seven flaps survived for an average follow-up time of 9.4 months. The outcome was compared to the virtual plan, superimposed on the mandible. The median deviation was 2.5 mm (IQR:1.9-4.8 mm) for the fibula segments and 3.1 mm (IQR:2.3-4.2 mm) for the implants. When superimposed on the fibula segments, a median deviation of fibula and implant placement of 0.5 mm (IQR:0.2-1.6 mm) and 2.1 mm (IQR:1.6-2.5 mm) was observed, respectively. The median mandibular resection planes deviated 1.9 mm (IQR:1.0-2.5 mm).

Conclusion

A patient-specific reconstruction plate is a valuable tool in the reconstruction of mandibular defects with fibula grafts and dental implants. Implant angulation showed a greater deviation from the virtual plans in patients with a sharp ventral fibula rim, where the guide is removed after pilot drilling of the implants.

Introduction

Reconstruction of mandibular defects is often performed by using autologous bone transplants. These bone transplants or free vascularized bone grafts have proven their benefit.[1] The free vascularized fibula flap is harvested from the lower leg and is the preferred flap for reconstruction of large mandibular defects.[2] To enhance functional outcome, in particular to facilitate dental rehabilitation, dental implants may be used.

Implant-supported prostheses have been shown to provide a good cosmetic result and adequate stability for chewing.[3] To decrease the risk of inappropriate positioning, dental implants may be inserted secondarily after fibula reconstruction of the jaw.[4,5] In the retrospective analysis by Anne-Gaelle et al.[6], several factors were identified for not accomplishing dental implant placement in fibula grafts used in mandibular reconstruction. The main reasons for not placing implants in the fibula bone graft at the time of reconstruction include incorrect positioning of the graft in the defect, and interference of the implant sites with the osteosynthesis screws. Implant placement after the grafted bone has healed is generally omitted due to risk of osteoradionecrosis (in cases of adjuvant radiotherapy), or due to malpositioning of the graft 'from an implant-prosthetic point of view', or because patients do not want to undergo additional surgery after completing the oncological treatment. Therefore, some studies report that implants are employed secondarily in less than 5% of reconstructed cases.[7] Recently, the quality of life has been shown to improve considerably if dental implants are placed to support a dental prosthesis during less complex surgery in oral cancer patients in their native mandibular bone.[8] Therefore, in reconstructing complex jaw defects, immediate placement of dental implants in the fibula bone graft is strongly advocated. The current study describes the possibility of using three dimensional (3D) technology to overcome the technical challenges of placing dental implants at the time of fibula reconstruction of jaw defects.

Three dimensional virtual surgical planning is gaining increasing attention, and its potential use in the planning of maxillofacial rehabilitation has been reported before.[9-11] 3D-printed cutting guides abutting on surrounding tissue such as bone, soft tissue or teeth are used intra operative to translate a 3D virtual surgical plan into reality. However, the accuracy with which these guides translate the surgical plan to the surgical outcome has rarely been assessed.[9,12,13] A precisely executed reconstruction of a mandibular or maxillary defect combined with implant insertion may reduce the risk of inappropriate positioning of the implants and could be more cost effective. The search for an accurate method to translate a 3D virtual surgical plan to the intra operative situation, and the report of its accuracy is, therefore, relevant.

Reconstruction plates are used for fixing the bone graft to the jaw. Recently, a patient-specific computer aided design/computer aided manufacturing (CAD-CAM) reconstruction plate that is commercially available was introduced. Such a plate can be integrated in 3D surgical reconstruction planning. These plates are designed to follow the contour of the patients' own bone and can be fixed with locking screws. Angulation of the screws in the plate and the inter-screw distance can be adjusted to some extent during the planning procedure. Besides individualization, patient-specific CAD-CAM reconstruction plates have another unintended potential powerful aspect, as they can be used to guide the reconstruction in the positioning of dental prostheses, and translate the 3D surgical plan to the reconstruction surgery. To our knowledge, the clinical accuracy of patient-specific CAD-CAM reconstruction plates as a guide for fibula graft positioning, including the insertion of dental implants in a one-stage 3D planned procedure, has not been reported.

The aim of this study was to assess the degree to which the surgical outcome of the fibula graft and the implants, inserted in a one-stage reconstruction of mandibular defects using 3D-planning and a patient-specific CAD-CAM reconstruction plate, correlate with the virtual surgical plan.

Materials and methods

Patients

This retrospective study evaluates the accuracy of positioning of the fibula segments, and the implants inserted in these segments, in patients who required reconstruction of the mandible with a free vascularized fibula flap. The reconstructions were carried out between 2013 and 2014 at the University Medical Center Groningen, University of Groningen, the Netherlands. The inclusion criteria were: (1) mandibular reconstruction using a free vascularized fibula graft, (2) the use of a patient-specific CAD-CAM reconstruction plate, and (3) immediate placement of dental implants in the graft. The only exclusion criterion was the absence of a post operative CBCT scan.

Virtual planning

The 3D virtual treatment plan started with a CBCT scan of the maxillofacial region and the mandible (i-CAT, Imaging Sciences International, Hatfield, PA, USA). The scanning protocol dictates that the patient is seated in an upright position using the chin rest and the headband for fixation. Upper and lower dentition must be in maximal occlusion, and in case of an edentulous or partially dentulous jaw, the denture should be worn. Scanning settings used were: 120KV, 5mA, 0.4 voxel with a field of view of 23 x 16 cm. A high-resolution CT angiography scan from the lower legs was acquired (Siemens AG, Somatom Definition Dual Source, Forchheim, Germany). An arterial contrast scan was made with a 0.6 mm collimation and a 30f kernel (medium smooth). Images were stored in an uncompressed DICOM format. Both scans were imported into ProPlan CMF 1.3 (Synthes, Solothurn, Switzerland and Materialise, Leuven, Belgium) to plan the reconstruction in a virtual environment. After converting to Simplant Pro 2011 (Materialize Dental, Leuven, Belgium), the implants were imported digitally into the plan. Next, in ProPlan CMF 1.3, the preferred contour of the reconstruction plate was marked. The planning was exported as a standard tessellation language (STL) file and sent to a company for the planning and production of the reconstruction plate (Synthes, Solothurn, Switzerland). In a web-based online planning session, the contour and size of the plate were planned, as well as the number of screws, together with the inclination and screw length. Subsequently, a guide design was made incorporating the bone-abutted resection guide for the mandible, with the drill guide to correctly position the screw holes for the plate. For the fibula segmentation a cutting guide was designed including guiding holes for the implants and for screw fixation of the plate. This guide was designed to be placed on the periosteum with a planned offset in the virtual plan of 0.4 mm to the bone surface. A surgical outcome model of the segmented fibula and the reconstruction plate were printed in acrylic, to check the shape of the planned fibula segments and plate in situ. This model was used intra operatively to ensure that the planned reconstruction would fit the resection defect before segmenting the fibula. Finally, the guides, the printed outcome model and the patient-specific reconstruction plates (PSP's) were sterilized with gamma irradiation to be used intra operatively.

Surgical procedure

The surgery was divided into three parts. First, the tumor or diseased bone (in the case of osteoradionecrosis) was removed by resecting the segment of mandible according to the preplanned, individually-designed cutting and drilling guide. The guide was fixed to the mandible with 8 mm long and 1.5 mm diameter screws (KLS Martin Group, Tuttlingen, Germany) using lateral holes in the guide planned for this purpose (1–2 holes per segment; Fig. 1). This was followed by guided resection of the segment of the mandible and guided drilling of the screw holes. Next, the surgical outcome model was placed into the mandibular defect to check the fit of the planned graft (Fig. 2). Second, the harvesting of the fibula was performed using a reciprocating saw with a 35 mm blade (Aesculap microspeed uni, Aesculap Inc., Center Valley, PA, USA). When the fibula was exposed the fibula guide was placed and fixed with 8 mm screws. The guide was used to drill and tap the implant sockets (Fig. 3). Subsequently, the implants (Nobel Speedy, Nobel Biocare AB, Götenborg, Sweden) were inserted into the fibula sockets according to the guide. In general, we use 10 mm length, 4 mm diameter implants, and because of the high stability we don't feel the need for bi-cortical drilling and implant placement. In the next step, the fibula was cut into segments with a reciprocating saw using the fibula guide as a template. Care was taken to preserve the periosteum to guarantee the vascularization of

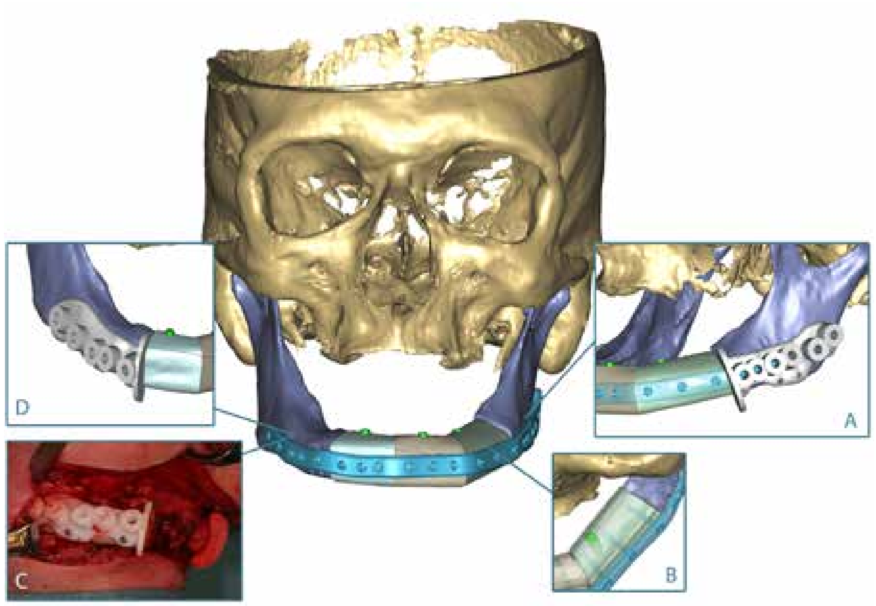


Figure 1 The virtual reconstructive plan is visualized using the left fibula in a three segment reconstruction of the mandible. Three implants and a CAD-CAM reconstruction plate were planned together. Insert A (right) shows the virtual plan of the resection guide of the mandible. This guide is designed to facilitate drilling of the screw holes. Insert B (right) shows the planning of the locking screws, the ventral screw is 15° angulated; all screws are planned to just reach the inner cortex of the fibula and to avoid planned dental implants. Inserts C and D (left) show the planning of the right mandibular resection/drilling guide (D) and the intra operative seating of this guide (C), fixated by two 1.5 mm screws (Synthes, Solothurn, Zwitserland).

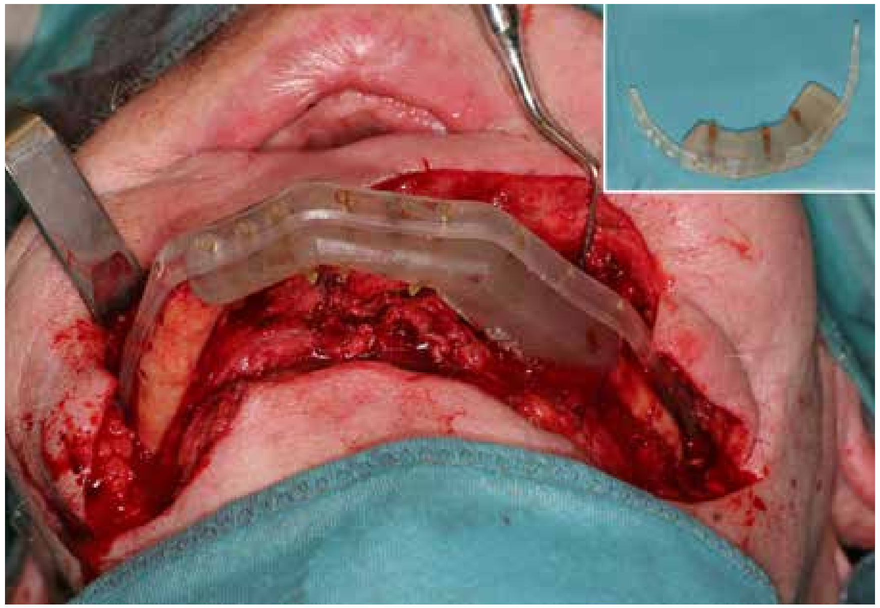


Figure 2 The insert shows a 3D printed (stereolithographic) anatomical model of the 3 fibula segments aligned according to the plan including the 3D-planned reconstruction plate. The overview shows the printed model seated intra operative after resection and pre-drilling of the screw holes in the both proximal mandibular segments. This 3D printed surgical outcome model is an essential part as it shows the outcome shape of the virtual plan combined with the preparation of the mandible and is used as a last check for the viability of the plan before harvesting and segmenting the fibula at the donor site.

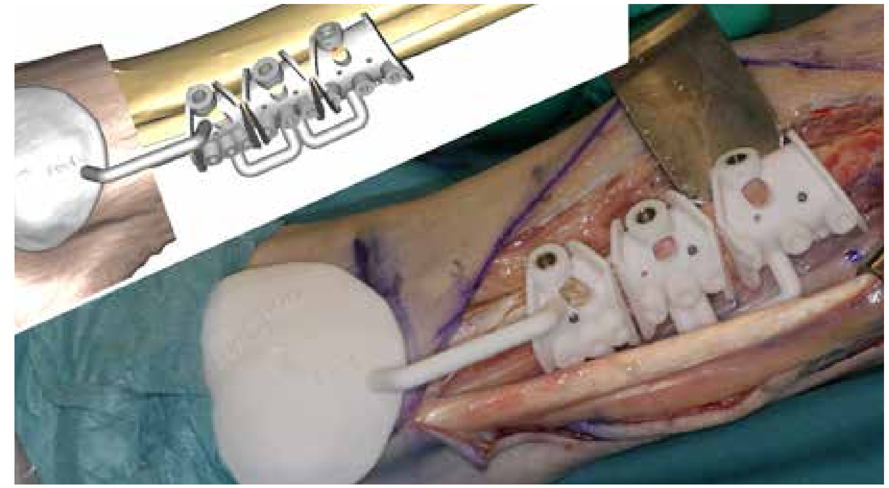


Figure 3 Virtual drilling and resection guide (left upper) and stereolithographic guide (right lower). The three segments are fixated with three 1.5 mm screws (8mm) to prohibit displacement of the guide after segmentation.

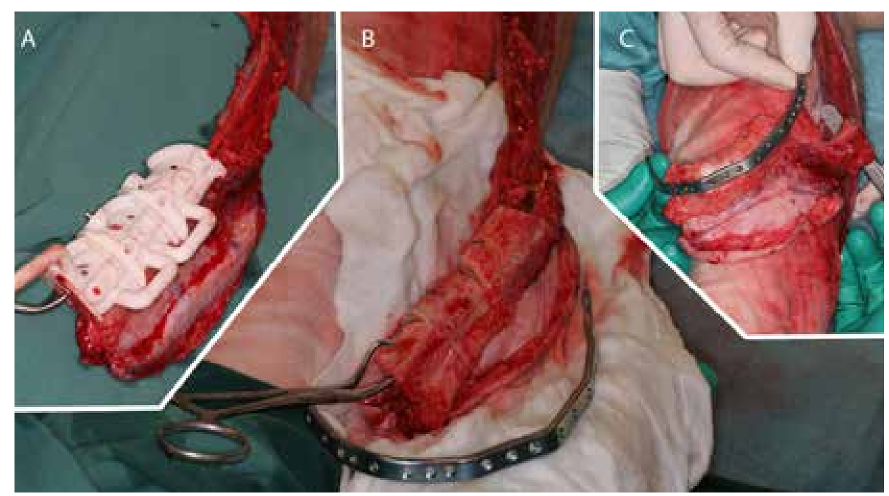


Figure 4 The sterolithographic guide (upper left panel) is situated on the fibula after segmentation, guided implant placement and pre-drilling of the screws of the reconstruction plate. After removing the guide (middle panel) the prefabricated fibula with skin paddle is shown. The fibula segments are screw-fixated on the CAD-CAM reconstruction plate (right panel) whit the native blood supply intact.

Figure 5 Fibula graft fixated on the right and left mandible side. The intra oral image (A) shows the implant reatianed prosthesis in the lower jaw and conventional prosthesis in the upper jaw. Note the excellent fit of the osteotomy lines and the proper alignment of the fibula segments and the mandible.

all segments. The fibula segments were fixated to the PSP using monocortical-locking screws so that the preplanned shape of the reconstructed mandible was reproduced (Fig. 4). Until this stage, the vascular pedicle of the fibula graft was kept intact, to preserve blood supply.

Third, the mandible was reconstructed by placing the fibula graft, with the patient-specific CAD-CAM reconstruction plate attached, into the defect. The guided drill-holes made earlier were used to fix the entire construction to the remaining mandible with bicortical locking screws (Fig. 5). Blood recirculation of the fibula graft was established by anastomoses of the peroneal vessels to recipient vessels in the neck. Three months post operatively an implant-supported denture was made on the reconstruction (Fig. 5).

Analysis of the results

A CBCT scan of the mandible was made within 2 weeks post operatively, as a routine, to judge the contact area between the fibula osteotomy planes. The mandible and the implants were segmented. It turned out that, due to scattering from the metal of the reconstruction plate, the fibula osteotomized parts could not be projected very well. To overcome this, the planned 3D fibula objects were imported into the post operative scan file in ProPlan CMF 1.3 and matched to the outline of the fibula segments. The mandible, fibula segments and the implants of the pre- and post operative ProPlan file were exported as STL files and imported in Geomagic Studio 2012 (Geomagic Gmbh). Surface-based superpositioning of the post operative CBCT scan onto the pre operative 3D plan was carried out. A best-fit match, using an iterative closest point registration algorithm, was performed on the mandibular outline of the mandibular part that was not involved in the resection. To perform the measurements, virtual cylinders around the fibula segments and implants were auto-generated by the software. These cylinders have a diameter corresponding with the maximum diameter of the fibula segment/implant and were aligned with the segment/implant. Subsequently, the centerpoints and centerlines of these cylinders could be determined automatically. Linear measurements were made between the centerpoints of the fibula segments and the implants to determine the deviation of the surgical outcome of the fibula reconstruction. Also, the angle between the centerlines of the fibula segments and implants was measured (Fig. 6). Furthermore, the resection

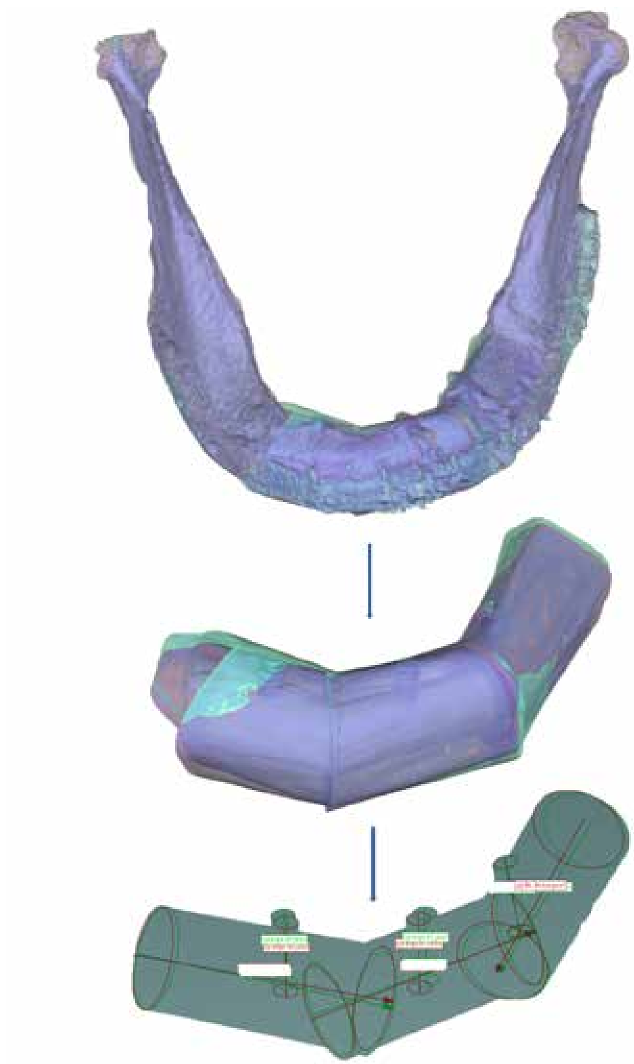


Figure 6 Superimposition of virtual reconstructive planning and post operative CBCT of the reconstructed mandible (upper). The alignment was performed on the mandibular parts using an iterative closest point algorithm Geomagic Studio (Geomagic Gmbh). The deviation of the post operative fibula segments (green) and virtual plan (blue) is shown (middle). Automated cylinders are situated on the fibula segments and implants by the software to determine centerpoint distances and axis deviations of the fibula and implants.

plane of the mandible was compared with the planned plane. This shows the accuracy of the fibula reconstruction in rehabilitating the mandibular defect. To investigate the accuracy of the implant insertion, fibula segmentation and screw fixation of the reconstruction plate on the fibula segments, the post operative scan was also matched using the fibula segments in the planning as a reference.

Even though this study is retrospective, the ethical board of our university hospital approved the study design and requirements for patient anonymity under reference number M14.160224.

Results

Patients

In the period between March 2013 and July 2014, seven consecutive patients met the inclusion criteria and were included in this study. No patients were excluded. The patients (five male and two female), with an average age of 60.4 years (range 43–84), required reconstruction of the mandible for a tumor of the mandible (four patients: desmoplastic fibroma (1) and squamous cell carcinoma (3), or osteoradionecrosis (three patients) with a free vascularized fibula flap (Table 1).

Accuracy

A total of 16 fibula segments were used, in which a total of 18 implants were placed. Six out of seven flaps survived for an average follow-up time of 9.7 months (range 5–16). Besides the implants within the graft that was lost due to flap necrosis, no other implants were lost. When the post operative scan was superimposed on the mandibular outline, the median centerpoint distance between the planned fibula segments and the post operative fibula segments was 2.5 mm (IQR:1.9-4.8 mm) and the median angulation was 3.1° (IQR:1.8-5.5°) (Table 2). The median centerpoint distance between the planned implants and the post operative implants was 3.1 mm (IQR:2.3-4.2 mm) and the median angulation was 12.3° (IQR:5.0-18.6°). The median deviation of the mandibular resection planes compared with the plan was 1.9 mm (IQR:1.0-2.5

Table 1 Patient characteristics

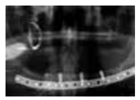
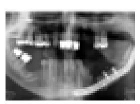
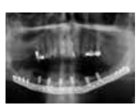
no.			Age	Sex M/F	Etiology	Follow up (month)
1			56	M	osteoradionecrosis	16
2			54	F	desmoplastic fibroma	15
3			61	M	osteoradionecrosis	12
4			44	M	osteoradionecrosis	11
5			84	M	squamous cell carcinoma	8
6			74	M	squamous cell carcinoma	5
7			54	M	squamous cell carcinoma	1 (flap-loss)

Table 2 Outcome measurements after superimposing the post operative CBCT scan over the pre-operative 3D virtual plan. Matching is performed using the mandible surface (iterative closest point algorithm) as a reference and secondarily using the fibula surface of the segments as a reference. The deviation of the implants and fibula segments is displayed for each of the seven patients. The central column displays the deviation of the midpoint of the resection plane post operative compared to the virtual plan displayed in the row of the adjacent fibula segment.

		Mandibular match		Mandibular resection plane	Fibular match	
Patients		axis deviation (°)	centerpoint deviation (mm)	midpoint deviation(mm)	axis deviation (°)	centerpoint deviation(mm)
1	implant 1	2,4	2		1,8	1,6
	implant 2	1,8	1,3		3	0,6
	implant 3	2,4	2,1		2,4	1,7
	fibula segment 1	5,2	0,9	2,1	2,8	0,2
	fibula segment 2	1,8	0,4		0,8	0,2
	fibula segment 3	1,2	1,1	2,4	0,6	0,1
2	implant	19	4,5		1,5	0,7
	fibula segment 1	10,9	5,4	1,1	3,9	1,6
	fibula segment 2	9,8	5,4	5,2	0,7	0,4
3	implant 1	6,8	4,1		2,5	2,6
	implant 2	7,5	3,7		4,3	2
	fibula segment	3,3	5,7	1,6		
				2,4		
4	fibula segment 1	2,4	2,3	0,8	6,5	1,3
	fibula segment 2	1,7	2,6	1,3	0,3	0,2
5	implant 1	5,8	4,8		14,2	2,5
	implant 2	5,9	5,7		14,1	2,1
	fibula segment 1	5,6	2,1	2,7	6	1,5
	fibula segment 2	2,6	3,1	2,3	2,8	0,5
6	implant 1	1,3	2,3		3,4	1,5
	implant 2	13,4	2,4		11,2	2,4
	implant 3	20,9	3,1		18,8	1,7
	implant 4	17,1	2		15,4	1,4
	implant 5	12,3	3,5		9,4	2,3
	implant 6	12,2	3,1		9,1	2,2
	fibula segment 1	0,9	3,1	3,6	1,6	0,4
	fibula segment 2	2,9	2		5,3	2,5
	fibula segment 3	3,7	5,5	0,7	4,4	0,8
7	implant 1	23,3	2,5		17,2	4,7
	implant 2	18,4	3,7		21,2	1,7
	implant 3	16,4	5,6		22,2	5,1
	implant 4	20,4	2,4		21,5	2,6
	fibula segment 1	9,8	2,2	1,3	5,2	1,9
	fibula segment 2	1,8	1,9		2,9	3,5
	fibula segment 3	5,2	2,7	0,6	2,1	0,4

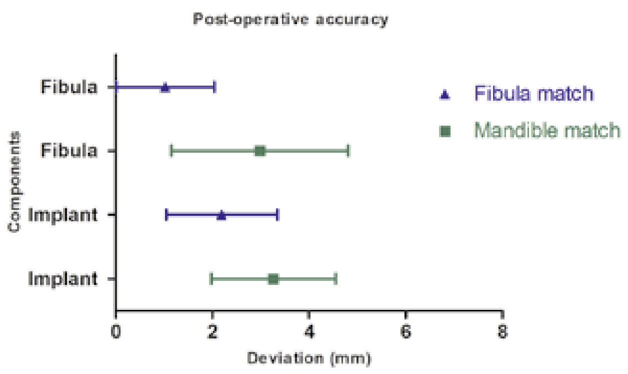


Figure 7 Plot showing the post operative accuracy of the fibula segments and implants (centerpoints) compared to the virtual planning. The vertical axis shows the implants and the fibula segments, either matched on the level of the mandible or with the fibula segments as a reference.

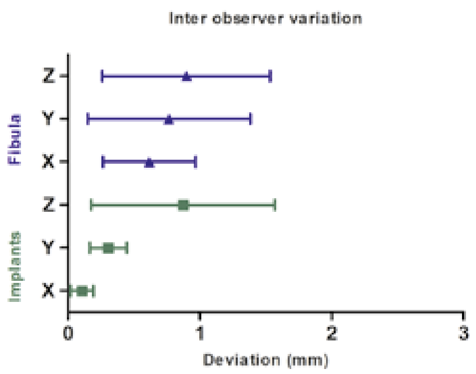


Figure 8 Plot showing the interobserver variation. The vertical axis shows the implants and fibula segments in dimension x, y and z between both observers. The horizontal axis shows the average implants and fibula segments centerpoints of deviation in mm and the 95% confidence interval. The interobserver deviation is the highest in the z-axis.

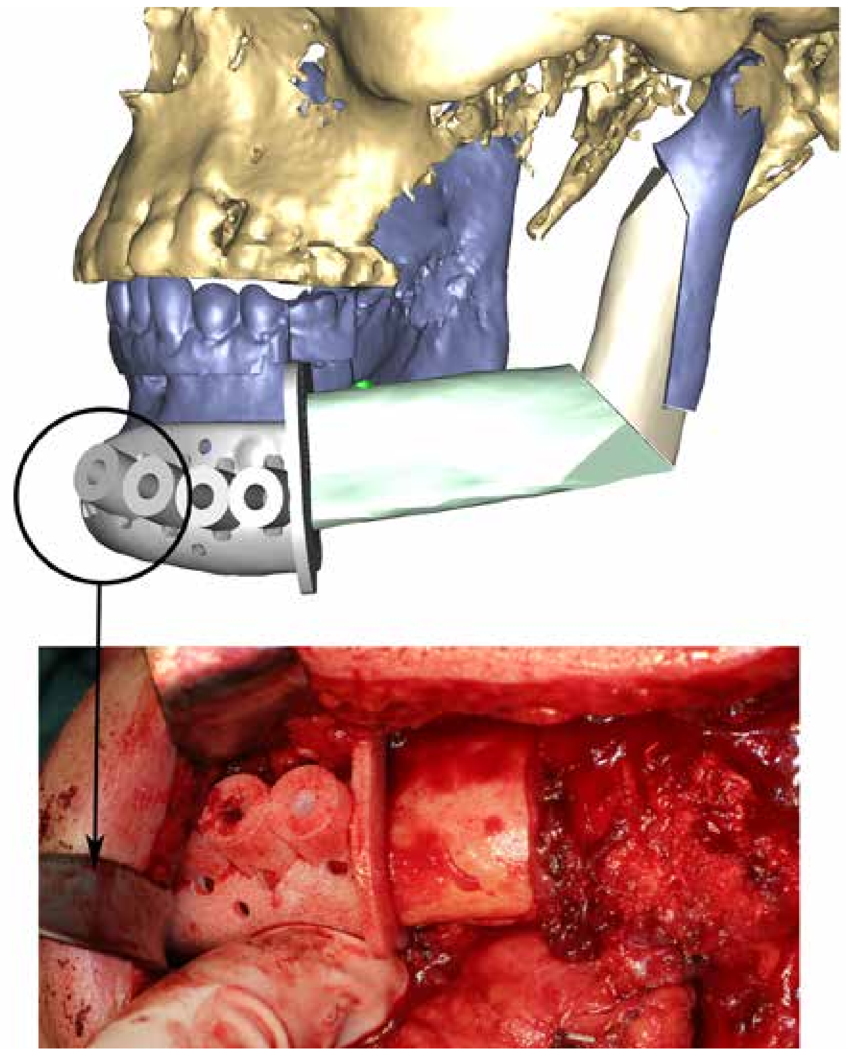


Figure 9 Planning (upper) and resection/reconstruction (lower) of a patient with a desmoplastic fibroma of the left mandibular corpus and ramus. Probably due to overriding and pressure of the skin (black arrow) in the mental region the guide was misplaced 5 mm dorsal, resulting in a subsequent deviation of the entire reconstruction.

mm). When the fibula segments were used as a reference of superposition, the median centerpoint distance between the planned fibula segments and the post operative fibula segments was 0.5 mm (IQR:0.2-1.6 mm) and the median angulation was 2.8° (IQR:0.8-5.2°). The median centerpoint distance between the planned implants and the post operative implants was 2.1 mm (IQR:1.6-2.5 mm), and the median angulation was 10.3° (IQR:2.9-17.6°) (Fig 7). To evaluate the matching of the planned fibula segments on the fibula outline of the post operative scan, two observers performed the matching of these files manually. The first five files were also matched by both observers to provide the inter-observer correlation (Fig. 8). The deviation of the centerpoints of the fibula segments were compared and expressed as average Euclidean distance of the centerpoints, which was 1.2 mm for the implants, and 2.0 mm for the fibula segments.

Discussion

This study shows that it is possible to combine the placement of dental implants in fibula bone grafts used for complex mandibular reconstruction with 3D-planning and printing of surgical guides and using patient-specific CAD-CAM reconstruction plates as a translation tool during the operation.

Including the patient-specific CAD-CAM reconstruction plate in the virtual planning of reconstruction, results in accurate reconstruction with a clinically acceptable average deviation of 3.0 mm. The use of 3D virtual planning and 3D printing allows preparation of the fibula with dental implants. A key factor in the accuracy of fibula segment reconstruction is proper positioning of the mandibular resection guide. Analysis of the second patient's data showed a large deviation of 5.2 mm of the anterior mandibular resection plane from the guide that was planned for the mental region (Table 2). This was probably caused by incorrect positioning of the guide, caused by overriding of the soft tissue underneath the guide in the mental region. Better visual control would have only been possible through the more extensive exposure and degloving of the mandible (Fig. 9). After identification of this problem the guide design for subsequent patients was altered by creating

a viewing window providing direct visibility of the position of the guide in relation to the lower border of the mandible.

Evaluation of the prefabrication of the fibula was performed using the fibula segments as a reference for superpositioning. These showed remarkably little deviation of the fibula segments. The orientation of the fibula segments is mainly determined by the accuracy and shape of the plate and drilling of the screw holes. The accuracy of stereolithography and CAM techniques is high compared with the deviation of the fibula and implants we found.[14,15] This CAD-CAM reconstruction plate has an individualized contour, allowing proper placement on the fibula. Other advantages of this plate are the individual planning of the angle of the locking screws and inter-screw distance allowing the use of locking screws to be inserted in the optimal position regarding bone quality and anatomical location.

Ciocca et al.[16] reported on the accuracy of fibula segments using the patient-specific CAD-CAM reconstruction plate compared with the careful use of bent of reconstruction plates. There are no other studies that report on the use of such a plate when combined with dental implant placement in the same operation. Roser et al.[9] have reported the potential contribution to placement errors when using manually pre-bent plates for fixation. Moreover, in accordance with the findings of this study, the total deviation from pre-operative planning is the sum of multiple small deviations in the different steps of the procedure.

The post operative fibula volume in our patients could not be used for comparison with the planned fibula segments because of scattering from the metal of the reconstruction plate. Even though there are studies which compare segmented CBCT scans of the reconstructed jaw with the virtual plans, [9, 12] these studies probably also experienced scattering as they report volume reductions of up to 30% of the post operative fibula osteotomized parts. Also differences in the CBCT scanner or the scan protocol can account for the amount of scattering we experienced in our post operative scans. We decided to use centerpoint and axis deviations of the fibulas and implants to report on the accuracy of the procedure and provide better insight into the type of deviation (rotation/translation) of the fibula segments and the implants. When considering the angulation of the implants, the wide range in angulation from 1.3°–20.9° was surprising, because guided implant insertion

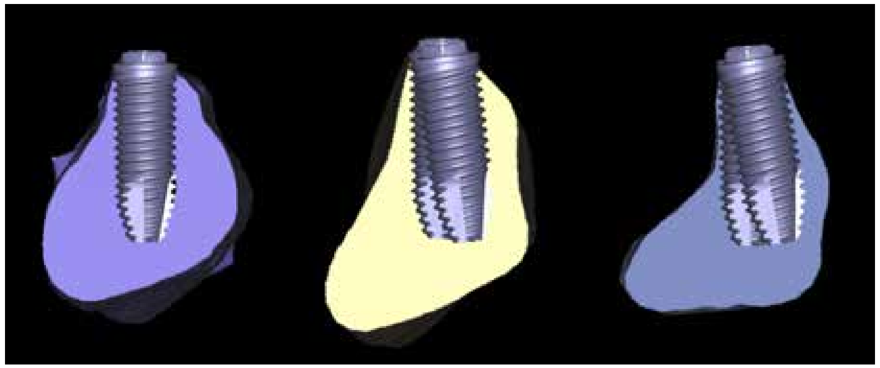


Figure 10 Axial slice through three different fibula bones 15 cm cranial from the distal end to show the variety in geometry in between the patients of the group. The fibula on the left has a relative round shape guided drilling and implant placement is possible with low risks. The middle fibula has a more sharp edge, guided drilling is possible, but with more risk of sliding and the insertion angulation is preferably more angulated than planned. The right fibula has a sharp edge, guided drilling is risky and the implant is placed preferably more angulated than planned. The right and more or less the middle fibula are implanted safer when the guide is removed after the pilot drill and the drilling of higher diameter drills including implant placement in these cases was performed under direct vision, accepting the angulation difference compared to the plan.

does not allow for this degree of freedom in angulation. To differentiate whether the deviation was due to implant insertion or that the deviation was caused by rotation of the fibula segments including the implants, the fibula segments derived from the post operative CBCT were also matched with the fibula parts from the plan using the fibula parts as a reference. Even then the median axis deviation of the implants in the fibula differed 10.3° from the plan. This implies that the deviation is caused by angulation of the implant during placement in the fibula segment. An explanation for this can be found in the wide variation in the shape of the fibula. Fibula geometry differed grossly in our patient group, especially the variation in sharpness of the ventral rim (Fig. 10). Where there was a noticeable sharp ventral rim, the guide was removed after the pilot drilling was done to prohibit drifting of the drill. The drilling to a wider diameter and tapping of the implants was then performed under direct vision without the drilling guide. The surgeon aimed to drill in the direction of the pilot guide, but when necessary changed the direction to prohibit side perforation of the drill. The position was determined by the guide, but the angulation differed due to manual drilling and implant placement, obviously resulting in a wide range of implant angulation differences compared with the 3D plan. We have no data yet as to whether the angulated placement of the implants creates problems for dental rehabilitation.

A critical issue in immediate reconstructions following tumor resection is how to plan a proper tumor resection margin. In the three patients in our group who had a malignant tumor we used clinical landmarks combined with anatomical findings on the CBCT to determine the virtual resection plane and planned a 1 cm tumor free margin. In the case of the desmoplastic fibroma we also used MRI data to determine the resection plane by visually comparing this to the virtually planned resection. During surgery we checked that these margins were still good before resecting according to the guide. We did not have to alter the resection plan in our patients. There are two problems that can occur; first of all, tumor growth in the period between planning of the surgery and execution can cause an intra operative change to the resection plane. It is possible that in these cases the patient-specific CAD-CAM reconstruction plate cannot be used. Second, a soft tissue deficit in the implant area can lead to implants that cannot be used for dental rehabilitation.

Immediate implant placement was first described by Urken et al.[17] to be a safe procedure. If immediate implant placement is not administered, it is general practice to wait for 6 months, delaying oral rehabilitation.[6] In cases of immediate implantation, osseointegration can begin before radiation therapy is administered, in cases where that is needed. In most cases, especially in immediate reconstruction following ablative surgery, the chances of implant-supported dental rehabilitation, therefore, will increase. Recently, Avraham et al.[18] showed that in their digitally planned fibula reconstruction group 11 of 14 patients with immediate implant placement achieved dental rehabilitation. We believe dental implant placement in the fibula while attached to the leg (before harvesting) provides clear advantages over secondary placement. The overview of the fibula geometry is better in the lower leg than intraorally, providing a good opportunity to place implants centrally so that they are surrounded by bone, even in a sharp ventral rim. Virtual planning makes it possible to plan the implants in a functional position, in line with the antagonist dentition. A temporary implant-supported denture following abutment connection is made at least 3 months after the reconstruction; in patients requiring post operative radiotherapy, abutment connection is delayed up to approximately 6 months after the end of radiotherapy. Initially, more often a fixed temporary acrylic prosthesis with temporary cylinders in the prosthesis is made and positioned during the abutment connection surgery for better control of the surrounding soft tissues. Extra care is taken to provide abundant space between the prosthesis and the soft tissue to facilitate healing and initial intra oral hygiene in the inter-implant spaces. These prostheses are fabricated with lower costs than a bar-supported prosthesis and can easily be reshaped to adhere better to patient-specific anatomy and allow adjustment for muscle function changes that appear in the post operative years. More often in a later stage, based on a patient's oral functions, the prosthesis can be changed into a removable bar-clip retained prosthesis to facilitate aspects such as support for the soft tissues of the cheek and lip, food impaction and cleaning.

Conclusion

Use of a CAD-CAM patient-specific reconstruction plate as a guide to position the fibula osteotomized parts, which have been prepared with dental implants inserted into the fibula before segmentation, allows both steps to be combined in one surgical procedure in a relatively accurate way. This allows the placement of dental implants in the fibula before segmentation and harvesting, resulting in immediate implant placement for the best chance of functional prosthetic rehabilitation following free fibula flap grafting.

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6

Integration of oncologic margins in 3D virtual planning for head and neck surgery, including a validation of the software pathway

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Summary

Objectives

Three-dimensional virtual planning of reconstructive surgery, after resection, is a frequently used method for improving accuracy and predictability. However, when applied to malignant cases, the planning of the oncologic resection margins is difficult due to visualisation of tumors in the current 3D planning. Embedding tumor delineation on an MRI, similar to the routinely performed radio therapeutic contouring of tumors, is expected to provide better margin planning. A new software pathway was developed for embedding tumor delineation on MRI within the 3D virtual surgical planning.

Methods

The software pathway was validated by the use of five bovine cadavers implanted with phantom tumor objects. MRI and CT images were fused and the tumor was delineated using radiation oncology software. This data was converted to the 3D virtual planning software by means of a conversion algorithm. Tumor volumes and localization were determined in both software stages for comparison analysis. The approach was applied to three clinical cases.

Results

A conversion algorithm was developed to translate the tumor delineation data to the 3D virtual plan environment. The average difference in volume of the tumors was 1.7%.

Conclusion

This study reports a validated software pathway, providing multi-modality image fusion for 3D virtual surgical planning.

Introduction

The use of three-dimensional (3D) virtual planning in oncologic- oral and maxillofacial surgery provides more predictable outcomes in terms of tumor resection, free flap placement and dental implant based prosthetic rehabilitation.[1-3] 3D planned tumor resection using either 3D printed resection guides[4] or computer assisted intra operative guided resection[5] has shown to provide precision for surgeons during ablative procedures. Currently, reconstruction of maxillary or mandibular discontinuities, with vascularized free flaps, is based more and more on 3D virtual planning using 3D printed surgical guides and/or intra operative navigation.[5-10] An increase in reconstructive accuracy and pre-operative insights are two examples of direct benefits from 3D virtually planned surgery. In order to translate this virtual planning to the actual surgical procedure, several methods are available. A commonly used method is the 3D printed, bone abutted, surgical guide, for cutting and drilling. In addition to the guided harvesting of the free flap, the guided insertion of implants was reported.[1] Computer Assisted Surgery (CAS) with intra operative navigation systems (e.g. Brainlab, Medtronic or Scopis) enables 3D virtual planning of tumor resection as well.[11] These systems use intra operative skull anchored reference points for finding pre operative marked points on an MRI or CT and are very accurate for maxilla resection. However, these systems are not validated by the manufacturer for use in the mandible due to a lack of a fixed reference point, although the use of CAS in mandibular resection was already reported.[10] The use of a recently developed method including a patient specific fixation plate enables such a rigid and predictable fixation in the mandible and maxilla; both free-flap reconstruction and implant insertion in that flap can be combined within a single surgical procedure[12,13] This primary reconstructive technique has already been implemented for benign cases or patients with osteoradionecrosis. When, however, applied to primary malignant cases, the risk of incorrect determination of the resection margins is a substantial clinical problem.[9] The decision to extend the margins during the surgical procedure can imply that the surgical guides and customized fixation plate cannot be optimally used or are no longer serviceable.Determination of oncologic margins is an applicable issue in primary malignant situations, as guidelines state that at least a ten millimeter tumor free margin is required in the case of erosive bone defects.[14] The potential discrepancy between planned and actual surgical margins are caused by a lack of 3D information concerning bony infiltration and tumor spread derivable from computed tomography (CT) imaging. Hence, in current practice, the malignancy is removed during the first procedure with some uncertainty about the bony marginal status; the free-flap reconstruction is then placed in the resected area. 3D planning allows accurate surgical resections by means of 3D printed surgical guides. But if the margin-planning is not performed adequately, the 3D planning method results in uncertainty with regard to resection margins. It may be necessary to revert to the conventional surgical approach during surgery, or result in a positive bone margin. Current 3D virtual planning is regularly based on Cone Beam CT (CBCT) or CT images. With CT imaging, the bony structures are segmented and included in the 3D virtual plan. However, because of the inherent properties of the acquisition device, Magnetic Resonance Imaging (MRI) is preferable to obtain more detailed soft tissue- and tumor expansion and invasion information (tumor delineation).[15] Combining both tumor expansion and invasion information as derived from MRI with the corresponding bone anatomy from the CT provides essential decision making information concerning the degraded bony tissue and thereby the localization of bone resection margins. In order to combine both image modalities, image fusion is required. By using multi-modality image fusion and tumor delineation the oncologic margins can be potentially included in the 3D virtual planning. The aim of this study is to provide a validated software pathway for the integration of tumor margins into 3D virtual surgical planning for both the maxilla and mandibula. This pathway can enable accurate primary reconstruction, even for the insertion of dental implants during primary surgery in benign and malignant cases. Development of a compatibility algorithm which enables multimodal image fusion and margin delineation during the 3D virtual planning is the first step. Acquiring data from animal cadavers with phantom tumor objects can provide an insight as to whether the developed software pathway is reliable and leads to reproducible margin data in 3D planning. The primary outcome is a validated software pathway for comparison of the measured volume of the phantom tumor objects before and after the translation; the final aim is surgical plan software.

Material and Methods

In this study a validated software pathway was developed for combination of image fusion, oncologic margin delineation, 3D virtual planning of the resection and 3D planned reconstruction of the defect. Figure 1 represents a schematic overview of the software pathway. The already available software architecture of both the department of radiation oncology and the 3D planning center in the hospital was used. The Mirada (Mirada Medical, Oxford Centre for Innovation, United Kingdom) software was used for the data fusion and margin delineation. The 3D virtual surgical planning was performed with the Pro Plan CMF 2.0 (Materialise, Leuven) software. To translate the 3D tumor volume determined in the MRI to the 3D plan based on the CT file, a compatibility algorithm was developed by Matlab (Mathworks, Natick, Massachusetts, USA).

A series of five bovine cadaver mandibles were used to test and validate the software pathway. A standardised phantom tumor, in the shape of a plastic sphere filled with a solution of barium sulfite and water, represented a malignancy. The phantom tumors were fixed onto the cadaver jaws at different locations with two-component dental impression paste (Provil Novo Putty®, Heraeus Kulzer GmbH,Hanau, Germany), as illustrated in figure 2. All the cadavers with the phantom tumors were CT scanned (Siemens AG Somatom Sensation 64) and MRI modalities (Siemens Magnetom Aera, 1.5 Tesla). Regular head and neck protocols were used for the CT imaging and MRI sequences. In addition to the 3D MRI sequence, the regular protocol, T1 vibe tra-isotrophic, was used as a comparison.

Manual global positioning of the MRI images, projected onto the CT images, was performed for data fusion. This is a standard technique in image fusion and is typically supported by radiotherapeutic planning software. This was followed by automatic rigid registration with a focus on the selected region of interest including the phantom tumor and surrounding tissues. The image fusion was visually inspected in order to detect any mismatches after the fusion process.

Figure 1 Schematic overview of software pathway.

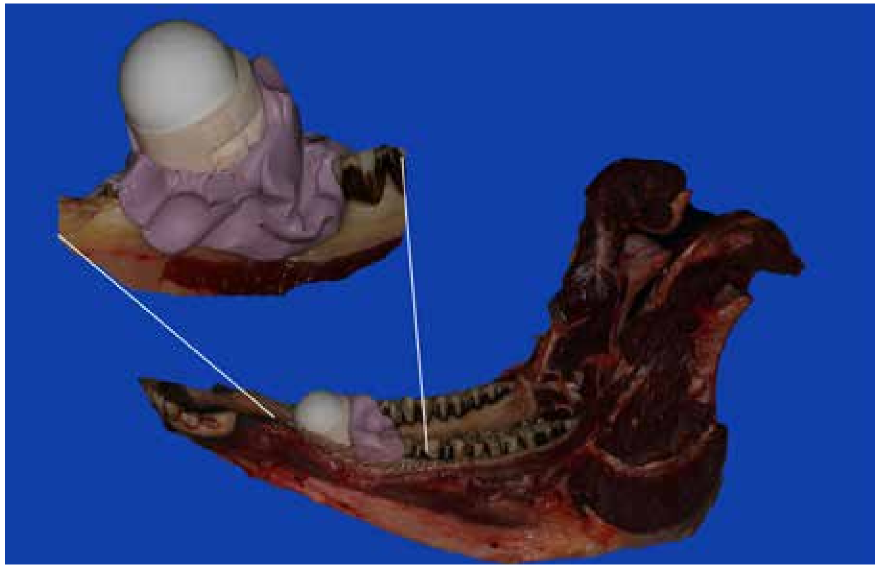

Figure 2 Picture of the bovine cadaver set-up, including the phantom tumor object (enlarged image).

Delineation of the gross tumor volume (GTV) was performed by a contouring brush tool in the software. The phantom object, being a spherical object, enabled straight forward contouring. The sphere was amply selected on the MRI images. The contour was decreased with an automated shrinkage tool until the exact borders of the phantom were found; then the total volume of the GTV was registered, as presented in figure 3. The delineation of the entire object was visually inspected again on both the MRI and CT images. The CT dataset was then exported together with a radio therapeutic structure set (RTSS)-file of the contour.

Both the RTSS-file and the CT dataset were combined using the developed compatibility algorithm. The algorithm produces a digital image and helps in the communication between the medicine (DICOM)-file and the CT images as well as the information from the RTSS-files and thus functions as the basis for the 3D virtual surgical planning.

To determine the validity of this software pathway, the volumes calculated in the Mirada- and Pro Plan software were compared using a ratio. The average ratio of the five samples quantified the accuracy of volume representation after completion of the software pathway.

Once the bovine setup was validated, the same software pathway was applied to a series of three clinical cases to validate the procedure for use in clinical practice. Delineation of the tumor after image fusion provided segmentation of the tumor in the 3D virtual planning. Determination of resection margins of the maxilla/mandible was performed based on the 3D visualization of the tumor. Figure 4 represents a 3D virtual model of an example case with the resection margins, colored in blue, derived from the 3D projected model of the tumor.

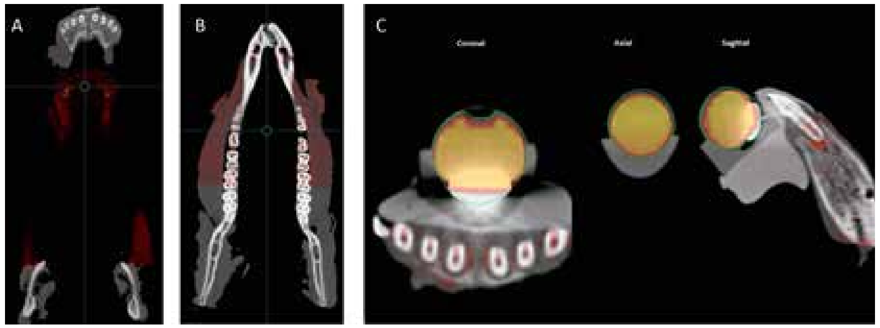

Figure 1 A. Fusion of MRI (red) and CT (grey) data of bovine cadaver. B. Fused images. C. Delineation of phantom tumor object (green).

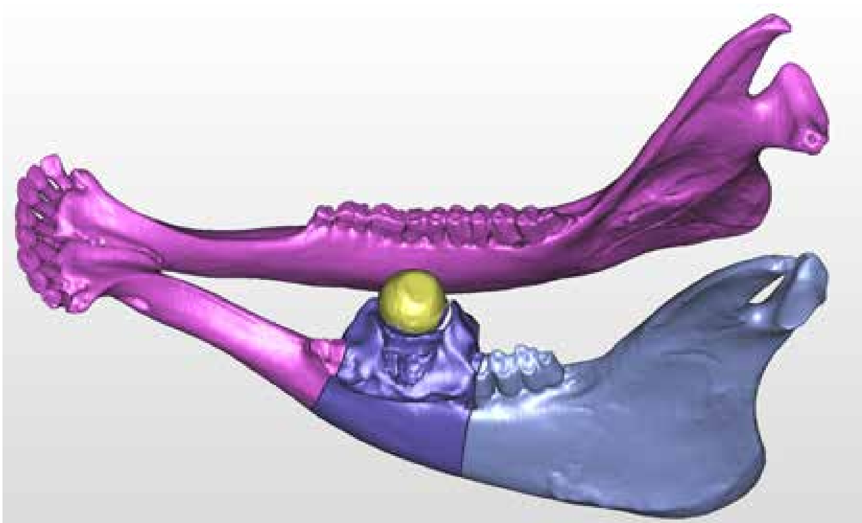

Figure 4 Three-dimensional virtual model of CT bovine cadaver data, including a segmentation of phantom tumor object (yellow) and an example resection margins.

Results

A compatibility algorithm was developed to combine data fusion and 3D virtual planning software. This algorithm, as part of the 3D software pathway, enabled the combination of radio therapeutic data fusion- and tumor delineation (Mirada) principles with 3D virtual surgical planning (Pro Plan).

In more detail, the algorithm introduces a voxel-highlight on the CT image for every voxel coordinate present in the RTSS-file. This means a highlight for every selected voxel within the GTV delineation. The highlight was achieved by increasing the value (in Hounsfield units) of the corresponding voxels, to a maximum distinctive white value (baseline value +2500 HU). This enabled distinctive visibility of the delineated GTV on the newly created DICOM file. The tumor was segmented in Pro Plan as a separate 3D object, and the volume was measured using the volume tool.

The objective was to determine whether the delineated volume in Mirada had been altered while converting the volume, using the compatibility algorithm, to the 3D virtual planning environment. This study validated the developed software pathway by means of pre and post comparisons of the phantom tumor volumes on the five cadavers. The mean variation in volume of the compared measurement points was 1.7%. Table 1 presents the compared measured volumes of each of the phantom tumor objects.

The CT images were obtained using regular head and neck protocols, as described in the method section. Regarding the MRI images, the regular head and neck sequences as well as the 3D vibe sequence were used. The initial tumor delineation was performed on the T1- TSE images. The same delineation was also performed on the T1-vibe tra-isotrophic sequence for comparison purposes, but this had no influence on the delineation of the phantom objects.

Application of the procedure to a (first) clinical case, ameloblastoma in the maxilla, resulted in a comparable difference in delineated volume, 1.7%, as represented in Figure 5. Two additional cases, with a squamous cell carcinoma invading the mandible, are represented in figure 6. Postoperative analysis,

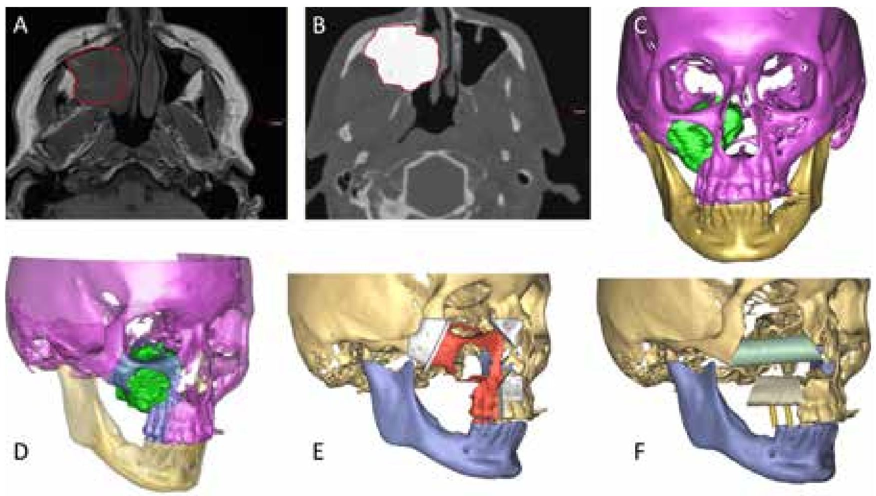

Figure 5 A. Tumor delineation on MRI imaging. B. Projection of tumor area on CT images C. 3D model of with the delineated tumor in green. D. The resection margins determined, in blue. E. Guide design for resection. F. Reconstructive plan with fibula including dental implants, represented by the yellow cones.

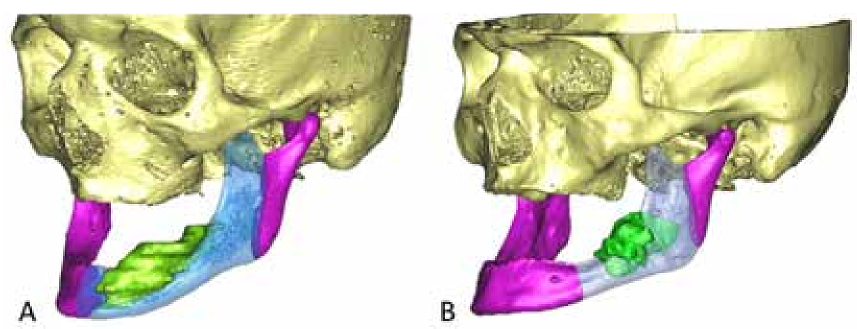

Figure 6 A. First example of a case with mandible related malignancy, tumor delineated in green and oncologic margins in blue. B. A second case example with a mandibula related malignancy.

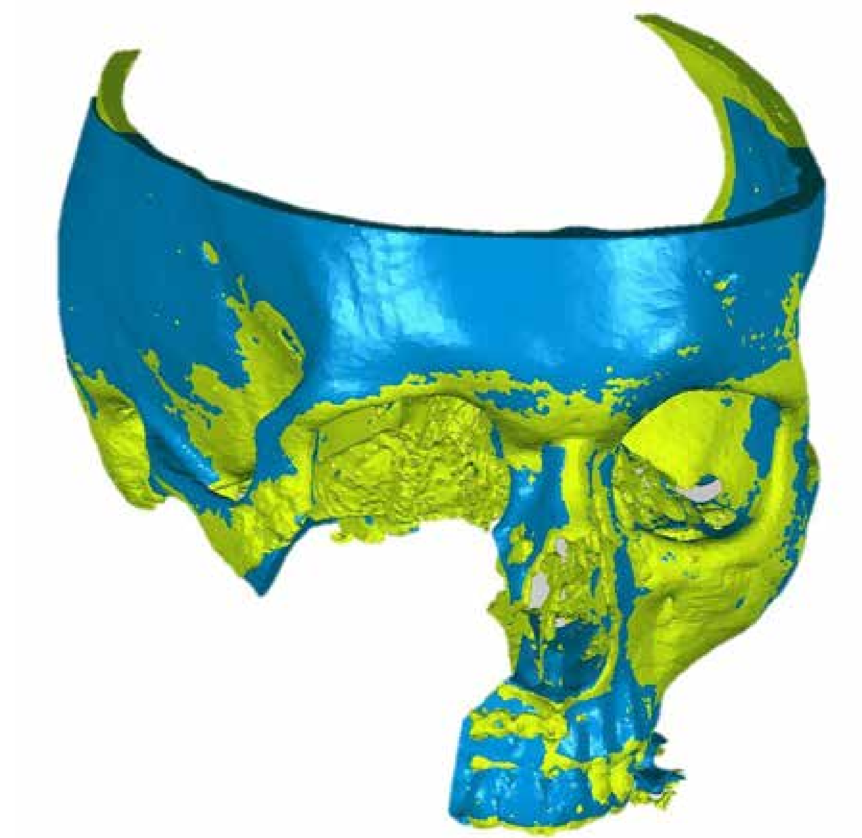

Figure 7 A 3D representation of the post operative resection-result (yellow) superimposed on a 3D model of the planned resection (blue).

Table 1 Results of volume measurements after initial tumor delineation (Mirada) and after conversion to a 3D virtual model (Proplan).

	Tumour 1	Tumour 2	Tumour 3	Tumour 4	Tumour 5	Mean	SD
Mirada (cm^3)	33,90	33,40	33,80	33,00	33,90		
Simplant (cm^3)	34,40	34,40	34,16	33,20	33,00		
Difference (%)	1,45	2,91	1,05	0,60	2,73	1,75	0,91

based on a post operative CT scan, showed that the reconstruction was performed according to the 3D virtual planning. Figure 7 shows an example of a 3D representation of the post operative result, using the first case with the ameloblastoma. The pathology report confirmed tumor free-margins of the resection, and thereby complete tumor removal based on a guided resection.

Discussion

A reliable software pathway for pre-operative integration of oncologic resection margins was realized by this study with a deviation of only 1.7 % in volume. The use of five cadavers with phantom tumor objects provides a validation for the delineation of tumors and this information, as an enhanced DICOM data set, can be used for surgical and consequently for reconstructive plans.

The concept of using the software with regular protocols for both MRI sequences and CT scans should not increase the workload of the imaging resources. The phantom tumor objects were relatively easy to delineate due to the symmetrical spherical shape but improved scanning protocols may be required to translate actual oral cancer malignancies with irregular shapes. These protocols could include a 3D sequence in order to gain additional detailed information on the z-axis. In this study, additional T1-vibe tra-isotropic sequence scans were made. During the tumor delineation the regular T1-TSE- sequence provided sufficient information, and there was no direct need for 3D sequences in the case of these phantom tumor objects. Finding the optimal scan protocols for head and neck oncology was not within the scope of this study, therefore the validated approach of tumor delineation within the radiation oncology principles was utilized.

The volumes of the phantom tumors did not correspond 100% when measured by both software entities. Despite the careful delineation, small areas outside the delineated volume may have been included in the high-threshold

segmentations of the 3D object volumes due to contrast deposits at the bottom of the phantom. However, this did not interfere with the purpose of our study since the objective was to see whether defined volumes would be altered on an MRI by the new software approach.

Due to the conversion algorithm, multiple combinations of software packages can be used. Therefore this method does not require the purchasing of a specific software package. Alternatives can be found in the navigation systems as well (e.g. Medtronic, Brainlab, Scopis), these have other (dis) advantages in terms of guided implant placement and tumor delineation. Several software packages are commercially available which provide efficient image fusion and/or tumor delineation features (e.g. I-plan, Brainlab or Eclipse, Varian Medical Systems). Application of these packages are reported for head and neck treatment planning as well.[10,16] Multidisciplinary 3D virtual planning, based on navigational planning was reported in combination with post operative radio therapeutic planning by Bittermann et al.[17], as well combining different software packages. Compared to this study method, these examples provide efficient solutions for mainly the maxilla, and no validated solution for the mandibular malignancies due to lack of fixed reference points. Secondly, the method described in this study enables multidisciplinary 3D virtual surgical planning, including single phase resection reconstruction and insertion of dental implants, within the existing software architecture using essential 3D printed surgical guides. The alternative software packages do not meet the requirements for treatment planning including accurate, guided dental implant insertion[13] and therefore do not provide an all-in-one solution which favors the prosthetic rehabilitation for the patient. Combining physiological information derived from the MRI with the corresponding anatomy from the CT images for tumor delineation in the head and neck area has been reported.[18] It was demonstrated that tumor delineation on MRI/CT scans can be performed with acceptable precision, although the MRI margins can be overestimated.[19] In essence, our approach is not different from tumor delineation routinely performed by radiation-oncologists.[20] However, the use of such radio therapeutic principles for pre-operative 3D surgical planning of oncologic resection margins, reconstruction planning (including dental implants) and translation by surgical guides has not been reported to our knowledge. Current applications of 3D virtual surgical planning of primary resections in the maxilla or mandible including reconstructions with insertion of dental implants are restricted to benign cases. Several authors state that the exact determination of oncologic margins for malignant cases restricts the application of this 3D virtual planning concept in the primary situation.[21,22] This study demonstrated that primary 3D virtual planning of resection margins in oncologic cases can be included in regular 3D virtual planning. The inclusion of the resection margins in the 3D virtual plan will result in a single surgical procedure, with added benefits in terms of predictability and accuracy and being able to place dental implants during a single procedure. Other authors have described the placement of dental implants in free flaps prior to radiation therapy. One might debate if this is feasible in terms of survival of the flap. These results prompted us to design a clinical study based on the 3D planning principle, aiming for added value for patients.

Conclusion

This study reports a validated software pathway, providing multi-modality image fusion for 3D virtual surgical planning. The all-in-one resection and reconstruction approach is applicable to malignant cases whereby soft-tissue information derived from MRI scans is included in the 3D virtual planning and the region of interest is carefully examined clinically. This study provides application of the all-in-one approach to larger target groups, including malignancies, with a decrease of the risk for irradical bone margins.

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7

General discussion

Free flap reconstruction of oncology patients

At the start of this PhD project knowledge about 3D reconstructive planning of maxillofacial defects was rather limited. A pubmed search on 3D planned fibula reconstructions of the jaw yielded 4 results.[1-4] While commercial software to plan fibula reconstructions was already available in 1988, only one study reported about accuracy of graft position using this method.[3] The aim of this thesis is to add on knowledge about the accuracy of 3D planned fibula graft reconstructions of maxillofacial defects. Because dental implants have proven to favor chances of dental rehabilitation we included immediately placed dental implants in the planning and measurements on accuracy.

In chapter 2 we performed a systematic review on the functional outcome of fibula grafts of the jaw. We learned that the overall survival rate of dental implants, placed in a osteocutaneous Free vascularized Fibula Flap (FFF) is high with an survival rate of 95% (662 implants in 210 patients). The oral function in head and neck oncology patients after cancer treatment is better when they receive an implant-retained denture than a conventional denture.[5-7] However, though implant-retained oral rehabilitation is favorable in head and neck cancer patients, implant placement in a FFF is often not straightforward and may result in non-used implants or even a failure of the prosthodontist of being able to make a functioning implant-retained overdenture.[8,9] The problem with implant placement in FFFs is that proper positioning of the implants in a FFF is not easy due to loss of anatomical landmarks after tumor resection, especially when immediate placement in strived for.[10] When implants are placed as a second stage surgery, scarification of mucosa, a bulky mucosa and/or a tender mucosa contribute to this problem.[11] E.g., due to the resection of soft tissues a deficit of peri-implant soft tissue and often absence of a buccal sulcus remains. The latter conditions difficult the creation of healthy peri-implant soft tissues. These circumstances agree with the observation that more peri-implantitis is observed around implants placed in the often bulky, mobile soft tissues that are present in the reconstructed area.[11] For these reasons either implants

are not placed in FFF or cannot be used for retaining prosthetics in case it was attempted to place implants in these unfavorable soft and hard tissue conditions. As a result the implants become infected or are left buried as sleeping implants.[12] The sum of the reported problems regarding implant-retained prosthodontics in oncology cases and our experience made us realize that proper planning of the reconstruction might be on the basis of optimal positioning of the graft and implants favoring a functional oral rehabilitation. Also combining efforts by involving both the surgeon who performs the reconstruction, the surgeon who places the implants (if not the same) and the prosthodontist who has to make the prosthodontic rehabilitation in composing the virtual reconstructive treatment plan, will to our opinion result in a viable, anatomical and clinical plan.

When focusing on planning of FFFs and its functional outcome the concept introduced by Dennis Rohner is promising, but in need of refining. The first step is to gain more anatomical insight and to reduce or even omit the multiple laborious steps of his method. The technique described in chapter 3 shows that the planning can be executed virtually as well as that the guides can be fully designed virtually thus overcoming the multiple, often time consuming and expensive, laborious steps. The in chapter 3 described cases also learned us that the errors between the virtual planning and the final result are rather small. This, however, does not necessarily mean that the error of the implant placement or cutting in itself is also small. But as we scan the actual implant position in the fibula with the Lava COS intra oral scanner and import the obtained data into the virtual plan, the result is an inherent correction of the implant position with regard to the final prosthodontics where after an rather accurate CAD-CAM bar or bridge can be milled. This way, there is an inherent compensation for surgical inaccuracies during implant placement. We tested this favorable outcome from our first cases in a case series (chapter 4). As expected the accuracy of the combination is larger than fibula reconstruction or implant placement alone. However, what was rather unexpected was the occlusal freedom the prefabricated prosthetics allowed the surgeon to place the segmented FFF without resulting in an improper occlusion. Thus the surgeon had the freedom to place the graft and denture entity as a whole in occlusion and even allowed for slight movement of the graft to maximize bony contact at key-points in the donor area of the bony graft edges to the jaw. On the other hand we also noted that placing the prefabricated graft, including the implants and prosthetics, was sometimes difficult due to scar tissue as a result of previous surgery or radiotherapy. Hence reconstruction of large defects in these patients remains to be complex surgery. Authors who perform 3D planning of their reconstructions, noted that planning helped them to perform more complex reconstructions.[13] Though the surgery can be complex, this does not mean that every FFF has to be planned digitally. The more straightforward a reconstruction is, meaning less fibula segments and easy positioning and landmark recognition, the less there is a need for 3D planning to our opinion.

As with every new technique, 3D planning and guided reconstruction also has a learning curve. Not only a surgical learning curve on how to manage guided surgery, but also a planning learning curve to efficiently perform a clinical viable plan. One can discuss who has to perform the 3D planning? It can be done by the surgeon or by someone with a technical background and sufficient medical knowledge to interpreted the clinical possibilities and limits. Also the 3D planning does not have to be performed in the hospital, it can also be performed outside the hospital and results and fine-tuning can be discussed in a web-meeting with the clinical team. Literature shows this variety of options well and there seems to be no golden standard or strong argument to choose one over the other.[2,3,14-19]

Fixating the graft in occlusion and at the same time placing osteosynthesis plates is probably a limiting step in obtaining the maximum end result. Roser et al. (2010) mentioned already that adapting the osteosynthesis is a key factor with regard to a proper positioning of a 3D planned fibula grafts, especially when large reconstruction plates have to be shaped to match the planned position of the segments.[3] Thus, the next logical step was to integrate a custom 3D shaped reconstruction plate into the virtual plan and fixate the graft using this CAD-CAM milled reconstruction plate (chapter 5). The same virtual treatment planning method was adopted as in the previous chapters to present a functional virtual reconstructive plan.[17,20] The difference is that now the reference for placement of the graft is not the occlusion but

the plate and the pre-drilled screw-fixation holes. Therefore this method is suitable to apply to immediate reconstruction after tumor ablation. This approach resulted in a higher accuracy compared to the approaches used in chapters 3 and 4. There are two major reasons underlying this favorable outcome, viz. primary wound closure is possible (the implants in the fibula that is transplanted to the oral cavity are buried which is necessary to bear post operative radiotherapy), and second; the time frame for the planning and fabrication of the guides an plate is less than 4 weeks, so the tumor resection and reconstruction can be performed within the time frame of 30 days according to the guidelines of the Dutch head and neck cancer taskforce which are based on international publications.[22] Our clinical studies are focused on mathematical outcome compared to the virtual plan. Our time frame was relatively short to address the functional outcome of our patients. Besides this there is gross heterogeneity in the groups of patients. In total we treated 18 patients in total in 2 studies, 13 had a mandibula defect and 5 a maxilla defect. Six patients had osteoradionecrosis due to primary radiotherapy treatment. Nine patients had a primary diagnosis of squamous cell carcinoma, three had a ameloblastoma, the other 4 had varying other types of tumors. This heterogeneity can also influence functional outcome and the timeframe in which dental rehabilitation can be executed. We believe that our patients benefit of 3D planning and guided reconstruction and more patients receive a prosthetic and they receive the prosthesis earlier, compared to our traditional staged reconstruction. This is coherent with the paper of Avram et al. (2014) who reported about unprecedented rates of dental rehabilitation.[13] It is known that prosthetic concepts may be changed during the treatment due to unfavorable soft tissue conditions which can lead to sleeping implants.[22] One of our patients received 6 planned implants in the reconstructed mandible and due to the lack of a labial vestibule the 2 ventral implants could not be used to retain the denture (Fig. 1). This case illustrates that the soft tissue problems we encountered before 3D planning are as expected are not all overcome, but by planning more implants in a functional position we can probably compensate for the majority of technical problems that arise in these complex patients. One of the major advantages of the Rohner procedure for secondary reconstruction is the transplantation of a fixed peri-implant layer of soft tissue. We noted that in this group we

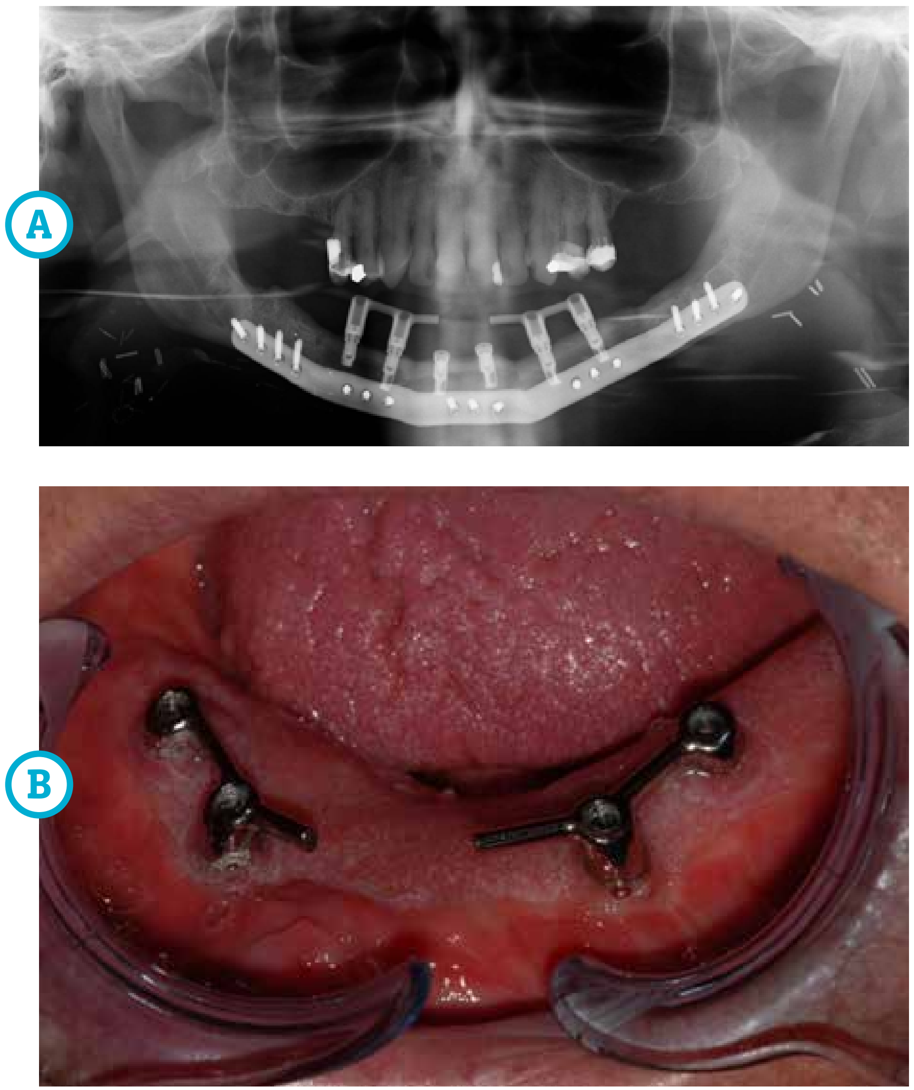

Figure 1 Fibula reconstruction of the mandible, In a one stage procedure 6 implants were inserted in the graft in an immediate reconstruction using 3D planning and a CAD-CAM reconstruction plate. The orthopantomogram (A) and the intra oral image (B) shows the lack of a buccal vestibule anterior, for this reason 2 anterior implants were not used for retention of the prosthesis and left as sleeping implants. The remaining 4 implants were used to retain a well-functioning denture.

had substantial less problems with the peri-implant soft tissues (Fig. 2). We hope to provide insight into the functional outcome of our 3D planned reconstructions in the future.

When the virtual planning method is applied to primary malignant cases, the risk of incorrect determination of the resection margins is a substantial clinical problem.[23,24] The potential discrepancy between planned and actual surgical margins is caused by a lack of 3D information concerning bony infiltration and tumor spread that can be learned form CT imaging. When combining CT data with MRI data, allowing for a more detailed image of the soft tissue, this clinical issue can be surpassed as is shown in chapter 6. The true clinical value of data fusion and the resulting virtual planning still has to be proven. We expect this will lead to improvement of the amount of tumor free margins after resection of large tumors. MRI tends to moderately overestimate the tumor size. Pathology reports will clear this out and hopefully give enough consistent data to provide an algorithm for safe resection margin determination and prohibit excessive overresection.

Conclusions and suggestions for future research

As described in the previous paragraph, virtual treatment planning and guided surgery in FFF reconstructions combined with dental implants of maxillary and mandibular defects offers sufficient accuracy for a predictable outcome as well as that image fusion of MRI and (CB)CT provides proper resection margins determination, contributing to safe planning of immediate reconstructions of the resection of malignant oral tumors. Virtual planning of primary implant placement in FFFs is currently the standard treatment in our department for patients who are reconstructed for a large maxillary or mandibular defect.

Figure 2 Fibula reconstruction of the lower jaw. The fibula was prefabricated with a split skin graft and dental implants, note the good aspect and amount of peri-implant split skin graft.

Virtual treatment planning offers a good anatomical insight and therefore can be of great help to plan tumor resections and complex reconstructions. The resulting optimal anatomical virtual treatment plan might not be the most realistic clinical plan, however. To convert the optimal anatomical plan into the optimal executive plan needs the involvement of a multidisciplinary team. This team should asses the virtual plan and make an estimation for the virtual plan to be clinically applicable regarding the patients local situation. Open, mutual collaboration between all team members, including the person who does the virtual treatment, facilitates a steep learning curve of the whole team and helps to prepare a realistic best virtual treatment plan, foresee surgical problems and get the best outcome for the patient. Moreover, virtual treatment plans are only as good as the scanning data is, so optimizing scanning protocols to obtain (CB)CT data that facilitates 3D planning best is therefore important.

Introducing the CAD-CAM reconstruction plate into the 3D workflow has proven to be a valuable step in controlling the translation of a virtual treatment plan to the surgery. This reconstruction plate is yet a bulky plate, which is only applicable in the mandible. The planning of smaller individual tailored osteosyntheses with a sufficient strength might be valuable in the reconstruction of the maxilla to use the same principle in translation pathway. Also in the mandible smaller plates might be of benefit. It also has to be tested whether indeed a rigid large reconstruction plate is needed or that smaller osteosyntheses can also do the job, e.g., two smaller plates at each osteotomy line, like is done in the treatment of mandibular fractures. Besides being easier to apply, less bulky plates also will reduce the risk on developing dehiscence's of the osteosynthesis as is not uncommon for large reconstruction plates.

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Summary

Prosthetic rehabilitation of head and neck cancer patients with large composite maxillary or mandibular defects is challenging. Yet, the most favorable treatment for large defects is the combination of a bony free vascularized graft to reconstruct the defect with implants to retain prosthetic constructions. The Free vascularized Fibula Flap (FFF) is a versatile flap that commonly is used to reconstruct such bony and soft tissue defects. It is also a versatile flap for implant placement as, probably due to the presence of dense cortical bone, stability and survival of implants is high.
When applying a FFF, a major challenge is arranging the FFF segments as such that they can provide a proper basis for implants optimally placed for implant-retained dental prosthetics. E.g., precise 3D placement of the FFF and implants to allow for implant-retained prosthetics is mandatory. In this respect, freehand positioning of a FFF is not without drawbacks and inaccuracies. When combined with freehand implant placement such an approach is even more prone for inaccurate positioning and therefore hardly administered. Therefore, virtual 3D surgical planning using CT (computed tomography) or CBCT (cone-beam computed tomography) data has been introduced to support an effective and efficient reconstruction. Such virtual planning should include the required margins for tumor surgery. Therefore, the overall aim of this PhD study was to develop an accurate digital planning method for mandibular and maxillary reconstructions of maxillofacial defects resulting from tumor surgery with FFFs combined with dental implants (chapter 1).

In chapter 2, a systematic review of the literature is described of the impact of oral rehabilitation with or without dental implants on functional outcome and quality of life (QoL) following reconstruction of large maxillary and mandibular defects with FFFs. The search yielded a total of 557 unique publications of which 10 studies were eligible according to our inclusion and exclusion criteria, viz., two prospective and eight retrospective case-series. When rating these 10 studies according to eligibility and a research quality criteria score (MINORS), the quality of the studies ranged from 44% to 88% of the maximum score. In these 10 studies, a total of 260 patients were described. These 260 patients were subjected to reconstruction with 261 FFFs, viz. 55 FFFs to reconstruct the maxilla and 206 FFFs to reconstruct the mandible. The survival rate of FFFs was 99%. Nine studies reported about the outcome of implant placement (662 dental implants in 210 patients), with an implant survival rate of 95%. Five studies reported on mastication including one prospective study. The results of the prospective study revealed that patients with implant retained dentures had less problems with mastication than patients rehabilitated without implants. The four retrospective studies could not identify significant improvements in occlusal force or masticatory performance. Furthermore, speech intelligibility was good to excellent in most patients. Overall aesthetic outcome was rated by both patients and physicians as 'good' to 'excellent' too. Finally, no changes in QoL were observed. Even though the reported results are probably biased by the retrospective nature of most studies, the overall conclusion was that oral rehabilitation with implant-supported dental prostheses after reconstruction of the mandibular or maxillary defects with segmented FFFs results in acceptable function, and good to excellent speech intelligibility and aesthetics.

Chapter 3, describes the virtualization of the "Rohner" method. In chapter 3.1, a case report of a 54 year old male who developed osteoradionecrosis of the mandible is described in whom a fully 3D digitally planned reconstruction of the mandible and immediate prosthetic loading using a fibula graft in a two-step surgical approach was performed. The essence of the applied technique is that planning starts with the preferred dental alignment of the prosthetic construction. Next, the FFF and the implants are planned in a position that allows for the wished reconstruction of the mandibula. The resection, cutting and implant placement in the fibula were all virtually planned. Cutting/drilling guides were 3D printed and the superstructure was CAD-CAM milled. The reconstruction was planned using SurgiCase CMF software (Materialize NV, Leuven, Belgium) and Simplant Crystal (Materialize Dental, Leuven, Belgium). In the first operation, the implants were inserted in the fibula and their position registered by an optical scanning technique. This scan defines the final planning of the superstructure. After the original virtual planning, the plan was updated with the real implant positions, the implant retained dental prosthetics was made. In the second operation and the area with osteoradionecrosis was resected, where after the fibula with

the integrated implants was harvested and, with the prosthetics fixed on the pre-inserted implants, placed in the mandibula guided by the occlusion. The outcome of this case was that it is possible to fully virtual plan a mandibular reconstruction with FFFs and implant retained dental prosthetics.

In chapter 3.2, a rather comparable case is described, comparable to the case described in chapter 3.1, with the exception that a screw retained bridge on the implants placed in the FFF was fabricated. The abutment of the bridge structure was individually CAD-CAM made of titanium and finished with composite. Placing the bridge in occlusion and accordingly fixating the graft with osteosynthesis plates resulted in a functional position of the FFF and bridge.

In chapter 3.3, it is illustrated that the virtual planning software and its application is also suitable for other free vascularized flaps through the planning of 2 cases: a free vascularized iliac crest flap and a free vascularized scapula flap. In the first case, virtual planning of a midface defect resulting from tumor resection was applied for a free vascularized iliac crest flap. The immediate reconstruction of the maxillofacial defect was followed by implant placement in a second stage. The second case describes the virtual planning of a prefabricated scapula flap for the secondary reconstruction of a mandibular defect. The scapula flap is prefabricated with dental implants and a split skin graft, comparable to the approach as described in chapters 3.1 and 3.2. On the implants an implant-retained fixed prosthetics was placed. Both cases were planned digitally and the surgery was facilitated guided through 3D printed guides resulting in a functional position of the implant-retained superstructures.

In chapter 4, an analysis of the accuracy of a complete virtual planning of a reconstruction in 11 consecutive reconstructive patients is described. The planning and surgery were executed according to the method described in chapter 3.1. The accuracy of placement of the fibula grafts and dental implants was correlated to the pre-operative 3D virtual plans by comparing pre-operative and post operative CBCTs. When superimposing the CBCT scans on the antagonist jaw, to represent the outcome of occlusion, a median deviation of the fibula segments and implants of 4.7mm (Inter Quartile Range(IQR):3-6.5mm) and 5.5mm (IQR:2.8-7 mm) from the planned position was observed, respectively. In addition, superimposing of the CT scans on the fibula segments was performed to represent the surgical outcome of the implant placement, cutting of the fibula and placement of the prosthetics. This approach revealed a median difference of fibula and implant placement of 0.3mm (IQR:0-1.6mm) and 2.2mm (IQR:1.5-2.9mm), respectively. All implant-retained prosthetic constructions functioned well. We concluded that the accuracy of 3D surgical planning of reconstruction of maxillofacial defects with a fibula graft and the implants is sufficient to ensure a favorable functional position of the implants and fibula graft.

In chapter 5, a computer-aided designed and computer-aided manufactured (CAD-CAM) reconstruction plate is introduced. The purpose of the study described in this chapter was to analyze the accuracy of mandibular reconstructions using patient-specific CAD-CAM reconstruction plates as a guide to place fibula grafts and dental implants in a one-stage procedure using pre-operative 3D virtual planning. Seven consecutive patients were analyzed. In all patients the 3D accuracy of placement of the fibula grafts and dental implants was compared to the virtual plan. When the post operative CBCT was compared to the virtual plan, superimposing on the mandible, the median deviation was 2.5 mm (IQR:1.9-4.8 mm) for the fibula segments and 3.1 mm (IQR:2.3-4.2 mm) for the implants. The median mandibular resection planes deviated 1.9 mm (IQR:1.0-2.5 mm). When superimposed on the fibula segments, a median deviation of fibula and implant placement of 0.5 mm (IQR:0.2-1.6 mm) and 2.1 mm (IQR:1.6-2.5 mm) was observed, respectively. All implant-retained (fixed) prosthetics functioned well. We concluded that the patient-specific reconstruction plate is a valuable tool in the reconstruction of mandibular defects with fibula grafts and dental implants.

3D virtual planning of secondary reconstructive surgery is a frequently used method for improving accuracy and predictability of the reconstruction. However, when primary applied to malignant cases, planning of the oncologic resection margins is difficult due to a lack of reliable visualization of tumors in the current 3D planning. Embedding tumor delineation on a magnetic

resonance image (MRI), similar to the routinely performed contouring of tumors ((CB)CT) in the radiotherapy plan, is expected to provide better margin planning thus bringing 3D virtual planning of primary reconstructions within reach. In chapter 6, a new software pathway is described embedding tumor delineation on MRIs within the 3D virtual surgical planning. The software pathway was validated in five bovine cadavers implanted with phantom tumor objects. MRI and CT images were fused and the tumor was delineated using radiation oncology planning software. This data was converted to the 3D virtual planning software by means of a conversion algorithm. Tumor volumes and localization were determined in both software stages for comparison analysis. After having proved that the 3D virtual planning worked in the bovine cadavers, the approach was also applied to three clinical cases. The results revealed that indeed the developed conversion algorithm allowed for translation of the tumor delineation data to the 3D virtual plan environment. The average difference in volume of the tumors was 1.7%, well within the limits allowing for a safe resection margin. It was concluded that a reliable software pathway has become available allowing for multi-modality image fusion for 3D virtual surgical planning. This software is currently in use to determine resection margins in primary 3D planned reconstructions of malignant tumors of the maxilla and mandible.

In the general discussion (chapter 7) the main results of the previous chapters are placed in a broader perspective. Based on the results of the research described in the previous chapters, it is concluded that accuracy in 3D planning and surgery is a sum of individual errors per step. Yet, the prefabrication of the fibula with implants is more accurate than positioning of the graft in the maxillofacial region. However, the magnitude of this error allows for general application of the developed technique in clinical practice.

Samenvatting

Verwijdering van een tumor in de boven- of onderkaak of middengezicht resulteert vaak in een groot defect. De prothetische rehabilitatie van een dergelijk defect is uitdagend. De mogelijkheden voor een goed houvast van de vaak grote prothetische voorziening zijn veelal beperkt. Mede hierdoor is de functie van de prothetische voorziening vaak matig. Met de opkomst van tandheelkundige implantaten voor een beter houvast van de prothetische voorziening, zijn de mogelijkheden om een fraaie, goed functionerende prothetische voorziening te vervaardigen sterk toegenomen. Een voorwaarde voor het toepassen van implantaten is echter dat er voldoende bot op de juiste plaats aanwezig is voor verankering van de prothetische voorziening. Daarom moet vaak eerst het defect in de boven- of onderkaak worden gereconstrueerd alvorens op de juiste plaats de implantaten te kunnen plaatsen. Kleine defecten in de boven- of onderkaak kunnen worden gereconstrueerd met een vrij bottransplantaat en/of botsubstituut. Voor grotere defecten zijn veelal vrij gevasculariseerde bottransplantaten noodzakelijk. Momenteel wordt vooral het Vrij gevasculariseerde Fibula Transplantaat (VFT) hiervoor gebruikt. Het VFT is vanwege de aanwezigheid van voldoende botvolume van een dichte cortex erg geschikt om hierin implantaten met goede primaire stabiliteit te plaatsen. De overleving van implantaten in een VFT is hoog. Van groot belang voor het welslagen van de prothetische behandeling is het om het VFT zodanig vorm te geven en te positioneren in het kaakdefect dat deze een optimale basis biedt voor de aan te brengen implantaten en de daarop te fixeren prothetische voorziening. Met andere woorden: voor een zo groot mogelijk kans op een functionele implantaatgedragen gebitsprothese of vaste brug is een precieze planning van de vormgeving van het VFT en de positionering van de implantaten daarin cruciaal. De ervaring heeft namelijk geleerd dat het uit de vrije hand positioneren van een VFT regelmatig leidt tot een suboptimale of ontoereikende reconstructie van het kaakdefect, zeker als het uit de vrije hand plaatsen van de VFT wordt gecombineerd met het uit de vrije hand plaatsen van implantaten. Het is geen uitzondering dat het dan voor de tandarts zeer moeilijk, zo niet onmogelijk is, om op deze implantaten een goede functionele prothetische voorziening te vervaardigen. Derhalve is in het kader van dit promotieonderzoek gezocht naar mogelijkheden om zowel de planning van de vormgeving van het VFT als het plaatsen van de implantaten in het VFT te verbeteren. Een goede mogelijkheid daartoe lijkt een virtuele driedimensionale (3D)-chirurgische planning van de in de vorige alinea beschreven behandeling met behulp van computertomografie (CT) of cone-beam computed tomography (CBCT) data. Als een dergelijke planning haalbaar is, lijkt het bovendien haalbaar om de planning van het VFT (of een andere vrij gevasculariseerd bottransplantaat) te combineren met het virtueel plannen van de implantaten in het VFT. In dat geval kunnen gelijktijdig met de reconstructie van het kaakdefect ook de implantaten worden aangebracht, al dan niet direct gecombineerd met het aanbrengen van de prothetische voorziening. Bovendien, mocht het mogelijk zijn om ook veilige marges voor de tumorresectie in de virtuele planning mee te nemen, dan is het naar verwachting ook mogelijk om de reconstructie uit te voeren tijdens dezelfde chirurgische ingreep waarin de tumor wordt verwijderd. Gezien deze wensen kende dit promotieonderzoek twee doelen: ten eerste het ontwikkelen van een virtuele 3D methode voor het plannen van een VFT en daarin het plaatsen van implantaten ten behoeve van de reconstructie van defecten in de boven- en/of onderkaak en ten tweede het onderzoeken of de accuratesse van de ontwikkelde methodiek voldoende is voor algemene toepassing (hoofdstuk 1).

In hoofdstuk 2 worden de uitkomsten van een systematisch literatuuronderzoek naar de effecten van een rehabilitatie van een defect in de boven- en/of onderkaak, met of zonder implantaten, beschreven. In dit literatuuronderzoek werd zowel gekeken naar de functionele uitkomst van een reconstructie van een groot kaakdefect met een VFT als naar de kwaliteit van leven van de betreffende patiënten. De literatuur tot april 2015 werd onderzocht. 557 Publicaties werden gevonden. Na toepassing van de inclusie- en exclusiecriteria resteerden 10 publicaties voor een gedetailleerde analyse, namelijk twee prospectieve en acht retrospectieve case-series. De wetenschappelijke kwaliteit van de in deze 10 publicaties gerapporteerde onderzoeken werd gescoord met behulp van de ‘Methodological Index of Non-Randomized Studies’ (MINORS) criteria. Uit de scores kwam naar voren dat ook de kwaliteit van de geïncludeerde publicaties matig is. In totaal werden 261 VFT reconstructies uitgevoerd, waarvan 55 in de bovenkaak en 206 in de onderkaak. De overleving van de VFTs was 99%. In negen van de 10 studies werden tandheelkundige implantaten in de VFTs geplaatst (262 implantaten), 95% van de implantaten overleefde. Vijf studies beschreven

de kauwfunctie, waarvan één prospectieve studie. De prospectieve studie toonde aan dat patiënten met een overkappingsprothese op implantaten een betere kauwfunctie hebben dan patiënten zonder implantaten. In de vier retrospectieve studies kon geen significante verbetering van het kauwvermogen worden aangetoond. Wel bleek het spraakvermogen sterk te zijn verbeterd en waren zowel de patiënten als de behandelaars (zeer) tevreden over de esthetiek. Een verbetering van de kwaliteit van leven kon niet worden aangetoond. De uitkomst van dit literatuuronderzoek geeft vermoedelijk een wat vertekend beeld gezien het retrospectieve karakter van de meeste studies. Desondanks kan worden geconcludeerd dat een reconstructie van een kaakdefect met de combinatie van een VFT en een overkappingsprothese op implantaten resulteert in een acceptabele kauwfunctie en een (zeer) goede spraak en esthetiek.

In hoofdstuk 3 wordt de ontwikkeling van een 3D-reconstructieve planning naar analogie van de”Rohner”-methode beschreven. In hoofdstuk 3.1 wordt de planningsmethode volgens Rohner geïllustreerd aan de hand van een casus. Het betreft een 54-jarige man met een defect van de onderkaak ten gevolge van osteoradionecrose. De reconstructie van het defect werd volledig 3D digitaal gepland. Op basis van deze planning werd het defect in twee operaties gereconstrueerd met behulp van een VFT en een overkappingsprothese op implantaten. De essentie van de toegepaste techniek is dat de planning begint met de ideale opstelling van de te vervangen dentitie. Vervolgens worden zowel het VFT als de implantaten gepland in een optimale positie voor de uiteindelijke prothetische voorziening met behulp van SurgiCase CMF software® (Materialise NV, Leuven, België) en Simplant Crystal® (Materialise Dental, Leuven, België). Om de implantaten te plaatsen in de gewenste positie werd gebruik gemaakt van een 3D geprinte boormal. Ook voor de resectie van de fibula en de segmenten hiervan werd gebruik gemaakt van 3D geprinte zaagmallen. Tijdens de eerste operatie werden de implantaten in de fibula geplaatst. De positie van de implantaten in de fibula werd vastgelegd met behulp van een optische intra orale scanner. Het oorspronkelijke virtuele 3D plan werd aangepast aan de middels de scan vastgelegde echte implantaat posities. Tevens werd op basis van deze gegevens een gebitsprothese vervaardigd.

Tijdens de tweede operatie werd de regio met de osteoradionecrose in de onderkaak eerst verwijderd alvorens de fibula met de daarin inmiddels geosseoïntegreerde implantaten werd geoogst en gesegmenteerd. Voor het oogsten werden de steg en overkappingsprothese op de implantaten geplaatst op de fibulasegmenten. Het VFT met daarop de overkappingsprothese werd, geleid door de occlusie, in de juiste positie geplaatst en in die positie aan de resterende kaakdelen gefixeerd met osteosynstheseplaten. Deze casus toont dat het mogelijk is om volledig virtueel een onderkaaksreconstructie te plannen met een overkappingsprothese op implantaten. In hoofdstuk 3.2 wordt een vergelijkbare casus beschreven, echter nu met een vastgeschroefde brug op de implantaten. De onderstructuur van de brugconstructie werd CAD-CAM vervaardigd van titanium en afgewerkt met composiet. De implantaatgedragen brug op het VFT kon in een functionele occlusie worden geplaatst.

In hoofdstuk 3.3 wordt geïllustreerd dat met behulp van de ontwikkelde virtuele planningssoftware ook reconstructies met andere vrij gevasculariseerde transplantaten dan het VFT kunnen worden gepland. Twee casus worden beschreven: een casus waarbij een vrij gevasculariseerd bekkenkamtransplantaat werd gebruikt en een casus waar een vrij gevasculariseerd schouderbladtransplantaat werd toegepast. In de eerste casus werd een reconstructie van een defect van het middengezicht virtueel gepland. De directe reconstructie met het vrij gevasculariseerde bekkenkamtransplantaat werd gevolgd door het plaatsen van drie implantaten in een latere fase. Deze patiënt had geen behoefte aan een gecombineerde reconstructie. De tweede casus beschrijft de virtuele planning van een secundaire reconstructie van een onderkaaksdefect. Conform de casus uit hoofdstuk 3.1 werd eerst het schouderbladtransplantaat voorbereid door het plaatsen van tandheelkundige implantaten en een vrij huidtransplantaat, tijdens de tweede operatie werd vervolgens op deze implantaten een verschroefde prothese geplaatst en in functionele positie in het kaakdefect gefixeerd. Beide casus werden volledig digitaal gepland en de operaties werden uitgevoerd met behulp van 3D geprinte boor- en zaagmallen.

In hoofdstuk 4 werd de mate van nauwkeurigheid beschreven van de kaakreconstructies in 11 opeenvolgende patiënten. De planning en de operatie werden uitgevoerd volgens de in hoofdstuk 3 beschreven methode. De nauwkeurigheid van plaatsing van de VFTs werd bepaald door de pre-operatieve 3D virtuele planning te vergelijking met de post operatieve CBCT. Bij superpositie op de antagonistische kaak, een weerspiegeling van de occlusie, werd een gemiddelde afwijking van VFTs en implantaten gevonden van, respectievelijk 5,5mm (Interkwartielafstand {IKA}: 2,8-7 mm) en 4,7mm (IKA: 3-6,5mm) ten opzichte van de geplande positie. Om te kunnen beoordelen hoe nauwkeurig de implantaten in de fibula werden geplaatst en hoe nauwkeurig de resectie van de fibulasegmenten was verlopen, werd een superpositie uitgevoerd op de fibulasegmenten. Op niveau van de fibulasegmenten bedroeg de afwijking 0,3 mm (IKA: 0-1,6mm), op implantaatniveau was de afwijking 2,2mm (IKA: 1,5-2,9mm). Op basis van deze resultaten werd geconcludeerd dat de nauwkeurigheid van de 3D-chirurgische planning van de reconstructie van maxillofaciale defecten met VFT en implantaten voldoende is om een functionele positie van de implantaten en fibulatransplantaat te realiseren.

In hoofdstuk 5 wordt beschreven dat een zogenaamde CAD-CAM vervaardiging van de reconstructieplaten als onderdeel van de virtuele planning en uitvoering van onderkaaksreconstructies een geschikt hulpmiddel is. Het doel van deze studie was om de nauwkeurigheid te bepalen van reconstructies van de onderkaak waarbij gebruik is gemaakt van de patiëntspecifieke CAD-CAM reconstructieplaten ter fixatie van een VFT. Zeven opeenvolgende patiënten werden geanalyseerd waarbij een reconstructie met een VFT werd gecombineerd met het direct plaatsen van een prothetische voorziening op implantaten. De VFT segmenten werden gefixeerd met een CAD-CAM reconstructieplaat. De 3D nauwkeurigheid van plaatsing van de fibulatransplantaten en implantaten werd vergeleken met het virtuele plan. Daartoe werd de postoperatieve CBCT-scan gesuperponeerd op de virtuele planning. Bij superpositie op de onderkaak bedroeg de mediane afwijking 2,5 mm (IKA: 1,9-4,8 mm) voor de fibulasegmenten en 3,1 mm (IKA: 2,3-4,2 mm) voor de implantaten. De mediane resectievlakken van de onderkaak weken 1,9 mm (IKA: 1,0-2,5 mm) af. Wanneer werd gesuperponeerd op de segmenten van de fibula bedroeg de mediane afwijking van fibula en implantaten, respectievelijk 0,5 mm (IKA: 0,2-1,6 mm) en 2,1 mm (IKA: 1,6-2,5 mm). Op basis van deze gegevens werd geconcludeerd dat de CAD-CAM vervaardigde patiëntspecifieke reconstructieplaat een waardevol hulpmiddel is bij de reconstructie van defecten van de onderkaak met VFTs en tandheelkundige implantaten.

In de 3D virtuele planning van reconstructieve chirurgie ten behoeve van de planning van primaire reconstructies is het belangrijk om de tumorgrenzen betrouwbaar te kunnen bepalen en weergeven. Planning van oncologische resectiemarges is echter moeilijk, omdat de tumor niet betrouwbaar kan worden gevisualiseerd met behulp van de huidige 3D software. Deze omissie is mogelijk op te vangen door tumorafgrenzing op magnetische resonantie beeldvorming (MRI) in de virtuele planning te implementeren conform de routinematige intekening van tumoren ten behoeve van radiotherapeutische planningen. In hoofdstuk 6 wordt een softwarematige conversie beschreven waarmee het mogelijk blijkt om de tumorintekening op basis van de MRI beelden in te voeren in de 3D virtuele chirurgische planningssoftware. De nauwkeurigheid van deze softwarematige omzetting werd gecontroleerd aan de hand van vijf runderkadavers waarin ‘imitatie tumorobjecten’ van een bekend volume waren aangebracht. De MRI en CT-beelden van deze kadaverhoofden werden gefuseerd. Vervolgens werd de tumor ingetekend met behulp van radiologische planningssoftware. Door middel van een conversie-algoritme werden deze ingetekende tumoren omgezet naar de virtuele 3D planningssoftware. De tumorvolumes en lokalisatie werden zowel bepaald met behulp van de radiologische als de 3D reconstructieve plansoftware en vervolgens met elkaar vergeleken. Het gemiddelde verschil in volume van de met beide methodieken berekende tumoren bedroeg 1,7%. Met andere woorden: middels het ontwikkelde conversie-algoritme kan op valide wijze de met MRI bepaalde lokalisatie en afgrenzing van de tumor worden geïncorporeerd in de 3D virtuele chirurgische planning. Deze methodiek werd vervolgens met succes toegepast in de primaire reconstructie van drie patiënten met een tumor in het maxillofaciale gebied.

In hoofdstuk 7 worden de belangrijkste resultaten van de voorgaande hoofdstukken in een breder perspectief geplaatst en bediscussieerd. Geconcludeerd wordt dat de nauwkeurigheid van de 3D planning en chirurgie een optelsom is van individuele fouten per stap in de totale procedure. Hierbij is het plaatsen van implantaten in het VFT en de segmentatie van de fibula nauwkeuriger gebleken dan de plaatsing van het transplantaat in het kaakdefect. De huidige foutmarge is zodanig dat 3D virtuele planning van reconstructie van defecten in de boven- en/of onderkaak voldoende voorspelbaar is voor algemene toepassing. In de toekomst zal deze foutmarge mogelijk nog verder kunnen worden beperkt.

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Curricilum Vitae

Rutger Schepers was born in Almelo, the Netherlands, on June 16, 1975. After completing MAVO, HAVO and pre-university secondary education (VWO) in Hardenberg, the Netherlands, he started dentistry in 1995 at the University of Gent, Belgium. After one year he switched to the Radboud University of Nijmegen, the Netherlands, where he graduated as a dentist in 2001. After his graduation he was trained in dento-alveolar surgery at the Maxillofacial surgery department of the St. Elisabeth hospital in Tilburg, the Netherlands. In 2005 he graduated from medical school at the University of Nijmegen. Hereafter, Rutger started a full-time training program at the Department of Maxillofacial Surgery at the University Medical Center Groningen (UMCG), the Netherlands. After his graduation as maxillofacial surgeon in 2010 he started working on his PhD thesis. At that same time he joined a private practice in the Martini hospital in Groningen. In 2011, he became a staff member at the UMCG Department of Oral and Maxillofacial Surgery (4 days/week) which he combines with his work at the Martini (1 day/week). He has a special interest in 3D virtual treatment planning, orthognathic surgery, cosmetic facial surgery and cleft-, lip- and palate surgery. He is living together with Miriam Bildt. They have two daughters, Leonie (5) and Vera (3), and two sons, Florian (3) and Ditmar (3).

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