Department of Plastic Surgery Department of Oral and Maxillofacial Surgery Helsinki University Hospital Faculty of Medicine University of Helsinki Helsinki, Finland

# RECONSTRUCTION OF SURGICAL MAXILLOMANDIBULAR DEFECTS: A clinical study

Tommy Wilkman

Academic Dissertation

To be presented, with the permission of the Faculty of Medicine of the Unviversity of Helsinki, for public examination in Auditorium 1 at Tölö Hospital, Topeliuksenkatu 5, on June 14<sup>th</sup>, 2017 at 12 noon.

Helsinki 2017

Supervised by

Docent Patrik Lassus Department of Plastic Surgery Helsinki University Hospital University of Helsinki Helsinki, Finland

and

Docent Jyrki Törnwall Department of Oral and Maxillofacial Surgery Helsinki University Hospital University of Helsinki Helsinki, Finland

Reviewed by

Docent Outi Kaarela Department of Surgery Oulu University Hospital University of Oulu Oulu, Finland

and

Docent Ilpo Kinnunen Department of Oto-Rhino-Laryngology Turku University Hospital University of Turku Turku, Finland

**Official Opponent** 

Bohdan Pomahac, MD Professor of Surgery, Harvard Medical School Co-Director of Center for Facial Restoration Director of Plastic Surgery Transplantation Medical Director of BWH Burn Center Brigham and Womens's Hospital Boston, MA, USA

ISBN 978-951-51-3188-1 (paperback) ISBN 978-951-51-3189-8 (PDF) <u>http://ethesis.helsinki.fi</u>

UNIGRAFIA Oy Helsinki 2017

To Erika, Lukas, Linus and Isak

## TABLE OF CONTENTS

# List of original publications

## Abbreviations

1 Abstract
2 Introduction
3 Review of the literature

3.1 Indications for maxillomandibular reconstruction
3.1.1 Oral cancers
3.1.1.1 Introduction to oral cancers

3.1.1.2 Incidence of and survival from oral cancers

3.1.1.3 Treatment of oral cancers

3.1.1.4 Prognostic factors in oral cancers

3.1.2 Other indicators of mandibular and maxillary reconstruction

3.2 Classification of surgical maxillomandibular defects

3.2.1 Maxillary defects

3.2.2 Mandibular defects

3.3 Maxillary and mandibular reconstructions

3.3.1 General aspects and historical milestones of the reconstruction of surgical maxillomandibular defects

3.3.2 Free bone grafts

3.3.3 Local flaps in maxillomandibular reconstructions

3.3.3.1 Palatal flaps

3.3.3.2 Tongue flap

3.3.3.3 Facial artery musculomucosal flap

3.3.3.4 Nasolabial flap

3.3.3.5 Platysma flap

3.3.4 Pedicled flaps in maxillomandibular reconstruction

3.3.4.1 Temporal flap

3.3.4.2 Submental flap

3.3.4.3 Supraclavicular flap

3.3.4.4 Deltopectoral flap

3.3.4.5 Trapezius flap

3.3.4.6 Pectoral flap

3.3.4.7 Latissimus dorsi flap

3.4 Microvascular maxillomandibular reconstruction

3.4.1 Soft tissue free flaps in mandibular and maxillary reconstruction

3.4.2 Osseal free tissue flaps in maxillomandibular reconstruction

3.4.2.1 Fibula flap

3.4.2.2 Iliac crest flap

3.4.2.3 Scapula flap

3.4.2.4 Other free osseal flaps

3.4.3 Tissue engineering in maxillomandibular reconstructions

3.4.4 Stem cells in maxillomandibular reconstructions

3.4.5 Face transplant

3.5 3D planning and 3D printing in maxillomandibular reconstructions 3.6 Classification of surgical complications and risks

### 4 Aims of the study

# **5** Patients

5.1 Helsinki head and neck tumour board

5.2 Study I

5.3 Study II

5.5 Study IV

# 6 Methods

6.1 Data collection

6.2 Methods, analyses and statistical methods

6.2.1 Study I

- 6.2.2 Study II
- 6.2.3 Study III
- 6.2.4 Study IV

# 7 Results

7.1 Study I: Osseous scapular reconstruction study

7.2 Study II: Complications and outcomes of the DCIA, scapula and fibula flaps

7.3 Study III: Volume analysis of bone flaps over time

7.4 Study IV: Latissimus dorsi study

# **8** Discussion

8.1 General aspects of maxillomandibular reconstruction

8.2 Reconstruction algorithms

8.3 Properties of the free scapular flap in maxillomandibular reconstruction

8.4 Differences between scapula, fibula and iliac crest osseous flaps in maxillomandibular reconstructions

8.5 Graft resorption or remodelling in reconstructed bone

8.6 Salvage methods in the reconstruction of morbid patients

8.7 Methodological considerations: Study strengths and limitations

8.8 Conclusions regarding mandibular and maxillary reconstructions

8.9 Future prospects

# 9 Conclusions

## 10 Acknowledgements

References

# List of original publications

- 1. Wilkman T, Törnwall J, Vuola J, Lassus P. The free scapular flap with latissimus muscle reduces fistulas in mandibular reconstruction. *J Plast Reconstr Aesthet Surg* (2016), 69, 6, 802–808.
- 2. Wilkman T\*, Husso A\*, Lassus P. Maxillo-mandibular reconstructions with scapular, fibular and iliac crest composite flaps: our experience. *(submitted, under review)*
- 3. Wilkman T, Apajalahti S, Wilkman E, Törnwall J, Lassus P. A comparison of bone resorption over time. An analysis of the free scapular, iliac crest and fibular microvascular flaps in mandibular reconstruction. *J Oral and Maxillofacial Surg* (2016), doi: 10.1016/j.joms.2016.09.009
- 4. Wilkman T, Suominen S, Bäck L, Vuola J, Lassus P. The pedicled latissimus dorsi flap in head and neck reconstruction: an old method revisited. *J Reconstr Microsurg* (2014), 30, 3, 163–170.

These articles have been reprinted with the written permission of their copyright holders.

Publication 2. \*equal contribution

# Abbreviations

3D	Three dimensional
ĂLT	Anterolateral thigh flap
ASA	American Society of Anaestesiologists
ASIS	Anterior superior iliac spine
BMI	Body mass index
BMP-2	Bone morphogenetic protein-2
CAD/CAM	Computer assisted design and manufacturing
CBCT	Cone beam CT
CCI	Charlson Comorbidity Index
CFS	Circumflex scapular
COPD	Chronic obstructive pulmonary disease
DASH	Disabilities of the Arm, Shoulder and Hand questionnaire
DCIA	Deep circumflex iliac artery, including all variations
DICOM	Digital imaging and communication in medicine
DIEP	Deep inferior epigastric perforator
ECS	Extracapsular spread
FAMM	Facial artery musculomucosal
FOSC	Fibula osteteoseptocutaneous
HCL	Hemimandible, central or anterior segment and lateral
	segment
HPV16	Human papillomavirus 16
ICD-10	10 <sup>th</sup> revision of the International Statistical Classification of
	Diseases and Related Health Problems
ICU	Intensive care unit
LD	Latissimus dorsi
MRI	Magnetic resonance imaging
MSCT	Multislice computerised tomography
OR	Odds ratio
ORL	Oto-rhino-laryngology
PEG	Percutaneous endoscopic gastronomy
PET	Positron emission tomography
PMMC	Pectoralis major myocutaneous
RFA	Radial forearm
RR	Risk ratio
SCC	Squamous cell carcinoma
SIEA	Superficial inferior epigastric flap
SLE	Systemic lupus erythematosus
TAPAS	Temporal artery posterior auricular skin
TDA	Thoracodorsal artery
TNM	Tumour, node and metastasis
TPP-LD	Transpectoral pedicled latissimus dorsi
TRAM	Transverse rectus muscle
US	Ultrasound
VRAM	Vertical rectus abdominis muscle
WHO	World Health Organization
WUHNCI	Washington University Head and Neck Comorbidity Index

## 1 Abstract

## **Introduction**

The treatment of oral cancer may cause significant morbidity, with a wide-ranging impact on the patient given how central the area treated is to a variety of functions. These include mastication along with dentition, tongue functioning and the ability to swallow, as well as maintenance of the airway, breathing and the production of speech. Furthermore, the importance of a socially acceptable aesthetic appearance cannot be ignored. Primary healing represents the first goal in reconstructive surgery. In cancer patients, possible postoperative oncological treatment is postponed until primary healing is obtained. Primary healing also impacts an individual's mobilisation, nutritional status as well as psychological wellbeing. Such patients are often older and have general comorbidities. Prolonged hospitalisation is associated with secondary morbidity such as infections and pulmonary and cardiovascular events. Secondary osseous integration and the quality of the transferred bone are essential for dental rehabilitation with prostheses or implants and, ultimately, the quality of life. The treatment aim in reconstruction focuses on offering every patient the best option for his/her specific problem.

### Aim of the study

This study aims to evaluate the outcomes of reconstructive methods used in maxillofacial reconstruction through four substudies:

- 1. Examination of the scapular chimeric flap in maxillofacial reconstruction;
- 2. Comparison of complications and results across the most frequently used free osseous flaps—that is, flaps of the fibula, the scapula and the deep circumflex iliac artery (DCIA);
- 3. Examination of remodelling or resorption of the fibula, the scapula and DCIA osseous microvascular flaps during the follow-up period;
- 4. Analysis of the latissimus dorsi (LD) musculocutaneous pedicular flap using a transpectoral route.

### Patients and methods

This study included patients who underwent microvascular free tissue or pedicular tissue reconstructive surgery in the facial and neck region with a focus on mandibular and maxillary reconstruction. Patients were operated on at the Department of Plastic Surgery and the Department of Maxillofacial Surgery at Helsinki University Hospital, Helsinki, Finland between 2000 and 2013. All patients were routinely assessed pre- and postoperatively in a weekly multidisciplinary meeting consisting of oto-rhino-laryngology (ORL) surgeons, plastic surgeons, oral and maxillofacial surgeons, head and neck pathologists and radiologists. As a retrospective study, data were collected from patient hospital records, including medical records, operative and anestesiological as well as intensive care unit (ICU) records, laboratory databases, histopathological classifications and radiological databases.

#### Main results

We analysed scapular osteomyocutaneous flaps in the reconstruction of 34 patients. The flap demonstrated versatility in complex reconstructions and the scapular bone was shown to tolerate osteotomies without complications. Furthermore, we found that using the LD muscle prevents fistula formation. In a comparison of clinical outcomes and complications of reconstructions with scapula, fibula or iliac crest (DCIA) composite flaps among 163 patients, we found that the scapula was the most reliable flap. DCIA carried the most complications and patient recovery among those reconstructed with fibula and scapula flaps experienced the most positive and best outcomes. We also found that elderly patients tolerated extensive surgeries well. The volume analysis of the three most-used osseous reconstructive flaps in 38 patients over time showed that the fibula was the most stable and the scapula was the most prone to resorb; DCIA represented the intermediate option. This study also showed that true three-dimensional (3D) volume analysis is more accurate over previously used height-by-width measurements. Moreover, postoperative radiation therapy was not associated with a significantly higher volume loss. The LD flap showed its versatility in reconstructons among 10 patients with large defects in locoregionally advanced cancer, accompanied by few donor site complications and reliable outcomes. In addition, the size of the flap, its usefulness and donor site morbidity favoured the LD flap compared to the more widely used pectoral flap.

#### **Conclusions**

No ideal reconstructive method can be used on every patient. We identified several qualitative differences between the reconstructive options compared in this study, where no option proved ideal across all parameters. The scapula flap is very reliable and versatile, and results favour the inclusion of a muscular section in large reconstructions. In a comparison of osseous reconstructions, our results favour the fibula and scapula flaps over DCIA. The fibula and scapula flaps are more reliable, accompanied by few donor site complications. All osseous flaps analysed were shown to tolerate osteotomies and dental osseointegrated implants with a high reiliability. However, differences in the remodeling of bone flaps over time are clear, with the fibula representing the most stable and the scapula standing as the most prone to volume loss. In addition, 3D imaging represented the preferred method in bone analyses. In morbid patients, the pedicled LD flap is a large flap covering extensive resections, accompanied by a high reliability and few donor site complications. Thus, we conclude that a custom-made patient-specific reconstructive solution is preferred and all flap options analysed here can be justified.

## 2 Introduction

### Treatment indications

In general, cancer is the most common cause for large resections of oral and facial tissues, where patients often require composite tissue reconstructions to restore the surgical defect. Squamous cell carcinoma (SCC) accounts for 90% of these cancers.

In Finland between 2010 and 2014, the incidence of oral cancer—including cancers of the oral cavity and lip, but excluding skin cancers—reached 349 cases per year, with the majority occurring among men. During the same period, the incidence of cancers in the oral cavity affected 148 men and 127 women per year, representing 1% of all cancer types. Incidence has increased in recent decades, while mortality has remained constant. In Finland, the five-year survival rate of oral cancer across all stages combined stands at 60% for men and 70% for women. Patients are often elderly, whereby the incidence of oral cancer increases with age.

Surgery stands as the primary treatment modality for the primary tumour with resection of the tumour and associated affected lymph nodes with free margins. This treatment generally yields the lowest rates of recurrence and highest survival rates for patients.

In general, limited T1 and T2 tumours are treated with surgery as a single modality, while larger T3 and T4 tumours require adjuvant oncological treatment postoperatively. Sinonasal cancers invading the maxilla, large facial skin tumours, traumatic avulsive defects and radiation as well as medication-induced osteonecrosis may also cause significant defects. Complex units of facial and oral tissue are involved in a wide variety of functions, such as the masticatory function as well as functional dentition, the tongue functioning, the ability to swallow, maintenance of a functional airway and the production of speech. In addition, the importance of a socially acceptable aesthetical appearance affects patient wellbeing. This surgical defect must be restored and reconstructed as well as possible, with a high reliability, few donor site complications and quickly enough to enable postoperative oncological adjuvant therapy within a reasonably short waiting time. To achieve viable tissue reconstruction with bone, muscle and skin contents, a microvascular transfer of composite tissue is preferred.

### **Classifications of defects**

The classification of the surgical maxillomandibular defect determines the subsequent reconstruction. Several classifications of mandibular as well as maxillary defects have been outlined. Such classifications primarily aim to describe options for subsequent reconstruction and, thus, allow comparisons between various reconstructive methods. By classifying the defect, the description becomes more precise. Both soft and osseous tissues need to be addressed and described, given that more complex reconstructive algorithms are often published based on clinical opinion and retrospective results from a single-centre or indivudal reconstruction surgeon.

<u>Reconstruction of defects in the mandibular and maxillary region</u> Local and pedicled flaps are used in limited reconstructions. The free radial forearm (RFA) flap, lateral arm flap, anterolateral thigh (ALT) flap, rectus abdominal flap and parascapular or scapula soft tissue flaps represent the workhorses in free flap soft tissue reconstructions of the head and neck. In salvage or reoperative pedicular and perforator flaps, such as the LD, the pectoralis, trapezius and supraclavicular flaps are also used. The most frequently used osseous composite tissue flaps in mandibular and maxillary reconstructions are the free flaps of the fibula, the iliac crest and the scapula, which are the focus of this study. Each of these has unique properties.

In recent years, the fibula flap has emerged as the most widely used option. It features a reliable, long vascular pedicle. Up to 25 cm of bicortical bone can be harvested with minimal donor site morbidity carried out simultaneously with the tumour resection by a second team without needing to reposition the patient. The bone tolerates osteotomies in several segments to achieve a 3D form and is also well-suited for postoperative osseointegrated dental implantations. The drawbaks of the fibula flap include the limited size of the soft tissue involved in such reconstructions and the unreliable blood supply in the skin island section of such flaps. In addition, the flap also has a relatively small capacity of filling large soft tissue defects. Furthermore, in older patients, smokers and patients with diabetes, the risk of atherosclerosis and subsequent alterations in arterial flow must be addressed. The fibula flap is widely regarded as the first choice for large mandibular as well as maxillary bone reconstructions.

By contrast, the DCIA flap was the first composite flap to be used in large series. Here, the bone is thick and has a natural anatomic form resembling that of the mandibular body. Thus, the DCIA flap is also well-suited for postoperative osseointegrated dental implantation to restore dentition. The main drawbacks include its short vascular pedicle, the thick and unreliable skin island and morbidity along the donor site.

Finally, the scapula flap is a versatile flap with wide-ranging possibilities in reconstructions. The scapula suits two different vascular pedicles, providing branches to two separate skin islands, two separate bone pieces and a separate muscular section—the LD muscle or the serratus muscle. The scapula flap is consequently well-suited for more extensive soft tissue defects. Its primary drawback stems from the limitation of the 14-cm-long but thin bone, usually considered qualitatively inferior compared to other flaps. However, donor site morbidity is typically low.

Contrary to free non-vascularlised bone grafts and metal-plate reconstructions, long-term stability is achieved in these composite tissue reconstructions. The remodelling or resorption of free vascularised bone is considered insignificant, although few thorough studies exist on this topic.

### 3D planning and printing

In complex facial structures, a thorough radiological evaluation relying on multislice computerised tomography (MSCT) and magnetic resonance imaging (MRI) is essential. By using MSCT data, we can accurately and preoperatively plan the resection of a tumour with predictable margins in many cases, particularly those involving osseous structures. Through virtual planning, the tumour is marked and the resection planned, avoiding unnecessary damage to vessels and nerve structures. Patient-specific cutting guides can be printed, thus ensuring that resection is performed as planned. Moreover, corresponding guides can be manufactured to produce an exact shape for the reconstructive osseous section, particularly in fibula and scapula flaps. In addition, patient-specific titanium plates are produced to secure the correct positioning of the reconstruction. This saves time during surgery and renders results more predictable.

#### Classification of surgical complications and comorbidities

Complications in these types of surgeries are common. Postoperative infection, wound dehiscence, repeat operations for microvascular disturbance and flap losses as well as donor site morbidities and complications occur. Furthermore, patients with general morbidities and a prior treatment history for cancer are common amongst such surgical patients. By classifying complications, it is possible to more thoroughly analyse the benefits and disadvantages of various surgical and other treatment options for patients. This also provides additional evidence for the best surgical treatment options based on patient characteristics. Classifying comorbidities has revealed an association between elevated risk for complications and comorbidities among patients. By using a preoperative risk assessment, identifying patients with comorbidities can optimise medical and nutritional treatment, thus reducing the risks of postoperative events and shortening the recovery period. In patients with severe comorbidities, surgical reconstruction may be downgraded to local or pedicleled reconstructions.

## 3 Review of the literature

#### 3.1 Indications for maxillomandibular reconstruction

The primary indication for maxillomandibular reconstruction is the treatment of a surgical defect caused when resecting a malignant solid tumour, where the majority of cases involve SCC. Benign odontogenic locally aggressive tumours, avulsive traffic trauma as well as explosive and ballistic injuries constitute a smaller proportion of cases in Finland. Yet, war injuries played a primary role in the history of plastic surgery and the evolution of reconstructive methods.

#### 3.1.1 Oral cancers

#### 3.1.1.1 Introduction to oral cancers

Oral cancers, including lip, gingiva, floor of mouth, hard palate and tongue cancers, constitute diseases involving a central body part of patients. Oral cancers are divided into subgroups related to their classification, statistics and treatment using the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) developed by the World Health Organisation (WHO).<sup>1</sup> Among the classifications based on incidence and prevalence, these diseases are grouped into lip cancer and oral cavity cancer.<sup>2,3</sup> With the exception of lip cancer in men, all types of oral cancers are increasing. Across the Nordic countries in 2014, a total of 2 166 cases of lip, oral and pharynx cancers were reported. This equates to a rate of 16.6 per 100 000 inhabitants. More specifically, 199 lip cancer cases (excluding skin cancers) corresponding to a rate of 1.5 per 100 000, 716 oral cavity cancer cases at a rate of 5.5 per 100 000 and 834 oropharynx cancer cases corresponding to a rate 6.4 per 100 000 were reported.<sup>3</sup> In Finland between 2010 and 2014, the total number of lip, oral and pharynx cancers each year reached 615 cases, affecting 374 men and 241 women. More specifically, 74 lip cancers, 275 oral cavity cancers and 147 oropharyngeal cancers were reported.2-4 Moreover, 21 patients with nasal and para sinusoidal cancers were recorded. Among oral cancer patients, approximately 90% were identified as SCCs; other cases consisted of various carcinomas of the small salivary glands, malignant melanomas. sarcomas, lymphomas, leukaemia and metastases of other malignancies.

				U	0
TX	Tumour cannot be	NX	Lymph nodes cannot be	MX	Distant metastasis
	assessed		assessed		cannot be assessed
То	No evidence of primary tumour	No	No lymph node metatasis	Мо	No distant metastasis
Tis	Carcinoma in situ	N1	Metastasis is a single ipsilateral node <3cm	M1	Distant metastasis
T1	Tumour of ≤2 cm	N2a	Metastasis is a single ipsilateral node >3 cm but <6 cm		
T2	Tumour >2 cm but <4 cm	N2b	Metastasis in multiple ipsilateral lymph nodes, <6 cm		
Т3	Tumour >4 cm	N2c	Metastasis in bi- or contralateral lymph nodes, <6 cm		
T4a	Tumour invading through cortical bone, into deep or extrinsic muscle of the tongue, maxillary sinus or facial skin	N3	Metastasis in a lymph node >6 cm		
T4b	Tumour invading the masticator space, pterygoid plates or skull base or encases the internal carotid artery				

Table 1. T	umour. node	e and metastasis	s (TNM)	staging for	oral cancer
I UDIC II I	uniour, nou	and moustable	, (		or ar cancer

Tuble 2. Stage clussification				
Stage o	Tis	No	Мо	
Stage I	T1	No	Мо	
Stage II	T2	No	Мо	
Stage III	T1 to 2	N1	Мо	
	T3	No to N1		
Stage IVA	T1 to 3	N2	Мо	
	T4a	No to 2		
Stage IVB	Any T	N3	Мо	
	T4b	Any N		
Stage IVC	Any T	Any N	M1	
Stage IVB Stage IVC	T4a Any T T4b Any T	No to 2 N3 Any N Any N	Mo M1	

## Table 2. Stage classification

In tumour and lymph node classification, the size represents the maximal size of the tumour or metastasis, and the corresponding class is downgraded in borderline cases. Adapted from: *WHO 2017. International Agency for Research on Cancer, IARC, 150 Cours Albert Thomas, 69372 Lyon CEDEX 08, France*<sup>5</sup>

## 3.1.1.2 Incidence of and survival from oral cancers

In Finland, five-year survival rates for patients with lip cancer reach 95% for men and 100% for women. In other oral cancers, the rates reach only 53% to 54% in men and 58% to 70% in women.<sup>3,4</sup> In the United States in 2016, 48 330 new cases and 9 570 deaths from oral cavity and pharynx cancers were estimated to occur. These figures include 16 100 tongue cancers, 12 910 oral cavity cancers, 16 420 pharyngeal cancers and 2 900 cancerns in other locations. For all stages combined, the five-year survival rate for oral cavity cancer was 63% and 52% for pharynx cancer. The highest five-year survival rate was found for lip cancer (90%), while floor of the mouth cancer accompanied the lowest rate (51%). Between 2005 and 2011 in the United States, five-year survival rates by stage at diagnosis for oral cavity and pharynx cancers combined reached 83% for local disease, 62% for regional disease and 38% for distant disease.<sup>6</sup>

## Figure 1. Cancer statistics for oral cancer in Finland

Reprinted with permission from The Cancer Society of Finland and NORDCAN. Engholm G, Ferlay J, Christensen N, Kejs AMT, Hertzum-Larsen R, Johannesen TB, Khan S, Leinonen MK, Ólafsdóttir E, Petersen T, Schmidt LKH, Trykker H, Storm HH. NORDCAN: Cancer Incidence, Mortality, Prevalence and Survival in the Nordic Countries, Version 7.3 (8 July 2016). Association of the Nordic Cancer Registries. Danish Cancer Society. Available from http://www.ancr.nu, accessed on day/month/year.

# ø

#### Cancer stat fact sheets Finland - Oral cavity

	Male	Female
Number of new cases per year (incidence 2010–2014)	148	127
Proportion of all cancers (%)	0.9	0.8
Proportion of all cancers except non-melanoma skin (%)	1.0	0.9
Risk of getting the disease before age 75 (%)	0.4	0.2
Age-standardized rate (W)	3.1	2.0
<ul> <li>Estimated annual change latest 10 years (%)</li> </ul>	+2.0	+1.8
Number of deaths per year (2010-2014)	51	45
Proportion of all cancer deaths (%)	0.8	0.8
Risk of dying from the disease before age 75 (%)	0.1	0.1
Age-standardized rate (W)	1.0	0.6
<ul> <li>Estimated annual change latest 10 years (%)</li> </ul>	+3.0	+3.4
Persons living with the diagnosis at the end of 2014 (prevalence)	1076	1084
Number of persons living with the diagnosis per 100 000	39	38
Relative survival (%) with [95% CI] (2010-2014)		
1-year	77 [74–81]	85 [82-88]
5-year	60 [55–65]	70 [66–74]



NORDCAN, Association of the Nordic Cancer Registries – All Rights Reserved. 8.7.2016

#### 3.1.1.3 Treatment of oral cancers

Complex units of tissue are involved in a wide variety of functions, such as the masticatory function, which includes functional dentition, tongue functioning, the ability to swallow, maintenance of a functional airway and the production of speech. In addition, such tissue is important to maintaining a socially acceptable aesthetic appearance.<sup>7</sup>

The primary consideration in oral cancer treatment is surgical resection of the tumour and affected lymph nodes with free margins. This is achieved through a preoperatively planned and estimated intraoperative resection of the tumour of one to two centimetres of healthy tissue margins. This also includes a sentinel node biopsy or modifications of the dissection of the locoregional lymph nodes (neck dissection). The tumour and degree of lymphatic spread as well as possible distant metastasis are preoperatively evaluated using MRI and MSCT, and possibly ultrasound (US) and positron emission tomography (PET) imaging. Limited T1 and T2 tumours are often treated with surgery as a single modality, while larger T3 and T4 tumours require adjuvant oncological treatment postoperatively.<sup>8-10</sup>

Radiation therapy or oncological modalities are used as primary treatment on inoperable patients as well as for large tumours at the base of the tongue and on the tonsils, especially in human papillomavirus 16– (HPV16) positive cases.<sup>11</sup> The treatment regime for head and neck cancers in Helsinki follows a protocol produced and evaluated by the multidisciplinary tumour board (unpublished data).

The margins are generally considered free when a 5-mm-wide resection is found in the specimen and close when a 0- to 5-mm-wide resection is found; positive and close margins negatively impact both survival and recurrence even after repeat operations.<sup>12-14</sup> The prevalence of positive margins is about 7% in large materials; high-volume centres produce better results than low-volume centres and the highest rates of positive margins are found in the floor of the mouth, the buccal mucosa and the retromandibular trigone.<sup>15</sup>

In the resection of a tumour in close proximity to the alveolar bone, a decision must be taken about bone resection. In a high toothbearing alveolus, the amount of bone is often sufficient to safely allow partial, box or rim resection. If, however, the tumour infiltrates through the cortical bone or the height of the bone is low, such as that found in an edentulous patient, a continuity resection is warranted.<sup>13</sup>

Oral cancer spreads primarily to the cervical lymph nodes, an observation first published in 1906 by G. Crile. Crile operated on 36 patients with oral tumour and combined neck dissections, and found a three-year survival of 75% compared with 19% in patients without neck dissections.<sup>16</sup> The American Head and Neck Society and the American Academy of Otolaryngology, Head and Neck Surgery defined the current classification of cervical lymph nodes used in clinical practice.<sup>17</sup> Spread to the cervical lymphatic system is verified and primary treatment of oral cancer today includes a modified neck dissection to treat patients.<sup>13</sup> Furthermore, in a preoperatively assessed negative node with T1 to T2 local tumours in the neck, an elective dissection of the neck lymphatic node has been shown to clearly improve disease-specific survival and rates of relapses compared to a later performed therapeutic neck dissection.<sup>18</sup>

## 3.1.1.4 Prognostic factors in oral cancers

The majority of patients with oral cavity malignancies have SCC. As the primary modality of treatment of the primary tumour, surgery generally produces the lowest rates of recurrence and the best survival benefits for patients.<sup>19</sup>

A study by Rogers et al.<sup>20</sup> on survival following surgery for oral cancer among 489 patients revealed several factors that also affect the reconstruction method. The TNM class has been widely accepted as the primary prognostic factor. For instance, Stage 1 patients have an excellent disease-specific five-year survival of 96%, Stage 2 patient survival drops to 82% and Stages 3 and 4 drop further still to 78% and 57%, respectively. Overall survival is significantly lower with a five-year survival of 76% for Stage 1 patients and 37% for Stage 4 patients, indicating the burden of disease in general as well as treatment morbidity among this patient population. Factors leading to recurrence and to patient death were also analysed. As such nodal status proved important, whereby anything beyond pNo yielded hazard ratios of 2.5 (pN1) and 3.4 (pN2–3), respectively. Surgical margins were also important. As such, the involved margins had a hazard ratio of 2.8, falling to 2.3 for close margins (<5 mm). The presence of extracapsular spread (ECS) in the cervical lymph nodes is probably the highest risk factor. If lymph node metastasis has ECS, the five-year survival drops to 37% compared to 83% for no ECS.

Tumour biology and prognostic markers are increasing in importance. In 2013, Sharma et al.<sup>21</sup> identified the need to understand prognostic factors in oral cancer. The size of the tumour does not neccecarily correlate with the risk of metastasis. Analyses of cellular properties along the invasive front of a tumour are important. Several extracellulare proteins, such as laminin, tenascin, syndecan, fibronectin and cortactin, are of prognostic value. As shown by Almangush et al.,<sup>22</sup> the depth of invasion and tumour budding in particular are indicative of worse outcomes in tongue cancer. Similarly, Mäkinen et al.<sup>23,24</sup> presented the prognostic significance of toll-like receptors and matrix metalloproteinases in oral cancers. Several markers in the prognostic staging of oral cancers remain unestablished.

### 3.1.2 Other indications for mandibular and maxillary reconstruction

The vast majority of patients needing facial reconstruction have malignant disease. In addition to oral cancer malignancies such as sinonasal cancers invading the maxillae, facial and sinusoidal sarcomas and skin cancers may also require large resections of the maxillae and reconstruction of defects.<sup>25-29</sup> A minority of patients present with benign but locally aggressive tumours which tend to recur unless treated with a block resection. The most frequent benign lesions requiring a large-bone resection or continuity resection are ameloblastomas, central giant cell tumours and odontogenic myxomas.<sup>30-34</sup>

Osteonecrosis of the jaw, related to medication or induced by radiotherapy, when extensive is best treated with resection of the involved bone and microvascular reconstruction.<sup>35-39</sup>

High-energy traumas, such as those common among war casualties and accompanying high-velocity self-inflicted or other rifle shootings, traffic incidents and animal attacks, lack the tumour burden, yet may also present with large defects

in the maxillary and mandibular area. In Finland, 1.8 per 100 000 population fatal shootings occur each year. These patients are typically young men with significant head injuries.<sup>40</sup> In non-fatal shootings between 1990 and 2003, 35% injured the head and neck region, with patients surviving and needing hospitalisation ranging from 2.1 to 5.1 per 100 000 person-years.<sup>41</sup> No available data exists on patients needing reconstructive surgery secondarily to shooting injuries in Finland.

#### 3.2 Classification of surgical maxillomandibular defects

The classification of a surgical defect serves as the basis for subsequent reconstruction. By classifying the disease, we diagnose it, and then compare treatment options and plan a reconstructive algorithm for various defects in the facial area. These classifications primarily serve scientific purposes, but are not widely used in the clinical setting.

## 3.2.1 Maxillary defects

In Sweden in 1933, Öhngren published one of the first papers on the classification and treatment of maxillary tumours.<sup>42</sup> That paper aimed to distinguish between nasal and maxillary tumours, as well as to distinguish more benignly behaving lower anterior tumours from more malignant posterior tumours. In 1986, MacGregor and MacGregor<sup>43</sup> published their classification based on a vertical defect. In 1997, Spiro et al. published the first complex classification that considered defects of functional parts of the maxilla based on 403 maxillectomies.<sup>44</sup> That defect classification included the categories of limited (LM) where one wall of the anthrum was removed, subtotal defect (SM) to include at least two walls with the palate and total defect (TM) for a complete resection of the maxilla. Interestingly, only 41.9% of the malignant tumours were SCCs. Spiro et al.'s classification also included suggested access routes as well as extension possibilities.

In 2000, both Brown et al.<sup>45</sup> and Cordeiro et al.<sup>46</sup> published new classifications.

Brown et al. presented 45 patients classified as follows: Class 1 consisted of a maxillectomy without an oroantral fistula (i.e., low alveolar resection); Class 2 consisted of a low maxillectomy; Class 3 consisted of a high maxillectomy (including orbital floor and/or content partial); and Class 4 consisted of a total maxillectomy with excenteration. Subgroups (represented by A, B or C) further described the width of the horizontal or palatal component.

Cordeiro and Santamaria published their results based on 60 patients with maxillary resections, with the aim of presenting a new classification, as well as an algorithm for reconstruction based on that classification. Their classification is based on the description of the maxilla as a six-wall structure. As such, a Type I defect included the resection of one or two walls of the maxilla, but not the palate. Type II defects included the resection of the maxillary arch, the palate and the anterior and lateral walls (five walls), while the orbital floor remained intact. A Type III defect consisted of a total maxillectomy, including the resection of all six walls of the maxilla. Type IV defects consisted of the entire maxilla and the entire orbit, but spared the palate (i.e., midface resection).

Types I and II and Classes 1 and 2 are similar across the two classifications from

2000, while Types III and IV and Classes 3 and 4 diverge. The majority of Cordeiro et al.'s patients were reconstructed with a free flap (91.7%), mostly consisting of soft tissue flaps. The rectus was used in 82% of patients while the remaining 12% included radius fasciocutaneous or osteofasciocutaneous flaps (4 cases). A further 17 patients underwent free osseous grafts. No fibula, ALT or scapula flaps were used in their series. The subsequent algorithm recommends only radius or rectus soft tissue reconstructions for all types of defects. However, Type II represented the exception, where an osteofasciocutaneous radius is recommended. Detailed instructions for flap architecture were also provided.

In 2001, Okay et al.<sup>47</sup> published a classification taking to an account both the defect as well as reconstruction using prosthodontics and autologous tissue. In this classification of 47 patients, Class 1 consisted of only a palatal defect. Class 2 consisted of a hemimaxillectomy including only one canine or a transverse anterior resection. Class 3 included any resection involving >50% of the palate. Subclasses F and Z indicated the involvement of the floor of the orbit or the zygoma or both. The authors recommended that Class 1 defects undergo soft tissue reconstructions or obturation prosthesis reconstruction. In addition, class 2 should undergo prosthetic obturation with or without an osseous free flap. Finally, Class 3 defects should involve a free osseous flap reconstruction. This classification aims at a functional dentition and contains recommendations for biomechanical prosthodontics possibilities.

In 2007, Rodrigues et al.<sup>48</sup> presented a classification and proposal for the reconstruction of high-energy facial defects. In this study, 14 patients with high-velocity defects were reconstructed, where 6 underwent an iliac crest and 8 underwent fibula reconstructions. Both flaps were suitable for patient reconstruction needs.

In 2010, McCarthy and Cordeiro<sup>7</sup> presented a classification and algorithm for midface reconstructions based on the earlier classification of Cordeiro and Santamaria published in 2000. This later classification further refines and more thoroughly categorises palatal defects, while maintaining the primary classes. The reconstructive algorithm here includes an RFA for Type I defects and a skin graft and palatal obturator or osseous RFA for Type II defects. Type III and IV defects should consist of rectus abdominis flaps, including bone grafts for Type IIIa orbital floor defects.

Also in 2010, Brown and Shah<sup>49</sup> presented an update to their classification from 2000 based on 147 midface resections and reconstructions. Their materials described the methods used in the reconstruction of these patients, and which they used to classify defects as falling into six classes. Class 1 consisted of a low maxillary defect without an oronasal fistula, Class 2 consisted of a maxillectomy not involving the orbit, Class 3 involved the orbit but spared the eye, Class 4 included enucleation or excenteration, Class 5 consisted of an orbitomaxillary defect not involving the palate or alveolar ridge, and Class 6 involved a central nasomaxillary resection. Subgroups A through D serve to describe the extent of the palatal and alveolar defect. Furthermore, their literature review discusses and describes several options recommended for reconstruction. For Classes 1 and 2, local flaps such as temporoparietal and temporalis are recommended. Soft tissue free flaps, such as RFA and ALT, are presented for osseal reconstructions, while RFA, fibula, DCIA as

well as scapula variations are also described. Local flaps are not recommended for Classes 3 through 6. DCIA is recommended for Classes 2 through 4, osseal RFA should be used for Classes 2, 5 and 6 (midface), the fibula is only method appropriate for Class 2, the scapula is appropriate for Classes 2 through 4 and the thoracodorsal angular variant is recommended for Classes 2 through 6. Soft tissue only flaps are primarily recommended for Class 2 and 5 (RFA and ALT) and for Class 4 (rectus abdomini and LD). This thorough classification also provides detailed recommendations. Here, the paradigm shift from earlier algorithms, where mostly soft tissue reconstructions were recommended, is clear. In addition, free nonvascularised bone grafts are not included in their recommendations.

In 2012, Bidra et al.<sup>50</sup> published a review of maxillary classifications, where 14 different classifications were presented and analysed. They concluded that no classification proved ideal for both surgical and prosthodontic needs. Furthermore, the remaining dental status and the involvement of the soft palate is frequently missing from classifications.

Costa et al.<sup>51</sup> presented a recent classification. Based on 57 midface defects, the authors proposed a new classification to ensure a bone-bearing reconstruction of the palate and alveolar area. Their classification takes into account both the vertical proportions of the defect as well as the horizontal plane—that is, the area of the palate and alveolar area. Type 1 defects consist of limited maxillectomies. Type 2 defects consist of subtotal maxillectomies, while Type 3 defects consist of a complete maxillectomy including the orbital floor. A further 'm'-class indicates the involvement of a mandibular resection. Type 4 represents a total orbitomaxillectomy. Subclasses were added to all types to describe the extent of the defect. Some similarities between this recent classification and previous descriptions exist, although the horizontal palatal classification is a new addition and useful. Still, the classification is complex, resulting in a small number of cases per class. All patients and an algorithm are presented for reconstructions. Thus, the descriptions are quite detailed resulting in 15 different reconstruction outcomes ranging from obturator prosthesis to several free flaps. In contrast to the earlier but analogous to the Brown algorithm from 2000, more bony reconstructions are recommended; in Classes 1c, 2a, 2b and 3a, DCIA is recommended; and in Classes 2b, 3a and 3m, fibula flaps are recommended. Among the soft tissue options, RFA with or without bone, LD and rectus abdomini flaps are recommended.

### 3.2.2 Mandibular defects

Similar to maxillary classifications, several classifications exist for mandibular defects. These focus primarily on the osseous defects, while related soft tissue components of importance, including the tongue, the floor of the mouth and full thickness cutaneous defects are usually uncovered.

Rosemann's<sup>52</sup> 1972 classification is most likely the first publication detailing these surgical defects. Earlier classifications exist in the literature, but these cover trauma, miscellaneous diseases and deformation studies. In 1974, Pavlov<sup>53,54</sup> presented a three-class system not widely cited in the literature, the details of which remain elusive.

Jewer et al.<sup>55</sup> presented the first more widely used classification based on 60

patients reconstructed using the DCIA flap. In this study, the 'HCL' method was presented. Here, the mandible is divided into three segments, where 'C' is the central or anterior segment including both canines; 'L' refers to the lateral segment from the midline laterally excluding the condyle; and 'H' represents the hemimandible from the midline laterally including the condyle. The length of the lateral segments remains unspecified, but the three segments are combined to describe the defect.

In 1991, Urken et al.<sup>56</sup> presented their classification based on 71 mandibles reconstructed using free vascularised bone flaps, where the fibula represented the preferable option. Classes consisted of unilateral defects from the symphysis (S), ramus (R), body (B) and condyle (C).

In 2000, Disa and Cordeiro<sup>57</sup> based their classification primarily on the reconstruction algorithm. Bone segments were classified as long or short, with or without condyle involvement and taking into account the soft tissue needs in the classification. Ramus and condyle defects with large soft tissue resections are best completed using the scapula flap and the radius if more limited soft tissue needs exist. All other sites are best completed using the fibula, possibly accompanied by a supplementary RFA soft tissue flap.

In 2000, Disa and Cordeiro<sup>58</sup> also published a review of mandibular reconstruction discussing the fibula, iliac crest, RFA and scapula flaps. They also discussed an algorithm for reconstructions, favouring the fibula for most defects. They concluded that the fibula has the longest bone-up to 27 cm-and the best donor site for simultaneous harvesting and minimal donor morbidity. In addition, the fibula is suitable for osteotomies. They concluded that other options best suit cases with large soft tissue requirements and minimal bone requirements. They also noted that soft tissue reconstruction combined with reconstructive plates only result in a higher rate of complications and should only be used in the absence of reasonable osseous graft possibilities. DCIA emerged as the primary method of reconstruction in the 1980s. Bone can be shaped as a mandible with a sufficient amount of bone. However, the short pedicle and unreliable skin island, as well as donor site complications such as bulging, numbress and hernia, limit its use in their opinion. They regarded the radial osteoseptocutaneous flap as featuring the best donor vessels as well as a pliable skin island. The bone's quality, however, stands as a disadvantage. It is thin and unicortical, and according to the authors cannot tolerate osteotomies. Fracture of the donor radius represents the most significant complication.

The scapula is said to possess good vessel length and calibre, but the bone is considered inferior to the fibula or DCIA. Thus, Disa and Cordeiro conclude that the scapula bone does not tolerate osteotomies or osseintegrated implants reliably. They conclude that harvesting the flap is not possible through a two-team approach, although they cite no external studies in this section of their paper. Based on their algorithm, they recommend the scapula for short ramus defects with large soft tissue requirements, the radius for limited bone defects with large lining needs and the fibula for all other options. They omit DCIA from their recommendations.

In 2005, Takushima et al.<sup>59</sup> presented their classification and algorithm for reconstruction based on 178 reconstructed mandibles published previously.<sup>60</sup> Their

classification addresses both osseal as well as soft tissue defects, with either anterior or lateral bone defects. Here, soft tissue defects fell into three categories: 'none', 'skin or mucosal' and 'through-and-through'. This yields six categories: lateral defects without soft tissue resection; lateral DCIA with a partial soft tissue resection; and a fibula with through-and-through defects, for which the authors recommend a scapularflap. For anterior classes, the fibula represents the first choice across soft tissue defects, accompanied by a second free soft tissue flap as needed.

Hanasono et al.<sup>61</sup> presented their findings from multiple studies.<sup>62,63</sup> In this publication, the osseal defects are classified as central, lateral and hemimandible according to Boyd et al.<sup>64</sup> Their reconstructive algorithm primarily recommends the fibula for anterior central defects, and a soft tissue or a scapula flap to join large defects in this area. For lateral and hemimandibles, the authors only recommend the fibula for addressing the bone, although a separate soft tissue method may be used.

In 2015, Schultz el al.<sup>65</sup> published a new classification and algorithm used in 24 patients, detailing both bone defects as well as pedicle requirements. Type 1 defects included a unilateral mandibular body defect. Type 2 consisted of a unilateral defect beyond the angle. Type 3 included a bilateral defect of the mandibular body anterior to the angle. Type 4 consisted of a bilateral dentoalveolar defect extending posterior to one or both angles. In this classification, types were further subdivided depending on the availability of useful donor vasculature on the ipsilateral side (subtype A) or not (subtype B). Finally, subtype C was added for condylar involvement. Here, DCIA was considered best for dental implantation and recommended for Type 1 lateral reconstructions, with the fibula serving as an alternative option. In Type 2 defects involving the ramus, the fibula is the first choice followed by DCIA. In addition, the authors reommended the fibula, accompanied by a secondary flap if needed for Type 3 and 4 defects. Other options, such as the scapula or radius, were not included in their recommendations.

In 2016, Brown et al.<sup>54</sup> reviewed previous classifications and presented a new system. In their literature review, 167 studies were analysed resulting in a total of 1 766 mandibles reconstructed and classified from other studies. Their new reclassification is based on the four corners of the mandible, the two canines and both angles of the mandible. They presented four classes: Class I (lateral, not canine or condyle), Class II (hemimandibulectomy without condyle), Class III (anterior including the canines) and Class IV (extensive, both canines and at least one angle). Furthermore, subclass C indicates condylar involvement. The purpose of this classification is to recognise that a growing defect class captures the defect measurements, the need for osteotomy and the functional and aesthetic outcome. Their classification also aimed to guide the method of reconstruction. The authors also discussed the distribution and complication rates of flaps used based on this new classification system. As such, they discuss the usefulness of the most common options, but provide no formal recommendations or algorithms.

#### 3.3 Maxillary and mandibular reconstructions

#### <u>3.3.1 General aspects and historical milestones of the reconstruction of surgical</u> maxillomandibular defects

Large defects in patients undergoing resections for malignant tumours and facial trauma represent significant challenges to the specialities of oncological, plastic reconstructive, maxillofacial and head and neck surgery since they require complex reconstructive surgical modalities.

The range of operative plastic reconstructive surgical methods includes direct tension free closure of the wound, healing by secondary intention, mucosal or skin grafting, local flaps, distant pedicled flaps and the most complex distant free microvascular composite tissue transfer. Osseous reconstructions are possible with free osseous grafting of cancellous or cortical bone, alloplastic materials, metal plating and with free vascular composite bone transfer.<sup>66</sup> These complex reconstructions of different tissues and organs must be restored based on the principle of replacing like-with-like. This includes both functional and structural reconstructions using tissue consisting of skin, fat, bone, muscle and mucosal lining with an adequate blood supply and sensory abilities, as well as having the ability to withstand the mechanical and motion stress present in the area. The gold standard of replacing like-with-like requires the use of composite tissues. Distant tissue transfer using microsurgical techniques as well as pedicular flaps replaces the missing tissue and partially restores the functional requirements.<sup>58,67-70</sup>

In every surgical intervention, some sort of defect is addressed. From this point onwards, we will use the reconstructive ladder. The simplest method involves no attempt to close the defect, that is, spontaneous healing through secondary intention. The most common solution involves direct closure of the wound following delayed closure of the wound. This could be accomplished by, for instance, negative pressure wound therapy. This method as used today was first described in 1993 by Fleischmann et al.<sup>71</sup> Split and full thickness skin grafts have been used for centuries, with the first description appearing in 1869 by Reverdin as described by Ollier in 1972.71 In an 1870 review by Stele,72 the method was first described. In oral reconstructive surgery, the first description of the tissue expansion technique appeared in 1976 by Radovan, which appeared in print in 1984.73 Furthermore, it is likely that the father of plastic surgery Sushruta Samhita, who invented the classical forehead flap used in nasal reconstruction found in a Arabic translation from the seventh century, also used skin grafts as well as local flaps as early as 800 to 1000 BC.74 Random or axial flaps, which evolved in the Western literature, were first described in G. Tagliacozzi's De Curtorum Chirurgia per Insitionem, Venice 1597, published in England in 1794 in Gentlemen's Magazine. After this, a variety of local cutaneous flaps for the reconstruction of facial defects appeared in the literature.

Local, axial flaps used in head and neck reconstruction as described above were first used in nasal reconstruction. A more detailed description of surgical options as well as the microvascular flaps used in maxillofacial reconstruction will be presented in the following sections. Vascular studies in specimens performed by Manchot (1889), Spateholz (1893) and Salmon (1936) provide the basis for state-of-the-art publications by G. Ian Taylor and JH Palmer<sup>75</sup> when the angiosomes were presented. This initiated a new era of free perforator flaps as well as an emerging period of greater reliability among axial flaps.

## 3.3.2 Free bone grafts

Free nonvascularised bone grafts have been used in the repair of osseous defects for some time. The most used donor areas include the iliac spine, calvarial grafts, rib grafts and intraoral bone grafts from the mental region, as well as the zygomatic buttress and ramus of the mandible. The primary drawback to these stem from the extensive and rapid resorption where up to 60% of the grafted volume is lost within six months.<sup>76,77</sup> The amount of available donor tissue is also limited, especially for local transplantations.<sup>78</sup>

### 3.3.3 Local flaps in maxillomandibular reconstructions

Small- to medium-sized defects in the oral cavity can be managed using local mucosal or cutaneous flaps. The methods used in cleft surgery and primary lip reconstructions are excluded here.

### 3.3.3.1 Palatal flaps

The Rehrmann plasty, a procedure familiar to general dentists, represents the most commonly used local reconstruction in oral and maxillofacial surgery for the closure of oroanthral fistulas following dental extractions.<sup>79,80</sup> Palatal reconstructive flaps were first used by cleft surgeons Veau and Millard as discussed in a 2004 review by Jamali.<sup>81</sup> Palatal reconstructive flaps can be unilateral or bilateral, which are perforator flaps based on the palatal artery and vein. The entire palatal mucosa can be raised and rotated as a flap or a finger flap alone can be used. The donor area is left for secondary granulation and is mucosalised in three to five weeks yielding a smooth surface. The area should generally be protected during healing and can be painful to the patient. In total, up to 16 cm<sup>2</sup> can be harvested. A variant of submucosal harvesting only has been described. One method that leaves the donor site mucosa *in situ* and the flap consists of a fibro-fatty vascularised flap.<sup>82</sup>

### 3.3.3.2 Tongue flap

Tongue flaps, as reviewed by Strauss,<sup>83</sup> have been used in the reconstruction of local defects of the floor of the mouth as well as in palatal defects since introduced by Eiselsberg and Lexer 1909. The flap is easy to raise and can reach 4 to 5 cm depending on the donor site used; dorsal flaps are used for palatal defects and lateral or ventral flaps are suitable for the mandible or the floor of the mouth. The primary drawback stems from the donor site, the tongue specifically. The tongue is sensitive and all procedures cause scarring, resulting in potential morbidities for the patient that involve speech and feeding. Leaving the tip of the tongue unharmed is of primary importance.<sup>83</sup>

### 3.3.3.3 Facial artery musculomucosal flap

In 1992, Pribaz<sup>84</sup> introduced the facial artery musculomucosal flap (FAMM). This axial flap is an intraoral analogue to the nasolabial flap using the facial vessels and can be raised either as a superiorly or inferiorly based flap. In raising the flap, the mucosa and submucosa, the buccinator muscle and a slice of the orbicularis oris are incorporated into the flap since the vessels are lateral to these structures. The flap can be used to reconstruct the palate, nasal septum, floor of the mouth, lips, as well

as the tongue and alveolus. The flap can be up to 3-cm-wide and the full buccal height can be harvested. The Stensen duct of the parotid gland must be avoided and dentition in the arc of the rotation can serve as a contraindication. No external visible scars and a mucosal surface represent favourable characteristics in oral reconstruction.<sup>85-90</sup>

## 3.3.3.4 Nasolabial flap

The nasolabial flap was perhaps first described by Sushruta in 700 BC. Originally used as an inferiorly based axial patterned flap based on the facial artery, in the nasolabial flap, the vein follows the same route lateral to the artery. It can also be based superiorly. The nasolabial flap is useful in the reconstruction of the lateral nose, lips, alveolar ridge, buccal mucosa and anterior floor of the mouth. It is especially viable in elderly patients with excess skin producing an anatomically well-hidden scar and can produce a flap sufficient to reconstruct a defect of up to 5 cm by 5 cm. The flap can be used as a one-stage or delayed two-step reconstruction with subsequent division of the fulcrum point. Previous or simultaneous procedures involving the facial vessels must be kept in mind when planning the flap. Several studies have shown that the flap is still reliable and useful as a random pattern flap.<sup>86,91</sup>

### 3.3.3.5 Platysma flap

Futrell et al. first introduced the myocutaneous platysma flap in 1978. The anatomical basis was described in detail by Hurwitz et al. in 1983, while Coleman et al. published the first series of 24 patients in 1983.<sup>92-94</sup> The platysma flap has several advantages, including good colour match, a small donor site surgical field, low donor site morbidity and a suitable flap thickness. Defects of up to 50 to 75 cm<sup>2</sup> can be reconstructed using the platysma flap. This type of flap is based on blood flow either from an inferior, superior or posterior origin. The superior option from the submental artery stands as the most useful in oral reconstruction. The vascular pedicle is usally not exposed and the flap usually survives ligation of the facial artery via retrograde circulation.<sup>95</sup>

## 3.3.4 Pedicled flaps in maxillomandibular reconstruction

### 3.3.4.1 Temporal flap

In 1895, Lentz<sup>96</sup> first described the pedicled temporalis muscle flap in the reconstruction of a condylar resection (original manuscript not found). The external cheek, orbital excenteration, as well as maxillary and oral defects can be reconstructed using this flap. The temporal muscle elevates the mandible from its origin in the temporalis line and the infratemporal crest for insertion into the coronoid process. The temporal fascia consists of the superficial temporoparietal and deep temporal fascia, further divided into superficial and deep layers. The muscle lies beneath the deep temporal fascia stemming from the superficial temporal vessels and the temporal muscle stemming from the deep temporal arteries originating at the internal maxillary artery. When harvesting the muscle flap, temporary removal of the zygomatic arch provides additional length to the flap. The flap measures from 12- to 16-cm-long and 0.5- to 1-cm-thick. Major drawbacks

include a risk of injury to the facial nerve, postoperative trismus and temporal hollowing.97

### 3.3.4.2 Submental flap

In 1993, Martin et al.<sup>98</sup> presented the submental flap, a perforator or pedicled cutaneous flap from the submental region based on the submental branch of the facial artery. This flap features good colour match, good reach to the anterior mouth and the donor site is directly closed; typically, it offers an abundance of tissue, particularly in elderly patients. This flap has even been used in reconstructing the pharynx, larynx and superior oesophagus, as described in a 2014 review by Cheng.<sup>99</sup> The skin paddle can reach up to 10 cm by 16 cm, the pedicle reaches up to 5 cm and the platysma muscle, a part of the mylohyoid, as well as the anterior digastricus muscle are included.<sup>100</sup> When possible, care should be taken when using this flap on the ipsilateral side of a lymphatic dissection. The submental flap is also applicable in facial vessels proximally divided through a reverse flow, and can also be used as a free flap.<sup>99</sup> The submental flap is ideal for reconstructing bearded areas in men.<sup>101</sup>

## 3.3.4.3 Supraclavicular flap

In 2014, Ramires and Fernandes<sup>102</sup> reviewed the supraclavicular flap, first described by Mutter<sup>103</sup> in 1842 (original publication not found). The vascular basis typically originates in the thyrocervical trunk and the transverse cervical artery. The supraclavicular flap is easy to harvest, is thin and pliable and can reach the lateral temporal region as well as the lower face. This type of flap can measure 12 cm by 35 cm, although when wider than 7 cm a skin graft of the donor area is typically necessary. Since the vessels originate in the lymphatic level V, care must be taken when using the flap if the area was previously dissected and knowledge of possible vascular damage remains unknown. The presence of the vessel can be evaluated preoperatively by contrast-enhanced MRI or CT.<sup>104</sup>

### 3.3.4.4 Deltopectoral flap

The deltopectoral fascial or Bakamjian flap, based on perforating arteries from the third and fourth intercostal arteries, was described by Bakamjian<sup>105</sup> in 1965 for reconstruction of a pharyngoesophageal defect. The fasciocutaneous flap can be harvested from the acromioclavicular area and the lateral deltoid region, although the most distal part lateral to the cephalic vein can be unreliable. This option is useful in local reconstructions of the lower face. A special technical modification worth mentioning spares this option for secondary or salvage use in raising the pectoralis flap.<sup>105,106</sup> A refinement of this flap consists of the internal mammary artery perforator flap that produces a thin pliable island flap for lower facial and neck reconstruction.<sup>107-109</sup>

### 3.3.4.5 Trapezius flap

In 1972, Conley<sup>102,110</sup> described the trapezius flap, which can be used in the lateral neck as well as occipital region. The lower island trapezius flap has the longest arc of rotation and is the most widely used variation. It features dual blood flow from the occipital artery as well as the transverse cervical vessels, those which are most

commonly used.<sup>111</sup> As with the supraclavicular flap, the vessels should be kept in mind during resection and neck dissection.

### 3.3.4.6 Pectoral flap

The pectoralis major myocutaneous (PMMC) flap is a widely used workhorse in head and neck reconstruction, first used on thoracic defects by Pickrell<sup>112</sup> in 1947. In addition, in 1979, Arvian<sup>113</sup> used the pectoral flap in head and neck reconstruction on four patients. The vascular supply to PMMC includes the pectoral branch, the lateral thoracic artery, the superior thoracic artery and the intercostal artery with concomitant veins. The most commonly used supply is the pectoral branch originating from the thoracoacromial supply. PMMC is reliable and relatively easy to harvest, features a large volume of muscle and subcutaneous tissue and can fill large defects oblitering dead spaces in reconstruction. In addition, PMMC is used as secondary reconstruction if the primary microvascular option fails or if additional surfacing is needed. Its drawbacks include an unreliable skin island with increased necrosis and dehiscence and its limited reach. The reach of the flap as well as the complications caused by tunnelling the pedicle can be partially avoided using an externalised tubed course of muscular and vascular pedicle as a two-stage operation with subsequent division of the flap. This technique, currently enjoying a comeback, dates to the nineteenth century as outlined by Kadlub et al.<sup>114</sup> in 2013. Very obese patients or aplasia of the pectoralis muscle, characteristic of Poland syndrome, are considered contraindications. The use of the pectoral flap also impairs the functioning of the shoulder.115

### 3.3.4.7 Latissimus dorsi flap

In 1978, Quillen<sup>116</sup> first described the use of the latissimus dorsi (LD) flap in head and neck reconstructions. Bartlett et al.<sup>117</sup> and Barton et al.<sup>118</sup> subsequently described the pedicle and its variations as well as the reliability and absence of atherosclerotic disease in this system. LD provides a large amount of muscle and cutaneous lining with minimal donor site morbidity.<sup>119-121</sup> In addition, LD provides a reliable solution to both primary as well as secondary reconstructions, especially in a vessel-depleted neck.<sup>122</sup> Compared to other local options such as PMMC and trapezius flaps, LD features the longest reach, the fewest variations in the vascular bundle, easiest harvesting, most versatile soft tissue tailoring possibilities and highest success rate. LD also provides the largest musculocutaneous flap that can be harvested.<sup>123</sup> Its reach as a pedicled flap can be enhanced by tunnelling the flap through the pectoral muscle.<sup>124</sup>

# 3.4 Microvascular maxillomandibular reconstruction

The workhorses in soft tissue reconstructions of the head and neck area consist of the free RFA flap, the ALT flap, the rectus abdominis flap and parascapular or scapular soft tissue flaps. In salvage or reoperatiive pedicular and perforator flaps such as LD, pectoralis and supraclavicular flaps are also common. The most frequently used composite tissue flaps in mandibular reconstructions include free flaps of the fibula, iliac crest and scapula. Each of these techniques carries unique properties. In reconstructive surgery, the gold standard adheres to the rule of 'replacing like with like'.<sup>67,70,125,126</sup>

While other options such as soft tissue only reconstructions represent viable options for many patients, long-term results favour the use of osseous vascularised composite flaps for most cases.<sup>63</sup> That said, such options are not without their drawbacks. Flaps may fail, surgical morbidity is greater, hospital stays are longer and the primary costs are higher.<sup>127</sup> Favourable results accompanyting composite flaps include the stability of the reconstruction, well vascularised tissue along the defect site and freely movable tissue compared to local flaps.<sup>126</sup> The primary advantages of the free flaps include the possibility of reconstructing missing parts using tissue with similar properties. Such reconstructions are more reliable compared to local or pedicled flaps. Finally, the vascularised osseous flap integrates into the patient and yeilds the best long-term result.<sup>128</sup>

### 3.4.1 Soft tissue free flaps in mandibular and maxillary reconstruction

As discussed in the section detailing reconstructive algorithms, several options exist for soft tissue reconstruction. The most commonly used methods include RFA as described by Muhlbauer<sup>129</sup> in 1982, ALT as first published in 1985 in Chinese by Luo and popularised in 1989 by Koshima,<sup>130</sup> the lateral arm flap presented by Song et al.<sup>131</sup> in 1982, several variations of the rectus muscle including the transverse rectus muscle (TRAM) and vertical rectus abdominis muscle (VRAM) flaps as well as the perforator options (deep inferior epigastric perforator or DIEP flap and superficial inferior epigastric or SIEA flap). Other options include the ulnar artery flap,<sup>132</sup> the median sural artery perforator flap<sup>133</sup> and the temporal artery posterior auricular skin (TAPAS)<sup>134</sup> flap. As described above, the LD flap is widely used as a microvascular flap. Since the introduction of perforator flaps with Taylor et al.'s<sup>75</sup> initial studies on angiosomes and perforators and Koshima et al's.<sup>135,136</sup> later studies, the options available have become virtually limitless.<sup>137</sup>

# 3.4.2 Osseal free tissue flaps in maxillomandibular reconstruction

The use of a vascular-free bone transfer that includes soft tissue provides a powerful reconstruction method where a bony defect can be replaced yielding both structural stability and soft tissue support. The most common options include the fibula, iliac crest and scapula free flaps, while additional options are also used in maxillary and mandibular reconstruction.

#### 3.4.2.1 Fibula flap

The osseocutaneous fibula composite flap, as the most popular option, allows for harvesting of the fibula simultaneously with tumour resection by a second team without necessitating patient repositioning. Its primary drawbacks include the limited size of the soft tissue and a potential unreliable blood supply in the skin island along part of the flap. The osseocutaneous fibula composite flap also carries a relatively small capacity to fill large soft tissue defects. In older patients, smokers and patients with diabetes, the risk of atherosclerosis and subsequent changes to arterial flow must be addressed. In general, the fibula flap is widely regarded as the first choice for large mandibular reconstructions.

In 1975, Taylor<sup>138</sup> introduced the use of the fibula bone as a free graft. The fibular osteoseptocutaneous (FOSC) flap stands as the most common osseous flap in head

and neck reconstructions, with its favourability over other options increasing.<sup>139</sup> Currently, the fibula is the most widely recommended option among the various classifications and algorithms discussed above. The vascular pedicle is one of three major vessels in the lower leg, where the peroneal artery and its concomitant veins remain constant and feature sufficient length and size.<sup>140</sup> The osseous and skin components can be harvested as a single composite flap or as two separate skin islands given a favourable anatomy. The bone is of good quality allowing for multiple osteotomies and is suitable for dental implantation.

In 1999, Cordeiro et al.<sup>141</sup> published a study of 150 mandibular reconstructions of which 90% relied on fibula flaps. The success rate reached 100%, while confirming bony union in 97% of cases and installing osseointegrated dental implants in 20% of cases. Corderio et al. concluded that the fibula should be the first choice for most cases, particularly those requiring multiple osteotomies. The authors estimated that the length of useful bone reached 25 cm allowing for the reconstruction of very long segments. Furthermore, the skin island was reliable in 90% of cases. In their discussion, they concluded that large soft tissue defects are not the primary indication for a fibular graft. The mean length of the pedicle stood at 8 cm, although longer lengths could be achieved by stripping the bone periost and harvesting more distally. Donor site morbidity for the fibula was considered low, although the authors provided no data on this. In CT evaluations of the fibula, bone measurements reached on average 35.6 cm among men and 34.2 cm among women.<sup>142</sup> In general, donor site morbidity remains low.<sup>128</sup> Yet, some important variations in arterial supply to the lower leg, including both main arteries and local factors, lead to the loss of cutaneous islands.

In a 2015 review by Abou-Foul,<sup>142</sup> 5 730 limbs were analysed. A dominant peroneal artery was found in 5.2% of cases, thus precluding the use of the fibula flap. Variants consisting of the hypo- or aplastic posterior tibial artery (3.3%), the hypoplastic anterior tibial artery (1.5%) and peroneal arteria magna (0.4%) were found in the limbs analysed. The author concluded that clinical examination alone may be insufficient, recommending preoperative imaging as well. Using a contrast-enhanced CT may also assist in localising the cutaneous perforators of the skin island. By contrast, in a 1999 prospective study of 120 patients by Lutz et al.,<sup>143</sup> the authors concluded that routine angiography is not mandatory in the precence of a normal palpable or Doppler US–verified distal pulse. All patients with an abnormal arterial anatomy also presented with an aberrant distal pulse.

In 1998, Urken et al.<sup>144</sup> also published a report on 210 patients, 46 of whom underwent fibula flap reconstructions. The fibula became more popular towards the end of that study at the expense of DCIA. They reported that 81 patients underwent a total of 360 osseointegrated dental implants with a 92% success rate. Irradiation postoperatively lowered the rate to 86%, while implants installed in previously irradiated bone had a success rate of 64%. The fibula was recommended in total or subtotal mandibular reconstructions among bone only cases, atrophic mandibles, condylar reconstructions and among paediatric patients. Absent cutaneous perforators were documented in 9% of fibula cutaneous islands.

Later, in 2012, Garvey et al.<sup>145</sup> showed that 94.5% of perforators were found upon CT, and, among 40 patients, 25% had modified skin islands designed based on this finding while 2 patients had hypoplatic tibial vessels precluding a fibula flap. Ling et

al.<sup>146</sup> published a review of donor site morbidity based on 42 studies. Among early complications, 7% experienced wound dehiscence, 7.3% reported wound necrosis and a total of 17.4% experienced delayed wound healing including skin graft complications. Among late donor site complications, 6.5% reported chronic pain, 3.9% reported gait abnormality, 5.8% experienced ankle instability and 11.5% reported a limited range of motion. In this review, no serious complications such as ischemia were reported.

In a 2014 quality-of-life study by Moubayed et al.,<sup>147</sup> patients undergoing reconstructions using the fibula had the most favourable outcomes, keeping in mind that scapula reconstructions tend to be larger through-and-through resections.

#### 3.4.2.2 Iliac crest flap

The iliac crest osteomusculocutaneous or deep circumflex iliac artery (DCIA) flap was the first composite flap applied in large series. The bone is thick and has a natural anatomic curvature well-suited for angular and corpus defects of the mandible. The iliac crest is also well-suited for postoperative osseointegrated dental implantation aimed at restoring dentition. The primary drawbacks consist of the variable and short vascular pedicle, the thick and unreliable skin island and donor site morbidity including pain, a possibly altered gait and the risk of hernia.

In 1979, Taylor<sup>148</sup> conducted a vascular study of the groin flap resulting in the presentation of DCIA and osteomuscular iliac crest flaps. The same author also recently published a review of the history and evolution of these procedures.<sup>149</sup> The majority of iliac crest flaps are based on DCIA, which measures between 1 and 3 mm at its origin at the iliac artery and provides an ascending branch with its musculocutaneous blood supply to the skin island in 67% of cases. Comparing the time until bony union for osteotomies, DCIA requires less time than the fibula. In a study of 267 reconstructed mandibles and 19 maxillae, Taylor identified several advantages. Various designs can be obtained using the curved form of the iliac bone. For instance, the head of the mandible can be constructed from the anterior inferior iliac spine. Furthermore, the flap matches the height of the mandible with an ideal bone height for osseointegration. Likewise, sufficient bone is available to reach the opposite angle of the jaw with a single osteotomy at the chin. In addition, rapid union of the osteotomy is achieved, while cancellous bone tends to granulate and heal if exposed intraorally. In a long-term follow-up study, the iliac crest also retained its original shape, trabeculation and body height. The iliac crest flap's drawbacks include the bulky skin flap for intraoral use, the risk of abdominal hernias, transient damage to the lateral cutaneous femoral nerve, the more challenging dissection required compared with the fibula and the partially unreliable anterior segment of the skin island.

In 1989, Urken et al.<sup>150</sup> reported on 20 mandibular reconstructions using DCIA. They favoured the use of the iliac crest in mandibular reconstructions because of the natural curved form and bone length. They concluded that donor site morbidity was minor in the long term. In a subsequent study in 1998, Urken et al.<sup>144</sup> reported on 210 patients all reconstructed using DCIA (n = 137), fibula (n = 46) or scapula (n = 27) flaps, with an additional 30 cases involving double free flaps between 1987 and 1997. The fibula emerged as the most popular technique by the end of the study at the expense of DCIA. In total, 81 patients underwent a total of 360 osseointegrated

dental implants with a 92% success rate. Irradiation postoperatively lowered this rate to 86% and implants installed in previously irradiated bone carried a success rate of 64%. The authors discussed the implant success and safety of installing them during the primary operation. Radiation therapy is typically administered six weeks after surgery, with the detrimental effect to the bone achieved by the end of therapy another six weeks later. A three-month period is thus available for osseointegration, a time period considered sufficient. A total of 16 repeat explorations of the microsurgical vessels were required, half of which proved successful resulting in an overall success rate of 96% for the flaps. The DCIA bone was considered most wellsuited for mandibular reconstructions and favoured for lateral defects. Furthermore, the authors reported only one partially lost skin island in the DCIA group. The fibula was recommended in total or subtotal mandibular reconstructions, bone only cases, atrophic mandibles, condylar reconstructions and among paediatric patients. The scapula was recommended for large soft tissue defects, cases involving facial reanimation resulting from resected facial muscles and in patients with existing gait disturbances. The bone of the scapula was judged as possibly unsuitable for dental implants. Flap-specific results and donor sitespecific results were only briefly discussed and no statistical analyses or conclusions were presented.

Hanasono<sup>61</sup> recently reviewed DCIA against other commonly used options. While DCIA stood as the most popular option at the beginning of microvascular osseous mandibular repair, other options emerged as more favourable. In addition, DCIA is omitted from several classifications and reconstructon algorithms presented in the above sections. In a comparison of the fibula and scapula, donor site morbidity was highest in DCIA. The DCIA vessels emerged as the least reliable, while the pedicle emerged as the shortest. Furthermore, the cutaneous island was ranked as the lowest. In a quality-of-life analysis comparing several microvascular flaps completed by Moubayed et al.,<sup>147</sup> DCIA ranked third and fourth.

#### 3.4.2.3 Scapula flap

The scapula flap is a versatile flap with wide possibilities for reconstruction. The lateral margin of the scapula includes two different vascular pedicles—one marginal and one angular. These connect to the same subscapular trunk yielding branches to two separate skin islands via the vertical parascapula and the horizontal scapula flap, as well as muscular branches to the LD and serratus muscles. The relatively consistent pedicles allow for harvesting of a chimeric composite flap with possibilities for osteotomising the bone into two pieces with an associated muscle flap and a separate skin island mobile relative to the osseous flap. The flap is thus well-suited for the largest soft tissue defects. Its drawbacks include a maximum length of 14 cm while the thin membranous brittle bone is typically considered inferior to the fibula and the iliac crest flap. Donor site morbidity is low, although harvesting requires repositioning of the patient. Nevertheless, the scapula is used for lateral mandibular reconstruction with success in many centres. Dental implantation relying on a scapula flap has also enjoyed success.<sup>58,59,68,69,125,141,151,152</sup>

The scapula flap represents a versatile option featuring freely movable osseous, cutaneous and muscular components, and thus suits complex reconstructions in need of a larger soft tissue replacement. Teot et al. first described the vascularity in the scapular system, while, in 1982, Gilbert and Teot<sup>153</sup> described the free scapula

flap. In 1984, dos Santos<sup>154</sup> provided a thorough analysis of the flap, while, in 1986, Swartz<sup>155</sup> described the scapula in maxillofacial reconstructions. The subscapular artery originates from the axillary artery and is divided into two major vessels—the circumflex scapular (CFS) artery and the thoracodorsal artery (TDA). This allows for the construction of several different flaps from the same vessels. From the CFS artery, the lateral scapular osseous flap, we can establish parascapular as well as scapular cutaneous islands. From TDA, we can establish the LD muscle, serratus muscle as well as the angular tip and medial border of the scapula bone.

In 1990, Sullivan et al.<sup>156</sup> reported outcomes from 31 osteocutaneous scapula flaps and 5 cutaneous flaps. All flaps included the latissimus. In total, 30 osteocutenous flaps resulted in mandibular reconstruction. Furthermore, 15 patients were previously irradiated. The flap was harvested with the patient in the lateral position. The length of the transferred bone ranged from 8 cm to 14.5 cm, while wedge osteotomies were performed with minimal stripping of the periosteum. In addition, the teres muscles were reattached to the remaining scapula during closure. The authors reported a 100% success rate for cutaneous flaps and 90% for osteocutaneous flaps, two of which involved arterial thromboses and one resulting in venous thrombosis. All but two patients showed solid bony unions. Moreover, two patients had minor fistulas that resolved spontaneously and one needed treatment for a fistula. All patients considered their shoulder functionally adequate at six months postoperatively. The authors concluded that the scapula has a very predictable anatomy, and proposed the possibility of harvesting the flap using a two-team approach. In addition, the vessels are 'macrovascular' with a diameter of 2.5 mm to 4.0 mm and a pedicle length of 7 cm to 10 cm. Finally, the authors concluded that the properties of the scapula render it ideal for mandibular reconstruction. The bone is relatively easy to shape and features better handling than DCIA. Thus, they planned to install dental implants in the scapula flap during a secondary operation.

In 1997, Shimizu et al.<sup>157</sup> completed a clinicoanatomical study of 42 Japanese cadavers. They classified arterial supply as falling within two types: Type 1 indicated the subscapular arising from the axillary artery branching into circumflex scapular and thoracodorsal arteries; Type 2 indicated that circumflex scapular and thoracodorsal arteries arose separately directly from the axillary artery with the subscapular artery absent. They also classified veins. Type 1 represented a common trunk vein, where the thoracodorsal vein and the circumflex scapular vein join the subscapular vein. Type 2 involved two circumflex scapular veins and a thoracodorsal vein joining to form the subscapular vein. Another subclass indicated that the circumflex scapular vein and thoracodorsal vein directly ended separately at the axillary vein without a subscapular vein. These were classified as 'M' or 'L' depending on the medial or lateral entrance of the circumflex scapular vein with respect to the thoracodorsal vein. The common Type 1 trunk accounted for 95% of the arterial anatomies and 27% of the vein anatomies. Type 2 appeared more common in the vein anatomy, representing 62% of anatomies. The authors found a direct two-vessel system to the axillary vessels in 5% of arteries (subclass M) and 11% of veins (6% subclass M and 5% subclass L). The length of Type 1 vessels reached 93 mm for arteries and 91 mm for veins. In direct type anatomies, lengths reached 95 mm for arteries and 71 mm for veins. The authors also analysed the length of the scapular graft as well as the shape and volume of the lateral border. They found that the maximal length of a usable graft from the tip to the glenoid

border reached 133 mm  $\pm$  9 mm. The thickness of the bone reached 9 mm  $\pm$  2 mm near the tip and 11 mm or 12 mm  $\pm$  2 mm along the mid- and cranial points, respectively, of the scapular graft. The width of the graft along the mediolateral position *in vivo* reached 20 mm  $\pm$  3 mm, 10 mm  $\pm$  2 mm and 28 mm  $\pm$  7 mm measured at the superior third, mid-third and inferior third, respectively, of the lateral scapular bone.

In 2000, Uglesic et al.<sup>158</sup> presented the results of maxillary resections including the orbit on 27 patients reconstructed using the subscapular system. One flap was lost. They found that the pedicle reached up to 20 cm, and the scapula flap performed excellently in maxillary reconstructions. The scapula flap thus carries several advantages in complex reconstructions for both mandibular and maxillary defects as Brown et al.<sup>159</sup> discussed. The authors reported a good reliability for the flap, the highest for all composite flaps, reporting no flap losses in their series of 46 patients. In addition, its favourability is strengthened given the possibility of osteotomies and the relatively minor indications of atherosclerotic disease in the pedicle.

In 2009, Brown et al.<sup>159</sup> published their indications for scapular reconstructions among 46 patients. They favoured the scapula because of its reliability, the functional outcomes and minimal donor site morbidity. The best option for the scapula involves an extensive resection of the mandible, including the floor of the mouth and the tongue, requiring large soft tissue reconstruction in a functionally important area. Furthermore, scapula use in patients with doubtful vascularity of the fibula is worthwhile. The angular scapula flap in the reconstruction of radical maxillectomies proved particularly useful. In addition, the authors reported no total flap losses or nonunions. Using the lateral scapular border also offered additional possibilities for safe osteotomies. Furthermore, the skin island proved better when the ipsilateral side was used intraorally and the contralateral scapula was used for extraoral use. The subscapular vein was aberrant in 12% of cases, where the circumflex vein directly drained into the axillary vein, while the corresponding arterial variant was found in 4% of cases. Shimizu et al.<sup>157</sup> also presented similar findings as discussed above.

In a 2010 study, Chepaha et al.<sup>160</sup> summarised their findings from midface and maxillary reconstructions in 20 patients using the TDA scapular tip flap. They reported a 100% success rate and a very long pedicle. The bone used was small, with a mean length of 5.2 cm (range 2.5 cm to 9.0 cm) with a cutaneous island of 68 cm<sup>2</sup> (range 20 cm<sup>2</sup> to 250 cm<sup>2</sup>). They assessed shoulder function with a mean value of 87/100 and found a low rate of donor site morbidity.

Hasan et al.<sup>161</sup> presented their analyses of 42 scapula flaps in reconstructions on 41 patients in 2013. In total, their analysis consisted of 24 mandibular, 13 maxillary and 5 calvarial reconstructions. They also discussed the rationale for not using the scapula as reported by several authors. This rationale included the need to reposition the patient, its unsuitability for dental implants, the short pedicle and better familiarity with other flaps, and weighed these against other findings and published results. In particular, they favoured the scapular tip in the reconstruction of an entire maxilla with the palate. They also performed closing-wedge osteotomies in the scapula bone, especially when using both pedicles. They also presented an algorithm for the use of various options for the subscapular system. The authors concluded that the scapula flap provides an unparalleled range of options with

minimal donor site morbidity, and should be used in patients with comorbidities that may contraindicate the use of the fibula.

Thus, if dental implants are considered, they prefer the fibula or DCIA. As they point out, scapula CT scan will, however, reveal the amount of scapula bone available.

Finally, Clark et al.<sup>162</sup> studied donor site morbidity in their series of maxillary reconstructions using the scapular angle flap. They used the Disabilities of the Arm, Shoulder and Hand (DASH) questionnaire to examine shoulder and upper-limb morbidity in 14 patients. They calculated a mean score postoperatively of 10.6 (median 13), falling within the normal range for the reference group. All patients reported a full range of shoulder movement six months after reconstruction. They also reported a pedicle length reaching 20 cm, as well as osseal similarities between the scapular tip and the native maxilla.

From the above discussion of the literature, it is found that the scapula flap is recommended for complex restorations with extensive soft tissue needs as well as in palatal and maxillary reconstructions.

#### 3.4.2.4 Other free osseal flaps Radial bone flap

The osteocutaneous radial flap is considered one of the most common reconstruction options alongside those described above, and is included in several classifications and algorithms for oral reconstruction. The radial free flap evolved from the 'Chinese' flap described by Muhlbauer in 1982,<sup>129</sup> and was used as an osseous flap in oral reconstructions by Soutar et al.<sup>163,164</sup>

In 1999, Thoma et al.<sup>165</sup> presented a large study of 60 patients reconstructed using the radial osteocutaneous flap. In that study, they used the flap in 97% of oncological cases necessitating mandibular reconstructions, treating both lateral and anterior osseous defects. The mean bone length reached 9.4 cm (range 5 cm to 14 cm), with a microvascular success rate of 98.3%. Complications included fractures of the donor radius in 15% of cases and nonunion of the mandible in 5% of cases. The authors recommended the free radial osteocutaneous flap as a safe and reliable option for mandibular reconstruction, finding that it offered sufficient bone for reconstructing large defects. In particular, they noted a pedicle length offering the possibility of anastomosis to the contralateral neck.

In 2003, Villaret and Futran<sup>166</sup> published a review and their own study of 34 patients reconstructed using the radial bone flap, involving 7 maxillary and 27 lateral mandible reconstructions. During a follow-up period of 10 to 54 months, they reported no flap losses and no fractures along the donor site. In their method 40% of the available radius was harvested. In their study, they used rigid fixation by volar plating with 2.4-mm locking plates along the donor area. The most common complication was oral cutaneous fistula formation, reported in 14% of cases, all of which received a curative dose of radiotherapy and healed without operative treatment. The primary limitation reported including the amount of bone available. The authors did not mention osteotomies of the bone, concluding that the flap
superceeds plating and soft tissue reconstruction only in the lateral or posterior mandible.

Cordeiro et al.<sup>167</sup> reported on two patients with bilateral subtotal maxillectomy defects, where both the palate and maxillary arch were resected and reconstructed using the osteocutaneous radial flap. The bone was successfully osteotomised and contoured to recreate the maxillary arch, and the skin island was folded around the bone and used to reconstruct the palatal and nasal defect.

#### Metatarsal bone flap

The transfer of the metatarsal bone—typically the second metatarsal—has primarily been used in the reconstruction of the condyle of the mandible. As early as 1958, Entin<sup>168</sup> reported on four patients with hemifacial microsomia, in whom the rudimentary condyle was successfully reconstructed using the fifth metatarsal bone. Later, in 1964, Dingman et al.<sup>169</sup> described a bilateral reconstruction using fifth metatarsal bone grafts—not vascularised flaps—to correct an anterior open bite caused by a condylotomy performed previously. The patient was followed for 17 months, and the radiological evaluation showed no resorption while the occlusion remained stable.

In a 2002 paper by Vilkki et al.,<sup>170</sup> additional methods were discussed, including the use of costochondral grafts associated with asymmetry, over- or undergrowth as well as ankylosis and pseudoarthrosis. The authors presented the results from a first reconstruction consisting of a free microvascular second metatarsal reconstruction of the condyle on a 4-year-old Goldenhar patient. Surgery proved successful, and the patient left the hospital walking on the donor foot on the fifth day postoperatively, the symmetry was largely corrected and the mouth opening was 4 cm without deviation. Furthermore, no chewing restriction was observed at two months postoperatively. The author of this thesis augmented the soft tissues 12 years later in this patient, and the metatarsal graft had grown with the patient (personal communication, unpublished data).

Vascular variations in the dorsalis pedis arterial tree affecting the use of the second metatarsal were reported in a large anatomical review and specimen study by Kim et al.<sup>171</sup> They concluded that the second metatarsal features reliable vascularisation, making use of all regions of the bone. The bone was deemed suitable for defects of up to 8 cm and the skin island could reach areas up to 10 cm by 14 cm. The bone was also considered a viable host for dental osseointegrated implants.

Potter et al.<sup>172</sup> discussed the vascular options for mandibular condyle reconstruction. The complexity of the MT2 dissection renders it more difficult than the fibula. Published results remain quite limited. However, patients with foot trauma and peripheral vascular disease represent poor candidates for this reconstruction option.

#### Rib graft flap

The ribs have been used in mandibular reconstructions for some time already. In 1975, Ostrup et al.<sup>173</sup> published their experimental work on the microvaslular transfer of the rib in radiated mandibular reconstructions in dogs. They used the

posterior intercostal vessels and recipient anastomoses were completed on the lingual vessels. In this study, five of nine transfers were successful. In 1976 and 1978, Serafin et al.<sup>174,175</sup> described a series of 69 microvascular reconstructions, 23 of which involved the head and neck region including two composite rib grafts to the mandible. All 23 transfers were successful. Four more microvascular ribs were used in other locations. Futhermore, Harashina et al.<sup>176</sup> documented two successful free rib transfers to the mandibles of cancer patients.

In 1992, Guyuron<sup>177</sup> discussed the unpredictable growth of costal grafts, which may involve under- as well as overgrowth of the rib. Recurrence of ancylosis along the joint may also prove problematic. Guyuron recommended including sufficient cartilage in the graft, using the fourth or fifth rib, placing soft tissue in the glenoid fossa and postponing corrective osteotomies until growth is completed. Using the rib was also recommended only in patients with severe defects.

In a large series published by Takushima<sup>60</sup> in 2001, 178 microvascular cases were analysed, 11 of which involved free ribs. The results, which included donor and recipient site complications, described rates comparable to other flap options and indicated better results than DCIA. The microvascular rib option, however, was omitted from their classification and reconstruction algorithm. In a 40-year review of microsurgical bone transfers carried out by Taylor et al.,<sup>149</sup> only one rib transfer was completed compared to 383 other bone flaps. Publications on rib-bone transfers have declined. In fact, the use of microvacular rib flaps is considered a rarity today.

#### 3.4.3 Tissue engineering in maxillomandibular reconstructions

The most studied bone engineering tool consists of recombinant human bone morphogenetic protein-2 (BMP-2). Mandibular defects due to benign conditions have been reconstructed using a collagen carrier with BMP-2<sup>178</sup> and allogenic bone with BMP-2 and platelet-rich plasma yielding good results. These results held even for successful maturation of an erupting tooth in the area.<sup>179</sup> In addition, rib grafts were used as a carrier for BMP-2.<sup>30</sup> However, *in vivo* studies of the adverse effects in oral cancer cells using BMP-2 raised concerns regarding its safe use in cases of malignancies.<sup>180</sup>

#### 3.4.4 Stem cells in maxillomandibular reconstructions

The use of stem cells and growth factors in the reconstruction of large resections, primarily due to benign conditions, appears promising. Adipose stem cells have primarily been used in addition to tricalcium phosphate granules and recombinant human BMP-2. At Helsinki University Hospital, a complete maxillary reconstruction was performed by Mesimäki et al.<sup>181</sup> using this method and incorporating it into a titanium mesh. The ectopic bone was regenerated by implanting the synthetic neomaxilla in the rectus abdominis muscle, and subseuqently transferred to the maxillary defect. Sandor et al.<sup>182</sup> also documented a successful reconstruction of a 10-cm full defect of the mandible using adipose stem cells, tricalcium phosphate granules and recombinant human BMP-2 without ectopic bone maturation. After a 10-month maturation, dental implants were installed and bone formation was confirmed.

#### 3.4.5 Face transplant

Partial and complete face transplants have been conduced since 2005, the first of which was performed in France.<sup>183</sup> This treatment modality remains reserved for the most difficult defects, where no other options exist. In the last decade, we have witnessed rapid development in the field of facial vascularised composite allotransplantation with promising functional, aesthetic and psychological outcomes. A facial transplant represents the only reconstruction option available to successfully replace lost or severely damaged central facial features, such as oral commissure, the maxilla, the nose and evelids, since functional outcomes using conventional reconstruction techniques invariably fall short. The primary indication for a facial transplate involves traumatic avulsive defects, including both mandibular and maxillary reconstructions. Patient selection is critical, where the decision is always delicate and individual. To date, at least 38 facial transplantations (including Finland's first case) have been performed globally. This modality remains experimental, although early results appear promising.<sup>184-186</sup> Factors complicating this method include life-long medication with immunosuppressives and accompanying adverse affects, including secondary malignancies.187

#### 3.5 3D planning and 3D printing in maxillomandibular reconstructions

The emergence of 3D imaging and planning was first described by Mankovich et al.<sup>188</sup> in 1990. MSCT forms the basis of accurate planning and manufacturing today.<sup>189</sup> Methods including computer-assisted design and manufacturing (CAD/CAM) have enjoyed wide use in orthognathic planning and surgery as well as in the reconstruction of orbital defects.<sup>190-192</sup> In a Helsinki study by Suomalainen et al.,<sup>193</sup> 114 models from 102 patients were described. Among these, 29% were performed due to malignant disease. The majority of the models were examined using MSCT, as well as successfully using cone-beam CT (CBCT). The primary benefit of the model consisted of treatment planning, while the method also proved effective in the intraoperative setting. In addition, 3D digital imaging and printing of soft tissue produces patient-specific restoration for facial transplant donors.<sup>194</sup> The benefits in producing preoperatively patient-specific osteotomy guides and patient-specific plates are obvious.<sup>195</sup>

# Figure 2. Images of the 3D planning and manufacture of a fibular osseous reconstruction of a maxillary defect.

Patient-specific titanium plates. The arched plate from the base of the nose to the premaxilla serves as a guide plate not implanted in the patient. Patient underwent surgery in Helsinki in 2015 performed by Mesimäki, Lassus and Wilkman (unpublished data).



3.6 Classification of surgical complications and risks

Comparing results and complications in scientific settings requires measurable parameters. Minor complications treated at bedside or through medication may increase treatment costs. But major wound- or flap-related complications affect overall patient outcomes by delaying recovery and postponing oncological treatment. Comparing the severity of undesired events across various methods and hospitals requires standardised and reproducible parameters.

As such, the Clavien–Dindo classification of surgical complications represents the most-cited system used in the literature. Clavien's<sup>196</sup> first classification, published in 1992, used cholecystectomy as the model. Here, a four-level grading system was described:

- Grade I: Deviation from an ideal postoperative course, non-life-threatening and with no lasting disability. Necessitates bedside procedures only and no significant extension to the hospital stay.
- Grade II: Potentially life-threatening, but no long-term disability. Extension to the hospital stay to more than twice the median. Subclass IIa: only medication needed. Subclass IIb: invasive procedure needed
- Grade III: Complications causing a residual disability or persistent lifethreatening conditions.
- Grade IV: Death resulting from complications.

In 2004, Dindo<sup>197</sup> introduced a new classification based on a survey of 6 336 patients from 10 centres worldwide. After refining Clavien's original classification, the new system consisted of five classes:

- Grade I: Any deviation from normal not necessitating invasive treatment. Bedside treatment of wound allowed.
- Grade II: Complication requiring more extensive pharmacological treatment, blood transfusions or parenteral nutrition.
- Grade III: Surgical, endoscopic or radiological intervention needed. Subclass IIIa: general anesthesia not required. Subclass IIIb: general anesthesia required.
- Grade IV: Life-threatening complication. Subclass IVa: single organ failure, including dialysis. Subclass IVb: multiorgan failure.
- Grade V: Death resulting from complications.
- A 'd' suffix is added to any grade for disability if a patient suffers from a complication at discharge from hospital.

In their publication, the reproducibility and reliability across different centres was analysed, whereby they found a statistically significant correlation for the grouping of complications. They showed that the classification system correlated with the length of hospital stay for all types of surgeries analysed. The types of surgeries analysed consisted of bowel and general surgerical procedures.

In 2014, Monterio et al.<sup>198</sup> assessed this classification for complications in head and neck surgeries. Head and neck surgery carries its own specific needs and complications, which may differ in severity from those previously presented. Two surveys covering five hypothetical patient scenarios analysed by head and neck surgeons as well as trainees revealed interobserver reliability scores ranging from moderate to high. In general, the classification proved appropriate and useful. In addition, 371 microvascular reconstruction patients were studied and the respective complications and 41% consisted of medical complications. The length of hospital stay again correlated well with the grade recorded. The authors concluded by recommending the use of the Clavien–Dindo system, which proved adequate, with a high level of validity and reliability as well as general acceptability among clinicians. The development of a specific grading system for head and neck surgery would further significantly improve the classification.

In 2015, Awad et al.<sup>199</sup> published an individualised estimation for postoperative complications after surgery for oral cancer. They studied 506 patients with oral cancer with the objective of developing a statistical tool to predict the risk of an individual patient developing a major complication following tumour surgery. The endpoint in their study was complications indicative of Clavien–Dindo grades III to V. They presented a nomogram predicting the risk of major complications with a concordance index of 0.79 (high). In total, 36 pre- and perioperative parameters were included in the nomogram, which were subsequently reduced from the model based on the predictive value obtained. The preoperative parameters predicting major complications included a low body mass index (BMI), high Washington University Head and Neck Comorbidity Index (WUHNCI) score,<sup>200</sup> high white

blood cell count, low haematocrit value and planned neck dissection and/or tracheostomy. Postoperative factors predicting Clavie–Dindo grade III to V complications included those listed above excluding BMI and including the duration of anesthesia.

In 1987, Charlson et al.<sup>201</sup> introduced the Charlson Comorbidity Index (CCI) score. Their study aimed to develop a method for classifying comorbidities affecting mortality risk. They developed a weighted index taking into account the number and seriousness of the comorbid disease using 559 general medical patients. Myocardial infarction, congestive heart failure, peripheral vascular disease, dementia, lung disease, peptic ulcer, mild liver disease and diabetes all scored one point. Hemiplegia, moderate renal disease, diabetes with organ damage, any tumour within five years, lymphoma and leukaemia scored two points each, while moderate to severe liver failure scored three points and a metastatic solid tumour and AIDS scored five points. The age of the patient yielded one point per decade once over the age of 50 resulting in an age-adjusted CCI. In the original study, the mortality rates were 12% for a score of 0, 26% for scores of 1 to 2, 52% for scores of 3 to 4 and 85% for scores <5. The CCI scores predicted the risk of death in 685 other patients during a ten-year follow-up period with similar results. With each increase in the CCI score, mortality increases. In this thesis, an electronic version of CCI was used to score patient comorbidities.

In 2002, Piccirillo et al.<sup>200</sup> described the Washington University Head and Neck Comorbidity Index (WUHNCI) study, which aimed to determine the prognostic impact of comorbid conditions specifically in head and neck cancer patients. This served as an improvement from the general medical use of CCI published earlier. In total, 1 153 patients with oral SSC were included in this study. An 132-item comorbidity form was used to record the data initially, excluding rare (<1%) conditions. A serial cross-tabulation of preoperative factors and five-year survival was performed and significant parameters were identified. The significant parameters predicting the worst outcomes included an older age, being black, severe symptoms, a high TNM stage and low differentiation of the tumour grade. Gender, smoking and initial type of treatment did not affect survival. Comorbid factors related to unfavorable outcomes consisted of pulmonary disease, peripheral vascular disease, cardiac arrhythmia and congestive heart disease, renal disease and other uncontrolled cancer. The risk ratios (RRs) were highest for renal disease (9.62) and other cancer (4.49).

The WUHNCI score includes seven comorbid conditions, incluing those listed above and other controlled cancer with weighted points ranging from 1 to 4. In the clinical analysis of patient five-year survival, a score of 0 yielded 53% five-year survival, a score of 1 yielded 43%, 29% for a score of 2 and 26% for a score of 3. The maximum score in the study was 9, and no patients with a score higher than 7 survived for five years.

In 2016, Las et al.<sup>173</sup> analysed 1 530 free flaps in 1 274 patients undergoing breast, head and neck as well as extremity reconstructions between 1992 and 2012. They analysed general as well as local risk factors. Across the hospitals included in their study, roughly 20 flaps were performed per year in 1993 peaking at over 200 annually in 2012. Flap failure remained constant, at roughly 10% with a linear declining trend. The total number of head and neck free flaps reached 459 (36.8%).

Among these, the total flap loss rate stood at 6.4% while partial losses reached 4.6%. Pulmonary comorbidity (odds ratio (OR) 4.47) and anastomosis to the lingual vein (OR 7.17, for only six cases) were independent risk factors for partial flap loss. An anastomosis to the superficial temporal artery (OR 4.4) and postoperative flap circulation problems (OR 11.23) remained independent risk factors for total flap failures.

## 4 Aims of the study

The objective of this study was to evaluate the methods used in the reconstructive surgery of maxillomandibular defects and to analyse the outcomes for the most commonly used tissue options.

The specific aims were as follows.

- I. To identify the properties of and possibilities for the scapular osteomyocutaneous flap in the reconstruction of maxillomandibular defects.
- II. To determine whether clinical differences exist among patients reconstructed with scapula, fibula or iliac crest osseal free flaps regarding results, complications, donor site morbidities as well as perioperative and postoperative outcomes.
- III. To identify any differences in the long-term resorption or remodelling of the three most frequently used flaps—the iliac crest, the fibula and the scapula—in mandibular reconstruction.
- IV. To determine the usability of the pedicled LD musculocutaneous flap in head and neck reconstructions in patients with comorbidities or palliative indications who are unsuitable for microvascular reconstruction.

## **5 Patients**

#### 5.1 Helsinki head and neck tumour board

This study, approved by the Research Ethics Board of the Helsinki University Hospital, consisted of patients who underwent microvascular free- or pediculartissue reconstructive surgery in the facial and neck regions with a focus on mandibular and maxillary reconstructions. Patients were operated on in the Department of Plastic Surgery and the Department of Maxillofacial Surgery at Helsinki University Hospital, Helsinki, Finland from 2000 through 2013. We estimated our study would include 200 patients, and included all consecutive cases. All patients were routinely assessed pre- and postoperatively during a weekly multidisciplinary meeting that included ORL surgeons, plastic surgeons, oral- and maxillofacial surgeons, head and neck pathologists and radiologists. Each year, the multidisciplinary head and neck tumour board at the Helsinki University Hospital assesses approximately 520 patients pre- and post-operatively.

#### <u>5.2 Study I</u>

Between 2006 and 2013, 718 patients presented with a defect requiring microvascular reconstruction, 119 including an osseous component.

The scapular osteomyocutaneous flap was analysed in the reconstruction of 34 patients (22 men and 12 women), with a median age of 62 (range 39–78 years). All patients had malignant disease, and all but two presented with Stage IV disease while none had distant metastases. In addition, 13 patients had a history of previous microvascular reconstruction and radiation therapy with curative intent. We performed 26 mandibular, 6 maxillary and 2 orbital reconstructions.

Scapular reconstructions	Mandibla	Mavilla	Orbit	Total
n	26	6	2	34
Gender M / F		Ŭ	-	22 / 12
Age, in years				62 (39-78)
(range)				

Table 3. Patient data for Study I

#### 5.3 Study II

Between 2000 and 2012, a total of 163 patients requiring reconstruction of a maxillomandibular defect received either a scapular, fibular or DCIA osseous reconstruction in the Helsinki University Hospital's Department of Plastic Surgery and the Department of Oral and Maxillofacial Surgery. These patients were analysed regarding the reconstruction results, flap-specific complications, donor site morbidities as well as perioperative and postoperative outcomes. In total, we studied 92 DCIA, 42 scapula and 29 fibula flaps, performed on 105 men and 58 women. The reconstruction sites included 119 mandibles, 39 maxillas and 4 orbits.

	All	DCIA	Scapula	Fibula
n	163	92	42	29
Male / Female	105 / 58	62 / 30	26 / 16	17 / 12
Age, in years (range)	60 (17-89)	60 (17-89)	62 (33-78)	59 (20-87)
Malignancy	149	87	41	21

Table 4. Patient data for Study II

## 5.4 Study III

For Study III, we analysed the osseous segment of the reconstruction in 186 consecutive patients reconstructed with scapular, fibular or DCIA free osseous microvascular flaps between 2001 and 2013 in the Department of Plastic Surgery and the Department of Oral and Maxillofacial Surgery at Helsinki University Hospital. We included only mandibular reconstructions in our analysis to obtain equivalent material. The orientation of the osseal reconstruction and mechanical properties differs in maxillary and orbital reconstructions and were thus excluded.

We followed patients clinically and through imaging using MSCT with volume analyses of the bone.

## Figure 3. Patient data for Study III



#### 5.5 Study IV

In this study, ten consecutive patients were reconstructed using the pedicleled LD flap between 2008 and 2011 in the Department of Plastic Surgery at Helsinki University Hospital. The median patient age was 65 years (range 47–82 years), consisting of six men and four women. Five patients had oral cancer with mandibular invasion, two had laryngeal carcinoma requiring a laryngopharyngectomy, two had extensive neck metastasis of cutanous or unknown origin and one patient with tongue cancer underwent a complete glossectomy. All patients had severe comorbidities considered contraindicative for microvascular surgery. Among these patients, oncological therapy was also precluded leaving surgery as the only option.

	All
n	10
Male / Female	6 / 4
Age, in years (range)	65 (47-82)
Malignancy	10

## Table 5. Patient data for Study IV

## 6 Methods

#### 6.1 Data collection

In this retrospective study, we collected data from patient hospital records, including medical records, operative, anestesiological and intensive care unit (ICU) reports, laboratory database records, histopathological classifications and radiological database reports. We included the following parameters: running identification number, age, sex, smoking habits, general diseases, classification of tumour or trauma, type and width of resection or defect, reconstruction method, duration of the operation, blood loss intraoperatively, immediate complications and repeat operations (hereafter reoperatons) as well as later complications along both the donor and recipient sites, adjuvant oncological treatments, follow-up data including assessment of bone consolidation, volume, height and width as well as postoperative dental implantation. Follow-up also included evaluation of nutritional needs, possibility of oral feeding and estimate of speech ability. We routinely completed MRI and MSCT scans pre- and postoperatively according to the follow-up protocol.

In this study, we gathered relevant pre-, peri- and postoperative patient data, bone measurements from MSCTs and a volumetric analysis of the properties of the bone, and statistically analysed the data on operative results and complications.

#### 6.2 Methods, analyses and statistical methods

#### <u>6.2.1 Study I</u>

In total, we analysied 34 patients reconstructed using the scapula flap. In particular, we examined the following variables: age, sex, general disease, primary disease and classification, area of resection, size of the osseal flap, number of osteotomies in the flap, vascular pedicle used, skin island and muscle use, perioperative parameters (duration of the surgery and bleeding), primary flap-related and general complications, donor site complications (early and late), duration of hospital stay as well as ICU stay, details on speech ability and oral feeding, postoperative osseal consolidation of the osteotomies, placement and success of osseointegrated dental implants, pre- and postoperative oncological treatment and follow-up data on disease-specific and overall survival.

The surgical technique described the semidecubitus positioning of the patient, the rise of the flap using various vascular pedicles, the performance of the osteotomies and the reconstructive plating method. The majority of the patients underwent surgery through a two-team approach with the patient in a tilted decubitus position enabling simultaneous tumour resection and elevation of the flap. Patients undergoing bilateral resections and neck dissections were operated on in the supine position. The lateral and medial borders of the latissimus muscle were first mobilised allowing exposure to the scapula. The thoracodorsal, circumflex scapulae and angular branch of the serratus vessels were dissected and the osteotomy region of the bone was identified. Then, the muscles attached to the scapular transfer were cleared from the bone with a small muscle cuff. The osseal pedicle was based on either the CFS artery or the angular branch of the vessel or both. Open-wedge osteotomies, which leave intact the lateral scapular margin with its muscle cuff and an intact periosteum on the lateral side, were performed for part of the flap if

needed. Based on the planning, a desired length of scapula bone, with or without a cutaneous lining and a muscular component, was included. The surgical team chose the most suitable pedicle for the anatomical circumstances and planned osteotomies.

We used stereolithography models and manually manufactured osseous templates and prebent fixation plates at the beginning of the series and 3D CT virtual planning with patient-specific resection and reconstruction guides at the end of the series in two patients.

Statistical analyses were completed using SPSS version 20 (IBM Corporation, USA). For continuous data, we used the Mann–Whitney U-test for group comparisons. For categorical data, we used the Pearson's chi-squared test or the Fisher's exact test when appropriate. Results are given as absolute numbers or median values including the range.

#### 6.2.2 Study II

For Study II, we searched for all patients operated on between 2000 and 2012 for a head and neck microvascular reconstruction to obtain a final sample of 163 patients with osseous composite flap reconstructions using DCIA, the scapula or the fibula. Other flap options represented a minority of procedures, and we thus excluded them from our analyis. Patients included were followed from admission to hospital until the end of the study in May 2016.

In this study, we collected patient data on age, sex, smoking status, general diseases classified using CCI, classification of site-specific disease (malignant, benign or trauma), the TNM classification, site-specific previous oncological treatments or reconstructions, flap-specific properties, osteotomies along the flap, duration of ICU stay, tracheostomy and hospital stay, duration of the surgery and perioperative bleeding, early and late reconstruction-specific events and complications, early and late donor site–specific events and complications, speech and oral feeding capabilities, delay of postoperative oncological treatments and dental osseointegrated implants. We then analysed data for complication-related factors and flap-related determinants. As a retrospective study, we focused our analysis on the outcomes and complications related to the three most common reconstruction flaps.

As such, we analysed early flap-related complications accompanying vascular reoperations, wound dehiscence, hematomas and infections as well as partial or total flap necrosis, vascular complications and complications during recovery. Donor site and reconstruction-specific complications for each flap were recorded. Total and partial flap failures were recorded as well as fistulas and failing consolidation of the osseal segment. We also included data on smoking, previous oncological treatment, comorbidities and later dental implant therapy. Postoperative oral functioning was recorded specifically for speech and oral feeding. We also focused our analysis on complications causing a delay to oncolocical treatments.

We used SPSS version 20 (IBM Corporation, USA) for all statistical analyses. For continuous data, we used the Mann–Whitney U-test for group comparisons. For

categorical data, we used the Pearson's chi-squared test or the Fisher's exact test when appropriate. To compare several groups, we used the Kruskall–Wallis test. Results are provided as absolute numbers, percentages and medians that include a range.

#### 6.2.3 Study III

For Study III, we analysed data from 186 patients with osseous composite tissue flaps. To obtain reliable data to compare the scapula, fibula and iliac crest flaps, we included only patients with at least two follow-up MSCT scans using thin (0.5–2.5 mm) sections without tilt of gantry. We excluded all other patients with modalities such as MRI, CBCT, US, pantomography and plain x-rays.

Across all cases, 136 had mandibular, 44 maxillary and 7 orbital reconstructions. We included only mandibular reconstructions to ensure consistency within the study. As such, 21 patients fulfilled all inclusion criteria, and were included in the primary group.

We assessed the 3D semiautomatic volume of the bone flaps twice using the Advantage Workstation software version 4.4. (GE Healthcare, USA). For each follow-up image, two team members (SA and TW) independently analysed the images to verify the accuracy of the method. We assessed both the inter- and intraobserver variability in order to verify the results.

The secondary patient group consisted of 17 patients using MSCT scans completed according to various protocols, excluding these from the volume analysis. Thicker slices or a possible tilt of gantry rendered reliable measurements incomparable. We analysed this group using the height-by-width measurements of the bone flap 10 mm from the nearest osteotomy to exclude errors caused by callus or osteolysis along the gap. In addition, we analysed every osteotomy piece separately. To compare the two methods, the height-by-width measurements were also performed on the primary group. A total of 749 measurements were included in this analysis after combining both groups.

Follow-up imaging was not uniformly completed. Patients underwent two to seven MSCTs, during a follow-up period ranging from 8 to 132 months. The initial bone volume of the flaps differed, where DCIA featured the largest volume and the fibula the least. In addition, the bone shape varied. To obtain a comparable method to analyse the bone volume over time, the first available MSCT volume measured for each flap for every patient was specified as 1.00 regardless of the true volume and timing of the MSCT. The volume over time was calculated separately for the volume group as well as for the height-by-width group. To compare the volume analyses with the simpler height-by-width analyses, the height-by-width sum was also transformed to the same value (1.00) from the first measurement. To compare the different volumes registered at varying intervals during the postoperative follow-up for patients, we performed statistical analyses.

We analysed data using SPSS version 20 (IBM Corporation, USA). We used the Pearson's correlation coefficient to validate measurements and to assess correlations for continuous variables. We used the Mann–Whitney for the comparison of groups of continuous data and the Fisher's exact test for categorical data. For our statistical analysis and to estimate any decrease in the bone volume for various bone flaps over time, we used a simple linear curve fitting (NCSS 8, USA). Results are provided as median values and include the interquartile range.

#### 6.2.4 Study IV

For Study IV, we analysed data on 10 patients with an LD reconstruction. Here, we analysed the following data: patient age, sex, general disease, primary disease and classification, area of resection, perioperative parameters (duration of the surgery, bleeding, blood and fluid transfusion), size of the flap, primary flap-related and general complications, duration of hospital stay as well as ICU stay, details on patient speech ability and oral feeding, pre- and postoperative oncological treatment and follow-up data regarding disease-specific and overall survival.

The surgical technique detailed the semidecubitus positioning of the patient enabling a simultaneous two-team approach, and the rise and tunnelling of the flap through the partially released insertion of the pectoral muscle to reach the reconstructive site as a pedical flap.

Surgery was performed with the patient in the semidecubitus position, while two teams simultaneously performed the elevation of the flap and the tumour resection. The LD skin island longitudinally overlaid the anterior border of the muscle and as distally as possible. Otherwise, the LD flap was raised in the standard fashion, but all branches of the thoracodorsal pedicle up to the axillary vessels were ligated to prevent pedicle kinking. The thoracodorsal nerve was resected to prevent muscular contractions and the proximal part of the muscle was resected to avoid excess bulk in the pectoral tunnel. The tunnel was created from the axilla to the clavicle between the pectoralis major and minor muscles. A 5-cm segment of the pectoralis major muscle insertion was released and the tunnel was continued into the neck. The flap was then delivered to the neck or oral region via a short transverse supraclavicular incision for access and control of the pedicle.

The results from the analysis here are reported as medians including the range for descriptive purposes.

## 7 Results

The results from each study are presented in this chapter.

#### 7.1 Study I: Osseous scapular reconstruction study

In this series, 34 patients were operated on (see Table 3 in chapter 4 Patients). No flap losses occurred, and two early anastomosis revisions were successfully completed. Fistulas developed in three mandibular reconstructions, all reconstructed using scapula bone and a fasciocutaneous component only, while no fistulas occured in reconstructions including the LD muscle (p = 0.032). Openwedge osteotomies were performed on 19 scapula bone flaps, and no osseal consolidation failures occured. Furthermore, we found no association between open-wedge osteotomy and fistula formation (p = 0.215).

The type of pedicle used did not associate with fistula formation (p = 0.513) or with bone consolidation (p = 0.5). The patient age (p = 0.97), length of the bone flap (p = 0.27), ischaemic time of the flap (p = 0.41) or duration of surgery (p = 0.86) did not associate with flap-specific complications or patient outcomes.

The median duration of the surgery reached 10 h and 34 min. The use of preoperative computerised 3D planning did not affect duration. The median blood loss was 1 520 ml ( $650-10\ 000\ ml$ ) and the ischaemic time for the flap was 108 min ( $70-270\ min$ ). The median postoperative ICU stay stood at 6.5 days, tracheostomy duration at 7 days and hospital stay at 18 days.

Donor site morbidity was low with no immediate site-specific complications, with only one patient having pain and restricted motion at 12 months postoperatively.

Follow-up periods ranged from 15 to 1 431 days with a median of 473 days. In total, 14 patients died during follow-up—7 from metastasis of the primary disease and 7 from other causes (cardiac infarction, multiorgan failure, pneumonia and other malignancies).

Osseal healing was good with only one patient experiencing a radiological nonunion at the interface of the scapula and the mandible at 12 months. In total, 7 of the 26 patients (27%) with mandibular reconstructions received a total of 23 osseointegrated dental implants postoperatively along the scapula bone flap. All seven patients received radiation therapy (60–70 Gy)—three preoperatively only and four postoperatively for the scapula reconstruction. No implants were lost.

<u>7.2 Study II: Complications and outcomes of the DCIA, scapula and fibula flaps</u> A total of 163 patients received microvascular osseous composite reconstructions during the follow-up period. Here, DCIA was the most frequently used (n = 92, 56%), followed by scapula (n = 42, 26%) and fibula flaps (n = 29, 18%).

#### 7.2.1 Demographic results

We found no statistically significant differences between groups based on demographic characteristics. We found a slight tendency towards a lower age in the

fibula group and an older age and higher CCI score in the scapula group. Mandibular reconstructions covered more than 76% of DCIAs and scapulas and 59% of fibula flaps. The fibula was selected more often for nonmalignant cases (28%), whereas DCIA (95%) and scapula (98%) flaps were used in malignant reconstructions. Overall, 31% of patients received a previous radiation therapy.

#### 7.2.2 Peri- and postoperative results

Fibula flaps carried the shortest (530 min) median operation time, while scapula flaps were the longest (644 min; p = 0.001). The surgical duration for DCIAs reached 531 min. Fibula reconstructions also experienced the least blood loss during surgery (fibula, 1589 ml; DCIA, 2358 ml; scapula, 2197 ml; p = 0.013) and the shortest tracheostomy time (5 days; DCIA, 10 days; scapula, 8.6 days; p = 0.001). Across all flaps, 72% had an osteotomy along the transferred bone, where 15 flaps (9%) required more than 1 osteotomy. In addition, 49% of patients received postoperative oncological treatment. The primary reason for postoperative treatment not occurring was an earlier full-dose treatment. We found no statistical difference between reconstruction methods in the delay of initiating oncological treatment (median 42 days), although the median for fibula flaps reached only 31 days.

#### 7.2.3 Complications

In total, 14 total flap failures occured (8.6%). Most failures occurred among DCIA flaps (n = 13, 14%), six of which occurred in 2004, including one fibula and five DCIA flaps. Excluding 2004 from the analysis, the number of flap failures fell to 8 (5.4%). The difference between DCIA flap losses compared to other flaps was statistically significant (p = 0.001), which held when 2004 was excluded (p =0.038). In addition, 12% of all reconstructions necessitated reanastomosis, performed most often for DCIA flaps (p = 0.06). When including all early complications, every fourth reconstruction involved some complication. Among DCIA flap-specific early complications, we recorded 13 total flap failures, 7 cases of partial skin-flap necrosis, 2 cases of postoperative bleeding, 2 saved anastomosis occlusions and 1 early infection. Among scapula flap early complications, we recorded 2 partial skin island losses, 6 fistulas, 2 cases of bleeding and 3 saved anastomosis occlusions. Among fibula flap early complications, we recorded 1 total flap loss and 3 partial skin island losses as well as 1 saved arterial occlusion. Furthermore, early donor site complications in DCIA reconstructions consisted of 3 cases of bleeding, 3 hernias, 2 fractures and 1 case of partial femoral nerve paresthesia.

Among scapula reconstructions, we identified one case of seroma formation and one case of severe donor site pain. Among fibula flaps, four experienced early donor site complications, of which two consisted of early infections and two consisted of ischaemia or compartment syndrome.

Late reconstruction site complications in DCIA flaps consisted of 23 fistulas, 2 cases of flap osteonecrosis and two nonunions. Scapula flaps developed 10 fistulas and one case of mandibular osteonecrosis. In fibula flaps, we recorded five fistulas, four nonunions and two cases of flap osteonecrosis.

Late donor site complications in DCIA flaps consisted of four late hernias, three fractures of the anterior superior iliac spine (ASIS), one seroma and one case of chronic pain syndrome. In scapula flaps, an impaired range of motion of the scapula was identified in four patients. Fibula reconstructions with late donor site complications included two cases of chronic pain and one case involving exposure of the peroneal tendon. We found no statistically significant difference between groups.

When comparing the three different flaps, we found no significant differences in overall complications (p = 0.82), repeated microvascular anastomosis (p = 0.25), early and late donor site (p = 0.436 and p = 0.991, respectively) or reconstruction-specific complications (p = 0.328).

In total, 25 DCIA reconstructions included dental implants installed in the flap, of which 5 single implants failed. Furthermore, 9 scapular reconstructions involved implants with one failure and 11 fibula reconstructions involved implants, 3 of which failed. We found no statistical difference between flap type and implant failure (p = 0.38).

#### 7.2.4 Complication-related factors

We also analysed all patient and reconstruction site complications against preoperative risk factors including, age, sex, CCI score, smoking status, previous microvascular reconstructions and radiation therapy. We also recorded perioperative factors such as duration of surgery, bleeding and osteotomies of the microvascular flap. We found that previous radiation therapy significantly correlated with postoperative complications (p = 0.009). We found that age-related complications showed a statistically significant relation between groups, although the noncomplication group exhibited an older patient age (p = 0.028). Other parameters did not correlate with complications.

#### 7.2.5 Resection type

We used a modified Jewer classification to estimate the mandibular resection width. An anterior resection consisted of symphysis anterior to the canine, a lateral resection covered the body of the mandible with or without condyle and an extended resection combined anterior and lateral resections or an extended soft tissue resection. Most resections were lateral or extended. Over the last five years, the percentage of extended mandibular resections increased, particularly in the scapula flap group, from 51% to 64%.

#### 7.2.6 Oral functioning

We analysed postoperative oral functioning—as an evaluation of speech and ability to fully feed orally versus permanent dependency on percutaneous endoscopic gastronomy (PEG) feeding—related to three different flaps. We found no differences between flap types and oral feeding function. The scapula flap carried significantly better scores for speech ability than fibula (p = 0.007) and DCIA (p = 0.04) flaps, whereas no difference was found between fibula and DCIA (p = 0.5) flaps.

		Donor	Duration of	Duration			Total
	Flap loss	site	tracheostomy	OFEG	Speech	Bleeding	score
DCIA	3	3	3	ns	2, ns	2, ns	13
Scapula	1	1	2	ns	1	2, ns	7
Fibula	2	2	1	ns	2, ns	1	8

## Table 6. Results from Study II: Scores for flaps

1 = best option, 2 = second best option, 3 = worst, least favourable option; ns = not statistically significant.

Table 6 provides an analysis of the most significant outcomes for DCIA, scapula and fibular flaps. Here, we see the best overall outcomes occurred in the scapula (7 points) and fibula (8 points) groups, and the worst outcomes and events occurred in the DCIA group (13 points). In flap loss and donor site evaluations, DCIA alone appears less favourable.

7.3 Study III: Volume analysis of bone flaps over time

Among the 38 patients (22 men and 16 women) in this study, we recored a mean age of 61 (range 21–87 years), who underwent 25 DCIA, 5 scapula and 8 fibula flaps. The follow-up period using MSCT imaging ranged from 7 to 132 months. During the initial analysis of the bone flaps, a mean volume of 23.8 cm<sup>3</sup> was recorded for DCIA, 11.4 cm<sup>3</sup> for scapula and 7.2 cm<sup>3</sup> for fibula flaps. We validated the volume method through a double reading by two separate physicians (SA and TW), finding with an interobserver reliability of 0.997 (Pearson's correlation coefficient) and intraobserver reliabilities of 0.999 (SA) and 0.998 (TW).

In the 3D volume analysis, we analysed 11 DCIA, 7 fibula and 4 scapula flaps. In the height-by-width analysis, we included all 25 DCIA, 8 fibula and 5 scapula flaps.

The first volume comparison focused on bone flap CT data available at 6, 12 and 24 months ( $\pm 2$  months, n = 20) to provide comparable data for analysis. We found volume reductions of 7% for the scapula, 2% for DCIA and 0% for fibula flaps during the first year (up to 12 months) and 14% for scapula, 3% for DCIA and 1% for fibula flaps at 24 months.

The second comparison included all flaps using volume analysis as well as heightby-width calculations for all bone flaps. Using a longer follow-up of 48 months, the volume analysis showed a remaining volume of 0.69 for scapula (0.48-0.90), 0.88 for DCIA (0.67-1.08) and 0.95 for fibula (0.77-1.05) flaps. The height-by-width analysis showed a remaining relative volume of 0.89 for scapula (0.75-1.03), 0.89 for DCIA (0.77-1.01) and 0.96 for fibula (0.86-1.05) flaps.

Postoperative radiation therapy was administered to 24 of 38 patients with no statistically significant impact on volume reduction during the first 24 months. The volume reduction for all flaps reached 11% in radiated patients and 9% in nonradiated patients. We found no significant correlation between the bone volume reduction and patient age or sex.

The 3D volume analysis also showed a more pronounced volume loss due to the different shapes of the three bones not found by the simpler height-by-width measurements.

#### 7.4 Study IV: Latissimus dorsi study

7.4.1 Perioperative results

Among the ten patients in this study, we recorded a median surgical duration in the operating theatre of 7 h and 17 min (range 3 h and 20 min to 9.0 h), with a median blood loss of 1 035 ml (range 600–4 400 ml). In addition, we recorded a median skin island size for LD flaps of 8.5 cm by 16.5 cm (range 8 cm by 10 cm to 8 cm by 30 cm). We observed no total flap losses; however, in one case, a majority of the skin island was lost requiring a secondary operation. In all patients, tumour resection included a minimum of 3-mm margins verified by histology. The donor site was closed primarily in all cases.

#### 7.4.2 Complications and postoperative recovery

During their hospital stay, three patients experienced major early complications and two patients experienced major late complications. One patient died from multiorgan failure. Of the nine surviving patients, four were decannulated and five remained permanently tracheostomised. The nine surviving patients were treated in ICU for a median of four days (range 0–18 days) and the median total hospital stay reached 20 days (range 14–58days). All surviving patients were discharged from hospital.

#### 7.4.3 Follow-up results

Four of the nine patients died during follow-up due to cancer progression. One patient died two years later from an unrelated cause.

Table 7. LD patient characteristics by complication and survival						
Age and general health	Major complications	Survival, days				
Cerebral infarction, severe malnutrition, 82	Multiorgan failure	10 days				
Chronic obstructive pulmonary disease (COPD), smoker (100 pack years), 64	None	779 days unrelated cause				
Cerebral infarction, hypertension, atrial fibrillation, 66	None	166 d				
Hypertension, multiple venous thrombosis, permanent anticoagulation, smoker (50 pack years), 79	None	144 days				
COPD, aortic valve stenosis, smoker (40 pack years), 64	Fistula, partial flap necrosis	Alive				
COPD, hypertension, atherosclerotic disease, chronic kidney failure, 73	Paralytic ileus	226 days				
Alcoholism, smoker (25 pack years), 47	None	Alive				
Alcoholism, brain contusion, epilepsy, malnutrition, 51	Late hardware exposure	Alive				
Alcoholism, smoker, hypertension, 58	None	Alive				
Systemic lupus erythematosus (SLE), several prior malignancies, 70	No	Alive				

#### Table 7. LD patient characteristics by complication and survival

## 8. Discussion

#### 8.1 General aspects of maxillomandibular reconstruction

Several methods of composite flap reconstruction exist for maxillomandibular reconstruction. Many of the published methods have been used for decades by different centres, and results and recommendations for these have been published. Recommendations often result from a single-centre study based on retrospective analysis of patients operated on by the authors. This study follows that formula. Personal experience and familiarity with a certain flap or method likely influences patient treatment and may bias results. This will correspondingly affect the recommendations and algorithms presented. The results of our series comparing the three most frequently used osseous free flaps will give aspects of this matter.

Many previous publications discussed surgical results and donor site morbidity for one method of reconstruction. Others compared soft tissue and osseous reconstructions as well as surgical outcomes, results or complications from two osseous flaps. A small number of studies documented single-centre comparisons and follow-up for three different osseous reconstruction methods.

Studies on the behavour of the osseous segment of reconstructions remain few and long-term follow-up of bone volume appears less frequently. By contrast, clinical observations from these reconstructions demonstrate a reliabe stability and negligible loss of the load-bearing capacity.

Oral cancer is increasing among the elderly and otherwise morbid patients. Studies on extensive reconstructive surgery outcomes demonstrated that microvascular reconstructions are possible among these groups of patients. Preoperative evaluation of risk factors and assessment of complications are important tools in choosing the best options for a patient as well as in reducing the risk of postoperative complications. While microvascular options remain safe and enjoy wide use, some patients require simplified reconstructions such as pedicular flaps for salvage surgery.

#### 8.2 Reconstruction algorithms

Among the osseous microvascular options discussed, we can identify several trends from our results related to complications comparing published data and various published algorithms. In the tables (Tables 8 and 9) below, I summarise the results and recommendations put forth by various authors enabling a comparison between different algorithms.

Anterior		Lateral	Extended	
Jewer (1989)202	DCIA	DCIA	DCIA	
Disa (2000)57	Fibula	Fibula	Fibula or scapula	
Takushima	Fibula	DCIA or fibula	Scapula	
(2005)59				
Schultz (2015)65	Fibula	DCIA or fibula	Fibula	
Hanasono	Fibula	Fibula or soft tissue flap	Fibula and soft tissue or	
(2014)61		_	scapula	
Brown (2016)54	Fibula or DCIA	Fibula or scapula	Fibula	

 Table 8. Comparison of recent algorithms for mandibular reconstruction.

 For comparison, I reclassified reconstructions into three classes.

#### **Table 9. Comparison of recent algorithms for maxillary reconstruction.** For comparison I reclassified reconstructions into three clases

	Limited alveolar	Hemimaxilla	Extended or bilateral
Cordeiro (2000) <sup>46</sup>	RFA +/- bone graft	Rectus + bone graft or temporal muscle	Rectus
Rodrigues (2007) <sup>48</sup>	DCIA, FOSC	FOSC	FOSC, DCIA, multiple flaps
McCarthy (2010) <sup>7</sup>	RFA	Rectus abdominis muscle + bone graft	Rectus abdominus muscle
Brown (2010) <sup>49</sup>	Temporal, RFA, ALT	RFA, FOSC, DCIA, scapula	FOSC, DCIA, scapula +/- ALT or LD
Iyer (2014) <sup>203</sup>	No / local flap / RFA	ALT, RFA, fibula	ALT / rectus abdominus, fibula, DCIA
Costa (2015) <sup>51</sup>	RFA, DCIA	Fibula, DCIA	Fibula, rectus abdominis

We find a clear paradigm shift from earlier algorithms in the maxilla where mostly soft tissue reconstructions were recommended. Long-term results and 3D reconstruction appear to favour osseal vascularised flaps. Many authors now recommend DCIA, which lost most of its popularity in mandibular reconstruction, in the maxilla. Moreover, scapula and fibula come highly recommended for large reconstructions. In addition, free nonvascularised bone grafts are not included in more recent recommendations.

In mandibular DCIA where we began, trends clearly favour the fibula as the primary option. The scapula is also gaining popularity particularly in cases requiring large soft tissue reconstructions. In extended maxillary resections including orbital exenteration, large soft tissue flaps such as LD, rectus or ALT are recommended. In these cases, no functional need exists for reconstructing the orbital floor or rim.

Table 10. Algorithm for mandibular reconstruction and recommended uses of fibula, scapula and DCIA flaps based on the present study

	Anterior		Lateral		Extended	
	Α	В	Α	В	Α	В
Fibula	+++	++	++	+	+++	+
Scapula	+	+++	+	+++	++	+++
DCIA	++	+	+++	++	+	++

A = limited soft tissue defect; B = large soft tissue defect

+++ = highly recommended; ++ = good secondary option; + = can be used in select cases.

Several options exist for the reconstruction of osseous and soft tissue defects in head and neck surgery. The best patient outcome result from a composite tissue free flap. Microvascular surgery appears safe and reliable even among morbid and elderly patients. Applying algorithms and classifications are useful in the treatment of an individual patient, and particularly useful in analyses and studies comparing large datasets achieving better and more reliable results for our patients. Primary repair of the surgical defect without donor site morbidity and secondary surgeries, and a good quality of life for the patient for decades after treatment remain the goals of our work. We have witnessed some modifications and trends in reconstructive surgery in recent years and undoubtedly progression will continue in the years to come. We have not yet seen a technological evolution replacing microvascular reconstruction.

Our results and the recommendations above, indicate a clear preference for the osseous flap in the reconstruction of maxillomandibular oncological defects. The reconstructive flap should enable a near-functional and aesthetically tolerable solution without disabling donor site morbidity, with a high reliability without complications and reoperations to ensure as short as possible waiting time for further oncological treatment. We thus recommend the fibula and scapula. Both perform equally well across several parameters, although specific properties and targets vary. The fibula represents the best option in long osseal defects, particularly in younger patients, patients with limited soft tissue needs or when combined with a second soft tissue free flap. The scapula is the most reliable of all osseous flaps. It is well-suited for the most extensive defects with large soft tissue requirements and provides technical solutions for both simultaneous harvesting and recipient site surgery as well as successful dental implantation. As the primary workhorse in head and neck osseous reconstruction in the past, DCIA has been surpassed. Very few parameters analysed in this study or published elsewhere support the use of DCIA as the primary recommended flap. Its rate of flap failure remains high, the donor site experiences the most frequent and most disabling morbidities and the tailoring capacity of the bone and the adjacent soft tissue component remain low. Undoubtedly, DCIA has its place in the reconstructive vocabulary, and continues to be listed in modern algorithms with its justified uses. When planning the best reconstruction option for an individual patient, DCIA should not, however, be the solution for every defect, but merely an alternative for select cases.

<u>8.3 Properties of the free scapular flap in maxillomandibular reconstruction</u> Compared to the fibula and DCIA options, the scapula has enjoyed less use in facial reconstruction. Reasons mentioned in the literature include the posterior localisation of the flap rendering harvesting more demanding, the thin and cortical bone structure, the limited amount of bone, its unsuitability for dental implants and the risk of osteotomies.<sup>58,150,161</sup>

In this study, we analysed the scapula flap as a method of maxillomandibular reconstruction in 34 patients. A majority of patients relied on a two-team approach with the patient in the semidecubitus position for simultaneous resection and flap harvesting. Bilateral resections and neck dissections were performed with the patient in the supine position. Many authors previously discussed when the two-team approach was precluded and the duration of surgery was longer for scapula flaps. Disa and Cordeiro<sup>58</sup> as well as Hasan et al.<sup>161</sup> concluded that the scapula

should be harvested separately. However, we showed that the two-team approach is possible. In our study, the median surgical duration reached 10 h and 34 min for the entire procedure, which was statistically slower than for DCIA and fibular flaps in our setting. In addition, 3D–CT planning with patient-specific resection and reconstruction guides used for two patients did not affect the duration of surgery.

We found a high reliability for the scapula flap, whereby no flap losses occurred. A similar study by Sullivan et al.<sup>156</sup> from 1990 consisted of 31 osteocutaneous scapula flaps and 5 cutaneous flaps. All flaps included the latissimus. The authors reported a 100% success rate for cutaneous and 90% for osteocutaneous flaps. Furthermore, 30 osteocutenous flaps were used for mandibular reconstruction, and 15 patients were irradiated previously. A similarly high reliability was discussed by Brown et al.<sup>159</sup> in 2009 for scapula reconstructions among 46 patients. Here, the authors favoured the scapula because of its reliability, the functional outcome and minimal donor site morbidity.

The scapula flaps included either a fasciocutaneous component (scapula skin flap or TDA perforator flap) or a musculocutaneous component (LD) combined with an osseal segment. The osseal pedicle is based on either the CFS artery or the angular branch of the vessel or both. All patients had an angular pedicle and variations in vein drainage directly to the axillary vein as described by Brown et al.<sup>159</sup> and Shimizu et al.<sup>157</sup> were identified.

Open-wedge osteotomies, which leave intact the lateral scapular margin with its muscle cuff and intact periosteum on the lateral border, were performed on 19 of the flaps as necessary. Some flaps included two separate bone flaps based on the two pedicles, while some separate bones had secondary open-wedge osteotomies resulting in one to four bone segments. No osteotomies had failures of the osseal consolidation and we found no association between open-wedge osteotomy and fistula formation. The type of pedicle did not associate with fistula formation or bone consolidation. In current discussions, some disagreements exist regarding the benefits of performing osteotomies of the scapula. Dowthwaite et al.<sup>204</sup> and Hasan et al.<sup>161</sup> reported performing osteotomies of the scapula, while others including Disa and Cordeiro<sup>58</sup> regarded the scapula unsuitable for such prodedures.

In our study, scapula flaps including the LD muscle developed no fistulas, although 11 flaps that included a fasciocutaneous component only developed 3 fistulas. The higher incidence of fistulas in this flap type represents a noteworthy finding in our study. Similar findings have not been reported previously in the head and neck literature. Supporting evidence for the protective functioning of muscular tissue compared with fasciocutaneos flaps have appeared in the literature, although only in free flap reconstructions of defects in the extremities.<sup>205,206</sup> Somewhat surprisingly, we found no significant association between the patient's age at the time of surgery, the length of the bone flap, the ischaemic time for the flap or the total duration of the surgery and flap-specific complications or patient outcomes.

In total, 7 patients received 23 dental implants in the scapula flap, none of which failed. All implants were installed during a second operation after primary recovery, stabilisation of osteotomies and radiation therapy. The amount of bone did not serve as a limiting factor among patients not receiving implants, a finding supported by morphometric studies by Shimizu.<sup>157</sup> Many early studies concerning the scapula

flap regarded the amount and quality of available bone insufficient for osseintegrated implants,<sup>58,150</sup> although recent publications supported the use of implants.<sup>159,161</sup> Earlier studies described the use of dental implantations in free osseous flaps for oral rehabilitation, and long-term follow-up results are now available. Radiation therapy, functional mastication, mucosal versus cutaneous lining and bone stock influence the choice of dental rehabilitation.<sup>207-209</sup> Based on existing literature and the results from our study, it appears that the use of osseointegrated dental implants in the scapula bone in oral rehabilitation is possible and safe.

We recorded no early donor site complications needing attention primarily. We analysed shoulder functioning three months postoperatively to assess late donor site morbidity. In the majority of patients evaluated, shoulder movement fell within normal range accompanied by no pain and no restrictions in daily activities. Donor site morbidity remained quite low, a finding supported by the literature. Furthermore, the fibula and iliac crest were both reported as experiencing a greater number of donor site morbidities, particularly in elderly patients.<sup>162,210-213</sup>

## <u>8.4 Differences between scapula, fibula and iliac crest osseous flaps in</u> maxillomandibular reconstructions

In this study, we compared the three major options for osseal composite reconstruction of maxillomandibular defects—the scapula, fibula and DCIA flaps. Our material is coherent and employed the same treatment standards across flap types and patients.

In total, we analysed data from 163 patients requiring microvascular composite reconstructions of defects in the facial area with respect to complications and outcomes. DCIA stood as the most frequently used (56%) method, followed by the scapula (26%) and fibula flaps (18%). The distribution here differs from the crucial classifications and algorithms presented in the introduction to this thesis. Typically, fibula is the most commonly used technique, but this study reflects an overwhelming majority of cases employing DCIA at the beginning of the 21st century. In the maxillofacial department, where the majority of bone reconstructions were completed, DCIA was the first osseous flap employed.

We found the highest rate of flap loss in the DCIA group and while the fewest were found in the scapula group. This distribution mimics the literature, where the highest success rate belongs to scapula flaps, followed by fibulas and DCIAs. In 2001, Takushima et al.<sup>60</sup> published a series of 178 microvascular free flaps in mandibular reconstructions. Their study consisted of 11 costal grafts, 1 radius, 36 DCIAs, 51 scapulas, 34 fibulas and 45 soft tissue flaps with a reconstructive implant. In their series, the incidence of flap loss was the highest in the DCIA group (6/36), followed by the fibula (4/34) with the lowest occurring in the scapula group (2/51, p < 0.05). In Markiewicz et al.'s<sup>214</sup> 2015 meta-analysis and review on free flap survival consisting of 25 303 studies, they selected 17 studies for further analysis, including DCIA, fibula, scapular and RFA flaps in their analysis. In total, 1 221 patients had a total of 1 262 free flaps, 65 of which failed. The total success rate across all free flaps reached 94.8%. DCIA flaps were associated with an OR of 7.4 for failure compared to the RFA flap. In the analysis of fibula versus DCIA use and flap failure, the oldest publications favoured DCIA, while recent studies favoured the fibula, with the

weighted total slightly favouring the fibula. When comparing the scapula versus the DCIA flaps, the scapula clearly performed better with an OR of 3.2, although the number of patients was limited and not statistically significant. The OR for DCIA failure against all other flaps reached 1.7, while the scapula was favoured against the fibula with an OR of 2.3.

By contrast, Brown et al.<sup>215</sup> presented the results from 24 vascularised iliac crest grafts with an internal oblique muscle in the reconstruction of maxillectomy defects. They concluded that DCIA with bone and muscle is an ideal reconstruction method, with few and mild donor site complications not requiring intervention for patients in this series.

In cases involving flap loss, secondary reconstruction typically included a second free flap as recommended by Wei et al.<sup>216,217</sup> In their analysis of 3 361 free flaps, of which 1 235 consisted of head and neck reconstructions, they reported a partial and total flap loss rate of 3%. Furthermore, 40% of flap losses were further reconstructed by another free flap, 36% involved regional flaps and conservative treatments were used for the remainder of cases. The failure rate for regional flaps, however, remained high or involved the development of complications. They consequently recommended a second free flap as the solution to free flap loss.

The pedicle of the scapula is the longest with the largest diameter, followed by the fibula, while DCIA features the shortest and smallest vessels. The fibula and iliac vessels are also more often affected by atherosclerotic disease than the subscapular vessels.<sup>118,218-220</sup> The shorter DCIA vessels may withstand tension, particularly due to postoperative swelling, or necessitate a vein graft. Fibula vessels, however, may show possible peroneal dominance and atrophy of the other major vessels.<sup>142</sup> The scapula group underwent surgeries which were longest in duration for both reconstruction and in their entirety, this despite the technical means of performing a two-team procedure. This finding mimics similar findings from Dowthwaite et al.<sup>204</sup> Some cases consisted of bilateral neck dissections and extensive resections , where reconstruction using the scapula flap tends to be wider compared with other flaps. This follows most of the recommendations discussed above, where the scapula flap is favoured in cases with large soft tissue needs.<sup>159</sup>

Among perioperative parameters, several favoured the fibula flap. These included the lowest total blood loss, shortest tracheostomy duration and shortest ICU stay. These measurable results demonstrate a clear benefit to the fibula, and can partially be explained by some fibula flap properties. For example, the bone is easy to shape with osteotomies, minimal soft tissue is included and the skin island is thin. Swelling of the reconstruction itself can be less than that of the bulky skin island and the transverse muscle cuff in DCIA.

In this study, the scapula group enjoyed the best speech ability. This differs from Takushima et al.'s<sup>60</sup> results, who found no significant differences. Additionally, dental implant complications were lowest in the scapula group. Thus, a bone flap previously regarded as unsuitable for dental implants accompanied the best outcomes. Comparing overall results, we found no significant differences between flaps for repeat reconstructions of microvascular anastomosis, neck complications, early and late donor site or reconstruction–specific complications, usage of PEG,

length of hospital stay, postoperative oncological treatment modalities or delay of oncological treatment (days from operation to the start of treatment).

While we found no statistical difference between the overall complications associated with specifc flaps, the most disabling events typically occurred in DCIA patients. These patients experienced several fractures of the anterior superior iliac spine requiring repeat operations due to pain, bulging and hernias necessitating secondary operations as well as pain and paraesthesia of the femoral area. We recorded no donor complications needing treatment in the scapula group, while fibula-associated complications primarily concerned the skin graft and necessitated conservative treatment. One case of compartment syndrome caused by a too-tight donor site closure required a fasciotomy and opening of the donor area, and we recorded one case of critical ischaemia after a fibula harvest. Donor site complications and reconstruction-specific postoperative measurements all favoured the scapula, while the fibula performed almost as well and the most negative findings accompanied DCIA. In 2003, Rogers et al.<sup>221</sup> compared long-term morbidities among DCIA and fibula flaps for the reconstruction of head and neck defects, relying on 44 fibula and 73 DCIA free flaps. Among these, 16 patients with fibula flaps and 20 patients with DCIA flaps underwent clinical examination regarding donor site morbidities. They concluded that both flaps yielded comparable results among both subjective and objective parameters, including the Harris Hip Score and the American Orthopedic Foot and Ankle Society scores. Rogers et al. reported median DCIA scores of 90 for the hip score (where 90 to 100 is excellent and 80 to 90 is good). The fibula scored a median of 85 for the ankle score, the same value as the postoperative score for corrective metatarsal osteotomy. Thus, the fibula typically had more donor site healing problems and diminished muscular power as well as a loss of sensation.

In our analysis of the extent of the resections reconstruction flaps, we found that the scapula flap was the most popular for extended cases, whereas DCIA was more common for lateral mandibular reconstructions. This mirrors existing algorithms discussed earlier, where DCIA is recommended, when included, for lateral reconstructions including the floor of the mouth. The scapula is also frequently recommended for large soft tissue reconstructions, and, even in the most extensive cases, complications and flap losses remain remarkably low. Furthermore, the fibula flap also proved reliabile, resulting in only one total flap loss which occurred in 2004 and possibly stemmed from the COX-2 selective pain medication used at that time.<sup>222</sup>

The DCIA flap was used most often in reconstructions (n = 92), particularly at the beginning of this study. Most likely, its success rate suffered during the learning curve, and may also have been strongly affected by the COX-2 problem. In total, we recorded 13 DCIA flap losses, 5 of which occurred in 2004.

Previously irradiated patients also experienced significantly more complications as noted elsewhere in this field.  $^{\rm 223}$ 

Patient age differed statistically between groups experiencing complications versus those who did not, although mean age was in fact higher in the group without complications than among those experiencing complications (55.5 versus 60.5). This may stem from a bias caused by the primary selection of reconstructed patients. For instance, a younger patient with several comorbidities may undergo surgery resulting in complications, while an elderly patient with the same comorbidities receives a higher CCI score and perhaps receives other recommendations such as a reconstruction plate and soft tissue flap.<sup>224</sup> Elderly patients as a group tolerate large reconstructions with good postoperative treatment in recovery. Several studies reported similar findings.<sup>225-230</sup>

In 2015, Grammatica et al.<sup>226</sup> reviewed the literature concerning microvascular flap surgery among the elderly, an important issue since more than 50% of patients with SCC are over 65.<sup>231</sup> While the cut-off for 'old' remains undefined, 65 years is typically used, which then leaves the majority of our patients by definition classified as 'old'. Age itself is not a major risk factor for free flap surgery. For instance, in a study by Wester et al.<sup>232</sup> involving ten patients over the age of 90, they reported a success rate of 100% and a 0% mortality rate.

In 2011, Nao et al.<sup>233</sup> analysed results among 418 patients consisting of 323 patients under 70 and 95 cases older than 70. They found an overall rate of medical complications of 10% versus 21%, favouring the younger group. In addition, the surgical complication rates reached 32% versus 31%, while flap success rates reached 89% versus 94%, both better among older patients; however, the mortality rates stood at 1.8% versus 4.2%, clearly higher among older patients. Comorbidities assessed using the American Society of Anaestesiologists (ASA) classification and CCI<sup>201</sup> scores carried higher predictive values than age. Nao et al. recommended using an algorithm based on age and medical risk. In patients under 65, no contraindications existed for free flap surgery among patients with low as well as high comorbidity scores. Once over 65, patients with low comorbidity scores could be treated similarly to younger patients. Among elderly patients with high comorbidity scores, soft tissue or pedicled flaps were recommended.

In a 2016 publication by Szturz et al.<sup>231</sup> on the treatment of elderly patients with SCC in the head and neck regions, several important issues emerged. First, they emphasised the importance of geriatric counselling. Second, a review of oncological considerations among older patients found that current recommendations for chemoradiotherapy in patients over 70 revealed that most reject this treatment option. The authors found no survival benefit, although more acute and late toxicity occurred in elderly patients. Thus, the surgical option may prove even more important for the elderly. Third, the authors suggested that the higher rate of perioperative complications accompanying free flap surgery among the elderly most likely results from an increased prevalence of comorbidities than from their advanced age.

We found no significant difference in preoperative comorbidity CCI scores between groups. We analysed several pre- and perioperative parameters, and found no statistical differences between flap types and the related complications. In this analysis, our comparison included smoking habits, sex, previous microvascular reconstructions in the same area, duration of surgery, blood loss during surgery and osteotomies in the osseous flap. Furthermore, we found no differences in total hospital stay and recovery from surgery through the start of adjuvant oncological treatment, defined as oncological treatment delay. The mean oncological delay from the day of surgery to the start of oncological treatment stood at 42 days, or the exact six weeks of time discussed by Cordeiro above. An additional 42 days or subsequent six weeks also represents the gold standard for completing adjuvant radiation therapy.<sup>234</sup> The delay for radiation therapy was previously shown to correlate with a higher disease recurrence rate. In a review by Chen,<sup>235</sup> 44 studies consisting of 26 231 patients were analysed. Most studies involved head and neck as well as breast cancer patients. For definitive radiation therapy they calculated an RR of 1.28 for each month of delay. This results in a 6.3% absolute increase in local recurrence for every month of delay. Studies on RR for distant metastasis failed to establish a statistically significant difference in head and neck cancer. No randomised controlled trials, however, exist due to the strong indirect evidence on the impact of delay and worse outcomes.

Dental osseointegrated implants can be used in any of the flaps presented. In this study, 25 of 92 DCIA, 9 of 42 scapula and 11 of 29 fibula patients had implants. The proportion of implants installed and lost mirror those from other studies and demonstrate that implants can be used alongside all of the presented flaps as discussed in the literature.<sup>204,215,144</sup> The selection of patients receiving implants is tailored to the needs of a specific case and general recommendations are not supplied.

Finally, factors unrelated to the flap, patients and surgical techniques also influence outcomes. In the Department of Maxillofacial Surgery, six flaps (one fibula and five DCIAs) were lost in 2004 before the high complication rate leading to unexpected flap losses was linked to a pain medication<sup>236</sup> used postoperatively in ICU and on the ward. Between March and December 2004, the postoperative use of the COX-2 inhibitor valdecoxib and its intravenous prodrug parecoxib were associated with an overall success rate that fell to 71%. After cessation of the COX-2 selective inhibitors beginning in January 2005, the success rate returned to 96% resulting in one flap loss during that year. Similar adverse results with COX-2 inhibitors and flap necrosis were reported by Ren et al.<sup>237</sup> in 2013 in epigastric flaps in rats. In particular, after seven days, necrosis was more marked in that animal study.

#### 8.5 Graft resorption or remodelling in reconstructed bone

Free nonvascularised bone grafts have enjoyed use in the repair of osseous defects for some time. The most used donor areas consist of the iliac spine, calvarial, rib and intraoral bone grafts from the mental region, the zygomatic buttress and the ramus of the mandible. Extensive and rapid resorption of up 60% within six months proves problematic.<sup>76,77</sup> The amount of grafted tissue also remains limited, particularly with regards to regional transplants.<sup>78</sup>

A large resection of the maxillomandibular area requires a composite reconstruction with stable as well as durable vascularity to ensure patient recovery and to allow the patient to withstand subsequent adjuvant oncological therapy. Vascularised grafts appear to maintain their volume significantly better and provide viable bone marrow with a rapid capacity to heal even after radiation of the area.<sup>238</sup> A composite microvascular osseous transfer is thus the typical reconstructive arsenal. In a 2011 study by Rana et al.<sup>239</sup> of 178 patients, the authors followed free nonvascularised iliac grafts, microvascular DCIA, rib grafts, sternal grafts and microvascular fibula

flaps for a year to evaluate complications and bone mass. Their results favoured free vascularised grafts. Yet, knowledge of long-term outcomes related to the bone, changes in volume and possible atrophy remained limited.

Studies on various osseal flaps typically focus on measurements from plain or pantomographic radiographs in two dimensions as illustrated by Disa et al.<sup>240</sup> In their study, the fibula preserved its bone mass well. They measured each osteotomised bone using manual pantomographic radiographs during a 24 to 104 month follow-up period among 27 patients. Volume loss reached 5% to 10%, with the greatest loss found after radiation therapy (only three patients). Furthermore, loss of volume reached 5% to 7% in patients with dental implants and 3% to 7% in patients without implants, resulting in no significant difference. The greatest volume loss occured in the body of the mandible. Yet, they did not measure volume, but bone height instead.

Mertens et al.<sup>241</sup> presented material from 21 DCIA and 15 fibular flaps, followed for up to 17 months. Their analysis relied on digital measurements of panoramic images in digital imagining and communication in medicine (DICOM), classifying defects using the HCL method described by Jewer. After six months, vertical bone resorption reached 6.79% for DCIA, climbing to 12.58% at 17 months. Fibula grafts showed a resorption of 5.30% at six months, climbing to 16.95% at 17 months. Rana et al.'s<sup>239</sup> results discussed above stood at 16.7% for DCIA and 12% for the fibula at one year. Mertens et al. concluded that microvascular bone transplants, in contrast to nonvascularised bone transplants, result in low bone resorption rates independent of their origin. Futhermore, both options demonstrate sufficient stability for installing dental implants. In addition, DCIA provides a higher vertical dimension, which is beneficial in patients with residual dentition preventing vertical mismatch between the graft and the residual mandible. This may offer a more stable mechanical benefit in prosthetic rehabilitation.

Ylä-Kotola et al.<sup>242</sup> analysed fibula union and resorption. Using CT scans to evaluate the bone of 112 patients, they identified 24 with at least two CT scans for the evaluation of bony resorption. Measurements were made on a workstation with vertical and horizontal measurements taken 5 mm from the osteotomy line. Bone resorption was found only in vertical height measurements, and resorption was identified in both the mandible as well as in the fibula graft at one year during follow-up. They did not report the specific value of bone volume reduction, regarding it as minimal.

A literature search on the long-term stability or resorption of the osseal scapular microvascular flap turned up no publications. Volume analyses of other bones used also remain unpublished. Therefore, in our study, we understood the importance of including a comparison of single-centre material from DCIA, fibula and scapula osseous reconstructions and performing true 3D volume analyses of these.

As published by others, resorption or a volume decrease are observed over time. Osseous bone flaps all appear stable clinically and have been shown to permit dental implants. Nevertheless, significant differences between osseous flaps exist and were analysed in this study. For instance, the fibula flap emerged as the most stable with 95% remaining after 48 months, whereas the scapula flap involved the greatest loss of volume with 69% remaining at 48 months. DCIA had a volume of 88% at 48 months. When comparing results only using height-by-width or horizontal-byvertical measurements, the results for volume loss at two years were 8% for the scapula, 5% for DCIA and 2% for the fibula. The corresponding values at four years were 11% for the scapula, 11% for DCIA and 4% for the fibula. This two-dimensional method fails to record the even greater change in volume revealed by volume analysis. At two and four years, the scapula lost 18% and 31% of its volume, respectively, DCIA lost 8% and 12% and the fibula lost 5% of its initial volume. We assume that the different shapes of the bones influence this difference in volume loss, with the fibula appearing as a rounded triangular figure, DCIA appearing boxlike and the scapula resembling a thin, flat bone with a thicker lateral border. These volume changes are, therefore, not visible in a two-dimensional analysis.

Postoperative radiation therapy did not significantly impact volume loss during the first two years postoperatively. We found volume losses of 11% for all flaps in radiated patients and 9% in nonradiated patients. These figures fall within the limits of Disa et al.'s<sup>240</sup> findings, where resorption was indeed greater in radiated patients.

#### 8.6 Salvage methods in the reconstruction of morbid patients

Disease relapse, complications from previous microvascular reconstructions or oncological treatment complications may compromise reconstruction treatment. Patients may experience osteradionecrosis with a fistula, exposed reconstructive plates, scar tissue and thrombosised vessels in the neck requiring reoperations using other tissue. Specifically in patients with poor general health recovering from previous treatment, a minimally invasive reconstructive procedure may be necessary. The most common local or pedicled flaps consists of the pectoral muscle flap, trapezius muscle flap, LD and perforator flap, as well variations of these.<sup>111,123,243-247 68,144,248,249</sup>

The pedicular LD flap in secondary head and neck reconstructions yields reliable results.<sup>124,250,251</sup> The transpectoral pedicled LD (TPP-LD) flap used for salvage operations enables reconstruction of wide resections in morbid patients with a previous surgery or poor general health. The anatomy of the LD flap is stable and reliable with a long pedicle of good caliber, typically without atherosclerotic disease.<sup>117,252</sup>

The LD flap enables a two-team approach with simultaneous resection and reconstruction without requiring patient repositioning. PMMC is closer to the primary field and may not allow simultaneous harvesting of the flap, and the vascular pedicle from the thoracoacromial supply may lie in an irradiated field. Trapezius flaps are taken from the posterior back where patient repositioning is inevitable,<sup>111</sup> and the vascular supply depends on the transverse cervical vessels which may have been harmed during a previous neck dissection. The LD muscle segment is large and pliable, and the skin island can be positioned both vertically and horizontally with respect to the muscle as necessary during reconstruction. The muscular part is also considerably larger and thinner than in PMMC.<sup>244,253</sup> The LD flap also carries a good reach, with reconstructions extending to the vertex of the skull and contralateral orbit are possible.<sup>124</sup>

We studied the LD musculocutaneous flap tunnelled through the pectoral muscle to the recipient area in the head and neck area as a method to reconstruct large defects in patients unsuitable for microvascular surgery. The resection width of these patients was large, precluding local flaps as viable options.

The method of transferring LD through the axilla by releasing a part of the pectoral insertion was described by Sabatier<sup>124</sup> and summarised above. We presented a method here enabling a two-team approach that includes harvesting the flap in the decubitus position simultaneously with the resectioning of the head and neck area, thus shortening the duration of surgery. We found this type of flap was reliable and offered a pedicled version of a large flap unmatched in size by options such as the PMMC and trapezius flaps. Furthermore, the LD's reach proved better in the anterior facial area. PMMC is smaller in size and bulkier, although raising PMMC is easier with the patient in the supine position. The trapezius is better suited for use in posterior cervical reconstructions, but will not feauture the reach to the midface area. Furthermore, it is typically harvested when the patient is in the prone position, precluding a two-team approach and necessitating several repositionings. Another concern stems from the transverse cervical vessels needed by the trapezius compared to LD. These vessels may have been harmed during previous operations on the fifth lymphatic area of the neck and lie along the field of radiation of the neck<sup>111</sup>

Finally, donor site morbidity for LD flap harvest is normally well-tolerated and scars are aesthetically acceptable positioned on the patient's back.<sup>119,254,255</sup> The reliability of the trapezius flap is also good, with a success rate of over 97%, although patient repositioning and the shorter reach represent major drawbacks.<sup>256</sup> No systematic donor site analyses were found regarding postoperative donor site complications associated with the trapezius flap. By contrast, the pectoral flap is a workhorse particularly in ORL head and neck reconstructions. The flap is reliable and produces a good bulk of muscle and subcutaneous tissue with tolerable donor site complications.<sup>257,258</sup> Its drawbacks include the bulky flap for muscle and subcutaneous tissue reconstructions, while the donor site, particularly women's breasts, remain unsightly given the pectoral muscle scarring and result in possible shoulder impairment.<sup>244,259</sup> We therefore conclude that LD favours the donor site.

8.7 Methodological considerations: Study strengths and limitations The strength of these studies stems from the overall reliability of our materials—all data were gathered from a system within in the same hospital. Patients were all treated using the same recommendations and guidelines. All patients were evaluated pre- and postoperatively by the same multidisciplinary head and neck team, and underwent surgery largely by the same surgeons across years. As a singlecentre material, we can consider our dataset large.

Our material was collected retrospectively, and methods of reconstruction were not necessarily chosen on the basis of published classifications. A surgeon's own preference and familiarity with a method potentially biased our material. DCIA represents the first microvascular bone flap used in the Department of Maxillofacial Surgery, which is inevitably reflected both in the high proportion of this type of flap, particularly during the initial years in our study. This may also bias the higher rates of complications we observed. The general health of a patient during consultation also impacted flap selection. If a patient presented with atherosclerotic disease or diabetes accompanying weak leg pulses, the fibula flap was typically precluded without further comment. This then is reflected in better results for the fibula, since it most likely was only performed on patients with a more favourable health status. Furthermore, the scapula flap may require patient repositioning, and thus obese patients are not ideally reconstructed using this option, which may also impact our results.

Our analysis of patient-related complications associated with specific flaps suffers from a weakness related to how complications were scored. That is, we used no formal classification. Moreover, we only analysed complications registered in medical charts. Thus, complications or morbidities patients neglected to report may have been missed in the absence of a structured evaluation.

In our study of bone resorption over time, we found that only 21 of the original 186 patients evaluated fulfilled our strict criteria for study inclusion. We included a further 17 cases based on secondary specifications. We used the radiological modality as the determining factor, whereby drop out was most likely random and did not affect our results. Our results, however, represent new findings not previously presented in the literature.

A prospective study, particularly in Study II, would prove beneficial in recording complications more accurately. Retrospective collection of patient data depends greatly on the quality and accuracy of notes in patient medical records.

<u>8.8 Conclusions regarding mandibular and maxillary reconstructions</u> Based on this study and the literature analysed, we can draw the following conclusions regarding maxillomandibulary reconstructions. First, several measurable differences exist in the properties of the three most frequently used osseous flaps, with outcomes favouring the scapula and fibula flaps over DCIA flaps. Second, postoperative complications and donor site problems associate primarily with DCIA flaps. Third, volume analysis of the flaps showed a distinct difference in the remodelling of the bone in the years following reconstruction, where the fibula emerged as the most stable and the scapula the most prone to volume loss. This finding emerged most clearly from a true 3D volume analysis of all dimensions. Furthermore, all flaps tolerated both osteotomies for shaping as well as dental osseointegrated implants with a high reliability. Finally, patients unsuitable for microvascular reconstructions can be reconstructed using a large and reliable transpectorally rerouted pediceled LD flap, a particularly useful option for secondary and salvage procedures.

#### 8.9 Future prospects

The use of microvascular composite and osseous free flaps in the reconstruction of maxillomandibular defects will continue as the gold standard in the near future. Currently, 3D planning and manufacturing appears to aid greatly in surgery, which will likely further develop in the years to come. While promising reports of tissue engineering and stem cell–derived tissues exist, their roles remain unestablished. Tissue engineering and stem cell techniques appear too slow at present to treat patients with malignant disease. In addition, the role of pluripotent cells and growth factors along the site of a malignant tumour remain unclear. Furthermore, the total

cost must be addressed, although research on these methods continue to prove important.

In the near future, classifications of complications should be standardised across all patients in the head and neck group at Helsinki University Hospital. Preoperative risk factors will be assessed and a prospective analysis of the goal for each patient will be planned. Emphasis will be placed on early recovery and complication-free postoperative healing. Prospective studies on these factors are already drafted.

## **9** Conclusions

#### <u>9.1 Study I</u>

We analysed the scapula osteomyocutaneous flap and showed its versatility in complex reconstructions. The scapula bone tolerated osteotomies without complications. The use of the LD muscle prevented fistula formation compared to reconstruction with bone and skin flaps only. The scapula also allowed for the successful use of osseointegrated dental implants. In addition, donor site morbidity was considered low. We also eliminated earlier fears regarding inferior bone properties and the need to reposition the patient. Finally, this study encouraged the wider use of the scapula in reconstructive surgery of extensive defects.

#### 9.2 Study II

We analysed maxillomandibular defects reconstructed with scapula, fibula or iliac crest (DCIA) composite flaps looking specifically at patient outcomes and complications. We found several significant differences between the most frequently used flap options.

The scapula emerged as the most reliable option followed by the fibula. The overall general complication rate remained similar across groups, although DCIA patients experienced the most severe complications and the greatest number of flap losses. In postoperative recovery, the fibula and scapula flaps achieved the most positive properties and best outcomes. Finally, all flaps achieved similar results concerning dental implantation. Furthermore, elderly patients tolerated large surgeries well.

#### 9.3 Study III

The volume analysis of the bone over time showed that the fibula emerged as the most stable while the scapula is most prone to volume loss, with DCIA representing the intermediate option. In this study, we also showed that true 3D volume analysis is preferred as more accurate over previously used height-by-width measurements. Moreover, postoperative radiation therapy was not associated with a significantly higher volume loss. Here, we identified several aspects of remodelling or resorption for free vascularised osseous reconstructions not previously studied widely.

#### 9.4 Study IV

The use of the LD musculocutaneous flap illustrated its capacity to reconstruct large defects in locoregionally advanced cancer patients with few donor site complications yielding reliable outcomes. We also evaluated the size of the flap, its usefulness and donor site morbidity as favouring LD compared to the more widely used pectoral flap. Our results here also justify reconstructive surgery of advanced tumours as palliative treatment.

#### 10 Acknowledgements

This study was initiated during a congress on microsurgery in Barcelona, Spain in April 2011. The study was carried out at the Department of Plastic Surgery as well as the Department of Oral and Maxillofacial Surgery, Helsinki University Hospital. Financial support from Suomen Plastiikkakirurgiyhdistys- Chirurgi Plastici Fenniae and HUS-EVO is gratefully acknowledged.

I wish to express my sincere gratitude to the following persons involved in my scientifical development as well as important contributors in my clinical career:

My supervisors Docent Patrik Lassus and Jyrki Törnwall.

Patrik, my primary supervisor and mentor during these years. Thank you for your kind guidance and confidence in my work with a never-ending interest and patience, both during slow progression as well as in intense last minute correspondence and late discussions preparing manuscripts and this thesis. You always gave me your attention despite your own clinical work. We have had meetings and discussions on odd hours and places, including with your family and children at your home. You are true friend and colleague.

Jyrki, I thank you for your positive attitude and clinical support during this study as well as during my training in Oral and Maxillofacial Surgery. I especially value your skilful teaching in head and neck surgery and reconstructive planning and performance.

Erkki Tukiainen, as Professor and Head of Plastic Surgery. Thank you for giving me the opportunity to become a plastic surgeon and all the guidance you have given me during the years. I admire your as a broadly experienced scientist as well as an amazing surgeon and role model for younger doctors presenting and executing the most advanced solutions and innovations, and moreover, you have an outstanding attitude towards both patients and colleagues.

Christian Lindqvist, as Professor and former Head of Oral and Maxillofacial Surgery. You have been my professor already during my first dental training and you gave me your support to continue my studies in medical school. I am grateful for your confidence in me when you after my years in plastic surgery gave me the opportunity to join you and gave me the possibility to focus on head and neck reconstructive surgery. You were the Head of the Clinic for decades and managed to develop the speciality to the high standards and recognition we have today.

The reviewers of this thesis, Docent Outi Kaarela and Docent Ilpo Kinnunen, thank you for your kind and valuable comments and improvements of this thesis work. I especially value your time, while you performed your work after busy clinical work ours as well as during your Christmas holiday.

All of my co-workers and cowriters in this project. Docent Sinikka Suominen, thank you for your guidance in microsurgery as well as your valuable comments in the manuscript. Docent Jyrki Vuola, thank you for everything you taught me about burns as well as head and neck surgery. Your experienced and precise comments were valuable in preparing the manuscripts. Docent Leif Bäck, thank you for your comments and improvements in my scientifical writing. DDS, PhD, radiologist Satu Apajalahti, your extensive skills and hours and hours of analysing bone segments
were crucial in this work. You always have the patience and your kindness and I highly appreciate your contribution. MD Annastiina Husso, thank you for your cooperation in preparing our extensive data in the analysis of complications and your crucial role in structuring and finishing our shared manuscript. MD, DDS, PhD, ESICM Erika Wilkman, thank you for your valuable contribution in statistical analysis and developing the method for presenting the data in our manuscript.

I am also grateful to Peter Grönholm, your valuable skills in retrieving data from both ancient and new hospital data systems were critical in this work. MD, DDS Karri Mesimäki, my closest colleague and co-worker. Thank you for your friendship and clinical expertise. You have taught me a lot during the years, I highly value your surgical skills and expertise and your knowledge in 3D planning and manufacturing is crucial in our work. I will also always remember all the hours you covered my back when I was doing this book. Docent Risto Kontio, Head of Oral and Maxillofacial Surgery, thank you for your support and positive attitude during this work. You are the number one in virtual planning and also started the microvascular reconstructions in Oral and Maxillofacial Surgery in the end of the 20th century.

I also deeply respect and highly enjoy working together with all the colleagues in the Departments of Plastic Surgery, Oral and Maxillofacial Surgery, Radiology, Pathology, Oncology and Oto-Rhino-Laryngology, thank you for all the wisdom you have shared.

Finally, my love to my family. To my parents Margita and Peter, you have taken care of us and our sons and also showed that there is another world outside. To my sons Lukas, Linus and Isak. You have had to withstand both me and your mother working with our respective thesis alongside our clinical work and on-call duties for a substantial part of your lives. You are super and the best thing in my life! My greatest devotion and love to my Erika, you have been my lovely wife, my best friend, the mother of our three boys, my colleague, my science partner and partly mentor during two decades. I could never have done this without you!

In Esbo, 17th of April, 2017

Tommy Wilkman

## References

1. WHO. Www.who.int/whosis/icd10/.

2. Engholm G, Ferlay J, Christensen N, et al. NORDCAN--a nordic tool for cancer information, planning, quality control and research. *Acta Oncol.* 2010;49(5):725-736.

3. Engholm G, Ferlay J, Christensen N, et al. NORDCAN: Cancer incidence, mortality, prevalence and survival in the nordic countries, version 7.3 (08.07.2016). association of the nordic cancer registries. danish cancer society, Available from http://www.ancr.nu, accessed on day/month/year. 2016.

4. Syrjänen S, Grenman R, Lakoma A, et al. Oral cancer, *Current care guidelines*, Working group appointed by the finnish medical society duodecim and the finnish dental society apollonia, 24.01.2012 . . 2012.

5. International agency for research on cancer, IARC. 150 cours albert thomas, 69372 lyonCEDEX 08, france . hptt://screening.iarc.fr Web site. . Published 2017.

6. American Cancer Society. Cancer facts and figures 2016. <u>www.cancer.org</u> Web site. . Updated 2016.

7. McCarthy CM, Cordeiro PG. Microvascular reconstruction of oncologic defects of the midface. *Plast Reconstr Surg.* 2010;126(6):1947-1959.

8. Keski-Santti H, Kontio R, Tornwall J, et al. Sentinel lymph node biopsy or elective neck dissection for patients with oral squamous cell carcinoma? *Eur Arch Otorhinolaryngol.* 2008;265 Suppl 1:S13-7.

9. Kowalski LP, Sanabria A. Elective neck dissection in oral carcinoma: A critical review of the evidence. *Acta Otorhinolaryngol Ital.* 2007;27(3):113-117.

10. Binahmed A, Nason RW, Abdoh AA. The clinical significance of the positive surgical margin in oral cancer. *Oral Oncol.* 2007;43(8):780-784.

11. Chinn SB, Myers JN. Oral cavity carcinoma: Current management, controversies, and future directions. *Journal of Clinical Oncology*. 2015;33(29):3269-3276.

12. Rogers SN, Brown JS, Woolgar JA, et al. Survival following primary surgery for oral cancer. *Oral Oncol.* 2009;45(3):201-211.

13. Shah JP, Gil Z. Current concepts in management of oral cancer--surgery. *Oral Oncol.* 2009;45(4-5):394-401.

14. Williams MD. Determining adequate margins in head and neck cancers: Practice and continued challenges. *Curr Oncol Rep.* 2016;18(9):54-016-0540-y.

15. Luryi AL, Chen MM, Mehra S, Roman SA, Sosa JA, Judson BL. Positive surgical margins in early stage oral cavity cancer: An analysis of 20,602 cases. *Otolaryngol Head Neck Surg*. 2014;151(6):984-990.

 Silver CE, Rinaldo A, Ferlito A. Crile's neck dissection. *Laryngoscope*. 2007;117(11):1974-1977.

17. Robbins KT, Clayman G, Levine PA, et al. Neck dissection classification update: Revisions proposed by the american head and neck society and the american academy of otolaryngology-head and neck surgery. *Arch Otolaryngol Head Neck Surg.* 2002;128(7):751-758.

18. D'Cruz AK, Vaish R, Kapre N, et al. Elective versus therapeutic neck dissection in nodenegative oral cancer. *N Engl J Med*. 2015;373(6):521-529. 19. Brown JS, Blackburn TK, Woolgar JA, et al. A comparison of outcomes for patients with oral squamous cell carcinoma at intermediate risk of recurrence treated by surgery alone or with post-operative radiotherapy. *Oral Oncol.* 2007;43(8):764-773.

20. Rogers SN, Brown JS, Woolgar JA, et al. Survival following primary surgery for oral cancer. *Oral Oncol.* 2009;45(3):201-211.

21. Sharma M, Sah P, Sharma SS, Radhakrishnan R. Molecular changes in invasive front of oral cancer. *J Oral Maxillofac Pathol.* 2013;17(2):240-247.

22. Almangush A, Bello IO, Keski-Santti H, et al. Depth of invasion, tumor budding, and worst pattern of invasion: Prognostic indicators in early-stage oral tongue cancer. *Head Neck*. 2014;36(6):811-818.

23. Makinen LK, Hayry V, Atula T, et al. Prognostic significance of matrix metalloproteinase-2, -8, -9, and -13 in oral tongue cancer. *J Oral Pathol Med*. 2012;41(5):394-399.

24. Makinen LK, Atula T, Hayry V, et al. Predictive role of toll-like receptors 2, 4, and 9 in oral tongue squamous cell carcinoma. *Oral Oncol.* 2015;51(1):96-102.

25. Yasumatsu R, Nakashima T, Sato M, et al. Clinical management of squamous cell carcinoma associated with sinonasal inverted papilloma. *Auris Nasus Larynx*. 2016.

26. Patel TD, Carniol ET, Vazquez A, Baredes S, Liu JK, Eloy JA. Sinonasal fibrosarcoma: Analysis of the surveillance, epidemiology, and end results database. *Int Forum Allergy Rhinol.* 2016;6(2):201-205.

27. Lund VJ, Clarke PM, Swift AC, McGarry GW, Kerawala C, Carnell D. Nose and paranasal sinus tumours: United kingdom national multidisciplinary guidelines. *J Laryngol Otol*. 2016;130(S2):S111-S118.

28. Konuthula N, Khan MN, Parasher A, et al. The presentation and outcomes of mucosal melanoma in 695 patients. *Int Forum Allergy Rhinol.* 2017;7(1):99-105.

29. Jain S, Kaur R, Koul R. Malignant fibrous histiocytoma of maxillary sinus- a diagnostic challenge. *Indian J Surg Oncol.* 2015;6(3):259-262.

30. Johnson J, Jundt J, Hanna I, Shum JW, Badger G, Melville JC. Resection of an ameloblastoma in a pediatric patient and immediate reconstruction using a combination of tissue engineering and costochondral rib graft: A case report. *J Am Dent Assoc.* 2016.

31. Milman T, Ying GS, Pan W, LiVolsi V. Ameloblastoma: 25 year experience at a single institution. *Head Neck Pathol*. 2016;10(4):513-520.

32. Pogrel AM. The diagnosis and management of giant cell lesions of the jaws. *Ann Maxillofac Surg.* 2012;2(2):102-106.

33. Liu Y, Han B, Yu T, Li L. A large odontogenic myxoma of the bilateral maxillae: A case report. *Oncol Lett.* 2014;8(3):1328-1332.

34. De Melo WM, Pereira-Santos D, Breda MA,Jr, Sonoda CK, Hochuli-Vieira E, Serra e Silva FM. Using the condylar prosthesis after resection of a large odontogenic myxoma tumor in the mandible. *J Craniofac Surg*. 2012;23(5):e398-400.

35. Mucke T, Krestan CR, Mitchell DA, Kirschke JS, Wutzl A. Bisphosphonate and medication-related osteonecrosis of the jaw: A review. *Semin Musculoskelet Radiol.* 2016;20(3):305-314.

36. Kuroshima S, Kaku M, Matsuura T, Atsuta I, Ayukawa Y, Sawase T. Medication-related osteonecrosis of the jaw; what should we do as prosthodontists? *J Prosthodont Res.* 2016;60(4):229-230.

37. Kim TH, Seo WG, Koo CH, Lee JH. Evaluation of the predisposing factors and involved outcome of surgical treatment in bisphosphonate-related osteonecrosis of the jaw cases including bone biopsies. *J Korean Assoc Oral Maxillofac Surg.* 2016;42(4):193-204.

38. Neto T, Horta R, Balhau R, et al. Resection and microvascular reconstruction of bisphosphonate-related osteonecrosis of the jaw: The role of microvascular reconstruction. *Head Neck.* 2016;38(8):1278-1285.

39. Horta R, Monteiro D, Neto T, et al. Microsurgical reconstruction for radiation- and bisphosphonate-induced mandible osteonecrosis based on patient-specific physiopathologic mechanisms. *J Craniofac Surg.* 2014;25(5):1793-1796.

40. Makitie I, Pihlajamaki H. Fatal firearm injuries in finland: A nationwide survey. *Scand J Surg.* 2002;91(4):328-331.

41. Mattila VM, Makitie I, Pihlajamaki H. Trends in hospitalization for firearm-related injury in finland from 1990 to 2003. *J Trauma*. 2006;61(5):1222-7; discussion 1227.

42. Öhngren L. Malignant tumors of the maxillo-ethmoidal <br />region. *Acta Otolaryngol* (*Suppl*). 1933;19:1476.

43. MacGregor IA, Macgregor F. *Cancer of the face and mouth <br />* Edinburgh: Churchill Livingstone; 1986:pp. 544–568.

44. Spiro RH, Strong EW, Shah JP. Maxillectomy and its classification. *Head Neck*. 1997;19(4):309-314.

45. Brown JS, Rogers SN, McNally DN, Boyle M. A modified classification for the maxillectomy defect <br /> *Head Neck*. 2000:17-26.

46. Cordeiro PG, Santamaria E. A classification system and algorithm for reconstruction of maxillectomy and midfacial defects. *Plast Reconstr Surg*. 2000;105(7):2331-46; discussion 2347-8.

47. Okay DJ, Genden E, Buchbinder D, Urken M. Prosthodontic guidelines for surgical reconstruction of the maxilla: A classification system of defects. *J Prosthet Dent*.
2001;86(4):352-363.

48. Rodriguez ED, Martin M, Bluebond-Langner R, Khalifeh M, Singh N, Manson PN. Microsurgical reconstruction of posttraumatic high-energy maxillary defects: Establishing the effectiveness of early reconstruction. *Plast Reconstr Surg*. 2007;120(7 Suppl 2):103S-17S.

49. Brown JS, Shaw RJ. Reconstruction of the maxilla and midface: Introducing a new classification. *Lancet Oncol.* 2010;11(10):1001-1008.

50. Bidra AS, Jacob RF, Taylor TD. Classification of maxillectomy defects: A systematic review and criteria necessary for a universal description. *J Prosthet Dent*. 2012;107(4):261-270.

51. Costa H, Zenha H, Sequeira H, et al. Microsurgical reconstruction of the maxilla: Algorithm and concepts. *J Plast Reconstr Aesthet Surg*. 2015;68(5):e89-e104.

52. Rosemann G. Resection of the mandible in oral tumours. HNO. 1972;20(6):166-171.

53. Pavlov BL. Classification of mandibular defects. Stomatologiia (Mosk). 1974;53(5):43-46.

54. Brown JS, Barry C, Ho M, Shaw R. A new classification for mandibular defects after oncological resection. *Lancet Oncol.* 2016;17(1):e23-30.

55. Jewer DD, Boyd JB, Manktelow RT, et al. Orofacial and mandibular reconstruction with the iliac crest free flap: A review of 60 cases and a new method of classification. *Plast Reconstr Surg.* 1989;84(3):391-403; discussion 404-5.

56. Urken ML, Weinberg H, Vickery C, Buchbinder D, Lawson W, Biller HF. Oromandibular reconstruction using microvascular composite free flaps. report of 71 cases and a new classification scheme for bony, soft-tissue, and neurologic defects. *Arch Otolaryngol Head Neck Surg.* 1991;117(7):733-744.

57. Disa JJ, Cordeiro PG. Mandible reconstruction with microvascular surgery. *Semin Surg Oncol.* 2000;19(3):226-234.

58. Disa JJ, Cordeiro PG. Mandible reconstruction with microvascular surgery. *Semin Surg Oncol.* 2000;19(3):226-234.

59. Takushima A, Harii K, Asato H, Momosawa A, Okazaki M, Nakatsuka T. Choice of osseous and osteocutaneous flaps for mandibular reconstruction. *Int J Clin Oncol.* 2005;10(4):234-242.

60. Takushima A, Harii K, Asato H, Nakatsuka T, Kimata Y. Mandibular reconstruction using microvascular free flaps: A statistical analysis of 178 cases. *Plast Reconstr Surg*. 2001;108(6):1555-1563.

61. Hanasono MM, Matros E, Disa JJ. Important aspects of head and neck reconstruction. *Plast Reconstr Surg.* 2014;134(6):968e-80e.

62. Hanasono MM, Weinstock YE, Yu P. Reconstruction of extensive head and neck defects with multiple simultaneous free flaps. *Plast Reconstr Surg*. 2008;122(6):1739-1746.

63. Hanasono MM, Zevallos JP, Skoracki RJ, Yu P. A prospective analysis of bony versus soft-tissue reconstruction for posterior mandibular defects. *Plast Reconstr Surg*. 2010;125(5):1413-1421.

64. Boyd JB, Gullane PJ, Rotstein LE, Brown DH, Irish JC. Classification of mandibular defects. *Plast Reconstr Surg.* 1993;92(7):1266-1275.

65. Schultz BD, Sosin M, Nam A, et al. Classification of mandible defects and algorithm for microvascular reconstruction. *Plast Reconstr Surg.* 2015;135(4):743e-54e.

66. Thorne C, Beasly R, Aston S, Bartlett S, Gurtner G, Spear S. *Grabb and smith 's plastic surgery*. Philadelphia, USA: Lippincott Williams&Wilkins; 2007.

67. Daniel RK. Mandibular reconstruction with free tissue transfers. *Ann Plast Surg*.1978;1(4):346-371.

68. Deschler DG, Hayden RE. Head and neck reconstruction. *Neuroimaging Clin N Am*. 1996;6(2):505-514.

69. Hanasono MM, Zevallos JP, Skoracki RJ, Yu P. A prospective analysis of bony versus soft-tissue reconstruction for posterior mandibular defects. *Plast Reconstr Surg*. 2010;125(5):1413-1421.

70. Rinaldo A, Shaha AR, Wei WI, Silver CE, Ferlito A. Microvascular free flaps: A major advance in head and neck reconstruction. *Acta Otolaryngol (Stockh)*. 2002;122(7):779-784.

71. Fleischmann W, Strecker W, Bombelli M, Kinzl L. Vacuum sealing as treatment of soft tissue damage in open fractures. *Unfallchirurg*. 1993;96(9):488-492.

72. Steele C. Clinical lecture on the transplantation of skin. Br Med J. 1870;2(519):621-623.

73. Radovan C. Tissue expansion in soft-tissue reconstruction. *Plast Reconstr Surg*.1984;74(4):482-492.

74. Champaneria MC, Workman AD, Gupta SC. Sushruta: Father of plastic surgery. *Ann Plast Surg.* 2014;73(1):2-7.

75. Taylor GI, Palmer JH. The vascular territories (angiosomes) of the body: Experimental study and clinical applications. *Br J Plast Surg*. 1987;40(2):113-141.

76. Johansson B, Grepe A, Wannfors K, Aberg P, Hirsch JM. Volumetry of simulated bone grafts in the edentulous maxilla by computed tomography: An experimental study. *Dentomaxillofac Radiol.* 2001;30(3):153-156.

77. McAllister BS, Haghighat K. Bone augmentation techniques. *J Periodontol*. 2007;78(3):377-396.

78. Sittitavornwong S, Gutta R. Bone graft harvesting from regional sites. *Oral Maxillofac Surg Clin North Am.* 2010;22(3):317-30, v-vi.

79. Rehrmann A. On mandibular alveoloplasty. Zahnarztl Rundsch. 1953;62(18):505-512.

80. Rehrmann A. Plastic surgery of the facial-maxillary area. HNO. 1957;6(5):139-144.

81. Jamali JA. Palatal flap. Oral Maxillofac Surg Clin North Am. 2014;26(3):305-311.

82. Yamazaki Y, Yamaoka M, Hirayama M, Shimada H. The submucosal island flap in the closure of oro-antral fistula. *Br J Oral Maxillofac Surg.* 1985;23(4):259-263.

83. Strauss RA, Kain NJ. Tongue flaps. *Oral Maxillofac Surg Clin North Am*. 2014;26(3):313-325.

84. Pribaz J, Stephens W, Crespo L, Gifford G. A new intraoral flap: Facial artery musculomucosal (FAMM) flap. *Plast Reconstr Surg*. 1992;90(3):421-429.

85. Pribaz JJ, Meara JG, Wright S, Smith JD, Stephens W, Breuing KH. Lip and vermilion reconstruction with the facial artery musculomucosal flap. *Plast Reconstr Surg*. 2000;105(3):864-872.

86. Napolitano M, Mast BA. The nasolabial flap revisited as an adjunct to floor-of-mouth reconstruction. *Ann Plast Surg.* 2001;46(3):265-268.

87. Heller JB, Gabbay JS, Trussler A, Heller MM, Bradley JP. Repair of large nasal septal perforations using facial artery musculomucosal (FAMM) flap. *Ann Plast Surg.* 2005;55(5):456-459.

88. Hatoko M, Kuwahara M, Tanaka A, Yurugi S. Use of facial artery musculomucosal flap for closure of soft tissue defects of the mandibular vestibule. *Int J Oral Maxillofac Surg*. 2002;31(2):210-211.

89. Fassio E, Laure B, Durand JL, et al. The facial artery-buccinator musculo-mucosal flap for reconstruction of the palate. *Rev Stomatol Chir Maxillofac*. 1999;100(5):221-225.

90. Dupoirieux L, Plane L, Gard C, Penneau M. Anatomical basis and results of the facial artery musculomucosal flap for oral reconstruction. *Br J Oral Maxillofac Surg*. 1999;37(1):25-28.

91. Braasch DC, Lam D, Oh ES. Maxillofacial reconstruction with nasolabial and facial artery musculomucosal flaps. *Oral Maxillofac Surg Clin North Am.* 2014;26(3):327-333.

92. Futrell JW, Johns ME, Edgerton MT, Cantrell RW, Fitz-Hugh GS. Platysma myocutaneous flap for intraoral reconstruction. *Am J Surg.* 1978;136(4):504-507.

93. Coleman JJ,3rd, Jurkiewicz MJ, Nahai F, Mathes SJ. The platysma musculocutaneous flap: Experience with 24 cases. *Plast Reconstr Surg.* 1983;72(3):315-323.

94. Hurwitz DJ, Rabson JA, Futrell JW. The anatomic basis for the platysma skin flap. *Plast Reconstr Surg.* 1983;72(3):302-314.

95. Baur DA, Williams J, Alakaily X. The platysma myocutaneous flap. *Oral Maxillofac Surg Clin North Am*. 2014;26(3):381-387.

96. Lentz J. Re´section du col du condyle avec interposition d'un lambeau temporal entre les surfaces de re´section. gue´rison. Assoc franc, de chirur (paris) 1895;9:113–117. .

83

97. Hanasono MM, Utley DS, Goode RL. The temporalis muscle flap for reconstruction after head and neck oncologic surgery. *Laryngoscope*. 2001;111(10):1719-1725.

98. Martin D, Pascal JF, Baudet J, et al. The submental island flap: A new donor site. anatomy and clinical applications as a free or pedicled flap. *Plast Reconstr Surg*. 1993;92(5):867-873.

99. Cheng A, Bui T. Submental island flap. *Oral Maxillofac Surg Clin North Am*. 2014;26(3):371-379.

100. Faltaous AA, Yetman RJ. The submental artery flap: An anatomic study. *Plast Reconstr Surg.* 1996;97(1):56-60; discussion 61-2.

101. Demir Z, Kurtay A, Sahin U, Velidedeoglu H, Celebioglu S. Hair-bearing submental artery island flap for reconstruction of mustache and beard. *Plast Reconstr Surg*. 2003;112(2):423-429.

102. Ramirez CA, Fernandes RP. The supraclavicular artery island and trapezius myocutaneous flaps in head and neck reconstruction. *Oral Maxillofac Surg Clin North Am*. 2014;26(3):411-420.

103. Mutter T. Case of deformity from burns relieved by operation. *Am J Med Sci,*.1842;4:66-80.

104. Chan JW, Wong C, Ward K, Saint-Cyr M, Chiu ES. Three- and four-dimensional computed tomographic angiography studies of the supraclavicular artery island flap. *Plast Reconstr Surg.* 2010;125(2):525-531.

105. Bakamjian VY. A two-stage method for pharyngoesophageal reconstruction with a primary pectoral skin flap. *Plast Reconstr Surg.* 1965;36:173-184.

106. Morel F, Peron JM, Trost O. A plea for the systematic preservation of the deltopectoralis (bakamjian) flap in pectoralis major flap harvesting. *Int J Oral Maxillofac Surg*. 2014;43(9):1169.

107. Schellekens PP, Paes EC, Hage JJ, van der Wal MB, Bleys RL, Kon M. Anatomy of the vascular pedicle of the internal mammary artery perforator (IMAP) flap as applied for head and neck reconstruction. *J Plast Reconstr Aesthet Surg*. 2011;64(1):53-57.

108. Vesely MJ, Murray DJ, Novak CB, Gullane PJ, Neligan PC. The internal mammary artery perforator flap: An anatomical study and a case report. *Ann Plast Surg*. 2007;58(2):156-161.

109. Yu P, Roblin P, Chevray P. Internal mammary artery perforator (IMAP) flap for tracheostoma reconstruction. *Head Neck*. 2006;28(8):723-729.

110. Conley J. Use of composite flaps containing bone for major repairs in the head and neck. *Plast Reconstr Surg.* 1972;49(5):522-526.

111. Chen WL, Deng YF, Peng GG, et al. Extended vertical lower trapezius island myocutaneous flap for reconstruction of cranio-maxillofacial defects. *Int J Oral Maxillofac Surg.* 2007;36(2):165-170.

112. PICKRELL KL, BAKER HM, COLLINS JP. Reconstructive surgery of the chest wall. *Surg Gynecol Obstet.* 1947;84(4):465-476.

113. Ariyan S. The pectoralis major myocutaneous flap. A versatile flap for reconstruction in the head and neck. *Plast Reconstr Surg.* 1979;63(1):73-81.

114. Kadlub N, Shin JH, Ross DA, et al. Use of the external pectoralis myocutaneous major flap in anterior skull base reconstruction. *Int J Oral Maxillofac Surg*. 2013;42(4):453-457.

115. Patel K, Lyu DJ, Kademani D. Pectoralis major myocutaneous flap. *Oral Maxillofac Surg Clin North Am.* 2014;26(3):421-426.

116. Quillen CG, Shearin JC,Jr, Georgiade NG. Use of the latissimus dorsi myocutaneous island flap for reconstruction in the head and neck area: Case report. *Plast Reconstr Surg*. 1978;62(1):113-117.

117. Bartlett SP, May JW,Jr, Yaremchuk MJ. The latissimus dorsi muscle: A fresh cadaver study of the primary neurovascular pedicle. *Plast Reconstr Surg.* 1981;67(5):631-636.

118. Barton FE,Jr, Spicer TE, Byrd HS. Head and neck reconstruction with the latissimus dorsi myocutaneous flap: Anatomic observations and report of 60 cases. *Plast Reconstr Surg*. 1983;71(2):199-204.

119. Adams WP,Jr, Lipschitz AH, Ansari M, Kenkel JM, Rohrich RJ. Functional donor site morbidity following latissimus dorsi muscle flap transfer. *Ann Plast Surg.* 2004;53(1):6-11.

120. Haughey BH, Fredrickson JM. The latissimus dorsi donor site. current use in head and neck reconstruction. *Arch Otolaryngol Head Neck Surg.* 1991;117(10):1129-1134.

121. Salmi A, Tuominen R, Tukiainen E, Asko-Seljavaara S. Morbidity of donor and recipient sites after free flap surgery. A prospective study. *Scandinavian Journal of Plastic & Reconstructive Surgery & Hand Surgery*. 1995;29(4):337-341.

122. Har-El G, Bhaya M, Sundaram K. Latissimus dorsi myocutaneous flap for secondary head and neck reconstruction. *Am J Otolaryngol.* 1999;20(5):287-293.

123. Ong HS, Ji T, Zhang CP. The pedicled latissimus dorsi myocutaneous flap in head and neck reconstruction. *Oral Maxillofac Surg Clin North Am.* 2014;26(3):427-434.

124. Sabatier RE, Bakamjian VY. Transaxillary latissimus dorsi flap reconstruction in head and neck cancer. limitations and refinements in 56 cases. *Am J Surg.* 1985;150(4):427-434.

125. Urken ML, Buchbinder D, Costantino PD, et al. Oromandibular reconstruction using microvascular composite flaps: Report of 210 cases. *Arch Otolaryngol Head Neck Surg*. 1998;124(1):46-55.

126. Hurvitz KA, Kobayashi M, Evans GR. Current options in head and neck reconstruction. *Plast Reconstr Surg.* 2006;118(5):122e-133e.

127. Genden EM, Rinaldo A, Suárez C, Wei WI, Bradley PJ, Ferlito A. Complications of free flap transfers for head and neck reconstruction following cancer resection. *Oral Oncol.* 2004;40(10):979-984.

128. Wong CH, Wei FC. Microsurgical free flap in head and neck reconstruction. *Head Neck*. 2010;32(9):1236-1245.

129. Muhlbauer W, Herndl E, Stock W. The forearm flap. *Plast Reconstr Surg*.1982;70(3):336-344.

130. Koshima I, Fukuda H, Soeda S. Free combined anterolateral thigh flap and vascularized iliac bone graft with double vascular pedicle. *J Reconstr Microsurg*. 1989;5(1):55-61.

131. Song R, Song Y, Yu Y, Song Y. The upper arm free flap. Clin Plast Surg. 1982;9(1):27-35.

132. Lovie MJ, Duncan GM, Glasson DW. The ulnar artery forearm free flap. *Br J Plast Surg*. 1984;37(4):486-492.

133. Ozkan HS, Irkoren S, Aydin OE, Eryilmaz A, Karaca H. Medial sural artery perforator flap in head and neck reconstruction. *Eur Arch Otorhinolaryngol.* 2016.

134. Lassus P, Lindford AJ. Free temporal artery posterior auricular skin (TAPAS) flap: A new option in facial and intra-oral reconstruction. *Microsurgery*. 2016.

135. Koshima I, Yamamoto H, Hosoda M, Moriguchi T, Orita Y, Nagayama H. Free combined composite flaps using the lateral circumflex femoral system for repair of massive defects of the head and neck regions: An introduction to the chimeric flap principle. *Plast Reconstr Surg.* 1993;92(3):411-420.

136. Koshima I, Handa T, Satoh Y, Akisada K, Orita Y, Yamamoto H. Free rectus abdominis muscle perforating artery flaps for reconstruction of the head and neck defects. *Nihon Jibiinkoka Gakkai Kaiho*. 1995;98(1):1-7.

137. Cho A, Hall FT. Review of perforator flaps in head and neck cancer surgery. *Curr Opin Otolaryngol Head Neck Surg.* 2016;24(5):440-446.

138. Taylor GI, Miller GD, Ham FJ. The free vascularized bone graft. A clinical extension of microvascular techniques. *Plast Reconstr Surg.* 1975;55(5):533-544.

139. Okay D, Al Shetawi AH, Moubayed SP, Mourad M, Buchbinder D, Urken ML. Worldwide 10-year systematic review of treatment trends in fibula free flap for mandibular reconstruction. *J Oral Maxillofac Surg.* 2016.

140. Wei FC, Chen HC, Chuang CC, Noordhoff MS. Fibular osteoseptocutaneous flap: Anatomic study and clinical application. *Plast Reconstr Surg*. 1986;78(2):191-200.

141. Cordeiro PG, Disa JJ, Hidalgo DA, Hu QY. Reconstruction of the mandible with osseous free flaps: A 10-year experience with 150 consecutive patients. *Plast Reconstr Surg*. 1999;104(5):1314-1320.

142. Abou-Foul AK, Borumandi F. Anatomical variants of lower limb vasculature and implications for free fibula flap: Systematic review and critical analysis. *Microsurgery*. 2016;36(2):165-172.

143. Lutz BS, Wei FC, Ng SH, Chen IH, Chen SH. Routine donor leg angiography before vascularized free fibula transplantation is not necessary: A prospective study in 120 clinical cases. *Plast Reconstr Surg.* 1999;103(1):121-127.

144. Urken ML, Buchbinder D, Costantino PD, et al. Oromandibular reconstruction using microvascular composite flaps: Report of 210 cases. *Arch Otolaryngol Head Neck Surg*. 1998;124(1):46-55.

145. Garvey PB, Chang EI, Selber JC, et al. A prospective study of preoperative computed tomographic angiographic mapping of free fibula osteocutaneous flaps for head and neck reconstruction. *Plast Reconstr Surg*. 2012;130(4):541e-549e.

146. Ling XF, Peng X. What is the price to pay for a free fibula flap? A systematic review of donor-site morbidity following free fibula flap surgery. *Plast Reconstr Surg*. 2012;129(3):657-674.

147. Moubayed SP, L'Heureux-Lebeau B, Christopoulos A, et al. Osteocutaneous free flaps for mandibular reconstruction: Systematic review of their frequency of use and a preliminary quality of life comparison. *J Laryngol Otol*. 2014;128(12):1034-1043.

148. Taylor GI, Townsend P, Corlett R. Superiority of the deep circumflex iliac vessels as the supply for free groin flaps. clinical work. *Plast Reconstr Surg.* 1979;64(6):745-759.

149. Taylor GI, Corlett RJ, Ashton MW. The evolution of free vascularized bone transfer: A 40-year experience. *Plastic & Reconstructive Surgery*. 2016;137(4):1292-1305.

150. Urken ML, Vickery C, Weinberg H, Buchbinder D, Lawson W, Biller HF. The internal oblique-iliac crest osseomyocutaneous free flap in oromandibular reconstruction. report of 20 cases. *Arch Otolaryngol Head Neck Surg.* 1989;115(3):339-349.

151. Guo L, Ferraro NF, Padwa BL, Kaban LB, Upton J. Vascularized fibular graft for pediatric mandibular reconstruction. *Plast Reconstr Surg.* 2008;121(6):2095-2105.

152. Head C, Alam D, Sercarz JA, et al. Microvascular flap reconstruction of the mandible: A comparison of bone grafts and bridging plates for restoration of mandibular continuity. *Otolaryngol Head Neck Surg.* 2003;129(1):48-54.

153. Gilbert A, Teot L. The free scapular flap. Plast Reconstr Surg. 1982;69(4):601-604.

154. dos Santos LF. The vascular anatomy and dissection of the free scapular flap. *Plast Reconstr Surg.* 1984;73(4):599-604.

155. Swartz WM, Banis JC, Newton ED, Ramasastry SS, Jones NF, Acland R. The osteocutaneous scapular flap for mandibular and maxillary reconstruction. *Plast Reconstr Surg.* 1986;77(4):530-545.

156. Sullivan MJ, Carroll WR, Baker SR, Crompton R, Smith-Wheelock M. The free scapular flap for head and neck reconstruction. *Am J Otolaryngol.* 1990;11(5):318-327.

157. Shimizu T, Ohno K, Michi K, Segawa K, Takiguchi R. Morphometric examination of the free scapular flap. *Plast Reconstr Surg.* 1997;99(7):1947-1953.

158. Uglesic V, Virag M, Varga S, Knezevic P, Milenovic A. Reconstruction following radical maxillectomy with flaps supplied by the subscapular artery. *J Craniomaxillofac Surg*. 2000;28(3):153-160.

159. Brown J, Bekiroglu F, Shaw R. Indications for the scapular flap in reconstructions of the head and neck. *Br J Oral Maxillofac Surg.* 2010;48(5):331-337.

160. Chepeha DB, Khariwala SS, Chanowski EJ, et al. Thoracodorsal artery scapular tip autogenous transplant: Vascularized bone with a long pedicle and flexible soft tissue. *Arch Otolaryngol Head Neck Surg.* 2010;136(10):958-964. 161. Hasan Z, Gore SM, Ch'ng S, Ashford B, Clark JR. Options for configuring the scapular free flap in maxillary, mandibular, and calvarial reconstruction. *Plast Reconstr Surg*.
2013;132(3):645-655.

162. Clark JR, Vesely M, Gilbert R. Scapular angle osteomyogenous flap in postmaxillectomy reconstruction: Defect, reconstruction, shoulder function, and harvest technique. *Head Neck*. 2008;30(1):10-20.

163. Soutar DS, Scheker LR, Tanner NS, McGregor IA. The radial forearm flap: A versatile method for intra-oral reconstruction. *Br J Plast Surg*. 1983;36(1):1-8.

164. Soutar DS, Widdowson WP. Immediate reconstruction of the mandible using a vascularized segment of radius. *Head Neck Surg.* 1986;8(4):232-246.

165. Thoma A, Khadaroo R, Grigenas O, et al. Oromandibular reconstruction with the radialforearm osteocutaneous flap: Experience with 60 consecutive cases. *Plast Reconstr Surg*. 1999;104(2):368-378.

166. Villaret DB, Futran NA. The indications and outcomes in the use of osteocutaneous radial forearm free flap. *Head Neck*. 2003;25(6):475-481.

167. Cordeiro PG, Bacilious N, Schantz S, Spiro R. The radial forearm osteocutaneous "sandwich" free flap for reconstruction of the bilateral subtotal maxillectomy defect. *Ann Plast Surg.* 1998;40(4):397-402.

168. ENTIN MA. Reconstruction in congenital deformity of the temporo-mandibular component. *Plast Reconstr Surg Transplant Bull.* 1958;21(6):461-469.

169. DINGMAN RO, GRABB WC. RECONSTRUCTION OF BOTH MANDIBULAR CONDYLES WITH METATARSAL BONE GRAFTS. *Plastic & Reconstructive Surgery*. 1964;34:441-451. 170. Vilkki SK, Hukki J, Nietosvaara Y, Hurmerinta K, Suominen E. Microvascular temporomandibular joint and mandibular ramus reconstruction in hemifacial microsomia. *J Craniofac Surg.* 2002;13(6):809-815.

171. Kim JW, Choi YJ, Lee HJ, Yi KH, Kim HJ, Hu KS. Anatomic study of the dorsalis pedis artery, first metatarsal artery, and second metatarsal bone for mandibular reconstruction. *J Oral Maxillofac Surg.* 2015;73(8):1627-1636.

172. Potter JK, Dierks EJ. Vascularized options for reconstruction of the mandibular condyle. Seminars in Plastic Surgery. 2008;22(3):156-160.

173. Ostrup LT, Fredrickson JM. Reconstruction of mandibular defects after radiation, using a free, living bone graft transferred by microvascular anastomose. an experimental study. *Plastic & Reconstructive Surgery*. 1975;55(5):563-572.

174. Serafin D, Georgiade NG, Peters CR. Microsurgical composite tissue transplantation: A method of immediate reconstruction of the head and neck. *Clin Plast Surg.* 1976;3(3):447-457.

175. Serafin D, Georgiade NG. Microsurgical composite tissue transplantation. *Ann Surg*. 1978;187(6):620-628.

176. Harashina T, Nakajima H, Imai T. Reconstruction of mandibular defects with revascularized free rib grafts. *Plast Reconstr Surg.* 1978;62(4):514-522.

177. Guyuron B, Lasa CI,Jr. Unpredictable growth pattern of costochondral graft. *Plast Reconstr Surg.* 1992;90(5):880-6; discussion 887-9.

178. Herford AS, Boyne PJ. Reconstruction of mandibular continuity defects with bone morphogenetic protein-2 (rhBMP-2). *J Oral Maxillofac Surg.* 2008;66(4):616-624.

179. Melville JC, Couey MA, Tong MS, Marx RE. Regeneration of a tooth in a tissueengineered mandible after resection of a central giant cell tumor. demonstrating evidence of functional matrix theory and ectodermal origin of teeth in a human model-A case report. *J Oral Maxillofac Surg.* 2016.

180. Woo EJ. Adverse events reported after the use of recombinant human bone morphogenetic protein 2. *J Oral Maxillofac Surg*. 2012;70(4):765-767.

181. Mesimaki K, Lindroos B, Tornwall J, et al. Novel maxillary reconstruction with ectopic bone formation by GMP adipose stem cells. *Int J Oral Maxillofac Surg.* 2009;38(3):201-209.

182. Sandor GK, Tuovinen VJ, Wolff J, et al. Adipose stem cell tissue-engineered construct used to treat large anterior mandibular defect: A case report and review of the clinical application of good manufacturing practice-level adipose stem cells for bone regeneration. *J Oral Maxillofac Surg.* 2013;71(5):938-950.

183. Devauchelle B, Badet L, Lengele B, et al. First human face allograft: Early report. *Lancet*. 2006;368(9531):203-209.

184. Khalifian S, Brazio PS, Mohan R, et al. Facial transplantation: The first 9 years. *Lancet*. 2014;384(9960):2153-2163.

185. Kiwanuka H, Aycart MA, Bueno EM, Alhefzi M, Krezdorn N, Pomahac B. Patient recruitment and referral patterns in face transplantation: A single center's experience. *Plast Reconstr Surg.* 2016;138(1):224-231.

186. Sosin M, Rodriguez ED. The face transplantation update: 2016. *Plast Reconstr Surg*. 2016;137(6):1841-1850.

187. Lantieri L, Grimbert P, Ortonne N, et al. Face transplant: Long-term follow-up and results of a prospective open study. *Lancet*. 2016;388(10052):1398-1407.

93

188. Mankovich NJ, Robertson DR, Cheeseman AM. Three-dimensional image display in medicine. *J Digit Imaging*. 1990;3(2):69-80.

189. Cohen A, Laviv A, Berman P, Nashef R, Abu-Tair J. Mandibular reconstruction using stereolithographic 3-dimensional printing modeling technology. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2009;108(5):661-666.

190. Suojanen J, Leikola J, Stoor P. The use of patient-specific implants in orthognathic surgery: A series of 32 maxillary osteotomy patients. *J Craniomaxillofac Surg.* 2016.

191. Stoor P, Suomalainen A, Lindqvist C, et al. Rapid prototyped patient specific implants for reconstruction of orbital wall defects. *J Craniomaxillofac Surg*. 2014;42(8):1644-1649.

192. Stoor P, Mesimaki K, Lindqvist C, Kontio R. The use of anatomically drop-shaped bioactive glass S53P4 implants in the reconstruction of orbital floor fractures--A prospective long-term follow-up study. *J Craniomaxillofac Surg.* 2015;43(6):969-975.

193. Suomalainen A, Stoor P, Mesimaki K, Kontio RK. Rapid prototyping modelling in oral and maxillofacial surgery: A two year retrospective study. *J Clin Exp Dent*. 2015;7(5):e605-12.

194. Makitie AA, Salmi M, Lindford A, Tuomi J, Lassus P. Three-dimensional printing for restoration of the donor face: A new digital technique tested and used in the first facial allotransplantation patient in finland. *J Plast Reconstr Aesthet Surg*. 2016.

195. Bosc R, Hersant B, Carloni R, et al. Mandibular reconstruction after cancer: An in-house approach to manufacturing cutting guides. *Int J Oral Maxillofac Surg*. 2017;46(1):24-31.

196. Clavien PA, Sanabria JR, Strasberg SM. Proposed classification of complications of surgery with examples of utility in cholecystectomy. *Surgery*. 1992;111(5):518-526.

197. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: A new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg.* 2004;240(2):205-213.

198. Monteiro E, Sklar MC, Eskander A, et al. Assessment of the clavien-dindo classification system for complications in head and neck surgery. *Laryngoscope*. 2014;124(12):2726-2731.

199. Awad MI, Palmer FL, Kou L, et al. Individualized risk estimation for postoperative complications after surgery for oral cavity cancer. *JAMA Otolaryngol Head Neck Surg*. 2015;141(11):960-968.

200. Piccirillo JF, Lacy PD, Basu A, Spitznagel EL. Development of a new head and neck cancer-specific comorbidity index. *Arch Otolaryngol Head Neck Surg*. 2002;128(10):1172-1179.

201. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. *J Chronic Dis.* 1987;40(5):373-383.

202. Jewer DD, Boyd JB, Manktelow RT, et al. Orofacial and mandibular reconstruction with the iliac crest free flap: A review of 60 cases and a new method of classification. *Plast Reconstr Surg.* 1989;84(3):391-403; discussion 404-5.

203. Iyer S, Thankappan K. Maxillary reconstruction: Current concepts and controversies. *Indian J Plast Surg.* 2014;47(1):8-19.

204. Dowthwaite SA, Theurer J, Belzile M, et al. Comparison of fibular and scapular osseous free flaps for oromandibular reconstruction: A patient-centered approach to flap selection. *JAMA Otolaryngol Head Neck Surg.* 2013;139(3):285-292.

205. Yazar S, Lin CH, Lin YT, Ulusal AE, Wei FC. Outcome comparison between free muscle and free fasciocutaneous flaps for reconstruction of distal third and ankle traumatic open tibial fractures. *Plast Reconstr Surg*. 2006;117(7):2468-75; discussion 2476-7.

206. Chan JK, Harry L, Williams G, Nanchahal J. Soft-tissue reconstruction of open fractures of the lower limb: Muscle versus fasciocutaneous flaps. *Plast Reconstr Surg*. 2012;130(2):284e-295e.

207. Anne-Gaelle B, Samuel S, Julie B, Renaud L, Pierre B. Dental implant placement after mandibular reconstruction by microvascular free fibula flap: Current knowledge and remaining questions. *Oral Oncol.* 2011;47(12):1099-1104.

208. Vu DD, Schmidt BL. Quality of life evaluation for patients receiving vascularized versus nonvascularized bone graft reconstruction of segmental mandibular defects. *J Oral Maxillofac Surg.* 2008;66(9):1856-1863.

209. Gaggl A, Schultes G, Karcher H. Stability of dental implants in microvascular scapula and iliac crest transplants. *Mund Kiefer Gesichtschir*. 2001;5(5):293-298.

210. Fujiki M, Miyamoto S, Sakuraba M, Nagamatsu S, Hayashi R. A comparison of perioperative complications following transfer of fibular and scapular flaps for immediate mandibular reconstruction. *J Plast Reconstr Aesthet Surg*. 2013;66(3):372-375.

211. Nkenke E, Vairaktaris E, Stelzle F, Neukam FW, Stockmann P, Linke R. Osteocutaneous free flap including medial and lateral scapular crests: Technical aspects, viability, and donor site morbidity. *J Reconstr Microsurg*. 2009;25(9):545-553.

212. Hartman EH, Spauwen PH, Jansen JA. Donor-site complications in vascularized bone flap surgery. *J Invest Surg.* 2002;15(4):185-197.

213. Dowthwaite SA, Theurer J, Belzile M, et al. Comparison of fibular and scapular osseous free flaps for oromandibular reconstruction: A patient-centered approach to flap selection. *JAMA Otolaryngol Head Neck Surg.* 2013;139(3):285-292.

214. Markiewicz MR, Bell RB, Bui TG, et al. Survival of microvascular free flaps in mandibular reconstruction: A systematic review and meta-analysis. *Microsurgery*. 2015;35(7):576-587.

215. Brown JS, Jones DC, Summerwill A, et al. Vascularized iliac crest with internal oblique muscle for immediate reconstruction after maxillectomy. *Br J Oral Maxillofac Surg*. 2002;40(3):183-190.

216. Las DE, de Jong T, Zuidam JM, Verweij NM, Hovius SE, Mureau MA. Identification of independent risk factors for flap failure: A retrospective analysis of 1530 free flaps for breast, head and neck and extremity reconstruction. *J Plast Reconstr Aesthet Surg.* 2016.

217. Wei FC, Demirkan F, Chen HC, et al. The outcome of failed free flaps in head and neck and extremity reconstruction: What is next in the reconstructive ladder? *Plast Reconstr Surg.* 2001;108(5):1154-60; discussion 1161-2.

218. Blackwell KE. Donor site evaluation for fibula free flap transfer. *Am J Otolaryngol*. 1998;19(2):89-95.

219. Hartman EH, Spauwen PH, Jansen JA. Donor-site complications in vascularized bone flap surgery. *J Invest Surg.* 2002;15(4):185-197.

220. Ling XF, Peng X. What is the price to pay for a free fibula flap? A systematic review of donor-site morbidity following free fibula flap surgery. *Plast Reconstr Surg*. 2012;129(3):657-674.

221. Rogers SN, Lakshmiah SR, Narayan B, et al. A comparison of the long-term morbidity following deep circumflex iliac and fibula free flaps for reconstruction following head and neck cancer. *Plast Reconstr Surg.* 2003;112(6):1517-1525.

222. Al-Sukhun J, Koivusalo A, Tornwall J, Lindqvist C. COX-2 inhibitors and early failure of free vascular flaps. *N Engl J Med*. 2006;355(5):528-529.

223. Al Deek NF, Wei FC, Tsao CK. Fistulae after successful free tissue transfer to head and neck: Its prevention and treatment. *Clin Plast Surg*. 2016;43(4):739-745.

224. Grammatica A, Piazza C, Paderno A, Taglietti V, Marengoni A, Nicolai P. Free flaps in head and neck reconstruction after oncologic surgery: Expected outcomes in the elderly. *Otolaryngology - Head & Neck Surgery*. 2015;152(5):796-802.

225. Clark JR, McCluskey SA, Hall F, et al. Predictors of morbidity following free flap reconstruction for cancer of the head and neck. *Head Neck*. 2007;29(12):1090-1101.

226. Grammatica A, Piazza C, Paderno A, Taglietti V, Marengoni A, Nicolai P. Free flaps in head and neck reconstruction after oncologic surgery: Expected outcomes in the elderly. *Otolaryngology - Head & Neck Surgery*. 2015;152(5):796-802.

227. Howard MA, Cordeiro PG, Disa J, et al. Free tissue transfer in the elderly: Incidence of perioperative complications following microsurgical reconstruction of 197 septuagenarians and octogenarians. *Plast Reconstr Surg*. 2005;116(6):1659-68; discussion 1669-71.

228. Nao EE, Dassonville O, Poissonnet G, et al. Ablative surgery and free flap reconstruction for elderly patients with oral or oropharyngeal cancer: Oncologic and functional outcomes. *Acta Otolaryngol.* 2011;131(10):1104-1109.

229. Vandersteen C, Dassonville O, Chamorey E, et al. Impact of patient comorbidities on head and neck microvascular reconstruction. A report on 423 cases. *Eur Arch Otorhinolaryngol.* 2013;270(5):1741-1746. 230. Sacak B, Akdeniz ZD, Certel F, Kocaaslan FND, Tuncer B, Celebiler O. Risk assessment for free tissue transfers: Is old age a determining factor?. *J Craniofac Surg*. 2015;26(3):856-859.

231. Szturz P, Vermorken JB. Treatment of elderly patients with squamous cell carcinoma of the head and neck. *Front Oncol.* 2016;6:199.

232. Wester JL, Lindau RH, Wax MK. Efficacy of free flap reconstruction of the head and neck in patients 90 years and older. *JAMA Otolaryngol Head Neck Surg*. 2013;139(1):49-53.

233. Nao EE, Dassonville O, Chamorey E, et al. Head and neck free-flap reconstruction in the elderly. *Eur Ann Otorhinolaryngol Head Neck Dis*. 2011;128(2):47-51.

234. Hansen CR, Johansen J, Kristensen CA, et al. Quality assurance of radiation therapy for head and neck cancer patients treated in DAHANCA 10 randomized trial. *Acta Oncol.* 2015;54(9):1669-1673.

235. Chen Z, King W, Pearcey R, Kerba M, Mackillop WJ. The relationship between waiting time for radiotherapy and clinical outcomes: A systematic review of the literature. *Radiother Oncol.* 2008;87(1):3-16.

236. Al-Sukhun J, Koivusalo A, Tornwall J, Lindqvist C. COX-2 inhibitors and early failure of free vascular flaps. *N Engl J Med*. 2006;355(5):528-529.

237. Ren H, Lin D, Mou Z, Dong P. The adverse effect of selective cyclooxygenase-2 inhibitor on random skin flap survival in rats. *PLoS One.* 2013;8(12):e82802.

238. Benlidayi ME, Gaggl A, Buerger H, et al. Comparative study of the osseous healing process following three different techniques of bone augmentation in the mandible: An experimental study. *Int J Oral Maxillofac Surg.* 2014;43(11):1404-1410.

239. Rana M, Warraich R, Kokemuller H, et al. Reconstruction of mandibular defects clinical retrospective research over a 10-year period -. *Head Neck Oncol*. 2011;3:23-3284-3-23.

240. Disa JJ, Winters RM, Hidalgo DA. Long-term evaluation of bone mass in free fibula flap mandible reconstruction. *Am J Surg*. 1997;174(5):503-506.

241. Mertens C, Decker C, Engel M, Sander A, Hoffmann J, Freier K. Early bone resorption of free microvascular reanastomized bone grafts for mandibular reconstruction--a comparison of iliac crest and fibula grafts. *J Craniomaxillofac Surg*. 2014;42(5):e217-23.

242. Yla-Kotola TM, Bartlett E, Goldstein DP, Armstrong K, Gilbert RW, Hofer SO. Union and bone resorption of free fibular flaps in mandibular reconstruction. *J Reconstr Microsurg*. 2013;29(7):427-432.

243. Chia HL, Wong CH, Tan BK, Tan KC, Ong YS. An algorithm for recipient vessel selection in microsurgical head and neck reconstruction. *J Reconstr Microsurg*. 2011;27(1):47-56.

244. Dedivitis RA, Guimaraes AV. Pectoralis major musculocutaneous flap in head and neck cancer reconstruction. *World J Surg*. 2002;26(1):67-71.

245. Mogi G, Fujiyoshi T, Kurono Y, Kawauchi H, Yoshimura H. Reconstructive surgery of head and neck cancer using various pedicle flaps. *Auris Nasus Larynx*. 1985;12(Suppl 2):S24-9.

246. Schuller DE. Pectoralis myocutaneous flap in head and neck cancer reconstruction. *Arch Otolaryngol.* 1983;109(3):185-189.

247. Yu BT, Hsieh CH, Feng GM, Jeng SF. Clinical application of the internal mammary artery perforator flap in head and neck reconstruction. *Plast Reconstr Surg*. 2013;131(4):520e-6e.

248. Leonard AG. Musculocutaneous flaps in head and neck reconstruction. *Ann R Coll Surg Engl.* 1989;71(3):159-168.

249. Hurvitz KA, Kobayashi M, Evans GR. Current options in head and neck reconstruction. *Plastic & Reconstructive Surgery*. 2006;118(5):122e-133e.

250. Ferbeyre-Binelfa L. Lattissimus dorsi myocutaneous flap in head and neck surgery. *Cir Cir*. 2010;78(6):485-491.

251. Quillen CG. Latissimus dorsi myocutaneous flaps in head and neck reconstruction. *Plast Reconstr Surg.* 1979;63(5):664-670.

252. Olivari N. The latissimus dorsi flap, experience with 51 operations. *Acta Chir Belg*. 1980;79(2):111-114.

253. Schuller DE. Limitations of the pectoralis major myocutaneous flap in head and neck cancer reconstruction. *Arch Otolaryngol.* 1980;106(11):709-714.

254. Clough KB, Louis-Sylvestre C, Fitoussi A, Couturaud B, Nos C. Donor site sequelae after autologous breast reconstruction with an extended latissimus dorsi flap. *Plastic & Reconstructive Surgery*. 2002;109(6):1904-1911.

255. Russell RC, Pribaz J, Zook EG, Leighton WD, Eriksson E, Smith CJ. Functional evaluation of latissimus dorsi donor site. *Plast Reconstr Surg.* 1986;78(3):336-344.

256. Can A, Orgill DP, Dietmar Ulrich JO, Mureau MAM. The myocutaneous trapezius flap revisited: A treatment algorithm for optimal surgical outcomes based on 43 flap reconstructions. *Journal of Plastic, Reconstructive & Aesthetic Surgery: JPRAS.* 2014;67(12):1669-1679. 257. Castelli ML, Pecorari G, Succo G, Bena A, Andreis M, Sartoris A. Pectoralis major myocutaneous flap: Analysis of complications in difficult patients. *Eur Arch Otorhinolaryngol.* 2001;258(10):542-545.

258. Mehrhof AI,Jr, Rosenstock A, Neifeld JP, Merritt WH, Theogaraj SD, Cohen IK. The pectoralis major myocutaneous flap in head and neck reconstruction. analysis of complications. *Am J Surg.* 1983;146(4):478-482.

259. Nishi Y, Rikimaru H, Kiyokawa K, Watanabe K, Koga N, Sakamoto A. Development of the pectoral perforator flap and the deltopectoral perforator flap pedicled with the pectoralis major muscle flap. *Ann Plast Surg.* 2013;71(4):365-371.