# ADVANCING TREATMENT POSSIBILITIES IN ORO-MAXILLO-FACIAL REHABILITATION

**Ph.D. Thesis**

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# 1. INTRODUCTION

## 1.1 Overview of the topic

### 1.1.1. What are the topics?

We investigate the possibilities on scanning a face contactless for creating prosthetic appliances. We also studied the prognosis of quality of life in patients with post-maxillectomy defects whether prosthetic or surgical reconstruction provides the better-functioning outcome.

### 1.1.2. What are the problems to solve?

Due to the positive likeness of prosthesis-bearing tissues, creating lifelike facial prostheses is challenging. Low staffing and centralized patient care facilities cause inaccessibility.

Rehabilitating maxillectomy patients for optimal postoperative quality of life is another issue. One must chose surgery over prosthetic reconstruction. The option is still debated, with no convincing proof.

### 1.1.3. What are the importance of the topics?

#### *1.1.3.1. Facial defects*

Globally, over 650 000 people develop head and neck cancer annually, resulting in the death of 330 000 individuals. Patients with a tumor in the maxillofacial region often find themselves in a vulnerable situation after cancer ablation: the defect is surgically unrepairable using conventional interventions. Unrestored facial defects can lead to stigmatization, social isolation, and severe psychological issues. The number of patients requiring facial prostheses is increasing. Due to the high costs, complex

technicality, and unavailability of skilled caregivers, proper care is inaccessible for most people in need.

*1.1.3.2. Oroantral and oronasal defects*

Oral cancer affects the world significantly, with 377 713 new cases annually. As these tumors become more prevalent, adequate healthcare resources are essential for effective treatment and rehabilitation. Maxillary sinus cancer occurs in 0.5–1 per 100 000, and small salivary gland cancers in 0.16–0.4 per 100 000. Surgical resection is often the best treatment for these conditions, but it can impair speech, chewing, and swallowing due to nasal-oral connections. Conditions like maxilla mucormycosis, benign tumors, and traumatic injuries may also necessitate surgical excision.

### 1.1.4. What would be the impact of our research results?

Digital tools in anaplastology can transform rehabilitation by improving prosthesis accuracy, reducing costs, and streamlining production. While initially less accessible, these innovations are expected to become more widespread ("trickle-down effect"), enhancing care quality.

Clinicians need evidence-based information on the prosthetic and surgical restoration of maxillectomy defects to make educated decisions and provide the best rehabilitation plan. Access to high-quality care must be promoted to influence healthcare policy and resource allocation.

## 1.2. Understanding the complexity of rehabilitation plays a key role in the management of maxillofacial patients

### 1.2.1. Contactless imaging and digital planning

Anaplastology reconstructs facial defects alloplastically. It lags in adopting digital technology. Traditional methods are costly, inefficient, and require skilled professionals, with no standard for quality control. Digital tools may improve fit, accuracy, and edge quality while reducing production time and costs, which is essential for periodically refabricating prostheses over time.

### 1.2.2. Choosing the most appropriate postoperative rehabilitation

Preoperatively, a multidisciplinary team, including prosthodontists, should choose the rehabilitation method. Despite removability, retention, and cosmetic issues, prosthetic rehabilitation is cost-effective, fast, and allows surgeons to monitor the surgery site. Prosthodontists must be involved early to develop a rehabilitation strategy that takes into account patient age, defect size, and health to avoid unsatisfactory results.

Some say a surgical closure suits smaller defects, while larger ones often need prosthetics, but a universal approach rarely fits. General guidelines help but must adapt to each patient’s needs, finances, and defect complexity. Evidence-based algorithms can offer a structured yet flexible framework for better rehabilitation.

## 2. OBJECTIVES

### 2.1. Study I

No specialized hardware or software exists for facial prostheses, and industrial scanners lack validation for this purpose. Studies often overlook facial model accuracy, focusing instead on dimensional precision without considering prosthetics. Our systematic review analyzed the precision of scanning technologies by comparing interlandmark distances (ILDs) measured directly and virtually on volunteers' facial surfaces. We evaluated scanning methods' precision and accuracy across facial regions within a 3D coordinate framework.

### 2.2. Study II

Maxillectomy rehabilitation requires collaboration among specialists, including surgeons and prosthodontists. With rising maxillectomy cases, developing personalized rehabilitation algorithms is essential. This analysis evaluated the subjective and objective impacts of prosthetic and surgical interventions. The null hypothesis proposed no differences in quality of life, speech, or masticatory efficiency between the therapies.

## 3. METHODS

The systematic reviews and meta-analyses were performed in accordance with the PRISMA 2020 guidelines, following the instructions of the Cochrane Handbook. The study protocol was registered with PROSPERO (registration number of Study I: CRD42021282584, Study II: CRD42022334908), with adherence to its guidelines.

### 3.1. Literature search and eligibility criteria

We performed a systematic literature search in five databases (MEDLINE via PubMed, CENTRAL [The Cochrane Central Register of Controlled Trials], Embase, Scopus, and Web of Science) in Study I, and four medical databases (MEDLINE, CENTRAL, EMBASE, and Web of Science) in Study II. The original publications list the search dates and queries.

In Study I, studies reporting on human volunteers or live patients with or without facial deformity (Population). The distance between anthropometrical landmarks was used to indicate accuracy: the ILDs are measured on the virtual facial models made with any non-contact scanning technology (Index test, "Intervention"), and directly on the subjects' faces (Reference standard, "Comparator"). The deviation from the comparator in various ILDs was the desired outcome, confirming the accuracy of the virtual models (Outcome). Different scanning technologies were handled in subgroups. There were no restrictions regarding language or the time of publication. Studies measuring facial

deformity in patients were included, while cadavers or inanimate objects were excluded.

In Study II, the PICO format was used for eligible studies P: human patients who underwent surgical ablation of the maxilla that resulted in an open palatomaxillary defect. Defects originating from congenital causes were excluded. I: prosthetic restoration of the palatomaxillary defect, using either surgical or definitive obturators. C: surgical reconstruction using any flap or graft. Surgical restoration of oro-antral or oronasal communication after tooth extraction was excluded. O: both objective outcomes and subjective outcomes specifically in the form of patient-reported outcome measures (PROMs) and quality-of-life (QoL) questionnaires. No restrictions were placed on the time of publication or language. Experimental trials (randomized or nonrandomized controlled trials) and observational studies were included. Case-control studies and case reports were excluded.

### 3.2. Study selection and data collection

We utilized EndNote X9 (Clarivate Analytics, Philadelphia, PA, USA) for the selection of articles. Two independent writers evaluated the papers individually for the title, abstract, and complete text, with discrepancies addressed by a third author.

Two authors separately extracted data into a previously established Excel spreadsheet (Office 365, Microsoft, Redmond, WA, USA), while a third reviewer adjudicated the differences.

The following data were collected from each eligible article in Study I: first author, year of publication, number of subjects involved, nasolabial morphology of the involved subjects, age of the subjects, scanning technology, aspect of view, interlandmark distance, region, orientation, mean, and standard deviation. If the data were not presented in the article, it was excluded because of data insufficiency. Twelve authors were approached through an email directed to the corresponding author, inquiring about their willingness to submit data for the study; however, no responses were received. In Study II: first author, year of publication, study design, number of participants, age, sex ratio, maxillary dental status, defect size, number of patients who received radiotherapy, and which outcome measures were used by the authors and the outcome values. If multiple studies used the same compatible outcome, they were included in the quantitative analysis.

### 3.3. Quality assessment

The risk of bias assessment was carried out separately by two reviewers using the QUADAS-2 tool in Study I. According to the instruction manual of the tool, the signaling questions were tailored to accommodate the review's focus by adding a question (In the "Reference test" domain: "Were the examiners blinded to the results?") and omitting another one (In the "Index test" domain: "If a threshold was used, was it prespecified?"). The latter question was not applicable to any of the included studies, therefore we removed it. The same authors performed the risk of bias assessment using the ROB-2 for randomized and the

ROBINS-I tools for observational studies in Study II. A third author was involved if disagreements arose.

Egger's test and funnel plots were applied to report and visualize publication bias if there were a minimum of ten studies involved in the analysis.

### 3.4. Data synthesis and analysis

All statistical analyses were performed using a statistical software program (R version 4.2.0; https://www.R-project.org/), supplemented with the "meta" package. The recommendations of Harrer et al were followed throughout the analyses. As all the selected outcomes were continuous, the differences between the means of the intervention and control groups were used to measure the effect size. Random-effects meta-analyses were conducted on all of the datasets because significant heterogeneity between studies was anticipated.

In Study I, the mean differences (MDs) and their confidence interval were calculated for the most frequently measured ILDs. The standardized mean differences (SMDs) and their confidence intervals were calculated in the analysis regarding the comparison of regions and technologies. Since the different ILDs had different magnitudes, comparing the differences without any adjustments would result in distorted calculations. The MDs were transformed into SMDs to make them comparable. To keep track of the direction of the dimensional change, a negative sign denotes shrinkage, and a positive sign denotes magnification or expansion. Subgroup analyses were conducted based on

the three different major scanning technologies, assuming that the subgroups share a common $\tau^2$ value, as we did not anticipate a difference in the between-study heterogeneity. To assess the difference between the subgroups, Cochran's Q test was used between the subgroups.

Study II anticipated significant heterogeneity in populations and outcomes, leading to stratification by defect size (small/large) and edentulism status. Defect size was classified using Brown (1999, 2010) or Okay (2010) systems. QoL ratings were linearly transformed per EORTC QLQ-C30 guidelines, where a 20-point difference indicates clinical significance. Domains of life assessed with comparable questionnaires were analyzed on a 1–100 scale, with lower scores reflecting better QoL. Mean differences with 95% CIs were calculated for QoL domains, speech intelligibility, and nasalance. Subgroup analysis used a mixed-effects model with a common $\tau^2$ and Cochrane Q test ($\alpha$=0.05). Due to methodological heterogeneity in masticatory indicators, standardized mean differences (SMD, Hedges' G) with 95% CIs were applied instead.

In all situations, random-effects meta-analyses were performed by using an inverse variance weighting method. As for both large and small study numbers, the Hartung-Knapp adjustment provides a more reliable estimate. This adjustment was used for each analysis. Heterogeneity was assessed by using Higgins and Thompson $I^2$ statistics, and $\tau 2$ using the restricted maximum-likelihood estimator with the Q profile method.

The certainty of the evidence was evaluated by using the GradePro tool.

## 4. RESULTS

### 4.1. Study I

A total of 5090 studies were identified through the systematic search. Ten records were included in the quantitative synthesis. Publication dates range from 2004 to 2021.

The population included healthy adults in seven studies, with one study each on children, cleft patients, and edentulous prosthodontic patients. Stereophotogrammetry was the most used scanning technology, though landmark identification varied; three studies lacked prior marking, while seven employed marking techniques before scanning.

Most studies used commercial scanners with dedicated software, while one relied on manually stitched DSLR images. Common issues included hairline intrusion, blinking, facial expressions, motion artifacts, lighting, stitching errors, and flash interference.

Eight interlandmark distances (ILDs) were analyzed across facial regions (auricular, nasal, orolabial, periorbital) and Cartesian axes (X, Y, Z). Data were categorized into 12 groups, but auricular data and some periorbital axes lacked sufficient data for meta-analysis. Homogeneity was high ($I^2$ = 0–27%) due to consistent populations and methods. Confidence intervals narrowed in pooled analyses, eliminating individual study imprecisions, but no differences reached statistical significance. Subgroup analyses by scanning technology also showed no significant effects.

### 4.2. Study II

A total of 5383 studies were identified through the systematic search. A total of 36 full-text studies were identified and retrieved for careful evaluation. Thirteen records were included in the quantitative synthesis of the review. Publication of the studies occurred between 2003 and 2022.

The included studies were primarily cohort designs, with one randomized controlled trial by Aladashi et al. Among 466 participants, 206 underwent surgical reconstruction and 260 received prosthetic obturators. Participants were mostly male, aged 22–88, with a central tendency among middle-aged adults. All studies involved individuals with oncological diseases, but edentulism status was inconsistently reported.

Three studies assessed anxiety using the HAD and UW-QoL questionnaires, showing no significant difference between groups (MD=−18.99; CI: −55.54, 17.64). Pain data from four studies also showed no significant difference (MD=−5.19; CI: −18.59, 8.22). Swallowing outcomes from four studies yielded similar results (MD=−12.05; CI: −45.27, 21.18).

UW-QoL comparisons revealed a statistically significant but clinically negligible difference in the “activity” domain (MD=1.92; CI: 0.45, 3.40), with no significant differences in other domains. Speech quality, including nasalance and intelligibility, showed no significant differences between groups, except for one finding by Aladashi et al comparing submental flaps and surgical obturators. Pooled results for speech

intelligibility and nasalance were nonsignificant (MD=−0.47; CI: −4.41, 3.47; MD=0.14; CI: −13.50, 13.78).

Three studies assessing masticatory ability employed diverse methodologies, leading to pooled SMDs that showed no significant differences between interventions (SMD=−1.01; CI: −3.37, 1.35).

Overall, the findings indicate limited evidence of differences between surgical reconstruction and prosthetic obturators.

## 5. CONCLUSIONS

The present results suggest that there are no significant differences in linear dimensions, neither between direct caliper measurements nor between measurements taken on the scanned models, scanning technologies, or facial regions. However, this dimensional accuracy in the special clinical environment of facial prosthetics is insufficient. According to our thorough systematic analysis, acquiring a facial model using non-contact optical digitization is desirable over traditional moulage impressions. However, a streamlined device capturing the dimensions of the face reliably and consistently is still to be developed. Shifting the facial prosthetic workflow into a digital environment is vital for the field of anaplastology.

This comprehensive review and meta-analysis concluded that there was no significant difference in quality of life or objective clinical outcomes between obturator devices and surgical reconstruction. The current literature requires more thorough investigation to yield conclusive results. The limited evidence underscores the need for focused research, and established protocols could aid future decisions.

## 6. BIBLIOGRAPHY OF THE CANDIDATE'S PUBLICATIONS

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