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PhDthesis

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PAPERS

This PhD thesis is based on the following articles published in or accepted for publication in peer reviewed journals. The articles will be referred to by their Roman numerals (I–V).

Radiographic evaluation of clinical outcome:

I. Stokbro K, Thygesen T. 2018. "Surgical Accuracy in Inferior Maxillary Reposition." *J Oral Maxillofac Surg*. 76 (12): 2618–24. https://doi.org/10.1016/j.joms.2018.05.022.

II. Stokbro K, Liebregts J, Baan F, Bell RB, Maal T, Thygesen T, Xi T. 2019. "Does Mandible-First Sequencing Increase Maxillary Surgical Accuracy in Bimaxillary Procedures?" *J Oral Maxillofac Surg*. 77 (9): 1882-93. https://doi.org/10.1016/j.joms.2019.03.023.

III. Stokbro, K, Thygesen T, Marcussen L. 2019. "Inferior Maxillary Repositioning Remains Stable 1 Year after Surgery but Entails a High Risk of Osteosynthesis Failure" *J Oral Maxillofac Surg*. In press. https://doi.org/10.1016/j.joms.2019.08.014.

In vitro studies to improve the surgical outcome:

IV. Stokbro K, Bell RB, Thygesen T. 2018. "Patient-Specific Printed Plates Improve Surgical Accuracy In Vitro." *J Oral Maxillofac Surg*. 76 (12): 2647.e1-2647.e9. https://doi.org/10.1016/j.joms.2018.08.002.

V. Stokbro K, Borg SW, Andersen MØ, Thygesen T. 2019. "Patient-Specific 3D Printed Plates Improve Stability of Le Fort 1 Osteotomies in Vitro." *J Cranio-Maxillofacial Surg.* 47 (3): 394–99. https://doi.org/10.1016/j.jcms.2018.12.015

ACKNOWLEDGEMENTS

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ABBREVIATIONS

3D	3 dimensional
ABS	Acrylonitrile-butadiene-styrene (manufacturing 3D models)
CAD/CAM	Computer-aided design/computer-aided manufacturing
CBCT	Cone beam computed tomography
OMF	Oral and maxillofacial
PSP	Patient-specific, 3D printed (3D printed plates)
SLA	stereolithographic additive (manufacturing 3D models)
VSP	Virtual surgical planning

DEFINITIONS

Surgical accuracy: The correlation between the planned and obtained surgical repositioning. In this study, the surgical accuracy is measured as the distance from the planned position to the obtained surgical position of the maxilla. A negative value along the anterior axis means that the maxilla is placed posterior to the planned position. The surgical accuracy should be considered in reverse relation with the distance measurement, so the closer the distance comes to 0, the higher the level of surgical accuracy.

Skeletal stability: The skeletal movement of the maxilla from 1-week to 1-year follow-up after orthognathic surgery. A negative value along the anterior axis means the maxilla moved posterior during the first year after surgery. The skeletal stability should be considered as inverted from the distance measurement, so the closer the distance comes to 0, the higher the level of skeletal stability.

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BACKGROUND

Introduction

Orthognathic surgery is predictable and stable, and there is a high degree of patient satisfaction with the surgical outcome (Larsen and Thygesen, 2016). The overall goal of this study was not to save the surgical outcome from failure but rather to position the maxilla 1–2 mm closer to the planned position to improve the patient's facial appearance (Resnick *et al.*, 2018; Bengtsson *et al.*, 2019). If the virtual surgical plan is optimal, positioning the maxilla closer to the planned position should improve the esthetics of the surgical outcome and help to fully achieve the patient's esthetic potential.

Orthognathic surgery is undergoing a tremendous evolution regarding both virtual surgical planning (VSP) and three-dimensional (3D) printed supportive material (Hsu *et al.*, 2013; Mazzoni *et al.*, 2015). Three-dimensional VSP is common practice in Denmark, with surgical splints designed and fabricated directly from the virtual simulation of the surgery. Additional supportive material can be designed and fabricated directly from the patient's virtual plan to assist the surgeon in positioning the moving segments during the surgical procedure (Zinser *et al.*, 2013). Osteotomy guides, positioning guides and patient-specific, 3D printed (PSP) osteosynthesis plates can be tailored to fit each patient's bony contours while incorporating the planned reposition (Fig. 1) (Mazzoni *et al.*, 2015).

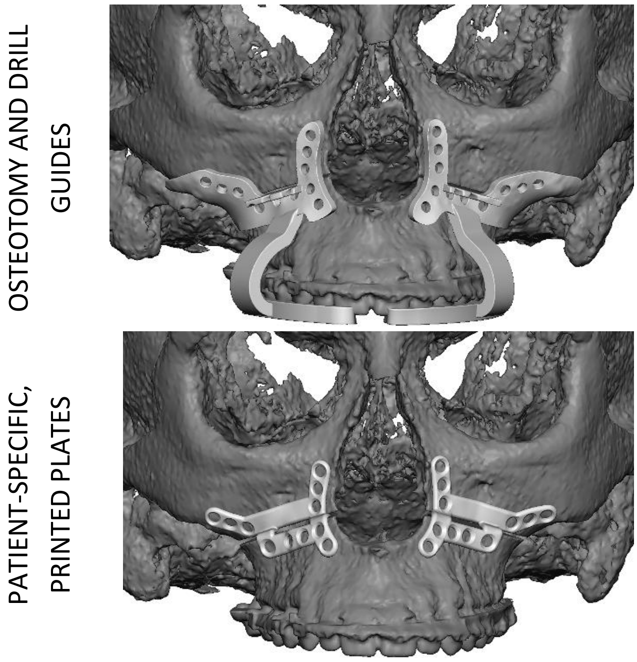


Fig. 1. Combined osteotomy and drill guides, and patient-specific, 3D printed plates. Used to assist the surgeon in obtaining the planned reposition of the maxillary dental segment.

Designing and manufacturing patient-specific supportive materials is time-consuming, and thus, more expensive than conventional and virtual surgical planning procedures with manually adapted stock plates (Resnick *et al.*, 2016). Furthermore, while there are numerous studies on procedures that are known to be predictable and stable, none have evaluated whether there still exists a need for further improvement of the most unpredictable and unstable orthognathic procedures after the introduction of 3D VSP (see updated review of the literature, Table 1).

Orthognathic surgical procedures are complex and have different clinical challenges and therefore different degrees of predictability and stability. The most unpredictable and unstable of the surgical procedures are the following: solitary mandibular setback, segmented maxillary procedures and inferior maxillary repositioning (Fig. 2) (Proffit, Turvey and Phillips, 1996, 2007). The new treatment possibilities afforded by patient-specific supportive materials should be used in the patients with the greatest needs, where the largest impact on outcome improvement can be expected.

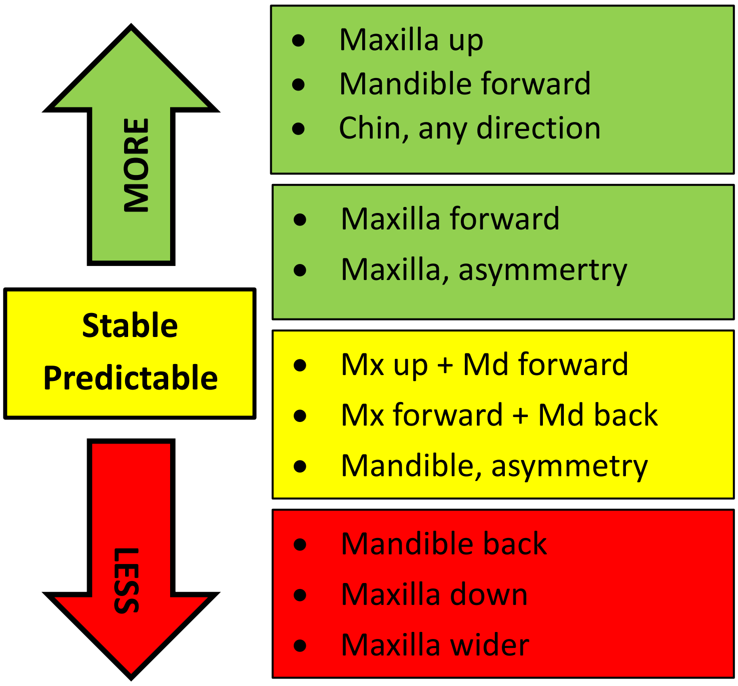


Fig. 2. Orthognathic surgical procedures have different degrees of stability and predictability depending on the direction of the repositioned bony segments (Proffit, Turvey and Phillips, 1996, 2007).

Therefore, this thesis seeks to evaluate whether there is a need to improve the surgical accuracy or postoperative stability of one of the most unpredictable and unstable procedures in orthognathic surgery: inferior maxillary repositioning.

Updated review of the literature

The literature and knowledge concerning clinical outcome 3D virtual surgical planning continue to expand. The systematic literature review on virtual surgical planning in orthognathic surgery (Stokbro *et al.*, 2014) was updated in December 2018 (unpublished). Inclusion criteria for studies were quantitative 3D analysis of the outcome of 3D VSP planned orthognathic surgery. Exclusion criteria were case series with less than 5 patients, reposition by surgical navigation and 2D lateral cephalometric analysis of outcomes. The included studies were analyzed regarding the above-mentioned patient inclusion criteria, the direction of surgical repositioning and the method of outcome measurement. The inclusion criteria were screened to find articles addressing the problematic procedures considered as unpredictable and unstable (inferior maxillary repositioning, segmented maxillary procedures and solitary mandibular setback) (Proffit, Turvey and Phillips, 1996, 2007).

Overall, 28 articles could be included in the updated review (Table 1). The review showed that most studies in orthognathic surgery included cohorts with mixed directions of inclusion or failed to properly express the inclusion criteria for the study. Furthermore, only a few articles included a control group or performed subgroup comparisons between different procedures. The prevailing method for outcome measurements was manual landmark identification in the 2 CBCT scans.

The inclusion of mixed directions of repositioning from consecutive cohorts is problematic as this may conceal problems in unstable procedures because of large numbers of predictable and stable procedures. Furthermore, including cohorts with mixed directions of repositioning makes it impossible to compare data across studies and compile knowledge regarding specific surgical procedures. The differences in outcome measurements also complicates comparison between studies. Since no studies specifically evaluated problematic procedures in the 2014 review, a pilot study was initiated to determine the surgical outcome in a cohort with mixed directions but with appropriate subgroup comparisons (Stokbro *et al.*, 2016).

Table I. Review of the literature (December 2018).

3D VSP with CAD/CAM splints

	Author	Year	Reference	N	Pro/retro	Cohort	Surgery	Direction	Subgroup analysis	Outcome measurement
1	Marchetti	2006	(Marchetti *et al.*, 2006)	25	NA	NA	16 Bimax 4 Mx 5 Md	Mixed	No	S-S distance
2	Xia	2007	(Xia *et al.*, 2007)	5	Pro	Mixed	Bimax	NA	No	Manual landmarks
3	Tucker	2010	(Tucker *et al.*, 2010)	20	Retro	Cl III	14 Bimax 6 Mx	Mx adv + Md setback	No	S-S distance
4	Centenero	2012	(Aboul-Hosn Centenero and Hernández-Alfaro, 2012)	16	NA	Mixed	15 Bimax (5 segm) 1 Md	NA	No	Manual landmarks
5	Zinser	2013	(Zinser *et al.*, 2013)	12	Retro	Cl III	Bimax	NA	No	Manual landmarks
6	Hsu	2013	(Hsu *et al.*, 2013)	64	Pro	Mixed	Bimax	NA	No	Manual landmarks
7	Hernandez-Alfaro	2013	(Hernández-Alfaro and Guijarro-Martínez, 2013)	6	Pro	Mixed	Bimax	Mx adv + Md adv	No	S-S distance

3D VSP with CAD/CAM splints (continued)

	Author	Year	Reference	N	Pro/retro	Cohort	Surgery	Direction	Subgroup analysis	Outcome measurement
8	Sun	2013	(Sun *et al.*, 2013)	15	NA	Mixed	Bimax	Mx adv	No	Manual landmarks
9	Bobek	2015	(Bobek *et al.*, 2015)	25	Retro	Mixed	24 Bimax (10 segm) 1 IVRO	NA	No	Manual landmarks
10	Borba	2016	(Borba *et al.*, 2016)	50	Retro	Mixed	Bimax	NA	Cl II vs Cl III	Manual landmarks
11	Stokbro	2016	(Stokbro *et al.*, 2016)	30	Retro	Mixed	Bimax (11 segm)	Mixed	Impact/dowgraft Segm/Unsegm	Manual landmarks
12	Koerich	2016	(Koerich *et al.*, 2016)	50	Pro	Cl III	25 bimax, 25 mx	Mx adv	Bimax/Mx adv	S-S distance
13	Chin	2017	(Chin *et al.*, 2017)	10	Pro	Mixed	9 Bimax 1 Md	NA	No	Manual landmarks
14	Lin	2017	(Lin et al., 2017)	15	Pro	Cl III	Bimax	NA	No	Manual landmarks
15	Bengtsson	2017	(Bengtsson *et al.*, 2018)	30	RCT	Cl III	NA	NA	2D/3D VSP	Manual landmarks
16	Liebregts	2017	(Liebregts *et al.*, 2017)	116	Retro, Controlled	Mixed	Bimax	NA	No	Semi-automatic method
17	Dreiseidler	2017	(Dreiseidler *et al.*, 2017)	92	Retro	Mixed	Bimax	Mixed	No	Manual landmarks
18	Stokbro	2018	(Stokbro and Thygesen, 2018b)	20	Retro	Vertical deficiency	13 Bimax 7 Mx	Inferior reposition	Bimax/Mx	Semi-automatic method
19	Ko	2018	(Ko *et al.*, 2018)	34	Pro	Cl III	Bimax	Mx adv + Md setback	No	Manual landmarks
20	Udomlarptham	2018	(Udomlarptham *et al.*, 2018)	19	Retro	Cl III	Bimax	Mx adv + Md setback	No	Manual landmarks

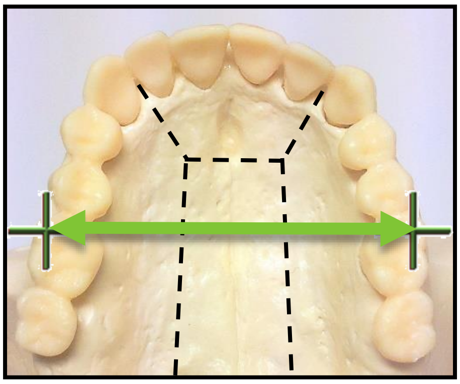
3D CAD/CAM Positioning guides

	Author	Year	Reference	N	Pro/retro	Cohort	Surgery	Direction	Subgroup analysis	Outcome measurement
1	Zinser	2013	(Zinser *et al.*, 2013)	8	Pro	Cl III	Bimax	NA	No	Manual landmarks
2	Shehab	2013	(Shehab *et al.*, 2013)	6	Pro	Mx excess	NA	Mx impaction	No	Manual landmarks
3	Li	2014	(Li *et al.*, 2013)	6	Pro	NA	Bimax	NA	No	Manual landmarks
4	Zhang	2016	(Zhang *et al.*, 2016)	30	Pro	Mixed	Bimax	NA	No	Manual landmarks

3D printed PSP plates

	Author	Year	Reference	N	Pro/retro-spective	Cohort	Surgery	Direction	Subgroup analysis	Outcome measurement
1	Mazzoni	2015	(Mazzoni *et al.*, 2015)	10	Pro	Mixed: 9 Cl III 1 Cl II	NA	NA	No	S-S distance
2	Brunso	2016	(Brunso *et al.*, 2016)	6	Pro	Mixed	5 Bimax 1 BSSO	5 Bimax-Adv.	No	S-S distance
3	Li	2017	(Li *et al.*, 2017)	10	Pro	Mixed	Bimax	NA	No	Manual landmarks
4	Heufelder	2017	(Heufelder *et al.*, 2017b)	22	Pro	Mixed	Mixed	Mixed	No	Manual landmarks

Pilot study in orthognathic surgery



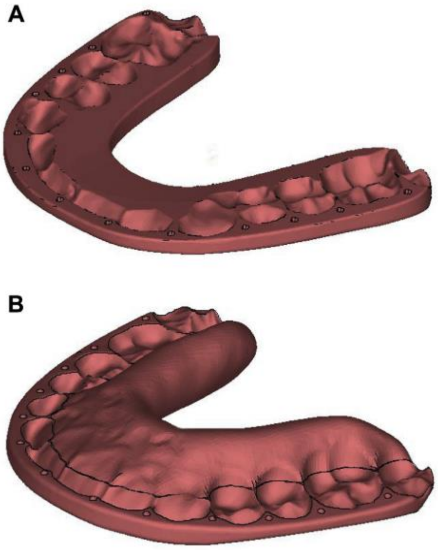


Fig. 3. The difference between planned and obtained maxillary expansion could be reduced by using a surgical splint with a reinforced palatal design. A: regular design. B: reinforced palatal design (Stokbro *et al.*, 2017).

The Odense pilot study evaluated 30 patients chosen at random from a pool of 72 patients in whom 3D VSP was planned (Stokbro *et al.*, 2016). The cohort included segmented maxillary procedures and inferior maxillary repositioning. In this study, the overall surgical accuracy was centered around 0, indicating no difference between the planned reposition and the obtained surgical outcome. However, when the subgroups were compared according to the direction of surgical procedures, patients treated with inferior maxillary repositioning were positioned 2.0 mm posterior to the planned position ($N = 7$, $P = .02$), while patients treated with superior maxillary repositioning were placed 0.3 mm anterior to the planned position ($N = 16$, $P = .80$). In addition, patients treated with segmented maxillary procedures were expanded 1.4 mm less between the first molars than planned. The results from the pilot study indicated that inferior maxillary repositioning and segmented maxillary procedures are still considered problematic procedures and may benefit from increased surgical accuracy and stability.

The lack of transverse expansion in segmented maxillary procedures was further explored in a retrospective study, where the transverse expansion was evaluated in a cohort of 30 new patients (Stokbro *et al.*, 2017). The study found that reinforcing the surgical splint with increased palatal coverage improved the obtained amount of transverse expansion. The difference between planned and obtained expansion was reduced from 1.3 mm (low palatal coverage) to 0.6 mm (high palatal coverage) ($P < .01$) (Fig. 3). Thus, the problem with transverse expansion appeared to be reduced by simply reinforcing the surgical splint design. Therefore, the cohort treated with inferior maxillary repositioning was chosen for further investigation, since improvement in surgical accuracy and stability would provide the greatest benefit to the patients.

Inferior maxillary repositioning

Apart from the Odense pilot study, the surgical accuracy in inferior maxillary repositioning has only been evaluated as a subgroup in a single study (Semaan and Goonewardene, 2005). The study evaluated 9 patients with inferior maxillary repositioning and found more than 2-mm errors in maxillary positioning in 3 patients. The orthognathic surgeries were planned on plaster cast models mounted in articulators with 2D lateral cephalometric analyses for treatment planning and outcome measurements.

In 2015, a systematic review evaluated the postoperative stability of inferior maxillary repositioning (Convens *et al.*, 2015). The review found that only 2 studies were of sufficient quality to be included, giving a combined cohort sample of 22 patients. Both studies were planned on plaster cast models mounted in a semi-adjustable articulator with use of 2D lateral cephalometric analysis for both treatment planning and outcome measurements. The findings in the 2 articles differed; 1 study found the surgical results to be stable with less than 0.3 mm difference between planned and obtained outcomes (Kretschmer *et al.*, 2010), while the other found a significant relapse of 1.6 mm in the superior direction during the first 6 months after surgery (Perez, Sameshima and Sinclair, 1997).

An additional systematic review of inferior maxillary repositioning was also performed in 2000, comparing stability of rigid fixation with wire fixation (Costa, Robiony and Politi, 2000). This review also found a large variance in relapse in both wire fixation and rigid fixation with bone grafting. The vertical relapse with rigid fixation and bone grafting ranged from 0.0 mm (0%) to 3.6 mm (49%) in the anterior maxilla and from 0.1 mm (16%) to 1.0 mm (167%) in the posterior maxilla. The mean vertical relapse of the anterior maxilla was 1.0 mm (15%) and that of the posterior maxilla was 0.7 mm (35%). Thus, the literature seems very heterogeneous regarding the stability of inferior maxillary repositioning, but the literature also shows that there was a larger relapse in the studies performed before 1995. This tendency toward an increased skeletal stability in older studies may be because mechanical factors (e.g. changes in the design and rigidity of the plates used for fixation) were not included in these studies (Fig.4). In this light, the findings of Kretschmer *et al.* (2010) could suggest that contemporary fixation methods are sufficient to stabilize inferior maxillary repositioning without need for additional improvement. However, this suggested trend must be verified in independent studies to evaluate whether this is a true development in stability or a single positive finding. Before studies I–III were performed, no study had evaluated surgical accuracy or skeletal stability in inferior maxillary surgery using 3D VSP or performed reliable 3D outcome measurements.

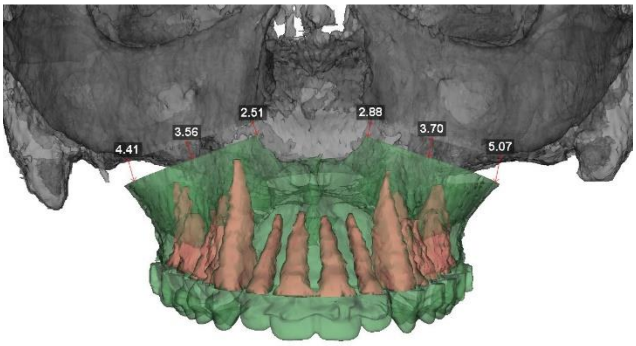


Fig. 4. Inferior maxillary repositioning is considered unstable and unpredictable due to the lack of bony support at the osteotomy; therefore, the repositioned segment is only stabilized by the osteosynthesis plates and the interpositioned bone.

Outcome measurement method

The obtained surgical outcome can be measured using conventional 2D lateral cephalometric analysis, 3D surface-to-surface distance measurements and by evaluating the difference between 3 reproducible landmarks positioned either manually or semi-automatically. The advantages and disadvantages of the methods are briefly described here.

The advantage of 2D lateral cephalometric analysis is that the method has been widely used, and therefore, the outcomes can be directly compared with similar studies. The disadvantage is the loss of information when the complex 3D VSP plan is reduced to a 2D X-ray image, especially in patients with asymmetry (Gateno, Xia and Teichgraeber, 2011; Bengtsson *et al.*, 2017; Borba *et al.*, 2018). The mean absolute errors in repeated measurements of 2D lateral cephalometric measurements exceed 1 mm (Ludlow *et al.*, 2009; Borba *et al.*, 2018).

The advantage of surface-to-surface distance measurements is the high degree of reproducibility, since the measurements are fully automatic between a 3D surface model positioned at the planned position and a 3D surface model positioned at the obtained position (Koerich *et al.*, 2016). The disadvantage of the method is that the reported mean distance only accounts for 40–50% of the true distance between the models (Jabar *et al.*, 2015). This underestimation is caused by all the measurements being performed on the surfaces running parallel to the repositioning direction because the surface measurements are performed to the closest point.

Using reference points to evaluate the obtained repositioning enables direct comparison with the VSP, where the surgical repositioning is also described by the 3D reposition at specific reference points. The disadvantage of manually inserting reference points is related to the reproducibility of the reference points. The mean absolute repeatability of manual reidentifying landmarks is approximately 0.5 mm (Ludlow *et al.*, 2009). The disadvantage of manually reidentifying landmarks is, that large outliers may occur and the range of measurement errors often exceeds 2 mm (Nebbe and Major, 2000; de Oliveira *et al.*, 2009; Titiz *et al.*, 2012; Lin *et al.*, 2017; Bengtsson *et al.*, 2018). This range of measurement errors may be minimized in large cohorts by use of the central limit theorem, but studies that measure outcomes in orthognathic surgery are often undertaken in small cohorts of less than 30 patients (Stokbro *et al.*, 2014; Haas Jr., Becker and de Oliveira, 2015). In small cohort studies, large outliers in measurement errors may either skew the data to create errors that were not found in the patients or mask problems that were not detected due to the variation in measurement errors. Thus, in small samples it is important to perform repeatable measurement of outcomes.

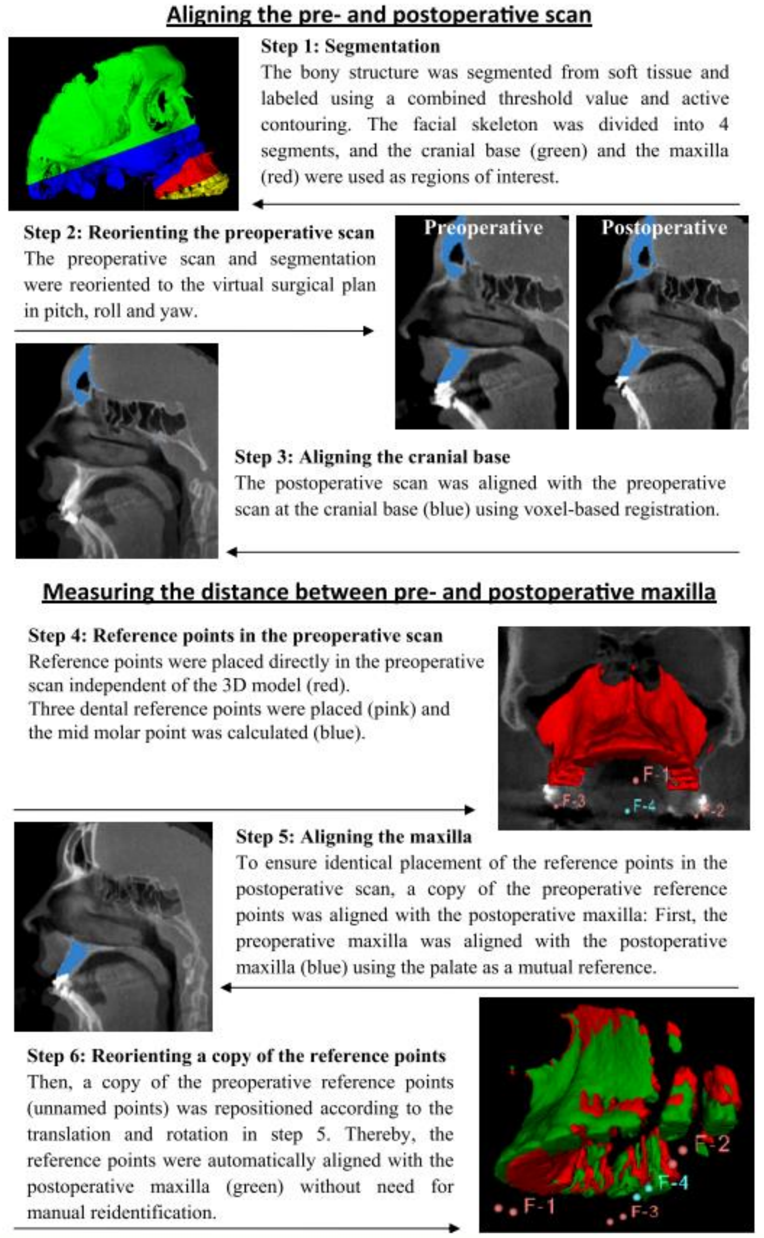


Fig. 5. The semi-automatic method for measuring the distance between the preoperative and the postoperative scan. The method automates the positioning of the reference points in the postoperative scan, thus eliminating errors due to manually reidentifying landmarks (Stokbro and Thygesen, 2018a).

To overcome the disadvantages of using reference points, a semi-automatic method was developed in which the reference points were positioned without need for manual reidentification of the landmarks (Fig. 5) (Stokbro and Thygesen, 2018a). The absolute mean repeatability of the method is less than 0.3 mm between repeated measurements, and the method has been validated by 3 independent study centers (Baan *et al.*, 2016; Stokbro and Thygesen, 2018a; Shaheen *et al.*, 2019). The method consists of manually inserting reference points in the preoperative scan and then aligning a copy of the reference points with the postoperative scans. The reference points are repositioned in the postoperative scan by aligning a bony reference structure (i.e. the bony palate for the maxilla) from the preoperative scan with the same reference structure in the postoperative scan using voxel-based registration. Thereby, the reference points do not need to be manually positioned, and the positioning can be performed independently of intraoperative resection of landmarks (i.e. anterior nasal spine) or postoperative orthodontic movement (moving the dental landmarks). Thus, more reliable measurements can be performed to evaluate the surgical accuracy and the postoperative skeletal stability of the obtained repositioning.

Combining the Odense cohort with the Nijmegen cohort:

In collaboration with the Department of Oral and Maxillofacial Surgery, Radboud University Nijmegen Medical Centre, the Netherlands, the hypotheses of study I could be analyzed in a larger dataset compiled from the 2 study centers (Odense and Nijmegen). A study was performed in Nijmegen Medical Centre evaluating 144 patients who underwent either a mandible first or a maxilla first procedure (Liebregts *et al.*, 2017). In the Nijmegen study, no subgroup analysis evaluated whether inferior maxillary repositioning influenced these results. Datasets from the two centers could be combined since the studies used similar measurement protocols with an equal level of accuracy. Thus, the findings of study 1 could be tested for validity in a large, combined dataset with sufficient statistical power to perform appropriate subgroup analyses.

In vitro studies – comparing in vitro results with surgical outcome

After establishing the level of surgical accuracy and skeletal stability, it is important to know whether the surgical outcome can be improved or whether we must simply accept the discrepancy between planned and obtained maxillary movement. Studies have shown that a high degree of surgical accuracy can be obtained with patient-specific, printed plates. However, no studies have demonstrated that 3D VSP orthognathic surgery performed with patient-specific plates improved surgical accuracy or skeletal stability compared with manually adapted plates. Ideally, improvement in surgical accuracy and stability should be tested using a “heads up” test between identical surgical situations or by operating on a single patient twice, but this is not clinically or ethically possible. The clinical improvement in surgical accuracy and skeletal stability can also be evaluated by randomized clinical trials (RCT). However, an RCT must include enough patients to be able to identify a statistically significant improvement. Currently, none of the clinical studies can provide any insights into the size of the cohorts needed to perform a sufficiently powered RCT. By using the patients’ data from the VSP, physical models can be 3D printed, thereby creating in vitro conditions closer to the identical twin scenario. The 3D printed models can be used to perform mock surgery on bone models that imitate the clinical conditions (Fig. 6). Thereby, the stability of manually adapted plated could be directly compared with that of PSP plates. Furthermore, since the model is a reproduction of the patient’s bony surface, the surgical accuracy obtained in the mock surgery can be compared with the surgical accuracy obtained in the patient. Comparing the surgical accuracy in vitro with the surgical accuracy obtained in the patient provides an estimate of the amount of improvement that could ideally be obtained by using PSP plates. However, a direct comparison should always favor the in vitro results, as these are not influenced by pull from the muscles or nightly bruxism.

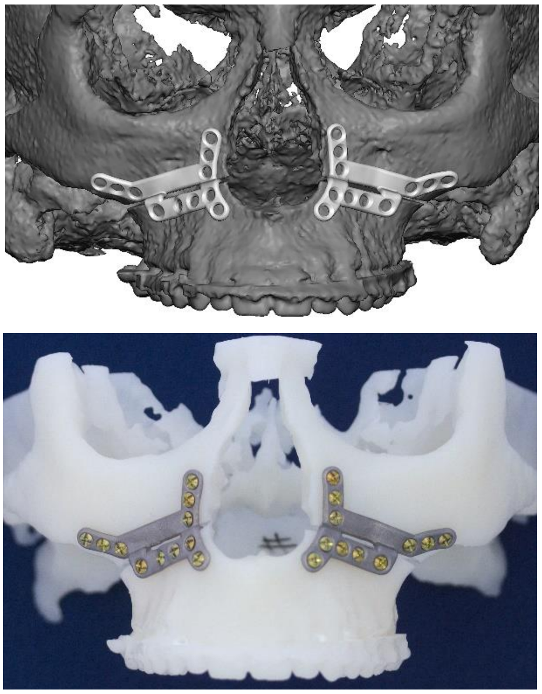


Fig. 6. Printed model with dentition to perform mock surgery. Model was printed from the preoperative VSP model. Patient-specific, 3D printed plates were used to reposition the moving, dental segment (Stokbro, Bell and Thygesen, 2018).

In vitro models may also be used to directly compare the stability of the osteotomy fixated by either manually adapted, stock plates or patient-specific, printed plates (Fig. 7). The identical conditions created in an in vitro setup enable direct comparison between the 2 types of plates. Thus, the stability of both types of fixation can be tested in identical setups mimicking the patients' clinical conditions regarding planned reposition, bone thickness and surface curvature.

Purpose and aims

The purpose of the studies that make up this thesis was to investigate the surgical accuracy and skeletal stability of the maxilla in orthognathic surgical patients treated with inferior maxillary repositioning and to evaluate whether PSP plates could improve the surgical accuracy and skeletal stability in vitro.

The following aims were tested in the thesis from the radiographic and in vitro studies:

I: The aim of study I was to quantify the difference between the virtual surgical plan and the obtained surgical movement of the maxilla at 1-week follow-up in a cohort treated with inferior maxillary procedures.

II: The aim of study II was to evaluate whether the results of study I could be confirmed in a large, mixed cohort study.

III: The aim of study III was to quantify the postoperative skeletal movement from 1-week to 1-year follow-up.

IV: The aims of study IV were to quantify how close PSP plates positioned the maxilla to the planned position in vitro and compare the in vitro results with the obtained orthognathic surgery.

V: The aim of study V was to measure and compare how much force was needed to eliminate the maxillary osteotomy stabilized by either manually adapted plates or PSP plates in vitro.

Null-hypotheses

The following null-hypotheses were tested in the radiographic and in vitro studies:

H_0-I: The obtained surgical reposition of the maxilla did not differ significantly from the virtual surgical planned repositioning.

H_0-II: The obtained surgical reposition of the maxilla in inferior maxillary repositioning did not differ significantly from superior maxillary repositioning in a large combined cohort.

H_0-III: The obtained surgical reposition of the maxilla was stable and did not relapse significantly in any specific direction.

H_0-IV: No difference existed between maxillary surgical accuracy of in vitro operations using PSP plates and the patients' obtained maxillary surgical accuracy following orthognathic surgery.

H_0-V: No difference exists in the force needed to eliminate the osteotomy gap between conventional plates and PSP plates.

METHODS AND MATERIALS

Patient sample

In **study I,** the authors implemented a retrospective cohort study. The cohort was derived from the consecutive population of patients treated at the Department of Oral and Maxillofacial Surgery, Odense University Hospital, Odense, Denmark, from January 1, 2013 to December 31, 2015. The inclusion criteria were orthognathic surgery with mono- or bimaxillary procedures, without segmentation of the maxilla, with a mean inferior maxillary repositioning measured at 3 dental reference points (upper incisor edge and the mesiobuccal cusps of the first molars). The exclusion criterium was deviations from the VSP during the orthognathic surgery.

In **Study II**, the study population consisted of the patients in 3 published studies from Odense and Nijmegen (Stokbro *et al.*, 2016; Liebregts *et al.*, 2017; Stokbro and Thygesen, 2018b). The inclusion criteria were bimaxillary procedures without segmented maxillary procedures. The exclusion criterium was missing information on the planned repositioning from the VSP in the dataset.

In **study III**, the inclusion criteria were identical to Study I. The exclusion criterium was not attending the 1-year postoperative follow-up.

The data from the CBCT scans of the cohort included in study I were used to print material for the in vitro studies IV and V.

In **study IV**, the VSP plans from the cohort analyzed in study I were included to produce 3D printed stereolithographic additive (SLA) models and PSP plates. No exclusion criteria were relevant.

In **study V**, the 7 patients with the largest osteotomy gaps from study I were included for in vitro compression testing of stability. No exclusion criteria were relevant.

Ethical considerations

All participants provided written consent prior to inclusion in the study. Permission to store the data digitally was granted by the Danish Data Protection Agency for all studies. All studies were exempt from ethical review by the Chairman of the Regional Committee on Health Research Ethics for Southern Denmark, since the studies were retrospective and without influence on the patients' treatment. All participants were treated in accordance with the Declaration of Helsinki.

Variables

All outcome, predictor and confounding variables included for analysis are listed in Table 2.

In **study I**, the primary outcome variable was the surgical accuracy, defined as the difference between the VSP maxillary reposition and the obtained maxillary reposition. The primary predictor variable was time from the preoperative scan to the postoperative scan. The secondary predictor was the VSP maxillary repositioning. Both the outcome and the secondary predictor variables were evaluated along the 3 axes (right, anterior, superior). Confounding variables are listed in Table 2.

In **study II**, the primary outcome variable was also the surgical accuracy along the 3 axes; the primary predictor was also time from the preoperative scan to the postoperative scan. The secondary predictor variables were the continuous variable of the VSP maxillary repositioning and categorical variables for counter-clockwise rotation and inferior maxillary repositioning.

In **study III**, the primary outcome variable was postoperative skeletal stability, defined as the difference between the obtained maxillary repositioning and the 1-year postoperative maxillary position. The primary predictor variable was time between the 1-week and 1-year cone-beam computed tomography (CBCT) scan. The secondary predictor variable was the amount of obtained maxillary repositioning.

In **Study IV**, the primary outcome variable was also the surgical accuracy of the in vitro surgery on the 3D printed model. The primary predictor was time from the scan before in vitro surgery to the scan after in vitro surgery. The secondary predictor was the VSP maxillary repositioning.

In **study V**, the primary outcome variable was the force needed to compress the 3D printed model with the osteotomy stabilized by the osteosynthesis plates. The primary predictor variable was the type of osteosynthesis plate used to stabilize the osteotomy.

Table 2. Summary of study variables in studies I–V.

Variables	Type	Unit	Study I	Study II	Study III	Study IV	Study V
VSP (T1)	Cont.	mm	X	X		X	
Obtained reposition (T2)	Cont.	mm	X	X	X	X	
1-year postoperative position (T3)	Cont.	mm			X		
Surgical accuracy (T2–T1)	Cont.	mm	X	X		X	
Skeletal stability (T3–T2)	Cont.	mm			X		
Linear	Cat.	Right	X	X	X	X	
		Anterior	X	X	X	X	
		Superior	X	X	X	X	
Rotation	Cat.	Yaw	X	X	X	X	
		Pitch	X	X	X	X	
		Roll	X	X	X	X	
Bimaxillary surgery	Dichot.		X		X		
Maxillary inferior repositioning	Dichot.			X			
Surgeon	Cat.		X				
Occlusion	Cat.	Angle Cl I	X	X	X	X	
		Angle Cl II	X	X	X	X	
		Angle Cl III	X	X	X	X	
Female gender	Dichot.		X	X	X	X	
Age	Cont.	Years	X	X	X	X	
Osteotomy gap size	Cont.	mm					X
Conventional plate size	Cat.	Regular					X
		Medium					X
		Large					X
Asymmetry	Dichot.						X
Compression force	Cont.	N					X
Displacement	Cont.	mm					X
2-mm displacement	Cont.	N/mm					X
E-modulus	Cont.	N/mm					X
Yield point	Cont.	N/mm					X

Abbreviations: Cont – Continuous variable; Cat – Categorical variable; Dichot – Dichotomous variable; N – Newton; VSP – Virtual surgical plan.

Surgical procedure and radiographic imaging

Cone beam computed tomography scans were obtained preoperatively and 1 week postoperatively using a NewTom 3G scanner (Field of view: 20 x 20 Cm; 110 kV; Voxel size: .36 x .36 x .45). The decompensatory orthodontic treatment was retained by passive wires from the time of the initial

CBCT scan until the time of the surgery. The VSP was performed in collaboration between a 3D Systems engineer and a maxillofacial surgeon using Dolphin 3D Surgery (Dolphin Imaging and Management, Chatsworth, CA, USA) and finalized by 3D Systems (3D Systems, Rock Hill, SC, USA) (Fig. 8).

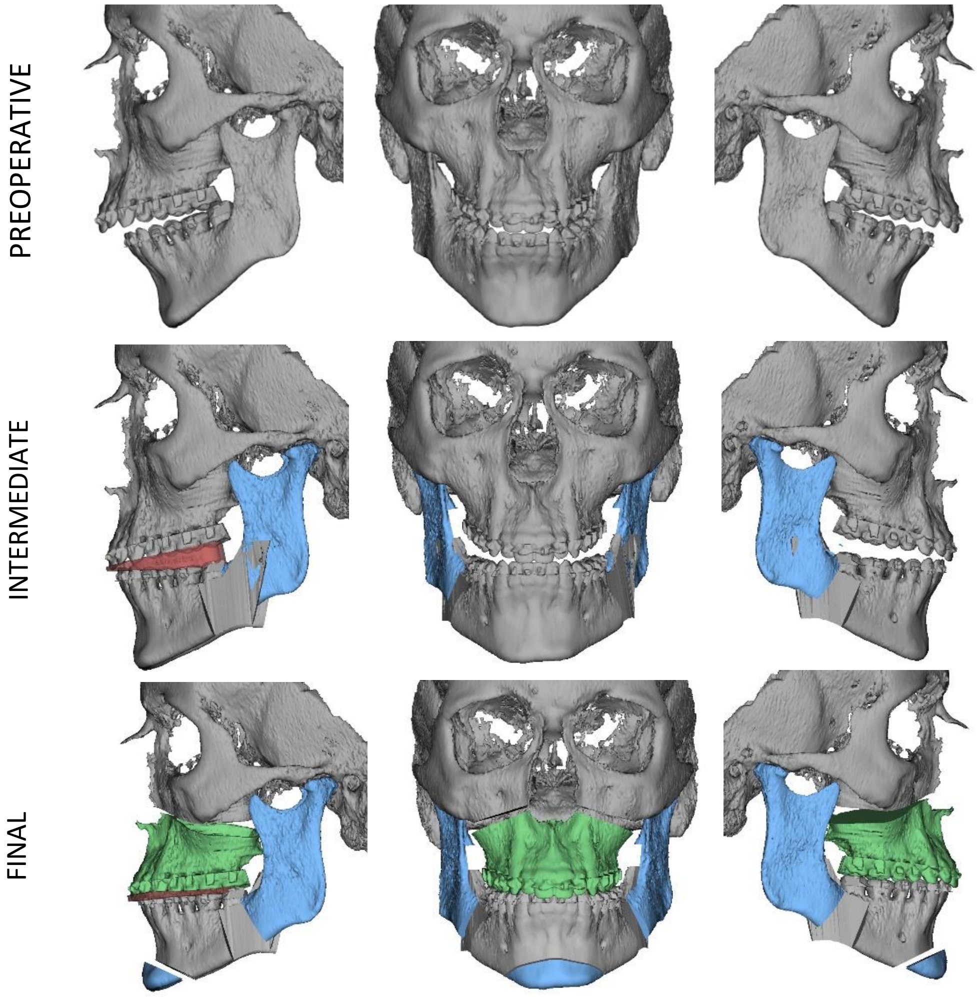


Fig. 8. Virtual surgical plan (VSP) produced by 3D Systems. Bimaxillary procedure planned with inferior maxillary repositioning, mandibular advancement and chin advancement. The surgical sequence is planned with a mandible-first approach.

In bimaxillary procedures in Odense, the mandible was operated on first. Surgical repositioning was obtained by an interdental surgical splint. The mandibular osteotomy was fixated by 3 bicortically fixated screws along Champy's lines. The vertical height was verified using external reference measurements with surgical calipers from the medial canthal ligament to the dental brackets. The maxillary osteotomy was fixated by 4 manually adapted L-shaped plates (Biomet 2.0 systems, Zimmer Biomet Corp, Warsaw, CA, USA). Bone grafting and repositioning were carried out by local resection, but no extraoral bone grafting was performed.

In bimaxillary procedures in Nijmegen, the surgical sequencing was changed from operating on the mandible first in 2010 to 2012 to operating on the maxilla-first in 2013 to 2014. The dental segments were positioned according to the interdental splints. The mandibular osteotomy was fixated by 1 miniplate along Champy's lines. The vertical height was verified with use of external reference measurements with surgical calipers from a bony anchored nasal reference pin to the dental brackets. The maxillary osteotomy was fixated by 4 manually adapted L-shaped plates (Champy 2.0 system, KLS Martin, Tuttlingen, Germany).

In vitro study setup

In **study IV**, the VSP was used to recreated the surgical conditions with a 3D printed model of the midface and print osteotomy guides and PSP plates, incorporating the planned maxillary repositioning. The 3D model and computer-aided design and computer-aided manufactured (CAD/CAM) surgical guides were designed and manufactured at 3D systems using SLA processing in a 3D printer (Fig. 9). The PSP plates were also designed and manufactured at 3D systems using direct metal printing by laser sintering of titanium alloy powder (Ti64Al4V).

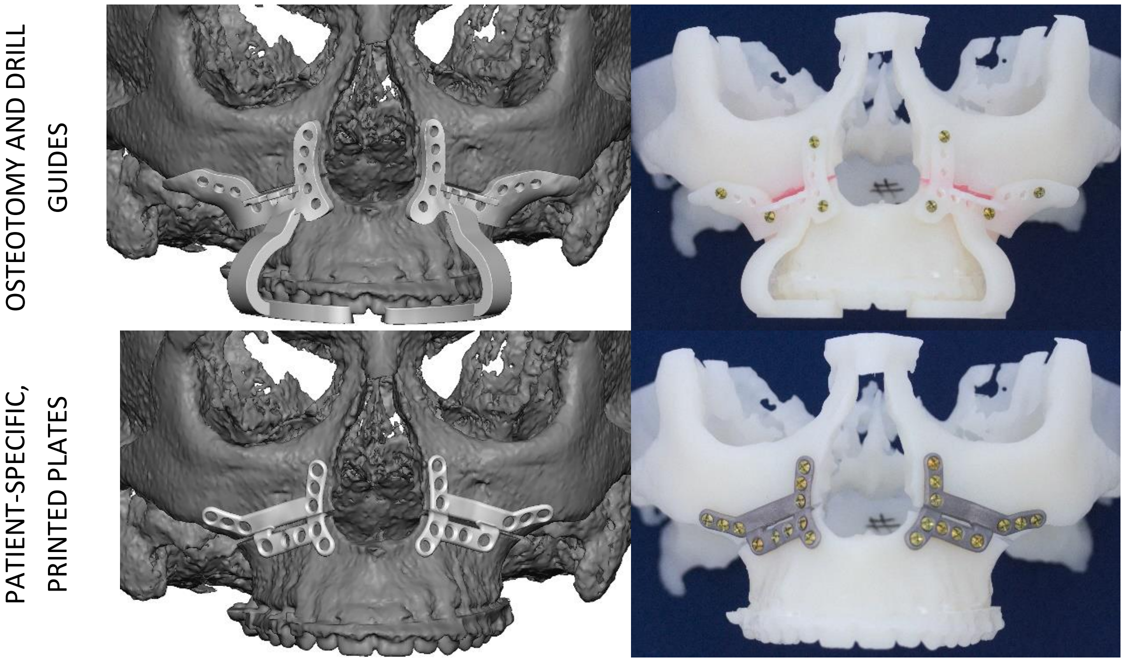


Fig.9. Osteotomy and drill guides, and patient-specific, printed plates. The osteotomy guide is mouned on the printed preoperative patient model. The osteotomy is marked with red wax. Plates are mounted on the model to reposition the dental segment.

The in vitro surgery was performed as in a clinical setting. A preoperative CBCT scan of the model was performed using the same setting as in the patient scans. Then, in vitro surgery was performed by mounting the osteotomy and drill guide and drilling the holes according to the drill guide-specified positions. The osteotomy was performed by an oscillating saw at the level specified by the osteotomy guide. The guide was removed and the osteotomy was completed by separating the dental segment from the cranial segment. The PSP plates were mounted with screws in the prespecified positions. To ensure close adaptation between the plates and model, the edge of the osteotomy was rounded using a pear-shaped burr, as the edge interfered with passive

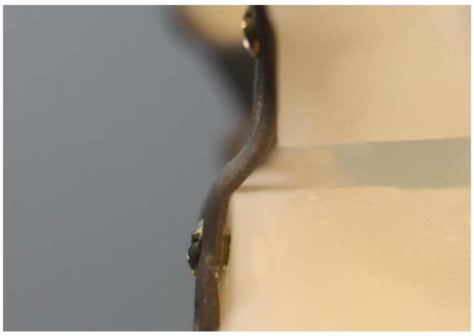


Fig. 10. Interference between the osteosomy edge and the patient-specific, printed plate. The interferences were removed to avoid displacement of the plates.

adaptation of the plates (Fig. 10). A postoperative CBCT scan of the model was performed with the same clinical settings as used in the patient scans.

In **study V**, the VSP virtual models in the postoperative position were used to print 2 identical sets of 3D models. The STL-file of the virtual model was exported from Dolphin 3D surgery-software and preprocessed in Autodesk MeshMixer (Autodesk Inc., San Rafael, CA, USA). Preprocessing ensured that the relationship between the midface and the dental segment was temporarily fixated. A disc was added, which ensured that the 2 parts of the midface did not move independently, and height of all models was calibrated to 46 mm. The models were printed on the Stratasys uPrint (Stratasys Ltd., Eden Prairie, MN, USA) in acrylonitrile-butadiene-styrene (ABS) material with a layer height of 0.254 mm, and the osteotomy was fixated with support material. Two identical model sets were made, one model in which the PSP plates were fitted and the holes were drilled, and in the other model the manually adapted, stock plates (Leibinger 2.0 L-shaped plates) were fitted. The support material was dissolved and the plates were fixated on the model to stabilize the osteotomy. Then, the models were mounted in a Zwick Roell Z050 testing machine (Zwick Roell, Ulm, Germany) (Fig. 11), with an upper compression plate mounted on a ball joint and a lower fixated compression plate. To engage the compression plates with the model, the model was preloaded with 50 newtons (N) before the test commenced. The test ended when the osteotomy gap completely disappeared.

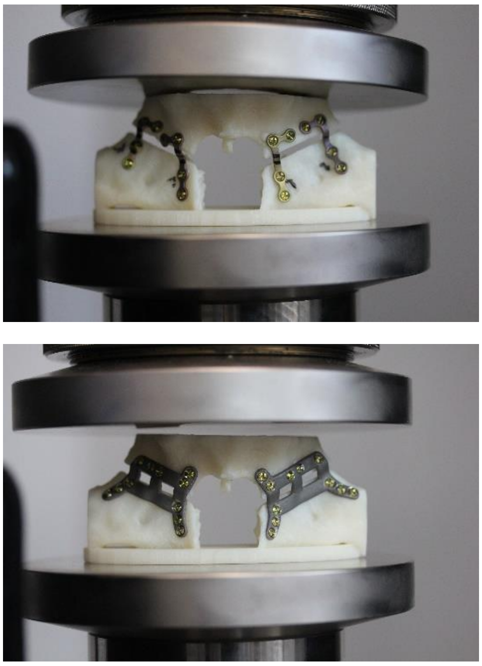


Fig. 11. Printed models placed between the compression plates in the testing machine (Zwick Roell Z050, Ulm, Germany). The models were compressed to measure the amount of force needed to eliminate the osteotomy.

Outcome measurements

3D measurements (I–IV)

The obtained surgical outcomes and postoperative relapses were measured by a previously validated, semi-automatic method (Stokbro and Thygesen, 2018a). The measurements were treated as 3D vectors and described in millimeters relative to the values of the 3 axes: right, anterior and superior.

In **study I**, the outcome was measured at 3 dental reference points: the upper incisors edge at the dental midline and bilaterally on the mesiobuccal cusp of the first molars. The mean of the dental reference points created a virtual centroid point (C) (Xia *et al.*, 2007; Hsu *et al.*, 2013). The linear surgical reposition was calculated as the difference between the centroid in the preoperative scan and in the 1-week postoperative scan. Rotational differences were calculated around the mid-molar point, positioned halfway between reference points on the first molars.

In **study II**, the linear measurements were changed from the centroid to the midline of the upper incisors edge, since this was the standard of measurements in the Nijmegen cohort. Rotational measurements were not affected by the change in measurement points.

In **study III**, the linear and rotational measurements were performed as in study I, but measured between the maxillary position in the 1-week CBCT scan and the 1-year CBCT scan.

In **study IV**, an approach similar to that in study I was used, but since the 3D printed model was homogeneous in density, voxel-based registration could not be performed, so surface-based registration was used instead.

Compression force (V)

In **study V**, the force (N) and amount of compression (mm) was measured continuously while testing the models in a Zwick Roell Z050 machine (Zwick Roell, Ulm, Germany). The test was terminated when the osteotomy gap was completely compressed and the amount of force needed to completely compress the model was recorded. The force needed to compress the model 2 mm was also recorded from the testing machine. The yield point was calculated on the force per mm compression recording as the intersection between a line running parallel to the steepest slope with a 2‰ (0.1 mm) offset.

Statistics

All data was analyzed using STATA version 14.2–15.0 (StataCorp LLC, College Station, TX, USA).

In the clinical studies I–IV, an overall mixed model regression analysis was performed to avoid multiple testing of multiple predictor and confounding variables. Thereby, all predictor and confounding variables were included in one global model, and significant predictor or confounding variables could be further explored in individual analyses to establish whether the findings in the global model translated to relevant statistical and clinical findings. Residuals between and within individuals were tested for normality of distribution before accepting the final statistical model. When performing mixed model regression testing on limited sample sizes, there is a risk of overfitting the model, and therefore, any significant findings in the global model must be verified in the clinical data before accepting the findings as significant.

The outcome variables were tested for normality of distribution by the Shapiro–Wilk test. In normally distributed outcomes, means were compared using one-sample *t*-test or Student's *t*-test. In non-normally distributed outcomes, the comparisons were performed by non-parametric testing with either the Wilcoxon sign-rank test or rank-sum test.

Clinical significant thresholds were initially set at 2 mm deviation from the planned position and 4 degrees, as proposed by several authors (Donatsky *et al.*, 1992; Padwa, Kaiser and Kaban, 1997; Xia *et al.*, 2007; Hsu *et al.*, 2013); however, this clinical threshold for mean measurements was lowered to a 1-mm threshold for study II, corresponding to updates in measurement accuracy (Borba *et al.*, 2018).

RESULTS

Study I

Twenty-five patients were invited to participate, but 2 patients declined and 2 patients did not respond to the invitation. Of the 21 patients who accepted participation, 1 patient was excluded because the surgical reposition was changed during surgery. Thus, 20 patients could be included in the final cohort. In the cohort, 13 patients underwent bimaxillary procedures.

The outcome was normally distributed along all 3 axes (Shapiro-Wilk test: P = 0.09–0.66). Overall, the maxilla was positioned 1.0 mm posterior (SD = 1.6 mm) and 0.4 mm superior (SD = 1.4 mm) to the planned position (Table 3).

In the mixed model regression analysis, only the VSP affected the surgical outcome along the superior and anterior axis. No other confounding variables, including bimaxillary surgery, affected surgical accuracy.

There was a linear correlation between the amount of planned repositioning and the surgical accuracy. Large inferior maxillary repositions were positioned further superior than planned (correlation coefficient R^2 = 0.46), likewise large advancements were positioned further posterior than planned (correlation coefficient R^2 = 0.49).

Table 3: Surgical accuracy in obtained maxillary reposition compared to the VSP (*N* = 20).

Mean measurements	Planned	Obtained	Difference	*P*-value
Linear measurements, mm (SD)				
Right	0.06 (0.77)	–0.05 (1.05)	–0.11 (0.79)	.592*
Anterior	2.93 (1.99)	1.95 (1.44)	–0.98 (1.57)	**<.001***
Superior	–1.75 (0.85)	–1.33 (1.01)	0.42 (1.36)	**.037***
Rotational measurements, ^{o} (SD)				
Yaw	1.01 (1.48)	0.71 (1.81)	–0.30 (1.18)	.270$
Pitch	–0.79 (3.32)	–1.48 (2.77)	–0.69 (2.14)	.321$
Roll	0.02 (1.21)	–0.21 (1.18)	–0.22 (1.14)	.688$

* Predictive margins with fixed proportions from mixed model analysis. The test incorporates all covariates and evaluates whether the obtained movement is statistically different from the planned movement.

$ One-sample *t*-test.

Study II

Among the 166 patients studied in the 3 published articles, 145 patients with bimaxillary procedure could be included in study II. All patients underwent bimaxillary procedures, and in 88 patients the mandible was operated on first, while in 57 patients the maxilla first was operated on first. Inferior maxillary repositioning was carried out in approximately half the participants.

Mixed model regression showed that both surgical sequencing and inferior maxillary repositioning had a statistically significant influence on surgical accuracy. The interaction between the surgical sequencing and the inferior maxillary repositioning showed that in inferior maxillary repositioning, the maxilla was positioned posterior to the planned position by a mean value of 2.0 mm (mandible-first procedure) to 1.7 mm (maxilla-first procedure) (See Table 4). In inferior maxillary repositioning, the difference between the mandible-first and the maxilla-first procedures was not statistically significant. The difference between inferior and superior maxillary repositioning was statistically significant for both mandible-first and maxilla-first procedures.

Table 4. The surgical sequence interaction with superior/inferior maxillary repositioning.

Linear distance (mm)	*N*	Mandible-first	*N*	Maxilla-first	*P* Value*
Superior maxillary reposition	43		24		
Right		0.32 (1.63)		−0.54 (1.64)	**.041**
Anterior		−0.93 (1.93)		1.45 (2.77)	**.000**
Superior		−0.34 (2.10)		0.53 (2.17)	.114
Inferior maxillary reposition	45		33		
Right		0.52 (1.69)		0.11 (0.95)	.211
Anterior		−2.03 (1.96)		−1.65 (1.60)	.370
Superior		−0.11 (1.36)		0.16 (2.01)	.484
P Value* superior vs inferior					
Right		.583		.064	
Anterior		**.010**		**.000**	
Superior		.541		.510	

* Student's 2-sample independent *t*-test.
Abbreviations: SD, standard deviation.
Note: Measurements are presented as mean (standard deviations).

Study III

From the 21 included patients, 1 patient was excluded because the patient did not attend 1-year follow-up (same patient was also excluded in study I) and 3 patients were excluded because they needed reoperations during the first year after orthognathic surgery. The reasons for reoperations were failure of the osteosynthesis material because of malocclusion, visible asymmetry or maxillary non-union after 12 months of healing. Thus, the final cohort for qualitative analysis consisted of 17 patients.

The maxillary position in the remaining cohort without postoperative complications was considered stable. Overall, the largest maxillary relapse was seen in the superior direction with a mean relapse value of 0.2 mm (SD: 0.3), which was statistically significant (P = 0.02) but not clinically significant. Mixed model regression analysis showed that the postoperative stability was significantly influenced by age, size of obtained repositioning and type of surgery (maxilla only compared with bi-maxillary procedures). The 3 excluded patients with postoperative complications all underwent bimaxillary procedures. Evaluating bimaxillary procedures showed that the maxilla relapsed slightly in a superior and posterior direction, while solitary maxillary procedures relapsed slightly in a superior and anterior direction (Table 5).

Table 5. Comparison between maxillary (N = 7) and bi-maxillary (N = 10) procedures.

Mean measurements, mm (SD)	Maxilla only	Bimaxillary	*P* Value*
Right	−0.02 (0.11)	−0.06 (0.20)	.634
Anterior	0.25 (0.28)	−0.16 (0.50)	.071
Superior	0.27 (0.11)	0.14 (0.32)	.395

* Student’s 2-sample *t*-test.

Study IV

The VSP from the 20 patients in study I was used to fabricate the in vitro study material (SLA model, PSP plates and CAD/CAM cutting and drill guides). In all models, the PSP plates interfered with the osteotomy edge at the dental segment, and the edge was therefore rounded with a burr. The PSP plates positioned the dental segment 0.5 mm anterior (SD: 0.6) and 0.3 mm inferior (SD: 0.3) to the planned position, which was statistically significantly different from 0 (*P* = .001). In rotational differences, the pitch was statistically significantly different from 0, with a small counter clockwise rotation of 1.3^{o} (SD: 1.5).

Comparing the surgical accuracy in vitro with the obtained surgical outcome in patients showed increased surgical accuracy and less variance in the in vitro setup in which the PSP plates were used. All in vitro surgeries were within the clinically acceptable threshold of 2 mm from the planned position (largest absolute difference 1.5 mm), while the obtained position was more than 2 mm from the planned position in 6 patients. The mean difference in absolute measurements showed that the in vitro outcome with PSP plates evidenced a significantly higher degree of surgical accuracy for all linear measurements.

Table 6: Absolute difference between orthognathic surgery and in vitro surgery (PSP plates)

Mean absolute measurements	Model Surgery	Orthognathic Surgery	*P*-value*
Linear difference – mm			
Right	0.18 (0.19)	0.57 (0.54)	**.004**
Anterior	0.61 (0.42)	1.49 (1.06)	**.005**
Superior	0.35 (0.23)	1.05 (0.94)	**.006**
Rotational difference – degrees			
Yaw	0.50 (0.38)	0.89 (0.80)	.052
Pitch	1.66 (1.05)	1.77 (1.42)	.794
Roll	0.60 (0.65)	0.94 (0.51)	.096

* One-sample *t*-test.

Study V

The 7 patients with the largest osteotomies were selected, and the stability of the osteotomy fixated by either PSP plates or manually adapted plates was compared directly. One of the 3 patients that required additional surgery in study III was included in the cohort.

In all tests, the PSP plates resisted more force than the stock plates before the osteotomy was completely compressed (Table 7). Furthermore, in all tests the PSP plates also resisted more force than the stock plates before the model setup was compressed 2 mm. In 6 out of 7 tests, both the yield points and the elastic modulus were higher for PSP plates than for manually adapted stock plates.

Qualitative evaluation of the plates' performance showed that the first point of failure for the stock plates was in the bend in the plates. In the PSP plates, the first point of failure was the first screws cranially to the osteotomy. During the preload of 50 N, 3 of the models fixated with stock plates yielded at one or all the plates. The 3 in vitro setups that yielded during preload were not produced from the patient that required additional surgery. The PSP plates did not fail during preload, but the screws did settle and rotate slightly away from the osteotomy. None of the PSP plates broke despite forces of more than 4000 N.

Table 7. Testing difference between patient-specific 3D printed plates and manually adapted stock plates (*N* = 7).

	Patient-specific plates		Stock plates		*P*-value*
	Median	(range)	Median	(Range)	
Osteotomy eliminated (N)	3047	(1171–4966)	1133	(50–4292)	**0.018**
2 mm displacement (N)	2299	(1779–4318)	637	(559–3205)	**0.028**
E-modulus (N/mm)	2119	(922–3042)	828	(487–2254)	**0.018**
Yield point (E + 0.1 mm)	1518	(759–3376)	538	(444–2416)	**0.018**

* Wilcoxon sign-rank test.

Abbreviations: N – Newton; E – elastic

DISCUSSION

The 3 digital, radiographic studies (studies I–III) investigated the surgical accuracy and stability of the maxillary position in orthognathic surgical patients treated with inferior maxillary repositioning. The 3 studies found that patients treated with inferior maxillary repositioning still has room for improvement regarding both surgical accuracy and postoperative stability.

In the 3 radiographic studies, the null hypotheses could be rejected in study I and study II, but not in study III. Study I found that the maxilla was positioned posterior to the virtual surgical planned position; thus H_0-I was rejected. Study II also found that the maxilla was positioned posterior to the virtual surgical planned position in a large combined cohort, thus H_0-II was rejected. Study III found that for patients without postoperative osteosynthesis failure, the obtained maxillary position was stable without significant relapse; however, 15% of the included patients needed reoperations during the first year after surgery due to osteosynthesis failure or non-union healing. Thus, H_0-III could not be rejected with regard to the patients without complications, but increased stability is considered clinically recommendable due to the high number of postoperative complications.

The 2 in vitro studies (studies IV–V) evaluated whether PSP plates could improve the surgical accuracy and stability of the maxillary position in vitro. Study IV showed that the maxilla was positioned significantly closer to the planned position in vitro using PSP plates compared with the patients' obtained maxillary reposition following orthognathic surgery, thus the H_0-IV could be rejected. Study V showed that the PSP plates resisted more force before the osteotomy gap was compressed compared with manually adapted stock plates, thus H_0-V could be rejected.

Interpretation of surgical accuracy results (I, II, IV)

Inferior maxillary repositioning is considered among the most unstable orthognathic procedures, and study I and study II confirmed that problems still exist despite advances in orthognathic surgical planning using 3D VSP. Studies I and II found that the maxilla was positioned posterior to the planned position, thereby confirming the problem found in the pilot study (Stokbro *et al.*, 2016). Positioning the maxilla 2 mm posterior to the ideal orthognathic position may not result in esthetic failure, but the patient's esthetic potential may not be fully achieved due to the deficiency in maxillary advancement. The mean posterior positioning was considered both statistically significant and clinically significant, and 3 findings were of interest in suggesting how the underlying mechanisms affected the surgical outcome in a posterior direction. First, the studies found an overall posterior position regardless of whether the maxilla or mandible was operated on first. Second, a linear correlation between the amount of posterior positioning and the amount of planned advancement, i.e. large maxillary advancements resulted in more posterior obtained positioning. Third, no correlation existed between the amount of inferior repositioning and the posterior maxillary positioning. These 3 findings suggest that inferior maxillary repositioning may not directly affect the posterior position in a linear way, but instead the lack of bony support may destabilize the maxillary repositioning. Additionally, the direct correlation between the amount of planned maxillary advancement and posterior repositioning suggests that elastic muscular forces pull on the maxilla in a posterior direction, thereby displacing the maxilla intraoperatively or during the first week postoperatively before the CBCT scan. The same underlying mechanisms also seem to have an influence on surgical procedures that involve maxillary advancement and inferior repositioning in comparative studies in the literature.

None of the studies on 3D surgical accuracy have previously evaluated surgical accuracy after inferior maxillary repositioning or maxillary advancement. Therefore, the comparative literature consists of studies on 2D lateral cephalometric tracings, which have reported diverse observations. Only the findings in 1 study were directly comparable with the reported surgical accuracy in both the vertical and horizontal directions in a subgroup of 9 patients treated with inferior maxillary repositioning (Semaan and Goonewardene, 2005). The study did not specify whether the maxilla or mandible was operated on first in the bimaxillary procedures. At the upper incisors edge, no mean vertical or horizontal discrepancy (mean < 0.3 mm) was found in inferior maxillary repositioning, but the study had a very large range in repositioning (SD > 2.0 mm). However, the study found the maxilla to be positioned anterior to the planned position (1.2 mm) when patients underwent superior maxillary repositioning, which is consistent with the findings in study II (1.5 mm, maxilla-first). Likewise, large maxillary advancements were positioned posterior to the planned position (–0.8 mm), which was consistent with the linear correlation between advancement and posterior positioning found in study I.

The amount of advancement may be correlated with the amount of posterior reposition; however, the comparative literature is divided on this subject. Like the findings of Semaan and Goonewardene, the maxilla was positioned posterior to the planned position in the following studies: –0.9 mm in 20 patients (Jacobson and Sarver, 2002), –0.76 mm in 16 patients (Kwon *et al.*, 2014), and –1.98 mm in 15 patients (Tankersley *et al.*, 2019). However, large studies of maxillary advancement found no difference between the planned and obtained horizontal position: –0.05 mm (SD 1.26 mm) in 30 patients (Ong, Banks and Hildreth, 2001), –0.05 mm (SD: 0.63 mm) in 14 patients (Choi, Choi and Baek, 2009), –0.18 (SD: 0.66 mm) in 67 patients (Donatsky *et al.*, 2011), and 0.19 mm (SD. 1.95 mm) in 72 patients (Meewis *et al.*, 2018). Thus, there does not seem to be a prevailing correlation between the maxillary advancement and posterior discrepancy across all studies. Perhaps the lack of consistency can be caused by the maxilla-first procedures that were used in most studies. This was also in alignment with the findings in study II, where the maxilla-first procedure resulted in both posterior or anterior discrepancy depending on whether the maxilla was repositioned in an inferior or superior direction, respectively.

Studies on surgical accuracy comparing the mandible-first and the maxilla-first procedures have only been performed in 3 previous studies. A systematic review from 2015 (Borba *et al.*, 2015) found only 1 study in the literature (Ritto *et al.*, 2014), but since then, 2 studies have been published (Liebregts *et al.*, 2017; Salmen *et al.*, 2018). The study by Liebregts et al. (2017) was included in study II. Salmen et al. (2018) found no difference between the procedures along the anterior axis, but they found differences between procedures along the superior axis, which is under the direct control of the surgeons. Likewise, Ritto et al. (2014) evaluated 5 patients treated with inferior maxillary repositioning, and in all 5 patients the maxilla was positioned superior to the planned position, but not posterior or anterior to the planned position. Thus, the findings in studies I & II were different from previous studies. It is impossible to evaluate whether these changes are new or were simply unnoticed due to measurement inaccuracies. In 2D lateral cephalometric tracing, the reproducibility of absolute repeated measurements ranged from 0.65 mm to 2.40 mm (calculated from the provided Dahlberg's analysis) (Salmen *et al.*, 2018).

The problem with the literature surrounding 3D measurements is the lack of uniform cohorts that can be used for comparison. In cohorts with multidirectional repositioned maxillary movements, the underlying mechanisms may not be evident in all cases if subgroup analyses are not performed. The studies with uniform inclusion criteria were mainly in patients with Angle class III occlusion (Tucker *et al.*, 2010; Zinser *et al.*, 2013; Koerich *et al.*, 2016; Lin *et al.*, 2017; Bengtsson *et al.*, 2018; Mulier *et al.*, 2019).

Study IV demonstrated that surgical accuracy could be improved by using PSP plates. Study IV evaluated the improvement in surgical outcome in vitro compared with the obtained surgical accuracy in orthognathic surgery; thereby, the problems with heterogeneous cohorts and different outcome measurements could be eliminated. A comparison of the results in study IV with those in a similar in vitro study on 9 printed maxillary models showed a difference of less than 0.2 mm with regard to both mean difference and standard deviation (He *et al.*, 2015). Likewise, comparing the results from study IV with the 2 clinical studies using PSP plates with similar outcome evaluations also found close correlations between mean differences and standard deviations (Table 8)

(Heufelder *et al.*, 2017a; Li *et al.*, 2017). The study by Li *et al*. also provided relative outcome measurements and standard deviation, but the study did not specify the direction of the measurement axes. Therefore, it was not possible to evaluate whether the reposition errors were in the same direction as those found in study IV, but the magnitude and frequency of errors were similar, as seen by the correlation between root mean squared deviation in the 2 studies. The results from the study IV seem to correspond with the findings in both in vitro and clinical studies of PSP plates. Thus, it can also be assumed that the proposed power calculation can be used in future RCT studies.

Table 8. Comparing study IV with the relevant literature

	Comparative study	Study IV (N = 20)
He et al. 2015, *N* = 9, in vitro study		
Right (abs)	.39 ± .30	.18 ± .19
Anterior (abs)	.81 ± .54	.61 ± .42
Superior (abs)	.44 ± .31	.35 ± .23
Heufelder et al. 2017, *N* = 22, clinical study		
Right (abs)	.30 (.00–.95)	.18 (.01–.85)
Anterior (abs)	.72 (.01–2.02)	.61 (.03–1.46)
Superior (abs)	.33 (.00–1.22)	.35 (.01–0.89)
Li et al. 2017, *N* = 10, clinical study		
Right (RMSD)	.38	.26
Anterior (RMSD)	.74	.74
Superior (RMSD)	.60	.41

Abbreviations: Abs, absolute outcome measurements. RMSD, Root mean squared deviation.

Note: Outcome of study IV compared with 3 studies using PSP plates (1 study with an in vitro setup and 2 studies with a clinical setup).

Interpretation of postoperative stability results (III, V)

Clinically, inferior maxillary repositioning was found to be stable between the 1-week and the 1-year postoperative scans; however, postoperative complications due to osteosynthesis failure occurred in 3 patients, who required additional surgery. The clinical outcomes were supported by the in vitro study (study V), where 3 model sets showed compression of a part of the osteotomy during the preloading by 50 N when the osteotomy was fixated with manually adapted plates. Thus, the results in study III and study V suggest that conventional, manually adapted plates can stabilize most inferior maxillary repositioning procedures, but there is a risk of failure of the plates that may result in the need for reoperation. In contrast, no preload failure occurred when the osteotomy was fixated with 3D PSP plates in the in vitro test.

The maxillary position of the included cohort without postoperative complications was stable with minimal relapse, which was in accordance with a previous study (Kretschmer *et al.*, 2010). The mean postoperative rate of relapse was almost identical, with only a slight difference in variance (0.5 mm compared with 1.3 mm). The increased variance found by Kretschmer *et al*. could be explained by differences in the surgical procedures, where larger inferior repositioning was planned and all procedures were bimaxillary. Both the planned movement and surgical procedure were also found to significantly influence stability in the mixed model regression analysis of stability. These results are in contrast with a previous study where a significant relapse of 1.6 mm was found in the superior direction during the first 6 months after surgery (Perez, Sameshima and Sinclair, 1997). The entire cohort (28 patients) included both single- (9 patients) and bi-maxillary (19 patients) procedures, one- (10 patients) and multiple-segment (18 patients) maxillary procedures, and grafting of the osteotomy with autogenous bone (3 patients) and hydroxyapatite (13 patients). Despite the cohort variations, no significant difference was apparent in the cohort, and all groups of patients experienced a mean superior relapse of more than 1.1 mm and posterior relapse of 0.7 mm. The reason for the difference in stability is not apparent, but several surgical factors could have improved the stability of orthognathic surgery in general from 1997 (Perez, Sameshima and Sinclair) to 2010 (Kretschmer *et al.*) such as improvement in rigidity of surgical plates, diet restrictions, patient information and compliance.

The postoperative stability and degree of relapse depend on the ability of the plates and screws to absorb the occlusal forces of the patient during healing of the osteotomy. Study V tested the rigidity of manually adapted plates and retention of the screws in vitro and found a lack of rigidity with manually adapted plates. In 3 of the 7 in vitro model setups, the plates yielded during the preload (50 N = 5 kg of occlusal force) and collapsed a part of the osteotomy. However, there was no direct connection between the patients that required additional surgery and the in vitro setup where the manually plates collapsed during preload.

Study V also found that PSP plates increased the stability of the osteotomy compared with manually adapted plates. The increased stability of the PSP plates may be caused by several differences in design between the plates: printed metal (Ti64Al4V) is stiffer than medical grade II titanium used for manually adapted plates (Liu *et al.*, 2014). The plates could be designed as a 1-piece, tripod plate with connections wider than the manually adapted plates. The PSP plates were designed to include 22 screws compared with the 16 screws used with conventional plates. The PSP plates were designed to allow placement of the screws in the maximum bone thickness. Thus, both the rigidity of the plates and the stability of the screws could be optimized by the design in the PSP plates.

In our study, the mechanical properties of manually adapted plates correlated somewhat with previous in vitro studies. The yield point has been correlated with amount of maxillary advancement, and in vitro testing found that loading the maxilla with 250 N was above the yield point when the maxilla was advanced by 6 and 9 mm (Huang, Lo and Lin, 2016). Likewise, in vitro testing of manually adapted stock plates failed between 534 and 1145 N (Araujo, Waite and Lemons, 2001). These findings concur with the median yield point (538 N) found in study V; however, the large individual variations of study V were not described in previous studies. The reason for the large variations could be explained by differences in the individual study setup mimicking the clinical conditions of the bony thickness and often asymmetrical advancements. The previous studies were all performed on thick stock models with symmetrical advancements. Thus, the previous studies solely evaluated the mechanical properties of stock plates, while study V compared the stock plates with PSP plates in a setup mimicking clinical conditions. Therefore, the large variation in yield point found in study V may better represent the variation encountered during orthognathic surgery, and thus, special consideration should be given to the fact that some plates yielded during preload of 50 N. A general drawback of all in vitro studies is that occlusal loading is tested as a linear force and does not represent realistic masticatory forces that occur during chewing or bruxism. Therefore, the individual yield point of the plates may have had even larger variances than found in vitro, and this may also have contributed to the large number of reoperations (15%) found in study III.

Study strengths and limitations

This study covers only the maxillary positioning of surgical accuracy in orthognathic surgery without evaluating the surgical accuracy of the mandible or the occlusion. Therefore, this study provides only a partial view of surgical accuracy in orthognathic surgery.

However, the reliability of this study's outcome is increased by focusing exclusively on the surgical accuracy of the maxillary measurements. Maxillary measurements are more reliable than mandibular measurements because of the mobility of the temporomandibular joint. Mandibular measurements are affected by the seating of the temporomandibular joints in centric relation with the fossa. If the condyles are not seated properly during the 1-week follow-up scan, the displacement will be interpreted as decreased surgical accuracy. At the 1-week follow-up scan, patients may still suffer from postoperative edema and paresthesia, and maintaining the joints in centric relation while keeping the mandible stable at the first point of occlusal contact can be difficult under such conditions, and errors in mandibular positioning may occur during scanning. Unlike the mandible, the maxillary position is fixated to the midface and cranial base and the position cannot be altered by the patient. Thus, the maxillary measurements used in this study are reliable without being dependent on the patient's cooperation.

An additional limitation of the studies on surgical accuracy and relapse (studies I, II & III) was that the scan was performed 1 week after surgery. Since the surgical outcome was evaluated 1 week postoperatively, the surgical accuracy measurements in study I and II reflected both the surgeon's ability to performed the planned reposition and the immediate relapse occurring within the first week after surgery, which is not under the surgeon's direct control. It remains unknown how much relapse occurs within the first week after surgery, and therefore, it is also unknown how much the rate of relapse influenced the outcome measurements. However, the patients' main focus lies on the outcome 1 year after surgery (Bengtsson *et al.*, 2018). If the long-term outcome is not satisfactory, then it is irrelevant whether the outcome was within satisfactory limits during the first week after surgery. Therefore, it is a strength that the included cohort in the surgical accuracy study was also followed up until 1 year after surgery. Thereby, the clinical outcome for the entire cohort can be evaluated while it is still possible to evaluate which parts of the surgical outcomes that need to be improved.

A final limitation involves the direct comparison between the surgical accuracy in vitro and surgical accuracy in the clinical studies (study IV). The in vitro surgery is not affected by soft tissue interference, pull from the masticatory and pharyngeal muscles or from incorrect condylar seating. Applying patient-specific plates in a clinical setup will challenge the plates and may cause outliers or systematic interferences than could change the surgical accuracy of the plates. Therefore, the outcome of the in vitro study must be interpreted with caution because it shows the best possible outcome obtained by PSP plates under idealized situations.

CONCLUSIONS

- Inferior maxillary repositioning entails that the maxilla is positioned posterior to the planned position (Studies I & II).
- In bimaxillary procedures, operating on the mandible first resulted in a more posterior maxillary position than operating on the maxilla first (Study II).
- Inferior maxillary repositioning was stable during the first year after surgery, but appears to suffer from a high degree of osteosynthesis failure (Study III).
- In vitro, PSP plates positioned the maxilla close to the planned position and closer than the obtained surgical outcome (Study IV). When using patient-specific plates, the edge of the osteotomy must be carefully inspected for any interference that could displace the maxilla from the planned position.
- In vitro, the PSP plates improved the stability of the Le Fort I osteotomies compared with manually adapted, stock plates (Study V).

Clinical implications and future perspectives

The 3 clinical studies (studies I–III) found that patients treated with inferior maxillary repositioning has room for improvement regarding both surgical accuracy and postoperative stability. The in vitro studies (IV & V) indicated that PSP plates could improve the surgical accuracy and skeletal stability. Future studies should focus on improving the surgical accuracy and skeletal stability by using PSP plates in a controlled, randomized setup. When designing a prospective RCT, it is important that the cohort is homogeneous regarding the vertical dimension before randomization, as the superior or inferior maxillary repositioning was seen to influence the surgical accuracy (Study II). However, until PSP plates become a standard part of orthognathic treatment, the findings of posterior maxillary positioning and risk of postoperative osteosynthesis failure should be addressed with the surgical tools currently at hand.

When the mandible was operated on first, the maxilla was on average positioned posterior to the planned position. The underlying cause of the posterior positioning was not identified in these studies, but it may be due to insufficient condylar seating intraoperatively or postoperatively by temporomandibular joint compression or immediate relapse or settling of the osteosynthesis materials within the first week after surgery. Since the underlying mechanisms cannot be corrected directly, it may be advisable to increase the maxillary advancement in the virtual surgical plan to compensate for the posterior positioning. Thereby, the maxilla will on average be placed closer to the planned position and in agreement with the intended position.

The postoperative skeletal reposition was stable, but inferior maxillary repositioning entailed a high number of osteosynthesis failures within the first year after surgery. The osteosynthesis plates can be supported by additional bone grafting and meticulous filling of the osteotomy with bone grafts. Increasing the mechanical support and the rate of bony healing across the osteotomy could help support the osteosynthesis materials.

Finally, future studies should assess segmental maxillary procedures, since these procedures are also considered to be unstable. Furthermore, there is also a need to develop an objective method to evaluate postoperative occlusion after orthognathic surgery, because it is among the most important parameters for the patient, but remains unaddressed in the literature on surgical accuracy.

ENGLISH SUMMARY

Inferior maxillary repositioning is one of the most unstable and unpredictable orthognathic procedures. However, no study has evaluated whether the use of 3D virtual surgical planning has improved the surgical accuracy or skeletal stability after surgery. Likewise, no study has evaluated whether patient-specific, 3D printed plates could improve the surgical outcome and postoperative stability.

The present PhD thesis presents the findings in 3 studies on 3D radiographic scans (I–III) and 2 in vitro studies on 3D printed models (IV, V). The 3D radiographic studies evaluated the surgical accuracy and skeletal stability in patients treated with inferior maxillary repositioning. Furthermore, the in vitro studies evaluated whether the surgical accuracy and skeletal stability could be increased by using patient-specific, 3D printed plates.

Study I measured the difference between the virtual surgical plan and the obtained surgical movement in 20 patients treated with inferior maxillary repositioning. The study found that the maxilla was positioned 1 mm posterior to the planned position.

Study II evaluated the results of study I in a 2-center study with a combined cohort of 145 patients. The study found that the direction of repositioning (superior versus inferior) and the surgical sequencing (maxilla-first versus mandible-first procedure) both significantly influenced surgical accuracy. Inferior maxillary procedures positioned the maxilla 2.0 mm (mandible-first) and 1.6 mm (maxilla-first) posterior to the planned position.

Study III measured the postoperative skeletal stability in inferior maxillary repositioning. Three patients were excluded since they required reoperation during the first year after surgery. The 17 included patients were stable and the mean maxillary movement was less than 0.2 mm in any direction.

Study IV measured the surgical accuracy of patient-specific, 3D printed plates in vitro, performed on 20 models printed from the preoperative scans of the patients included in study I. The in vitro

outcome was significantly closer to the planned position compared with the orthognathic surgical outcome.

Study V measured the amount of force needed to eliminate the maxillary osteotomy in vitro stabilized by either manually adapted plates or patient-specific, 3D printed plates. The patient-specific, 3D printed plates resisted more than twice the force of manually adapted stock plates regarding: total force, 2 mm compression, E-modulus and yield point.

In conclusion, orthognathic procedures with inferior maxillary repositioning seem to place the maxilla posterior to the planned position (studies I & II). The obtained surgical repositioning seems stable during the first year after surgery but entails a high risk of osteosynthesis failure (study III). The surgical accuracy and skeletal stability could possibly be improved by using patient-specific, 3D printed plates to reposition the maxilla (studies IV & V); however, clinical studies are needed to confirm the results of the in vitro studies.

DANISH SUMMARY

Sænkning af maksillen betragtes som et af de mest ustabile og uforudsigelige ortognat kirurgiske procedurer. Ingen undersøgelser har imidlertid vurderet, om indførelsen af 3D virtuel kirurgisk planlægning har forbedret den kirurgiske præcision eller stabilitet efter operationen. Ligeledes er det umuligt at evaluere, om patientspecifikke, 3D-printede plader kunne forbedre det kirurgiske resultat og den postoperativ stabilitet.

Denne ph.d.-afhandling inkluderer 3 undersøgelser med 3D-radiografiske scanninger (I-III) og 2 in vitro-studier på 3D-printede modeller. De radiografiske 3D-undersøgelser evaluerede den kirurgiske præcision og skeletale stabilitet hos patienter, der blev behandlet med sænkning af maksillen. Endvidere evaluerede in vitro-undersøgelserne, om den kirurgiske præcision og skeletale stabilitet kunne øges ved anvendelse af patientspecifikke, 3D-printede plader.

Studie I målte forskellen mellem den virtuelle kirurgiske plan og den opnåede kirurgiske bevægelse hos 20 patienter behandlet med sænkning af maksillen. Undersøgelsen fandt, at maksillen var placeret 1 mm bagved den planlagte position.

Studie II evaluerede resultaterne af studie I i et 2-center studie med en kombineret kohorte på 145 patienter. Studiet fandt, at retningen af repositionering påvirkede den kirurgisk præcision (impaktering versus sænkning af maksillen) og den kirurgiske sekventering (maksillen-først versus mandiblen-først) signifikant påvirkede kirurgisk nøjagtighed. Sænkning af maksillen placerede 2,0 mm (mandiblen-først) og 1,6 mm (maksillen først) bag ved den planlagte position.

Studie III målte den postoperative skeletale stabilitet når maksillen sænkes. Tre patienter blev udelukket, da de blev genopereret i det første år efter operationen. De 17 inkluderede patienter var stabile, og maksillens skeletale bevægelse var mindre end 0,2 mm i alle retninger.

Studie IV målte den kirurgiske præcision af patientspecifikke, 3D-printede plader in vitro, udført på 20 modeller printet fra scanninger af patienterne inkluderet i studie I. De patientspecifikke, 3D-trykte plader placerede det tandbærende segment 0,5 mm foran og 0,3 mm under den planlagte position. In vitro-resultatet var signifikant tættere på den planlagte position sammenlignet med det ortognatkirurgiske resultat.

Studie V målte den mængde kraft, der var nødvendig for at eliminere maksillens osteotomi på 7 sæt printede modeller, der var stabiliseret af enten manuelt tilpassede plader eller patientspecifikke, 3D-printede plader in vitro. De patientspecifikke, 3D-printede plader modstod mere end dobbelt så meget kraft som manuelt tilpassede plader angående: total kraft, 2 mm komprimering, E-modul og udbyttepunkt.

Som konklusion lader det til, at ortognatkirurgiske procedurer med sænkning af maksillen placerer maksillen bagved den planlagte position (studie I & II). Den opnåede kirurgiske flytning synes stabil i det første år efter operationen, men indebærer en høj risiko for svigt af osteosyntesematerialet (studie III). Den kirurgiske præcision og skeletale stabilitet kunne muligvis forbedres ved at bruge patientspecifikke, 3D-printede plader til at flytte maksillen (studie IV & V), men kliniske studier er stadig nødvendige for at bekræfte resultaterne af in vitro-studierne.

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Surgical Accuracy in Inferior Maxillary Reposition

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Purpose: Inferior maxillary repositioning is among the least stable and least predictable orthognathic procedures. The purpose of this study was to investigate whether posterior movement occurred with inferior maxillary repositioning and to analyze potential causes.

Materials and Methods: This retrospective observational study evaluated all consecutive patients treated at the Department of Oral and Maxillofacial Surgery of the Odense University Hospital (Odense, Denmark) with inferior maxillary repositioning from 2011 to 2013. The obtained repositioning was compared with the virtual surgical plan to determine surgical accuracy. Measurements were performed at 3 dental reference points. Linear and rotational measurements were performed along and around the right, anterior, and superior axes. Measurements were compared by paired *t* tests. Internal correlations and confounding variables were analyzed by mixed model regression analysis.

Results: Twenty patients were included for analysis. On average, the maxilla was positioned 1 mm posterior and 0.4 mm superior to the planned position. The virtual surgically planned reposition was statistically correlated with surgical accuracy. No other confounding variable influenced the outcome.

Conclusion: The correlation between planned advancement and inferior repositioning suggests that inferior repositioning destabilizes the maxillary position and that a perioperative or early postoperative relapse occurs in response to the advancement. This immediate relapse of 1 mm should be considered in the virtual surgical plan to ensure that the maxilla is placed closer to the desired position. Thus, this procedure could still benefit from increased surgical precision and stability based on technologic advancements, such as positioning guides or printed patient-specific plates.

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Vertical maxillary insufficiency is common in orthognathic surgical patients. Inferior maxillary repositioning is among the least stable and unpredictable orthognathic procedures.[1,2] A review in 2015 by Convens et al[3] found only 2 articles (22 patients) of sufficient quality to be included in an analysis of stability.[4,5] These studies focused on postoperative relapse without analyzing how much of the planned inferior repositioning was obtained during surgery.

Recently, only 2 studies have evaluated surgical precision in inferior maxillary repositioning. Semaan and Goonewardene[6] evaluated 9 patients in 2005 and found clinically relevant errors greater than 2 mm in 33% of patients. The authors' pilot study from 2016 included 7 patients and found the maxilla was positioned 2 mm posterior and 0.75 mm superior to the planned position. In these 2 studies (40 and 30 patients, respectively), the inferior maxillary repositioning cohort was derived by subgroup analysis. Thus far, no study has exclusively evaluated the surgical precision obtained with 3-dimensional (3D) virtual surgical planning in inferior maxillary repositioning.

Differences less than 2 mm between the planned and the obtained maxillary position might not

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constitute esthetic failure for the patient. However, when the maxilla is repeatedly placed posterior to the planned position, this difference should be considered in the virtual surgical plan. Including the difference in the surgical plan will assist in achieving the desired maxillary position. Therefore, it is important to know the direction and magnitude of any systematic errors that occur with inferior maxillary repositioning.

The purpose of this study was to investigate whether posterior movement occurred with inferior maxillary repositioning and to analyze potential causes of differences between planned and obtained outcomes. The null hypothesis was that no difference exists between the planned and the obtained outcome.

Materials and Methods

The authors implemented a retrospective observational cohort study. The cohort was derived from a population of patients treated in the Department of Oral and Maxillofacial at the Odense University Hospital (Odense, Denmark) from 2013 to 2015. Inclusion criteria were orthognathic surgery with inferior maxillary repositioning without segmentation of the maxilla. Exclusion criteria were deviation from the virtual surgical plan during surgery. All included surgeries were planned using 3D virtual surgical planning (3D Systems, Rock Hill, SC), and all patients provided written consent before inclusion. This study was exempt from ethical approval because of the retrospective nature of the study without direct involvement or influence on patients. Participants were treated according to the Declaration of Helsinki (October 2000).

VARIABLES

The primary outcome variable was the difference between the planned and the obtained surgical repositioning of the maxilla evaluated along the 3 axes. The primary predictor variable was the magnitude of the virtual surgically planned movement of the maxilla along the corresponding axis of the outcome. Confounding variables were age, gender, surgeon, preoperative occlusal relation (Angle Class I, II, or III), and bimaxillary procedure.

VIRTUAL SURGICAL PLANNING AND ORTHOGNATHIC SURGERY

Cone-beam computed tomographic (CBCT) scans were performed preoperatively and 1 week postoperatively using a NewTom 3G CBCT scanner (NewTom, Verona, Italy) with standard settings (field of view, 20 × 20 cm; 110 kV; radiation exposure, 59 μSv according to 2005 International Commission of Radiological Protection tissue weighing factors[7]). Orthodontic decompensation was retained with passive wires from preoperative scanning until surgery. Virtual surgical planning was performed by 5 calibrated departmental surgeons and a software engineer at 3D Systems using Dolphin 3D Surgery software (Dolphin Imaging and Management, Chatsworth, CA). All surgeries were planned according to the Houston protocol.[8]

In bimaxillary surgeries, the mandible was operated on first followed by the maxilla. The maxilla was repositioned according to the treatment plan using surgical splints. Vertical height was controlled by calipers, measuring from the right medial canthal ligament to the orthodontic bracket on the right first incisor. The maxilla was fixated by 4 L-shaped plates (BioMet 2.0 Systems, Zimmer Biomet Corp, Warsaw, IN). Local bone grafting was performed by excising bony interferences and interposing these in the osteotomies, but no extraoral block grafting was performed. All surgeries were performed according to the departmental standardized approach by 5 surgeons in accordance with the pilot study.[9,10]

LINEAR AND ROTATIONAL MEASUREMENTS

Analysis of the obtained surgical movement was measured using a previously validated semiautomatic protocol.[11] The linear reposition was calculated from 3 dental reference points: the top of the mesiobuccal cusp on the first molar on each side (M6L and M6R) and in the midline at the edge of the central incisors (U1I). The mean linear reposition was calculated from the mean of the 3 reference points, creating a centroid point, as described by Xia et al[12] and Hsu et al.[8] All measurements were recorded in relative numbers along each of the 3 axes. Measurements were recorded according to the positive values of the axes: right (mediolateral axis), anterior (anteroposterior axis), and superior (superoinferior axis).

Rotations were measured in degrees around the central mid-molar (MM) point calculated midway between the reference points on the first molars. The rotations were calculated as the difference between a dental reference point and the MM point. A positive yaw moved U1I to the left relative to the MM point. A positive pitch moved U1I superior to the MM point. A positive roll moved M6R superior to the MM point.

CALCULATING THE PLANNED ROTATIONAL MOVEMENT

The planned rotational movement was not measured in the virtual surgical plan; therefore, it was calculated from the obtained rotational measurements and dental reference points. Because all reference points were positioned at the same reference points, the distance from the dental reference point to the central point should coincide in the planned and obtained measurements. The following formula was used for sinus calculations:

$$\sin(A) = \frac{a}{c}$$

A corresponds to the degrees of rotation, *a* corresponds to the relevant dental reference point displacement relative to the central movement, and *c* corresponds to the distance between the central point and the dental reference point. When *c* coincides between the virtual surgical plan (VSP) and the obtained (OBT) measurements, the 2 formulas can be combined into 1 formula:

$$\sin(VSP) = \frac{a(VSP)}{c(VSP)} \text{ and } \sin(OBT) = \frac{a(OBT)}{c(OBT)}$$

$$\text{If } c(VSP) = c(OBT), \text{then } \sin(VSP) = \sin(OBT) \times \frac{a(VSP)}{a(OBT)}$$

Hence, the planned rotational movement could be calculated from the obtained rotation.

STATISTICS

Data were analyzed using STATA 15 (StataCorp LLC, College Station, TX).

The difference between the planned and the obtained surgical reposition was evaluated for normality of distribution formally by Shapiro-Wilk test and visually by a box-and-whiskers plot. If normally distributed, then the data would be presented with mean and standard deviation. The null hypothesis was tested by paired Student *t* test to establish whether the difference between the planned and the obtained surgical repositioning was meaningfully different from 0.

The primary outcome and the primary predictor variable depended on multiple spatial measurements along 3 axes in the same patient. Therefore, the data were treated as clustered data to allow for fixed and random effects. Linear mixed model analysis was performed to accommodate the multilevel analysis of the patients and correlate for confounding variables.

The level of statistical significance in all tests was set at a *P* value less than or equal to .05. Clinical success criteria were set at a difference of less than 2 mm and 4° between the virtual surgical plan and the actual surgical outcome, as proposed by previous studies.[8,12-14]

Results

Twenty-one patients agreed to participate and provided written acceptance, 2 declined, and 2 did not respond. Of the 21 participants, 1 was excluded (21-year-old woman, Angle Class I, bimaxillary procedure) because of changes in the virtual surgical plan during surgery.

The sample cohort was representative of the general orthognathic surgical population (mean age, 28 yr; range, 18 to 64 yr) and an equal gender distribution (Table 1). Bimaxillary surgery was performed in 65% of procedures. Five surgeons performed the operations. Surgeons 1 to 3 also performed the surgeries in the pilot study.[9]

A test for normality showed a normal distribution of the difference between the planned and the obtained repositioning (by Shapiro-Wilk test: right, $P = .093$; anterior, $P = .526$; superior, $P = .655$). A box plot of the difference between the planned and the obtained movement showed long tails with few outliers along the right and anterior axes (Fig 1).

The linear accuracy of surgical repositioning differed statistically from 0 along the anterior and superior axes (Table 2). On average, the maxilla was positioned 1 mm posterior and 0.4 mm superior to the planned position, which is within the clinical threshold of 2 mm. The difference between the planned and the obtained movement exceeded 2 mm in 6 participants (30%) along the anterior axis and in 4 participants (20%) along the superior axis.

The rotational accuracy differed less than 1° from the planned movement and was not found to be statistically or clinically relevant (Table 3).

Multilevel mixed model regression analysis of the surgical movements evaluated the influence of all

Table 1. DESCRIPTIVE COHORT ANALYSIS

Descriptive Data	
Participants, N	20
Women	8
Age (yr), mean	28
Age range (yr)	18-64
Occlusion (Angle classification)	
Neutral (I)	6
Distal (II)	6
Mesial (III)	8
Surgery	
Maxillary advancement	19
Additional mandibular surgery	13
Mandibular advancement	10
Mandibular setback	6
Surgeon	
1	4
2	6
3	3
4	6
5	1

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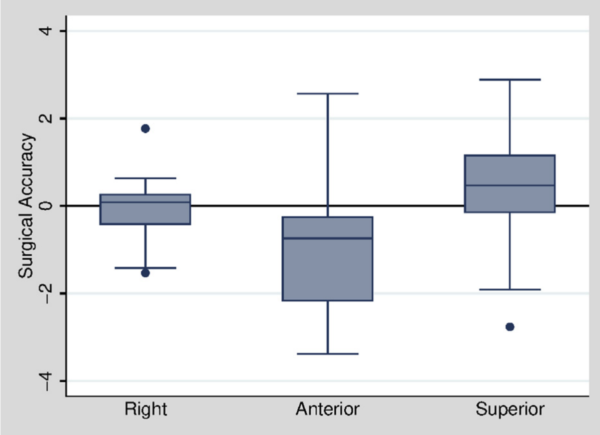

FIGURE 1. Box plot evaluating the difference between the planned and the obtained movement at 1 week after surgery.

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covariates to identify any potential confounding factors (Table 4). Assumptions for mixed model analysis were tested and residuals were normally distributed without heteroscedasticity. Bimaxillary surgery and other confounding variables did not meaningfully influence surgical accuracy. There was a relevant correlation in surgical accuracy between the anterior and superior axes. The interaction of the planned maxillary reposition on accuracy was statistically relevant. The direction and size of the planned movement correlated with the difference between the planned and the obtained surgical reposition, that is, large advancements correlated with large differences between the planned and the obtained surgical reposition (Figs 2, 3).

To verify the mixed model results, the correlation between surgical accuracy and planned maxillary movement was plotted along the anterior and superior axes (Figs 2, 3). The anterior and superior axes showed high correlations (R^2 = 0.49 and 0.46, respectively), thus confirming the mixed model results. Differences in the vertical dimension were evaluated in relation to posterior differences (Fig 4). There was no linear correlation between surgical accuracy along the inferior axis and surgical accuracy along the anterior axis (R^2 = 0.05). Thus, the posterior position of the maxilla was not caused by differences along the vertical axis.

Discussion

The purpose of this study was to further analyze the precision and accuracy of inferior maxillary repositioning and to analyze the potential causes of systematic differences between planned and obtained outcomes. The null hypothesis was that no difference existed between the planned and the obtained outcome.

This study confirms that a difference exists between the planned and the obtained position of the maxilla. Thus, the maxilla was positioned 1 mm posterior and 0.4 mm superior to the planned position. The difference was clinically relevant for 6 patients along the anterior axis and for 4 patients along the superior axis. There was a correlation between differences in the maxillary position along the anterior and superior axes. No confounding variables influenced surgical accuracy. This minor posterior discrepancy might not compromise the esthetic outcome for the patient; however, incorporating an additional millimeter of advancement into the surgical plan could help surgeons reach the desired maxillary position.

In the pilot study, the maxilla was positioned 2 mm posterior to the planned position in 7 patients.[9] The present results showed only half this difference; however, it also confirmed that a systematic error occurred with inferior maxillary repositioning. These findings contrast with those of Semaan and Goonewardene[6] who found no systematic errors in 9 patients who underwent downgrafting. However, the inferior repositions had a standard deviation greater than 2 mm and 33% were positioned more than 2 mm from the planned position vertically and horizontally.

The reason for the posterior discrepancy remains unclear. It is unclear whether the posterior repositioning is caused by downgrafting or advancement of the maxilla. In this study, 95% of participants received downgrafting and advancement of the maxilla. The

Table 2. LINEAR ACCURACY AND PRECISION IN OBTAINED MAXILLARY REPOSITION COMPARED WITH VIRTUAL SURGICAL PLAN (N = 20)

Measurements (mm), Mean (SD)	Planned	Obtained	Difference	*P* Value*
Right	0.06 (0.77)	−0.05 (1.05)	−0.11 (0.79)	.592
Anterior	2.93 (1.99)	1.95 (1.44)	−0.98 (1.57)	<.001
Superior	−1.75 (0.85)	−1.33 (1.01)	0.42 (1.36)	.037

Abbreviation: SD, standard deviation.

* Predictive margins with fixed proportions from mixed model analysis. The test incorporates all covariates and evaluates whether the obtained movement is statistically different from the planned movement.

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Table 3. ROTATIONAL ACCURACY AND PRECISION IN OBTAINED MAXILLARY REPOSITIONING COMPARED WITH VIRTUAL SURGICAL PLAN (N = 20)

Measurements (°), Mean (SD)	Planned	Obtained	Difference	*P* Value*
Yaw	1.01 (1.48)	0.71 (1.81)	−0.30 (1.18)	.270
Pitch	−0.79 (3.32)	−1.48 (2.77)	−0.69 (2.14)	.321
Roll	0.02 (1.21)	−0.21 (1.18)	−0.22 (1.14)	.688

Abbreviation: SD, standard deviation.

* By paired Student *t* test to evaluate whether the obtained movement is statistically different from the planned movement.

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literature is divided on this subject, with half the trials finding and the other half not finding posterior repositioning with advancement. A posterior systematic difference between planned and obtained outcomes was found in maxillary advancement procedures by Jacobson and Sarver[15] (−0.9 mm; N = 20), Semaan and Goonewardene[6] (−0.77 mm; N = 16), and Kwon et al[16] (−0.76 mm; N = 19). However, this is in contrast to the findings of Ong et al[17] (−0.05 mm; N = 30), Choi et al[18] (−0.05 mm; N = 16), and Donatsky et al[19] (0.19 mm; N = 67). Recently, Liebregts et al[20] found that the posterior discrepancy correlated with the mandible-first approach to bimaxillary surgery. However, this cannot entirely explain the posterior discrepancy because the pilot study also used the mandible-first approach for maxillary impaction without causing posterior discrepancy.

The vertical dimension was determined by using the medial canthal ligament as an external reference point. However, using the medial canthal ligament for vertical measurements might yield a less stable result than a bone-supported fixed reference point such as a Kirchner wire. The use of the medial canthal ligament could be responsible for errors in the vertical

Table 4. MIXED LINEAR REGRESSION ANALYSIS OF INTERNAL CORRELATION AND CONFOUNDING VARIABLES

			95% Confidence Interval	
	β	*P* Value	Upper Limit	Lower Limit
Internal correlation with anterior axis				
Superior	−2.12	.002	−3.48	−0.77
Right	−0.72	.116	−1.62	0.18
Interaction with planned movement				
Anterior (baseline)	−0.54	.000	−0.78	−0.30
Superior (addition to baseline)	−0.56	.042	−1.10	−0.02
Right (addition to baseline)	0.50	.105	−0.11	1.11
Female gender	0.02	.942	−0.54	0.58
Age (yr)	−0.02	.207	−0.04	0.01
Occlusion (Angle classification)				
Distal (II)	0.14	.738	−0.70	0.99
Mesial (III)	0.39	.359	−0.44	1.23
Surgery				
Bimaxillary surgery	0.55	.196	−0.28	1.38
Surgeon				
2	−0.08	.840	−0.88	0.72
3	0.76	.171	−0.33	1.85
4	0.37	.311	−0.35	1.10
5	0.59	.365	−0.69	1.86
Constant	0.29	.609	−0.83	1.41
SD (between patients)	1×10^{-12}		1×10^{-17}	9×10^{-8}
SD (within patients)	0.91		0.76	1.09

Note: Measurements for mixed model regression are the difference between the planned and the obtained movement.

Abbreviation: SD, standard deviation.

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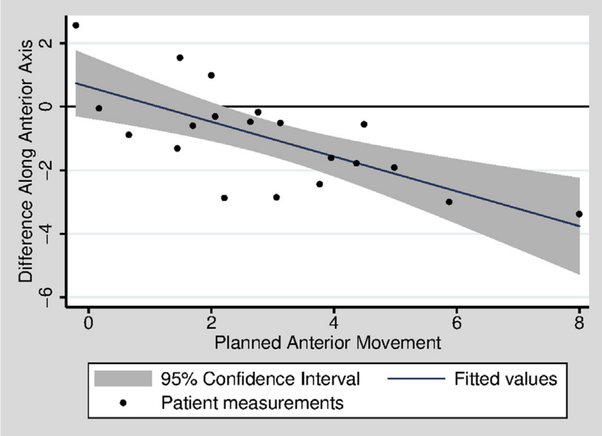

FIGURE 2. Correlation of surgical accuracy along the anterior axis with planned maxillary advancement. For each patient, the planned anterior movement was plotted against the difference between the planned and the obtained maxillary movement along the anterior axis (fitted line, $y = -0.55x + 0.62$; coefficient of determination, $R^2 = 0.49$). A strong correlation was found between planned advancement and immediate or early relapse.

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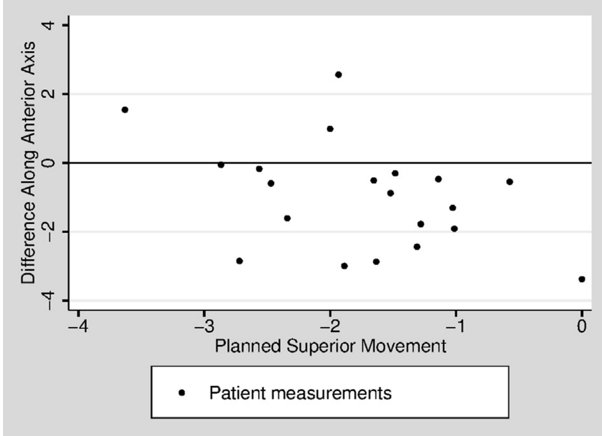

FIGURE 4. Correlation of surgical accuracy between the superior and anterior axes. For each patient, differences between the planned and the obtained maxillary movement in the superior axis were plotted against differences in the anterior axis. No linear correlation for surgical accuracy existed between the inferior and anterior axes ($R^2 = 0.05$).

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dimension of 0.3 mm.[21] Furthermore, the use of a single 2-dimensional measurement in a complex 3D movement also could incorporate errors into the vertical dimension.[22]

Therefore, the authors were concerned that errors in the vertical dimension could have caused or influenced errors in the anteroposterior dimension of the maxilla. However, although positioning the maxilla in the vertical dimension is under the direct control of the surgeon, the anteroposterior position is dictated by the surgical splint. A plot of the difference between the planned and the obtained maxillary position in the superior axis against the anterior axis showed no correlation (Fig 4). Thus, vertical differences from the planned position did not affect the posterior position of the maxilla. There also was no correlation between the vertical dimension and the posterior positioning. Therefore, the authors believe that using a bony anchored reference point and 3D measurements will correct only the vertical deficiency and not the posterior positioning of the maxilla.

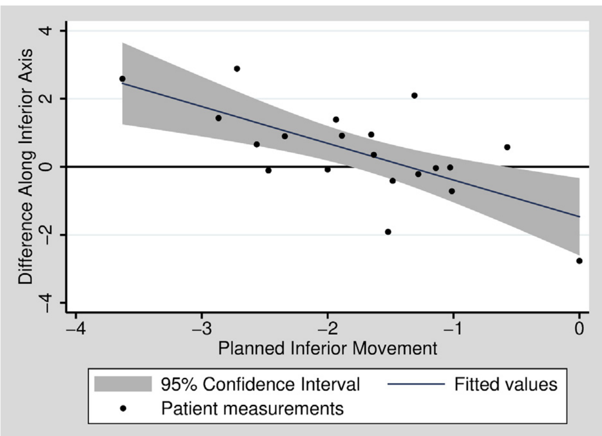

FIGURE 3. Correlation of surgical accuracy along the superior axis and planned inferior maxillary repositioning. For each patient, the planned inferior movement was plotted against the difference between the planned and the obtained maxillary movement along the inferior axis (fitted line, $y = -1.08x - 1.47$; coefficient of determination, $R^2 = 0.46$). A strong correlation was found between planned advancement and immediate or early relapse.

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These contradictions were further explored in this study with mixed model analysis and correlation plots. The planned advancement and the planned inferior repositioning were statistically correlated, with an equal β value. However, there was no correlation between inferior maxillary repositioning and posterior discrepancy in surgical accuracy. These results suggest that inferior maxillary repositioning decreases maxillary stability independent of the amount of inferior maxillary repositioning. The decreased stability causes an immediate or early posterior relapse of the maxillary advancement, dependent on the amount of advancement. The immediate relapse occurs during surgery or during the first postoperative week, probably from muscle contractions from stretched masticatory or pharyngeal muscles.[1,23,24]

The mixed model analysis of correlations and confounding factors is ideal for 3D analysis of the data, with multiple measurements for each participant. The combination of dependent measurements within patients (*x*-, *y*- and *z*-axes) and independent variables between patients (occlusion, gender, and surgeon) provides a challenge for properly analyzing the data.

Linear mixed modeling avoids the pitfalls of multiple testing and preserves the statistical power in the restricted sample size. This model encompasses the internal correlation between axes, the correlation with planned movement, and confounding variables in 1 model. Thus, the *t* tests were supported by the global model to avoid the risk of chance findings in multiple testing. However, because of the small sample and numerous confounding factors, there is a risk of overfitting the model. Over-fitted models can increase the statistical relevance and calculate too-high *P* values. Therefore, the model should be used to obtain an overview of the data to further explore correlations between statistically relevant findings.

Inferior maxillary repositioning is among the most unstable orthognathic procedures; thus, these procedures could benefit the most from technologic advances, although correlations have not yet been described. Although orthognathic surgery has undergone major changes regarding rigid fixation materials, virtual surgical planning, and printed surgical splints, the evidence to support how technologic advances improve surgical precision remains unclear. One expects improvements from printed positioning devices and patient-specific plates, but one should know whether the increase in surgical accuracy adds sufficient value to justify the added cost and time spent in planning and printing.[25,26]

In conclusion, the maxilla was positioned posterior and superior to the planned position. This error correlated with the planned advancement and inferior repositioning, suggesting that inferior repositioning destabilizes the maxillary position and that an early postoperative relapse occurs in response to the advancement. Thus, this procedure could still benefit from technologic advancements such as positioning guides or patient-specific plates in the quest for increased surgical precision and stability.

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Does Mandible-First Sequencing Increase Maxillary Surgical Accuracy in Bimaxillary Procedures?

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Purpose: In bimaxillary procedures, it is important to know how the chosen sequence affects the surgical outcome. The purpose of this study was to explore whether the theoretical advantages of using the mandible-first procedure were supported by clinical data.

Materials and Methods: The authors performed a retrospective investigation on a cohort compiled from 3 published retrospective studies. The sample was composed of patients treated at the Radboud University Nijmegen Medical Centre (Nijmegen, the Netherlands) from 2010 to 2014 and the Odense University Hospital (Odense, Denmark) from 2011 to 2015. The inclusion criterion was bimaxillary surgery without maxillary segmentation. The exclusion criterion was lack of a virtual surgical plan. The primary outcome variable was surgical accuracy, defined as the mean difference between the obtained outcome and the virtual surgical plan. The primary predictor variable was the comparison between mandible-first and maxilla-first sequencing. Secondary predictors were inferior maxillary repositioning and counterclockwise (CCW) rotation. The confounding variable was the virtually planned reposition. Results were analyzed by mixed-model regression encompassing all variables, followed by a detailed analysis of positive results using 2-sample *t* tests.

Results: Overall, 145 patients were included for analysis (98 women; mean age, 28 years). Operating on the mandible first notably influenced maxillary positioning and placed the maxilla 1.5 mm posterior and with 1.4° of CCW rotation compared with virtual surgical planning. The interaction of surgical sequence with maxillary rotation showed similar surgical accuracy between maxilla-first surgery with clockwise rotation and mandible-first surgery with CCW rotation. Inferior maxillary repositioning resulted in the maxilla being placed 1.7 mm (maxilla-first sequence) and 2.0 mm (mandible-first sequence) posterior to the planned position.

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Conclusion: Surgical accuracy was considerably influenced by sequencing in bimaxillary procedures. It remains important to know how the chosen sequence affects the surgical outcome so that the virtual surgical plan can be adjusted accordingly.

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Currently, the surgeon's preference dictates whether the mandible or the maxilla is operated on first in bimaxillary procedures.[1] This preference relies on old dogmas carried over from wire fixation or plaster cast models mounted in semiadjustable articulators.[2-5] With 3-dimensional (3D) virtual surgical planning (VSP), the old dogmas must be re-evaluated because previous strengths and weaknesses might no longer be relevant.[6,7] Surgeons might not wish to change the sequence they are familiar with, but it remains vitally important to know how the chosen sequence affects the surgical outcome. In this situation, the desired maxillary position can be achieved by adjusting the VSP to include the affected surgical accuracy.

The theoretical advantages of positioning the mandible first have been debated at length without a definite consensus being reached.[2-4,8,9] In theory, the surgical splint design should provide advantages for sequencing the mandible or maxilla first, depending on the rotation of the maxillomandibular complex. Clockwise (CW) rotation is believed to be more accurate using the maxilla-first approach, whereas counterclockwise (CCW) rotation should be more accurate using the mandible-first approach.[4,5] However, only 3 studies have compared the 2 sequences in large cohort studies, and none have evaluated how CW or CCW rotation influences the clinical outcome when the mandible or maxilla is sequenced first.[1,10-12]

Unstable procedures, such as inferior maxillary repositioning, also affect the clinical outcome and can cause the maxilla to be placed 1 to 2 mm posterior to the planned position.[13,14] Theoretically, the mandible-first approach should increase surgical accuracy in inferior maxillary repositioning because this sequence can be performed without autorotation of the condyles.[4,15] However, no one has evaluated the clinical effect on the surgical accuracy of sequencing the mandible or maxilla first in inferior maxillary repositioning.[16]

Although the surgical splint dictates the jaw's position in the sagittal and transverse directions, the vertical direction is under the direct control of the surgeon. Reliable measurement points are crucial for accurate vertical positioning of the maxilla. Using the medial canthal ligament instead of a bony fixated reference pin can affect the surgical outcome in the vertical dimension.[17,18] However, no previous study has evaluated the clinical influence of using the medial canthal ligament for vertical measurements in patients in whom 3D VSP is conducted compared with use of a fixed external reference pin.[6,7]

The purpose of this study was to evaluate whether the theoretical advantages of operating on the mandible first were supported by the clinical data. The null hypothesis was that no difference existed between sequencing the maxilla or the mandible first. This study sought to address the following research questions:

1. Was overall surgical accuracy affected by maxillary versus mandibular sequencing?
2. Was surgical accuracy in CCW rotation affected by maxillary versus mandibular sequencing compared with CW rotation?
3. Was surgical accuracy in inferior maxillary repositioning affected by maxillary versus mandibular sequencing compared with maxillary impaction?
4. Was vertical accuracy affected using the medial canthal ligament (Odense cohort) compared with an external reference pin (Nijmegen cohort)?

Materials and Methods

To address the research questions, the authors implemented a retrospective study using combined clinical data from 3 published retrospective studies.[10,19,20] The cohorts were derived from populations of patients treated at the Department of Oral and Maxillofacial Surgery of the Radboud University Nijmegen Medical Centre (Nijmegen, the Netherlands) and at the Department of Oral and Maxillofacial Surgery of the Odense University Hospital (Odense, Denmark). The studies could be combined because the data were measured by comparable protocols; however, the inclusion and exclusion criteria of these cohorts differed among studies. Study 1 (Nijmegen) analyzed 116 consecutive patients treated with bimaxillary procedures without maxillary segmentation from 2010 to 2014.[10] Study 2 (Odense) analyzed 30 patients with bimaxillary procedures, including maxillary segmentation, randomly selected from a population of 72 patients treated from 2011 to 2013.[19] Study 3 (Odense) analyzed 20 consecutive patients treated with inferior maxillary repositioning in a mono- or bimaxillary procedure from 2013 to 2015.[20]

The criteria for inclusion of participants in the combined cohort were *1)* they had been participants in the previously published studies and *2)* they had undergone bimaxillary orthognathic surgery without maxillary segmentation. The exclusion criterion for the combined cohort was the absence of VSP in the dataset. This study was exempt from ethical approval because of its retrospective nature, with no direct involvement of or influence on patients. Participants and data were treated in accordance with the Declaration of Helsinki.

VARIABLES

The primary outcome variable was the difference between the planned and obtained surgical repositioning of the maxilla. The primary predictor variable was sequencing with the maxilla- or mandible-first approach. Secondary predictors were planned CW or CCW rotation of the maxilla and planned inferior or superior maxillary repositioning. The primary confounding variable was the virtually planned reposition (continuous). Other clinical variables of interest were age and gender.

VSP AND ORTHOGNATHIC SURGERY

Cone-beam computed tomography (CBCT) was performed before surgery and within 7 days after surgery. All patients were scanned with the mandible in centric relation to the fossa by relaxing the muscles and maintaining the jaw position at the first occlusal contact during the scan. In Nijmegen, VSP was performed in house using Maxilim software (Medicim NV, Mechelen, Belgium); in Odense, VSP was performed in collaboration with 3D Systems (Rock Hill, SC) using Dolphin 3D Surgery software (Dolphin Imaging and Management, Chatsworth, CA). During VSP, the condylar segments were rotated around the condylar hinge point, set at the most lateral part of the condylar head, but not otherwise repositioned in the fossa.

The maxilla and mandible were repositioned according to the treatment plan using surgical splints. To ensure an unaltered position of the dentition and optimize the fitting of the surgical splint, no active orthodontics was carried out after the preoperative CBCT used for the VSP. The preoperative conditions were evaluated by visual inspection, and the fit of the surgical splint was appraised initially before the osteotomy to ensure that the preoperative conditions agreed with the VSP. The vertical height was controlled by calipers, measuring from a bony anchored nasion reference pin (Nijmegen cohort) or from the right medial canthal ligament (Odense cohort). The mandible was bilaterally fixated by 3 bicortical screws (Biomet 2.0, Zimmer Corp, Warsaw, IN; Odense cohort) or 1 miniplate fixated by 4 monocortical screws (Champy 2.0, KLS Martin, Tuttlingen, Germany; Nijmegen cohort). The maxilla was fixated by 4 miniplates using the 1.5-mm KLS Martin system (Nijmegen cohort) or the 2.0-mm Biomet system (Odense cohort). Local repositioning of bony segments was performed but without extraoral bone grafting.

The sequence for operating on the mandible or maxilla first was changed in the Nijmegen cohort for all consecutive patients from operating on the mandible first in 2010 to 2012 to operating on the maxilla first in 2013 to 2014. In the Odense cohort, the mandible was always operated on first.

OUTCOME MEASUREMENTS

Measurements were performed according to previously validated software algorithms: OrthoGnathicAnalyser[21] (Nijmegen cohort) and a semiautomatic algorithm using 3D Slicer[22] (Odense cohort). These systems have 95% reproducibility within 0.3 mm.

The mean linear reposition was calculated from the midline at the edge of the upper central incisors (UCIs). All measurements were recorded in relative numbers according to the positive values of the axes: right (mediolateral axis), anterior (anteroposterior axis), and superior (superoinferior axis).

Rotation was measured in degrees around the centroid (C) point. The C point was calculated as the mean of 3 dental reference points: the top of the mesiobuccal cusp on the first molar on each side and the UCI.[23,24] A positive yaw moved the UCI to the left relative to the C point. A positive pitch moved the UCI superior to the C point. A positive roll moved the right first molar superior to the C point (Fig 1).

STATISTICS

Data were analyzed using STATA 15.1 (StataCorp, College Station, TX). Descriptive variables were analyzed by χ^2 test, 1-way analysis of variance, and 2-sample *t* tests to evaluate cohort differences between procedures and centers. The primary outcome and predictor variables depended on multiple spatial measurements along the 3 axes in the same patient. Therefore, the data were treated as clustered to allow for fixed and random effects within and between patients. A linear mixed model was built by treating the outcome in 3 axes as repeated measurements within the same patient; therefore, all were influenced by the patient's response to the confounding and hypothesis-generating variables. All hypothesis-generating and confounding variables were included in the final model. Therefore, the linear mixed-model analysis could be performed to accommodate the multilevel analysis of patients and simultaneously adjusted for confounding variables. If the mixed-model regression was statistically relevant for

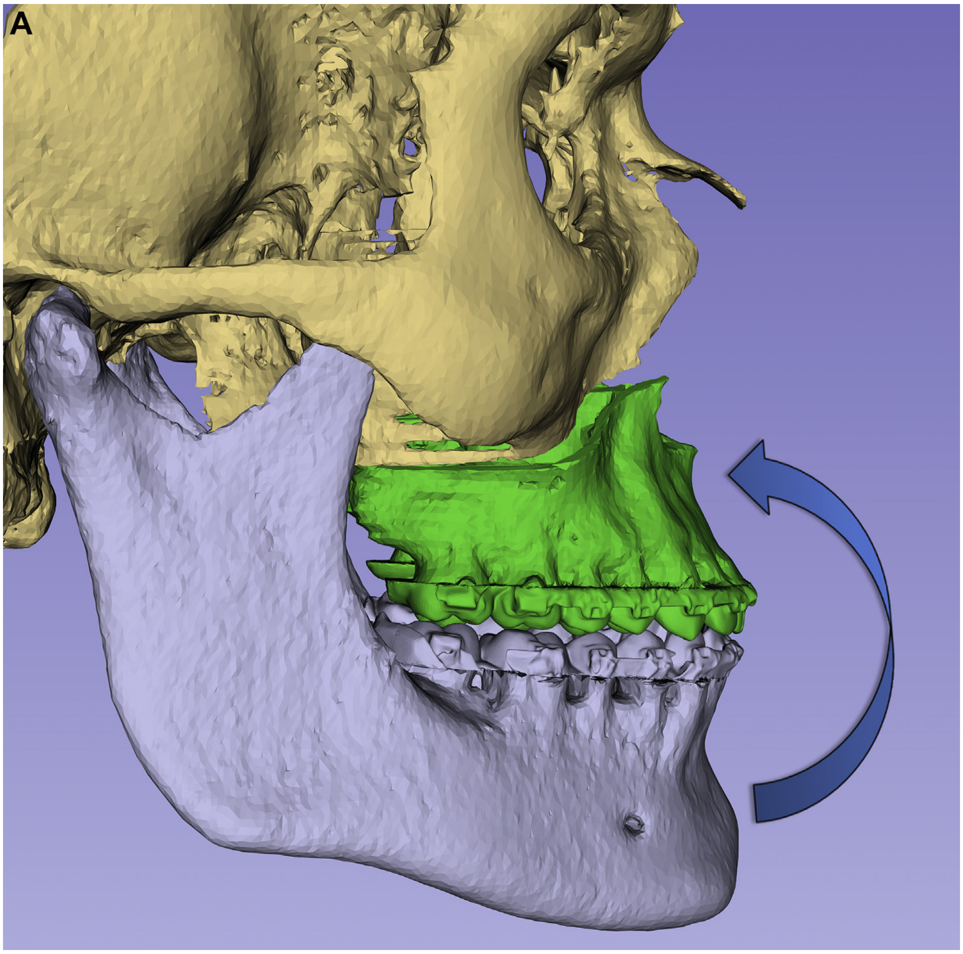

FIGURE 1. Rotation of maxilla. *A,* A positive pitch moved the upper central incisor cranially. **(Fig 1 continued on next page.)**

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predictor variables, then the data were further explored; differences within groups were analyzed by Student 1-sample *t* test, and differences between groups were analyzed by 2-sample *t* tests. The level of statistical significance in all tests was set at a *P* value less than or equal to .05. Clinical relevance was defined by the authors as differences in the mean of more than 1 mm and rotations of more than 2°, which indicate consistent unidirectional inaccuracies that are large enough to be addressed clinically by the surgeons.

Results

Of the 166 patients considered for this study, data on 145 patients were included (Fig 2). Of the total sample of 145 participants, 68% were women and participants had a mean age of 28 years (Table 1). All patients sequenced with the maxilla-first procedure were operated on in the surgical department at Nijmegen. Patients were evenly distributed and in sufficient numbers in the groups: mandible-surgery first, CCW rotation, and inferior maxillary repositioning. The linear planned repositioning did not differ statistically between the 2 study centers. The planned pitch was more negative in the maxilla-first group, and greater CCW rotation of the maxilla was planned in this group.

Incorporating all 3 hypotheses into 1 global statistical model showed that surgical sequencing and inferior maxillary repositioning markedly influenced surgical accuracy (Table 2). The mixed-model regression showed the VSP had a relevant influence on surgical precision. For each millimeter of advancement, the surgical accuracy decreased, indicating that larger advancements deviated more from the plan. Plotting the planned reposition against the surgical accuracy in the anterior axis showed a correlation that accounted for 15 to 34% of the difference in surgical accuracy (Supplementary Figure 4). Plotting the planned reposition against the surgical accuracy in the vertical axis showed almost no correlation (coefficient of determination, R^2 = 0.5 and 7%) despite a statistical correlation in the mixed-model regression (Supplementary Figure 5). Surgical sequencing and

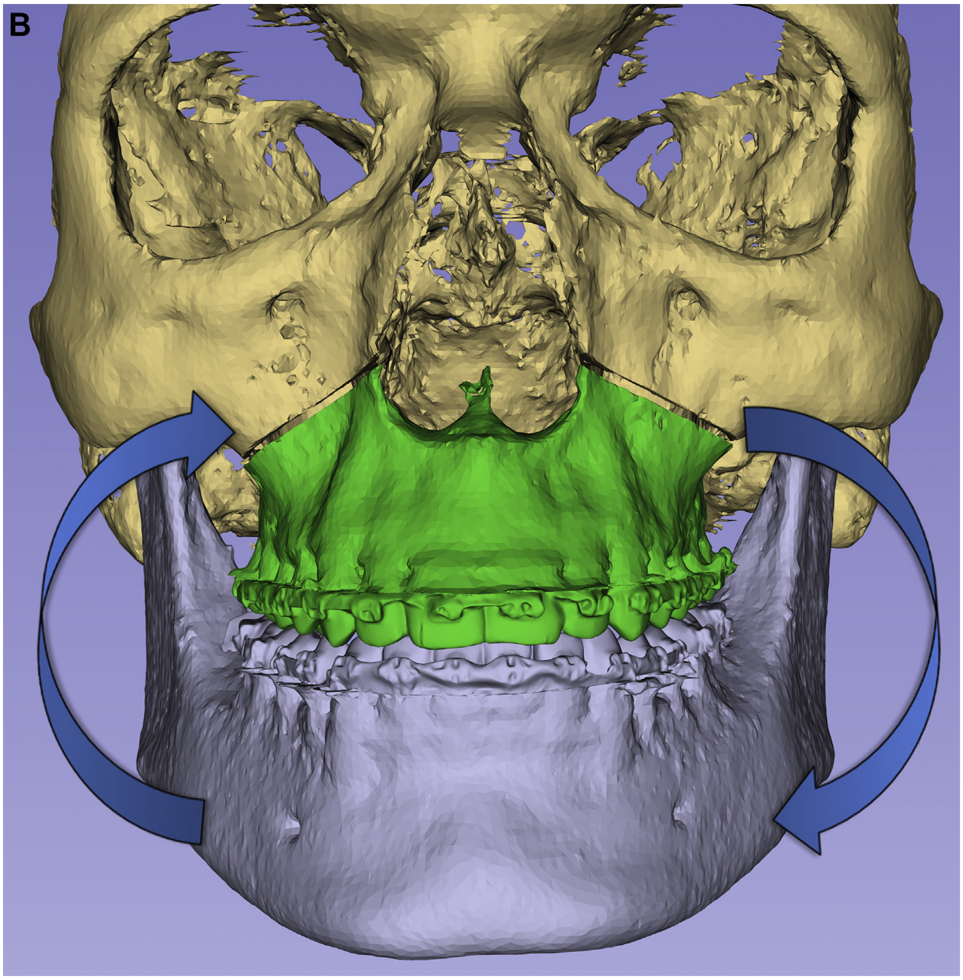

FIGURE 1 (cont'd). *B*, A positive roll moved the right first molar cranially. **(Fig 1 continued on next page.)**

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inferior maxillary repositioning markedly influenced surgical accuracy, but CCW rotation did not statistically influence surgical accuracy. However, to further analyze the influence on surgical accuracy, all 3 hypothesis variables were further explored.

When testing the primary hypothesis, there was a statistical difference between maxilla-first and mandible-first sequencing along the right and anterior axis and a difference in pitch (Table 3). Operating on the mandible first placed the maxilla posterior with additional CCW rotation (Fig 3). The maxilla-first approach had a larger variance than the mandible-first approach, and the standard deviation increased from 2.0 to 2.6 mm. Posterior positioning in the mandible-first approach was considered clinically relevant.

SURGICAL ACCURACY IN MAXILLARY ROTATION

Maxillary rotation influenced the surgical accuracy differently depending on whether the maxilla or the mandible was operated on first. The surgical accuracy was almost identical between the use of CCW rotation in the mandible-first procedure and the use of CW rotation in the maxilla-first procedure (Table 4). CCW rotation in maxilla-first sequencing positioned the maxilla 1.3 mm anterior to the planned position (Supplementary Figure 4). In contrast, CW rotation in the mandible-first procedure positioned the maxilla almost 2 mm posterior to the planned position. This difference was clinically relevant but not statistically different from the 2 reference procedures.

SURGICAL ACCURACY IN INFERIOR MAXILLARY REPOSITIONING

Inferior maxillary repositioning also statistically influenced surgical accuracy. In inferior maxillary repositioning, the maxilla was positioned 1.7 mm (maxilla-first approach) to 2.0 mm (mandible-first approach) posterior to the planned position, which was statistically relevant, regardless of whether the mandible or

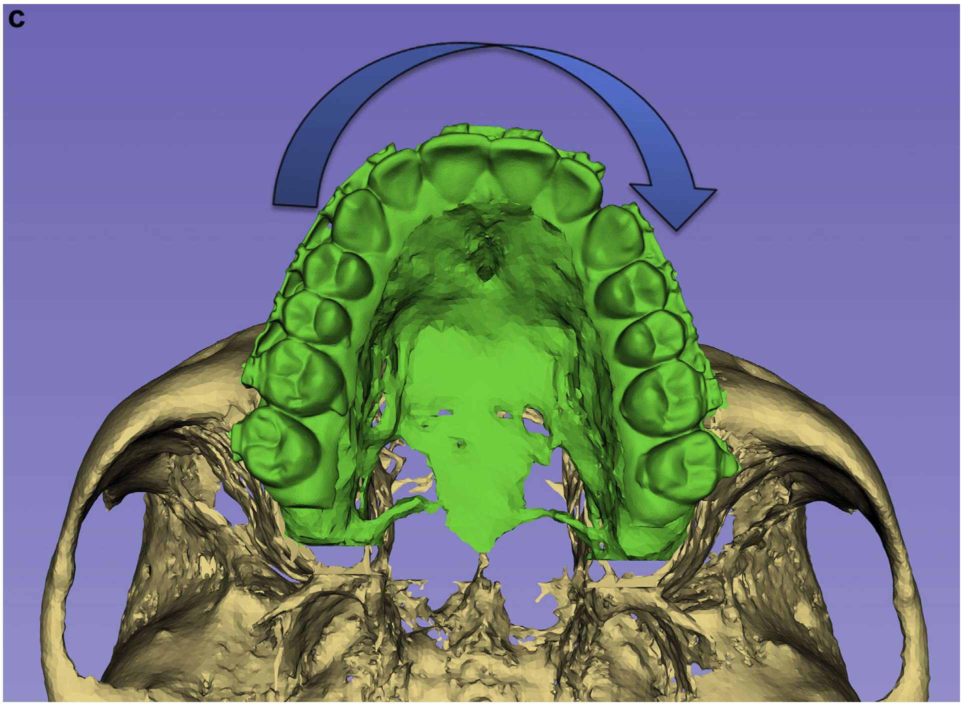

FIGURE 1 (cont'd). *C*, A positive yaw moved the upper central incisor to the left.

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maxilla was operated on first (Table 5). In superior maxillary repositioning, the maxilla-first approach placed the maxilla 1.5 mm anterior to the planned position (Supplementary Figure 5), whereas the mandible-first placed the maxilla 0.9 mm posterior to the planned position. The difference between the 2

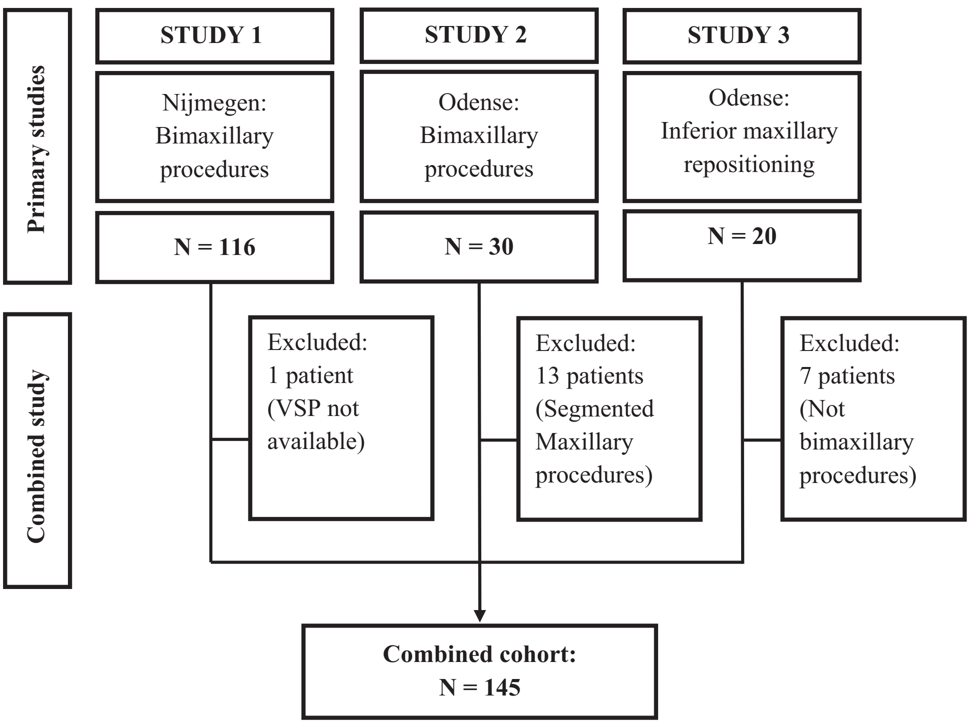

FIGURE 2. Inclusion and exclusion criteria for combined cohort.

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Table 1. DESCRIPTIVE COHORT ANALYSIS

	Nijmegen, Mx First	Nijmegen, Md First	Odense, Md First	*P* Value*	*P* Value†
Participants, n	57	58	30		
Women, n	43	37	18	.250	.104
Age (yr), mean (range)	29 (16-57)	28 (16-55)	27 (18-64)	.737	.459
Test of hypotheses					
Md-first sequence	0	58	30	.000	.000
CCW rotation	19	32	18	.006	.086
Inferior maxillary reposition	33	27	18	.354	.425
Planned maxillary translation					
Right	−0.04 (1.70)	−0.16 (1.42)	−0.58 (1.12)	.266	.295
Anterior	3.96 (1.67)	4.35 (1.83)	2.60 (2.91)	.001	.566
Superior	−0.31 (2.98)	−0.13 (2.92)	0.22 (2.49)	.716	.539
Planned maxillary rotation					
Pitch	−2.02 (3.94)	0.39 (5.99)	1.57 (4.31)	.003	.001
Roll	0.31 (2.07)	0.07 (1.99)	0.12 (1.72)	.801	.511
Yaw	−0.07 (1.49)	−0.14 (1.42)	0.10 (1.63)	.692	.981

Note: Translation and rotation measurements are presented as mean (standard deviation).
Abbreviations: CCW, counterclockwise rotation; Md, mandible; Mx, maxilla.
* By analysis of variance among all 3 groups.
† By Student *t* test between mandible-first and maxilla-first groups.

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sequences in superior maxillary repositioning was statistically relevant.

The interaction among sequencing, rotation, and inferior maxillary repositioning could not be further analyzed in this study because only 3 patients were operated on using inferior maxillary repositioning, CCW rotation, and the maxilla-first sequence.

MEDIAL CANTHAL LIGAMENT COMPARED WITH EXTERNAL REFERENCE PIN

Vertical surgical accuracy was not influenced by using the medial canthal ligament (Odense cohort) versus an external fixed reference pin (Nijmegen cohort). Comparing the planned, obtained, and surgical accuracy in the vertical axes showed no statistical

Table 2. MIXED LINEAR REGRESSION ANALYSIS OF INTERNAL CORRELATION AND CONFOUNDING VARIABLES

			95% CI	
	β	*P* Value	Lower Limit	Upper Limit
Interaction with planned movement				
Anterior (baseline)	0.14	.002	0.05	0.23
Superior (addition to baseline)	−0.34	.000	−0.50	−0.19
Right (addition to baseline)	0.06	.628	−0.17	0.28
Test of hypotheses				
Maxilla first	0.57	.003	0.19	0.95
Inferior maxillary repositioning	−0.98	.000	−10.42	−0.55
CCW rotation	0.31	.127	−0.09	0.70
Age (yr)	−0.01	.108	−0.03	0.00
Female gender	−0.10	.606	−0.49	0.28
Constant	−0.46	.106	−10.03	0.10
SD (constant)	2×10^{-13}		3×10^{-15}	1×10^{-11}
SD (residual)	1.84		1.73	1.97

Note: The outcome measurement for mixed-model regression was the difference between planned and obtained movements.
Abbreviations: CI, confidence interval; CCW, counterclockwise rotation; SD, standard deviation.

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Table 3. OVERALL DIFFERENCE BETWEEN PLANNED AND OBTAINED SURGICAL REPOSITIONING

	Md First (n = 88)			Mx First (n = 57)			
	Mean	SD	*P* Value*	Mean	SD	*P* Value*	*P* Value† for Md vs Mx
Linear maxillary difference							
Right	0.42	1.65	.019	−0.17	1.31	.341	.025
Anterior	−1.49	2.01	.000	−0.35	2.65	.327	.004
Superior	−0.22	1.76	.242	0.32	2.07	.253	.096
Rotational maxillary difference							
Pitch	1.42	2.86	.000	−0.25	2.90	.415	.001
Roll	−0.54	1.24	.002	−0.15	1.40	.329	.088
Yaw	0.12	1.52	.543	−0.19	1.57	.258	.236

Abbreviations: Md, mandible; Mx, maxilla; SD, standard deviation.
* By Student 1-sample independent *t* test.
† By Student 2-sample independent *t* test of the difference between the maxilla-first and mandible-first groups.

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difference between the 2 methods (Table 6). Visualizing the surgical accuracy for each patient according to the planned vertical reposition showed that the medial canthal ligament group was nested within the external fixed reference pin group (Supplementary Figure 6). Thus, using the medial canthal ligament did not seem to influence surgical accuracy or variation in the vertical dimension.

Discussion

The purpose of this study was to explore whether the theoretical advantages of operating on the mandible first were supported by the clinical data. All research questions were answered. *1)* Overall surgical accuracy was affected by maxillary versus mandibular sequencing. The maxilla-first sequencing

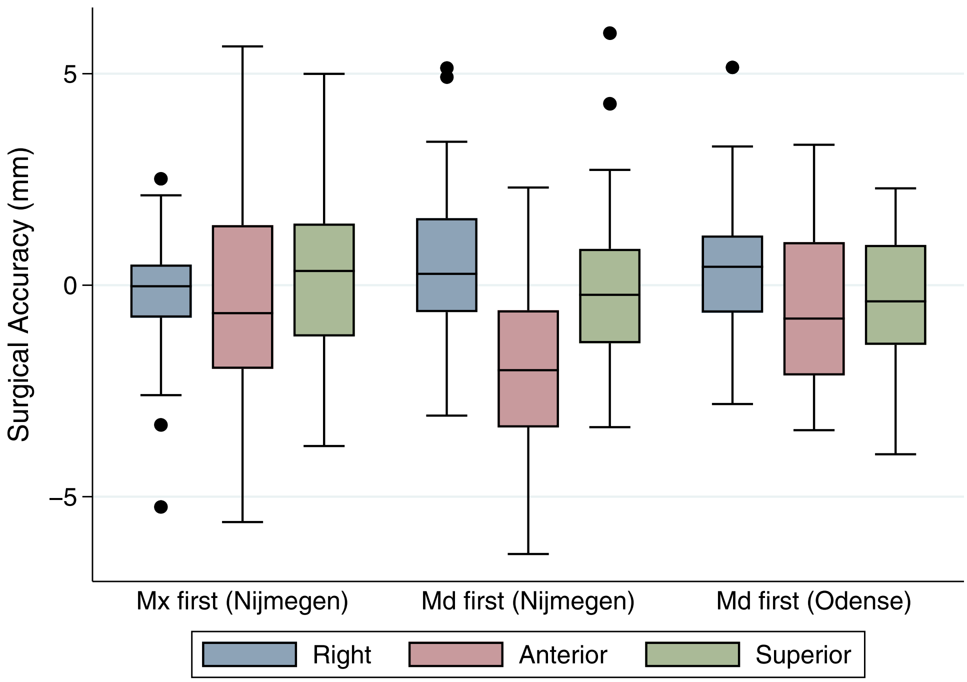

FIGURE 3. Distance between planned and obtained maxillary reposition between procedures and study centers. Surgical accuracy was determined according to center and maxillary-first and mandibula-first sequencing. The main difference was seen along the anterior axis; maxilla-first sequencing showed a larger variance, whereas mandible-first sequencing in the Nijmegen study showed a median of −2 mm. Md, mandible; Mx, maxilla.

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Table 4. SURGICAL SEQUENCE INTERACTION WITH MAXILLARY ROTATION

Linear Distance (mm)	n	Mandible First	n	Maxilla First	*P* Value*
CW	38		38		
Right		0.39 (1.37)		0.05 (0.99)	.222
Anterior		−1.93 (1.85)		−1.18 (2.35)	.127
Superior		−0.60 (1.58)		0.31 (2.04)	.035
CCW	50		19		
Right		0.45 (1.85)		−0.59 (1.74)	.037
Anterior		−1.16 (2.09)		1.33 (2.45)	.000
Superior		0.06 (1.84)		0.34 (2.18)	.602
P value* for CW vs CCW					
Right		.854		.081	
Anterior		.074		.000	
Superior		.080		.955	

Note: Translation and rotation measurements are presented as mean (standard deviation).
Abbreviations: CCW, counterclockwise rotation; CW, clockwise rotation.
* By Student 2-sample independent *t* test.

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was centered closer to the planned reposition than the mandibular-first sequencing, whereas the mandible-first approach resulted in a marked posterior reposition. The maxilla-first approach resulted in larger variances than the mandible-first approach. *2)* The surgical accuracy in the CW and CCW rotation was not statistically meaningfully influenced by the sequencing. However, the procedures appeared to be more accurate for the CCW rotation when the mandible was operated on first and for the CW rotation when the maxilla was operated on first. *3)* Inferior maxillary repositioning placed the maxilla posterior to the planned position regardless of sequencing. Sequencing the maxilla or mandible first affected surgical accuracy in superior maxillary repositioning. *4)* There was no relevant difference in vertical accuracy using the medial canthal ligament versus a bony fixated external reference pin.

Not all theoretical advantages of sequencing the mandible first could be found in the clinical data. Theoretically, operating on the mandible first should result in closer adaptation to the planned maxillary repositioning, because the condyles are initially seated in central relation during the operation. This will prevent any incorrect seating during the preoperative scan to be transferred to the surgical reposition. If the condyles are seated incorrectly on the preoperative scan, then the condyles will

Table 5. SURGICAL SEQUENCE INTERACTION WITH SUPERIOR AND INFERIOR MAXILLARY REPOSITIONING

Linear Distance (mm)	n	Mandible First	n	Maxilla First	*P* Value*
Superior maxillary reposition	43		24		
Right		0.32 (1.63)		−0.54 (1.64)	.041
Anterior		−0.93 (1.93)		1.45 (2.77)	.000
Superior		−0.34 (2.10)		0.53 (2.17)	.114
Inferior maxillary reposition	45		33		
Right		0.52 (1.69)		0.11 (0.95)	.211
Anterior		−2.03 (1.96)		−1.65 (1.60)	.370
Superior		−0.11 (1.36)		0.16 (2.01)	.484
P value* for superior vs inferior					
Right		.583		.064	
Anterior		.010		.000	
Superior		.541		.510	

Note: Translation and rotation measurements are presented as mean (standard deviation).
* By Student 2-sample independent *t* test.

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Table 6. SURGICAL ACCURACY IN VERTICAL DIMENSION USING EXTERNAL REFERENCE PIN AND MEDIAL CANTHAL LIGAMENT

Vertical Measurements	Reference Pin (n = 58)	Canthal Ligament (n = 30)	*P* Value*
Planned	−0.13 (2.92)	0.22 (2.49)	.561
Obtained	−0.31 (3.22)	−0.08 (2.31)	.701
Difference	−0.18 (1.83)	−0.30 (1.64)	.759

Note: Measurements are along the superior axis and presented as mean (standard deviation). Positive measurements are superior and negative measurements are inferior. In this analysis, all patients were operated on by the mandible-first approach.

* By Student 2-sample independent *t* test.

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reposition into centric relation when the patient is under general anesthesia, thereby changing the position of the mandible.[25] If the maxilla is positioned against the unoperated mandible, then an incorrect seating during the preoperative scan can cause the maxilla to be placed posterior to the planned position.[24] However, the clinical data did not support all theoretical advantages of operating on the mandible first. The maxilla-first approach did result in a larger variance in surgical accuracy; however, the mean was centered closer to the planned position than it was with the mandible-first approach. In contrast, operating on the mandible first resulted in the maxilla being positioned posterior to the intended position. This posterior positioning was further explored in the subgroups of patients in whom CW or CCW rotation of the maxillomandibular complex or superior or inferior maxillary repositioning was performed.

MAXILLARY ROTATION

Rotation of the maxillomandibular complex resulted in the same level of surgical accuracy in CCW rotation in the mandible-first group and CW rotation in the maxilla-first group. This is consistent with the proposed theoretical accuracy of the surgical splint design.[4,5] Choosing the maxilla-first sequence in association with CCW rotation placed the maxilla considerably anterior to the planned position, whereas CW rotation in mandible-first sequencing resulted in a clinically relevant 1.9-mm posterior positioning. If surgeons do not wish to alternate between sequencing the mandible or maxilla first, then this difference in surgical accuracy should be addressed in the VSP to achieve the desired maxillary position.

INFERIOR MAXILLARY REPOSITIONING

Inferior maxillary repositioning is among the least predictable and unstable surgical procedures. It is unknown whether the posterior position is caused by inaccuracy during the surgery or immediate postoperative relapse, but the posterior discrepancy occurred independent of the mandible-first or maxilla-first approach. This 1.7-mm (maxilla-first approach) to 2.0-mm (mandible-first approach) posterior discrepancy to the planned position should be considered in the design of the VSP. If the anticipated 2-mm inaccuracy is not judged to be esthetically acceptable, then additional maxillary advancement could be beneficial to the patient and should be considered in the final VSP.

ADJUSTING VIRTUAL SURGICAL PLAN

Adjusting for discrepancies between VSP and clinical outcome should be performed for CW or CCW rotation or inferior maxillary reposition but not for both. Because these discrepancies stem from the same cohort, adjusting for rotation and inferior reposition would adjust the patient's discrepancy twice. The interaction among sequencing, rotation, and inferior maxillary repositioning could not be further analyzed in this study because only 3 patients were operated on using inferior maxillary repositioning, CCW rotation, and the maxilla-first sequence. Thus, surgeons must choose to adjust the VSP according to CW or CCW rotation or inferior maxillary repositioning. Inferior maxillary repositioning seemed to influence the surgical accuracy more than CW or CCW rotation (larger β coefficient and lower *P* value).

POSSIBLE EXPLANATIONS FOR POSTERIOR MAXILLARY POSITION

The mechanisms that caused this posterior maxillary position were not evaluated, because this study was designed only to evaluate whether a systematic difference existed between the VSP and the obtained surgical outcome. In speculating on the possible cause, it is worth noting that during inferior maxillary repositioning, the maxilla was placed posteriorly independent of whether the mandible or maxilla was operated on first. Furthermore, superior maxillary repositioning was placed more anteriorly compared with inferior maxillary repositioning.

The authors believe that the posterior position in inferior maxillary repositioning might be caused by immediate relapse intraoperatively from additional compression of the temporomandibular joint or postoperatively from settling of the osteosynthesis material during the subsequent Le Fort I operation.[13,26,27] Furthermore, in superior maxillary repositioning, the maxilla can be displaced anteriorly if there are bony interferences at the pterygopalatine junction or surrounding the greater palatine nerve and artery. This anterior displacement will cause the maxilla to be positioned anterior to the planned position when the maxilla is operated on first, whereas the maxilla will be positioned anterior to the mandibular position when the mandible is operated on first. However, the authors can only speculate on the possible underlying mechanisms because the findings of this study do not provide a definite explanation. Identifying the mechanisms behind the posterior maxillary position will require prospective studies in more homogeneous cohorts in which a single surgical factor is evaluated at a time.

EXTERNAL REFERENCE MEASUREMENTS

Controlling the vertical dimension was not influenced by using different external reference points. Using the medial canthal ligament for measuring the vertical dimension has previously been described as accurate, affecting the vertical surgical accuracy with a mean of 0.3 mm.[17,18] This study's result of a 0.3-mm difference between the planned and obtained outcome was in accordance with the findings on 2-dimensional lateral cephalometric tracings and was considered well within acceptable limits. Likewise, visualizing each patient's vertical surgical accuracy, plotted against the planned reposition, showed the medial canthal ligament cohort matched the outcomes of the external reference pin cohort. Thus, using the medial canthal ligament can be considered a reliable alternative to using a fixed reference pin.

COMPARABLE LITERATURE

Apart from the included article (study 1),[10] only 2 retrospective cohort studies have evaluated the surgical accuracy of the maxilla-first versus mandible-first approach.[11,12] The 2 studies were planned with plaster cast models in a semiadjustable articulator, and the outcome was evaluated on lateral cephalometric tracings. Salmen et al[11] found a difference between groups (n = 16 patients per group) in the vertical direction but not in the horizontal direction. All patients were treated with advancement and impaction, similar to the maxillary superior repositioning group. The upper first incisor was positioned 0.8 mm posterior to the planned positioning in the mandible-first group and 0.3 mm posterior in the maxilla-first approach, which was not statistically different. In the vertical dimension, the upper first incisor was positioned 1.0 mm inferior to the planned position in the mandible-first approach and 0.1 mm superior in the maxilla-first procedures, which was considered statistically relevant. In contrast, this study found a marked horizontal difference between sequences, whereas there was no marked vertical difference. The study by Ritto et al[12] found no relevant influence in sequencing the maxilla or mandible first, and there was a slightly larger absolute variance in the maxilla-first group than in the mandible-first group (n = 20 patients per group). Thus, the results from this study do not reflect the results found in the literature. The difference between the present results and the literature can have several causes. The surgery was planned using VSP, which enables accurate placement of the condylar positioning and accurate occlusal plane re-creation. The outcome was measured in 3 dimensions with improved measurement tools with a reproducibility of less than 0.3 mm,[21,22] whereas the measurement reproducibility for cephalometric tracing was 0.46 to 1.68 mm.[11] Thus, this study should more accurately reflect the surgical outcome achieved by 3D planning and computer-assisted design and manufactured surgical splints.

LIMITATIONS AND FUTURE PERSPECTIVES

Some limitations and unanswered questions remain regarding the potential benefits of sequencing the mandible first. This study focused exclusively on the maxillary position compared with the planned position; therefore, differences in mandibular positioning and final occlusion were not addressed in this study. Especially the final occlusion is of interest because this is of major importance for the success of the surgical procedure. Operating on the mandible first should, theoretically, transfer any errors in condylar seating to the maxilla. Thus, it is acceptable that the maxilla is positioned posterior to the planned position to preserve the ideal occlusion in the final surgical splint. The final occlusion might not be evaluated sufficiently by CBCT scans but could be addressed more accurately by intraoral scans of the postoperative occlusion instead.

Future studies might wish to address whether interactions occurred between inferior maxillary repositioning and CCW rotation. In addition, there might be a threshold at which the benefit of the appropriate sequence becomes more obvious. In this study, the inferior reposition and CCW rotation were measured only overall, including minor and major repositions in 1 outcome, without interactions and detailed subgroup analysis. Combining additional future studies into a larger cohort analysis could enable researchers to further explore whether such interactions or thresholds exist. When combining future studies, it is important that the outcome measurements are sufficiently reliable to ensure the quality of each patient's data in a combined cohort study. Including less reliable outcome measurements could mask potential benefits of the appropriate sequencing in bimaxillary procedures.

The present study relied on 3D printed splints to position the moving segments. Although computer-aided designed and manufactured splints accurately fit and reposition the moving segments,[28] the looseness of the temporomandibular joint could affect the surgical accuracy and position of the segments.[24] The surgical accuracy is expected to improve if the moving segments can be positioned without relying on the opposite jaw position. Using 3D printed patient-specific plates to position the moving segments could improve surgical accuracy.[29,30] However, the clinical benefit of wafer-less maxillary positioning also must be evaluated in future randomized controlled studies.

In conclusion, it remains vitally important to know how the chosen sequence affects the surgical outcome. None of the sequences proved superior in all surgical outcomes, and no absolute "winner" could be identified. Operating on the mandible first decreased the variance in surgical accuracy but resulted in a maxillary position posterior to the planned position. Especially in the subgroup of patients treated with inferior maxillary repositioning, the maxilla was positioned posterior to the planned position in the mandible-first and maxilla-first approaches. This posterior discrepancy should be addressed by additional advancement in the VSP to position the maxilla closer to the planned position. Thus, these sequences could achieve closer adherence to the desired maxillary position by adjusting the VSP to include the effects on surgical accuracy.

Supplementary Data

Supplementary data associated with this article can be found in the online version, at https://doi.org/10.1016/j.joms.2019.03.023.

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Inferior Maxillary Repositioning Remains Stable 1 Year After Surgery but Entails a High Risk of Osteosynthesis Failure

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Purpose: Inferior maxillary repositioning has continued to be among the most unstable orthognathic procedures. The overall purpose of the present study was to measure skeletal stability after inferior maxillary repositioning.

Materials and Methods: We implemented a retrospective cohort study. The study cohort was derived from all orthognathic patients who had undergone treatment from January 2011 to December 2013 in Odense University Hospital. The inclusion criteria were orthognathic surgery with inferior maxillary repositioning in patients without maxillary segmentation or cleft lip/palate. The exclusion criteria were nonattendance at follow-up visits or requiring reoperation before the 1-year follow-up point. The primary predictor variable was the time from the 1-week follow-up examination to the 1-year follow-up examination. The primary outcome variable was maxillary skeletal movement. The other variables of interest were age, gender, preoperative occlusal relationship, maxillary movement obtained, and surgery type (mono- or bimaxillary procedure). Skeletal stability was measured at the centroid, anterior, and posterior nasal spines using the semiautomatic measurement technique. Skeletal stability was clinically defined as less than 2 mm of movement in any direction. The positive directions for the 3 axes were right, anterior, and superior. The data were analyzed using mixed model linear regression analysis and 1-sample *t* tests.

Results: A total of 17 patients were included in the present study (mean age, 28 years; female gender, 35%; bimaxillary surgery, 59%). Inferior maxillary repositioning was stable with less than 0.3 mm mean skeletal movement in any direction. Only 1 patient had experienced a relapse of more than 1 mm in the posterior direction; no movement exceeded 2 mm. However, 3 patients were excluded from the present analysis, because they had required reoperation during the first year after surgery for osteosynthesis failure.

Conclusions: Inferior maxillary repositioning was stable during the first year after surgery; however, the complication rate was high (15%). Thus, this procedure might still benefit from the use of more rigid patient-specific printed plates to increase postoperative stability.

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Reoperation after orthognathic surgical procedures entails both high financial and human costs. The human costs for patients include additional pain and extended sick leave. In addition, the patient could lose confidence in the surgeon. Inferior maxillary repositioning has been considered among the least stable and predictable of orthognathic procedures and has had a high risk of reoperation.[1,2] The latest systematic review from 2015 found only 2 studies of sufficient quality to be included for analysis, with a total of 22 patients.[3] The reported studies disagreed regarding the 1-year postoperative stability. Perez et al,[4] in 1997 (10 patients), reported a vertical relapse of −1.6 mm. In contrast, Kretschmer et al,[5] in 2010 (12 patients) reported almost no relapse (0.1 mm). Both studies had used articulator models, and the relapse was measured using 2-dimensional (2D) lateral cephalometric tracing. Only Liebregts et al[6] evaluated the overall 3-dimensional (3D) relapse for orthognathic surgery patients. However, to the best of our knowledge, no study has specifically evaluated 3D relapse or skeletal stability in inferior maxillary repositioning.[7]

The new 3D semiautomatic technique can be used to measure skeletal stability and relapse independently of postoperative orthodontic treatment.[8-10] The semiautomatic technique uses voxel-based registration to align the reference points in the moving maxillary segment from the preoperative scan to the 1-week and 1-year postoperative scans without the need to manually re-identify the reference landmarks. Thus, the measured distance between the reference points represents the true skeletal movement, independent of the resection of the anterior nasal spine (ANS) and postoperative orthodontic treatment.[9]

The overall purpose of the present study was to quantify the skeletal stability in patients who had undergone inferior maxillary repositioning. We hypothesized that the lack of bony stability in inferior maxillary repositioning would destabilize the maxilla and that significant relapse could occur in the superior and posterior directions. The specific aim of the present study was to measure the change in the maxillary position during the first year after surgery.

Materials and Methods

STUDY DESIGN

To address the research question, we implemented a retrospective cohort study. The study population included all patients who had undergone inferior maxillary repositioning in the Department of Oral and Maxillofacial Surgery at Odense University Hospital from January 1, 2013 to December 31, 2015. The cohort was also used to evaluate the surgical precision in these patients.[11] To be included in the study sample, the patients had to have undergone orthognathic surgery with inferior maxillary repositioning and to not have maxillary segmentation or cleft lip or palate. Inferior maxillary repositioning was defined as inferior repositioning at 3 dental reference points: the upper first molars and upper incisors edge. The patients were excluded if they had not attended the 1-year follow-up examination or if they had required reoperation during the first year after surgery. The patients who had undergone reoperation before the 1-year follow-up visit were also excluded from the quantitative analysis; however, these patients' data were qualitatively analyzed post hoc to evaluate the underlying causes of osteosynthesis failure. In observance with the Danish Code of Conduct for Research Ethics, all the patients had provided written informed consent before inclusion, and all included surgeries had used 3D virtual surgical planning (3D Systems, Rock Hill, SC). The ethics committee of Odense University Hospital reviewed the study design and determined that ethical approval was not required because the study did not directly influence the patients' treatment. The present study was performed in compliance with the 2000 World Medical Association Declaration of Helsinki.

VARIABLES

The primary predictor variable was the time from the 1-week postoperative follow-up examination to the 1-year postoperative follow-up. The primary outcome variable was the skeletal stability, measured as the distance between the maxillary position at 1 week and 1 year after surgery. Skeletal stability was measured as a continuous variable at the centroid point of the maxilla along the 3 axes: right, anterior, and superior. Skeletal stability was clinically defined as less than 2 mm of movement in any direction. The confounding variables were also recorded in the description of the sample (age, gender, preoperative occlusal relationship [angle Class I, II, or III)] and the orthognathic surgery (maxillary movement obtained and surgery type [maxilla-only or bimaxillary procedure]).

DATA COLLECTION METHODS

The mandibular and maxillary segments were positioned by intermaxillary surgical splints in accordance with the virtual surgical plan. In the bimaxillary procedures, the mandible was operated on first. The maxillary osteotomy was performed as a standard, horizontal Le Fort I osteotomy. The maxillary osteotomy was stabilized using 4 L-shaped plates (BioMet, version 2.0 systems; Zimmer Biomet Corp, Warsaw, IN). The osteotomies were grafted using local bone, and no extraoral block grafting was performed. The solid bone grafts were interpositioned around the plates or in the osteotomy between the plates to stabilize the vertical dimension. All participants attended postoperative orthodontic treatment for finalization of the occlusion.

Cone-beam computed tomography (CBCT) scans were performed at the 1-week and 1-year follow-up examinations using a NewTom 3G CBCT scanner (NewTom, Verona, Italy) with standard settings (field of view, 20 cm × 20 cm; 110 kV; radiation exposure, 59 μSV).[12]

SEMIAUTOMATIC 3D MEASUREMENT TECHNIQUE

To differentiate the skeletal movements from the postoperative orthodontic movements and bone remodeling at the ANS and posterior nasal spine (PNS), the maxillary movement was measured using a validated 3D semiautomatic protocol.[9] To position the reference points independently of the dental movements and bone remodeling, the hard palate on the postoperative scans was aligned with the hard palate on the preoperative scan. When the moving maxillary segments were aligned at the bony palate, the reference points could be positioned identically on the preoperative and follow-up scans, even if the reference landmarks had moved on the follow-up scans. Thus, the reference points were still positioned identically for both the 1-week and the 1-year scans relative to the bony palate, even if the teeth had moved orthodontically or bony remodeling had occurred. Thus, the reference points were positioned where the teeth and the ANS and PNS should have been on the follow-up scans if no orthodontic movements or bone remodeling had occurred. To align the global coordinate systems in the outcome measurements with the virtual surgical plan, the preoperative scan was rotated to align with the natural head position in the virtual surgical plan. Next, the cranial base on both the 1-week and the 1-year scans was aligned with the cranial base on the preoperative scan, and the distance between the respective reference points was measured.

Five reference points were positioned directly on the axial, coronal, and sagittal views. These were the top of the mesiobuccal cusp on the first molar on each side (M6L and M6R), the midline at the edge of the central incisors (U1I), PNS, and ANS.

The mean linear reposition at the dentition was measured between the virtual centroid points in the scans. The centroid points were created from the mean of the 3 dental reference points (M6L, M6R, and U1I).[13,14] All measurements were recorded in relative numbers according to the positive values of the 3 axes: right, anterior, and superior. Right was defined from the patient's perspective and was, thus, the patient's right side.

Rotations were measured in degrees around the central midmolar (MM) point, calculated as the mean of the first molars' reference points. The rotations were calculated as the difference between a dental reference point and the MM point: a positive yaw moved the U1I to the left, a positive pitch moved the U1I upward, and a positive roll moved the M6R upward.

STATISTICAL ANALYSIS

The data were analyzed using STATA, version 15.0 (StataCorp Ltd, College Station, TX). Descriptive variables were compared between the analyzed cohort and the patients with osteosynthesis failure. Descriptive variables were analyzed using the Fisher exact test and the Wilcoxon rank sum test for unpaired data. The skeletal stability was recorded as the mean ± standard deviation and visualized in a box plot. The primary outcome was tested using 1-sample *t* tests to establish whether the postoperative skeletal movement was significantly different from 0. Multilevel regression analysis was performed because each patient had multiple measurements along the 3 axes for both the outcome and the predictor variables. Therefore, the data were considered as clustered, and linear mixed model regression analysis was performed to accommodate both fixed and random effects of the individuals and to correlate for confounding variables. The level of statistical significance in all tests was set to $P \leq .05$.

Results

Twenty-five patients fulfilled the inclusion criteria and were invited to participate in the present study. However, 2 declined to participate and 2 did not respond, leaving 21 patients. Of the 21 patients, 4 were excluded: 1 had not attended the 1-year follow-up visit and 3 had required reoperation before the 1-year follow-up examination. Thus, the final cohort for quantitative analysis of the postoperative skeletal movement included 17 patients (Table 1).

Overall, all included patients were clinically stable, and all skeletal movements were less than 2 mm in any direction when measured at the centroid. Only 1 patient experienced a skeletal relapse of more than 1 mm in the posterior direction (20-year-old woman with neutral occlusion who had required bimaxillary surgery). The maxillary skeletal stability of the cohort showed a distribution with 2 negative outliers along the anterior axis (Fig 1). The mean relative skeletal change was less than 0.2 mm, and the mean absolute skeletal movement was less than 0.4 mm (Table 2). The vertical stability at the PNS was slightly less stable, with a standard deviation of more than 1 mm and a

Table 1. DESCRIPTIVE COHORT ANALYSIS OF INCLUDED COHORT AND PATIENTS EXCLUDED BECAUSE OF REOPERATION DURING THE FIRST YEAR AFTER SURGERY

Descriptive Data	Included Cohort	Excluded Because of Reoperation Before 1-Year Follow-Up Point	*P* Value
Participants (n)	17	3	
Female gender (n)	6	2	.54*
Mean age (yr)	28	26	1.00†
Range (yr)	17-64	19-37	
Occlusion (angle classification)			1.00*
Neutral (Class I)	5	1	
Distal (Class II)	5	1	
Mesial (Class III)	7	1	
Type of surgery			
Maxillary advancement	16	3	1.00*
Bimaxillary surgery	10	3	.52*
Mandibular advancement	9	2	
Mandibular setback	1	1	

* Fisher's exact test.
† Wilcoxon rank sum test of unpaired data.

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mean absolute skeletal movement of 0.7 mm. Likewise, the rotational differences were also minimal, with rotations of less than 0.3 degrees (Table 3).

Multivariable analysis of the included patients' confounding variables showed a correlation between the skeletal movement in the superior and posterior directions (Table 4). The relapse correlated negatively with the obtained inferior repositioning; thus, a large inferior repositioning would relapse in a superior direction. Finally, the skeletal movements correlated with bimaxillary repositioning, indicating that bimaxillary surgery was less stable than solitary maxillary repositioning.

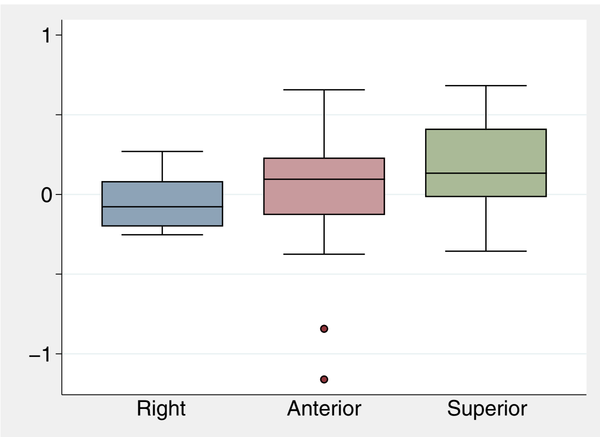

FIGURE 1. Box plot of skeletal movement during the first year after surgery (n = 17). The maxillary skeletal movement was measured along 3 axes. Maxillary skeletal movement was measured between the 1-week and 1-year postoperative scans. Patients requiring reoperation during the first year after surgery were not included.

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In the bimaxillary procedures, the maxilla moved in a posterior direction. In the solitary maxillary procedures, the maxilla moved in the anterior and superior directions (Table 5). This difference between the solitary and bimaxillary procedures was not statistically or clinically significant.

The 3 excluded patients who required reoperation before the 1-year follow-up visit were evaluated post hoc for factors that could explain the osteosynthesis failure. The need for reoperation had been diagnosed 2, 5, and 12 months after surgery. The reasons for additional surgery were failure of the osteosynthesis plates with malocclusion, failure of the osteosynthesis plates with clinically significant asymmetry, and nonunion of the maxilla after 12 months of healing. All 3 patients had undergone bimaxillary surgery with maxillary advancement; however, no other confounding variable was consistently present for all 3 patients (Table 1; Supplemental Table 1). The CBCT scans were inspected to evaluate the maxillary bone quality or quantity; however, none of the patients presented with bony abnormalities or unusually thin biotypes that could explain the osteosynthesis failure.

Discussion

The purpose of the present study was to evaluate skeletal stability in patients who had undergone inferior maxillary repositioning. We hypothesized that

Table 2. LINEAR SKELETAL MOVEMENT MEASURED AT THE CENTROID POINT AND AT ANTERIOR AND POSTERIOR NASAL SPINES (N = 17)

	Measurements (mm)		Skeletal Movement (mm)		
Variable	At 1 wk	At 1 yr	Absolute	Relative	*P* Value*
Centroid					
Right	−0.06 ± 0.87	−0.11 ± 0.18	0.15 ± 0.08	−0.05 ± 0.17	.280
Anterior	2.03 ± 1.51	2.05 ± 0.34	0.34 ± 0.30	0.01 ± 0.46	.916
Superior	−1.37 ± 1.01	−1.18 ± 0.22	0.27 ± 0.22	0.19 ± 0.30	.018
ANS					
Right	−0.18 ± 1.15	−0.22 ± 1.10	0.13 ± 0.11	−0.04 ± 0.17	.344
Anterior	2.42 ± 1.85	2.53 ± 1.84	0.21 ± 0.22	−0.10 ± 0.07	.166
Superior	−1.79 ± 1.65	−1.54 ± 1.36	0.41 ± 0.31	0.25 ± 0.46	.037
PNS					
Right	0.48 ± 0.89	0.58 ± 0.77	0.22 ± 0.25	0.10 ± 0.32	.228
Anterior	2.66 ± 1.79	2.46 ± 1.92	0.23 ± 0.42	−0.20 ± 0.44	.085
Superior	−0.56 ± 1.51	−0.38 ± 1.05	0.69 ± 0.83	0.19 ± 1.08	.480

Data presented as mean ± standard deviation.

Abbreviations: ANS, anterior nasal spine; PNS, posterior nasal spine.

* One-sample *t* test used to evaluate whether the relative skeletal movement differed from 0.

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the lack of bony stability in inferior maxillary repositioning would destabilize the maxilla and that significant relapse could occur in the superior and posterior directions. The specific aim of the present study was to measure the change in maxillary positioning during the first year after surgery. To the best of our knowledge, the present study is the first to analyze postoperative skeletal stability after inferior maxillary repositioning using 3D measurements. Inferior maxillary repositioning was quite stable, with a mean skeletal movement of less than 1 mm in patients without postoperative complications. However, 3 patients were excluded from the study because they required reoperation during the first year after surgery.

The stability of inferior maxillary repositioning in patients without complications was consistent with the findings reported by Kretschmer et al,[5] indicating that inferior maxillary repositioning is quite stable. Although Kretschmer et al[5] reported skeletal stability that was almost identical to the findings in the present study (0.1 mm vs. 0.25 mm), the standard deviation was greater (1.3 vs. 0.46 mm). This increase in variation might have resulted from their use of a larger inferior repositioning of the maxilla (ANS, 3.2 mm inferior vs. 1.65 mm) or because the 2D outcome measurement method was less accurate than our 3D technique.[5]

The high complication rate (15%) in our study indicated that many patients might still benefit from increased stability after inferior maxillary repositioning. Stabilizing the obtained maxillary position could be achieved by incorporating additional rigidity into the plates (ie, 3D patient-specific printed plates)[15] or by increasing the support of the plates (ie, extraoral bone grafting).[16]

Only a few common traits were found for the patients who required reoperation during the first year after surgery. All had undergone bimaxillary

Table 3. ROTATIONAL SKELETAL MOVEMENT MEASURED AT THE OCCLUSAL LEVEL (N = 17)

	Measurements (°)		Skeletal Movement (°)		
Rotational Movement	At 1 wk	At 1 yr	Absolute	Relative	*P* Value*
Yaw	0.70 ± 1.58	0.82 ± 1.39	0.25 ± 0.21	0.12 ± 0.31	.117
Pitch	−1.39 ± 2.83	−1.13 ± 2.04	0.87 ± 0.88	0.25 ± 1.23	.411
Roll	−0.27 ± 1.17	−0.35 ± 1.12	0.34 ± 0.37	−0.09 ± 0.50	.476

Data presented as mean ± standard deviation.

* One-sample *t* test to evaluate whether the relative skeletal movement differed from 0.

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Table 4. MIXED LINEAR REGRESSION ANALYSIS OF INTERNAL CORRELATION AND CONFOUNDING VARIABLES MEASURED AT THE CENTROID (N = 17)

Variable	β	*P* Value	95% CI
Internal correlation to superior axis			
Right	−0.14	.359	−0.45 to 0.16
Anterior	−0.31	.007	−0.56 to −0.06
Interaction with obtained movement			
Superior (baseline)	−0.12	.010	−0.21 to −0.03
Right (addition to baseline)	0.06	.470	−0.10 to 0.22
Anterior (addition to baseline)	−0.00	.993	−0.17 to 0.17
Type of surgery			
Bimaxillary surgery	−0.38	.005	−0.63 to −0.11
Occlusion (angle classification)			
Distal (Class II)	−0.01	.956	−0.25 to 0.23
Mesial (Class III)	−0.12	.236	−0.33 to 0.08
Female gender	0.10	.199	−0.05 to 0.26
Age (yr)	0.01	.030	0.00 to 0.02
Constant	0.21	.185	−0.10 to 0.53
SD (between subjects)	4×10^{-10}	NA	3×10^{-14} to 6×10^{-6}
SD (within subjects)	0.25	NA	0.21 to 0.31

The measurements for mixed model regression are the difference between the planned and obtained movement.
Abbreviations: CI, confidence interval; NA, not applicable; SD, standard deviation.

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procedures with maxillary advancement. In the mixed model analysis, bimaxillary procedures were also found to be a significant confounding variable for skeletal movement in the patients without complications, indicating that bimaxillary procedures are less stable. Bending the plates multiple times could have reduced the rigidity of the plates; however, no evidence of this was found. Also, all operations were performed by experienced consultant surgeons. The preoperative occlusal relationship did not seem to influence the incidence of postoperative complications or skeletal stability. Finally, when comparing the planned and obtained surgical repositioning in the patients with postoperative complications, no distinct pattern emerged. Most planned and obtained movements in the patients with complications were within 1 standard deviation of the mean obtained maxillary repositioning (Supplemental Table 1). Thus, except for bimaxillary procedures with maxillary advancement, none of the other registered confounding variables indicated an increased risk of postoperative complications.

The present study was limited by the small sample size, although the cohort equaled the combined sample size reported in the latest systematic review.[3] The limited sample size resulted in a risk of overfitting of the statistical model. Overfitting the statistical model might increase the correlation of the measurements and can result in significant *P* values that would not correspond to the raw data analysis. Thus, the *P*

Table 5. COMPARISON BETWEEN MAXILLA-ONLY AND BIMAXILLARY PROCEDURES

Measurement (mm)	Maxillary Only (n = 7)	Bimaxillary (n = 10)	*P* Value*
Right	−0.02 ± 0.11	−0.06 ± 0.20	.634
Anterior	0.25 ± 0.28	−0.16 ± 0.50	.071
Superior	0.27 ± 0.11	0.14 ± 0.32	.395

Data presented as mean ± standard deviation.
* Student's *t* test.

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values from the mixed level regression models must be interpreted with caution and must be validated by future independent studies.

To compensate for the limited sample size, measurement errors were minimized to decrease the variance in measurements and increase the reliability of the outcome measurements. The semiautomatic measurement technique used in the present study has several advantages regarding analysis of the postoperative skeletal movement. First, the semiautomatic technique shows a high degree of reproducibility, with a less than 0.3-mm difference between the repeated measurements.[8-10] Second, using 3D information to determine the skeletal movement was more accurate and informative than conventional lateral cephalometric analysis.[17-19] Third, the reference points were positioned automatically without the need to re-identify the landmark; thus, skeletal stability and relapse can be measured independently of the postoperative orthodontic treatment.[9,10] Thus, the semiautomatic measurement technique was ideal for analyzing postoperative skeletal stability, providing reliable results on skeletal relapse.

The use of the centroid as the main point of measurement for skeletal stability has potential limitations. The clinical indication for inferior maxillary repositioning has often been to increase the incisor display. However, although no skeletal movement will occur at the centroid, the vertical reposition of the incisors could still relapse in a superior direction. In the present study, both the centroid and the pitch were stable, indicating stability of the incisor display. Likewise, the skeletal change at the ANS was stable and might be a more clinically relevant indicator of stability of the central incisor display. Because the dental reference points used to calculate the centroid are not equally relevant clinically, future studies should consider using the central incisors edge as the primary measurement point, instead of the centroid.

Despite the reliability of the outcome measurements, not all problems concerning skeletal stability were addressed in the present study. Skeletal relapse occurring before the 1-week postoperative scan was not included in the present study but has previously been reported to indicate surgical inaccuracy. The previous studies of surgical accuracy found a much larger variation between the virtual surgical plan and the obtained reposition.[11,20] It is unknown how much of the surgical inaccuracy was caused by early skeletal relapse, and the problem of skeletal instability might, therefore, be larger than that reported in the present study. Thus, it is still advisable to increase the skeletal stability in inferior maxillary repositioning using bone grafting or 3D patient-specific printed plates. It is hoped that the increased skeletal stability will increase the surgical accuracy and decrease the number of postoperative complications, reducing both the financial and the human costs involved in reoperation.

In conclusion, inferior maxillary repositioning was stable during the first year after surgery but entailed a high complication rate and the risk of reoperation. Further studies are needed to validate these findings in larger samples, preferably in a multicenter study setup. Future studies should also explore whether inferior maxillary repositioning could benefit from the use of more rigid, patient-specific, printed plates to increase postoperative stability.

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Supplemental Data

Supplemental Table 1. EVALUATION OF REOPERATIONS DURING THE FIRST YEAR AFTER SURGERY

	Obtained Maxillary Reposition (Virtual Surgical Plan) (mm)					
Pt. No.	Right	Anterior	Superior	Yaw	Pitch	Roll
1	0.25 (0.00)	1.76 (2.06)	−1.90 (1.48)	−0.97 (−0.59)	−3.88 (−1.88)	−0.17 (−1.05)
2	−2.85* (−1.43†)	3.07 (4.98†)	−1.73 (−1.01)	4.64* (0.09)	−3.37 (−1.25)	−0.20 (0.27)
3	1.38 (−0.39)	2.88 (5.88†)	−0.97 (−0.97)	−1.39* (0.01)	1.34 (0.59)	1.35* (0.11)

Measurements of the surgical accuracy of patients requiring reoperation within 1 year postoperatively. The standard deviation was calculated in a previous study of surgical accuracy in the same cohort.[11]

Abbreviation: Pt. No., patient number.

* The obtained reposition differed by more than 1 standard deviation in surgical accuracy.

† The virtual surgical plan differed by more than 1 standard deviation from the average planned reposition.

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Patient-Specific Printed Plates Improve Surgical Accuracy In Vitro

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Purpose: It remains unclear to what extent patient-specific printed plates can improve surgical outcomes in orthognathic procedures. This study aimed to quantify the surgical accuracy of patient-specific printed plates in vitro and to compare the results with patients' actual surgical outcomes.

Patients and Methods: This in vitro study enrolled 20 postoperative orthognathic surgical patients, all treated with inferior maxillary repositioning. The preoperative midfaces were re-created in a 3-dimensionally printed model. The osteotomy and screw holes were placed at prespecified positions using a 3-dimensional guide. The dental segment was repositioned by means of the patient-specific plates. The primary outcome was the mean reposition at 3 dental reference points. The primary predictor variable was the obtained surgical reposition in vitro compared with the virtual surgical plan. Confounding variables were gender, age, occlusion, and bimaxillary surgery. The secondary outcome was surgical accuracy, and the secondary predictor was the in vitro outcomes versus the patients' surgical outcomes. Surgical accuracy was defined as the difference between the obtained reposition and the virtual surgical plan on a continuous scale. The differences were recorded in 3 dimensions according to the positive value of the 3 axes: right, anterior, and posterior. The results were analyzed using mixed-model regression and 1-sample *t* tests.

Results: In the 20 patients (age, 18 to 64 years; 40% of patients were women), the mean planned reposition was 2.9 mm anterior and 1.8 mm inferior. In all models, the osteotomy edge was rounded off to position the plate in the predetermined position. Overall, the maxilla was positioned 0.5 mm anterior and 0.3 mm inferior to the planned position using patient-specific plates.

Conclusions: The patient-specific plates positioned the maxilla in close approximation to the planned position without surgically relevant differences. The osteotomy edge must be carefully inspected for interference with the patient-specific plates to avoid displacement of the planned maxillary repositioning.

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Patient-specific printed (PSP) plates offer new opportunities to potentially improve the surgical precision in orthognathic surgery. The use of PSP plates should bridge the gap between increased precision in virtual surgical planning and increased precision in the surgical outcome. Clinical case series have confirmed that clinical implementation has a high degree of precision.[1-7] However, the lack of control groups makes it impossible to evaluate to what extent PSP plates increase surgical precision.

Evaluating to what extent PSP plates increase surgical accuracy should ideally be performed in a randomized controlled trial (RCT). Unfortunately, it is impossible to determine how many patients to enroll

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to ensure sufficient power because the current literature consists of mixed directional repositioning without any control groups. Furthermore, little is still known regarding the long-term clinical impact of using PSP plates (ie, risk of fracture in the case of nightly bruxism or increased risk of infection during the first year after surgery). Therefore, it would be unethical to undertake an RCT without proper power calculations that would ensure inclusion of cohorts of adequate size. To estimate the accuracy of PSP plates, they are evaluated under in vitro conditions that mimic orthognathic patients' clinical conditions. This setup may overestimate the surgical accuracy of PSP plates, but it provides a reference for the limit of accuracy for PSP plates. Furthermore, the surgical accuracy in vitro could be compared with the patients' actual surgical outcomes to evaluate how much the surgical outcomes could be improved under ideal circumstances. Thus, it is possible to calculate power for a prospective RCT from this study, but the power calculation must incorporate the bias incurred when an in vitro study is compared with the actual surgical outcome.

When one is choosing the study cohort, technologic improvements should benefit those patients in whom the least stable and least precise procedures are planned.[8,9] Thus far, studies of printed plates have mainly focused on stable procedures, such as superior maxillary repositioning and advancement, often with variable directional movements.[1-7] Variable directional movements may mask systematic errors and make it impossible to find a suitable control group in the literature. Similar to other investigators,[8-10] our pilot study found that inferior maxillary repositioning still proposes a challenge with regard to achieving the planned surgical repositioning.[11] The maxilla was systematically placed 2 mm posterior and 0.8 mm superior to the planned position, despite 3-dimensional (3D) virtual surgical planning.[11] Thus, inferior maxillary repositioning still has potential for improvement.

The purpose of this study was to investigate to what extent PSP plates can improve the surgical outcome under ideal in vitro conditions. We hypothesized that PSP plates tested in vitro would be accurate and may be able to improve the surgical outcomes of orthognathic surgical patients undergoing unstable procedures such as inferior maxillary repositioning. A comparison of in vitro results with actual surgical outcomes must be interpreted with caution as in vitro testing is performed under idealized conditions. This study aimed to *1)* quantify the surgical accuracy of PSP plates in vitro and *2)* compare the results with the patients' actual surgical outcomes to evaluate to what extent the surgical accuracy could be improved.

Patients and Methods

To address the research purpose, we designed and implemented an in vitro study on printed models to test the surgical accuracy of PSP plates. The in vitro material included a printed reproduction of the preoperative midface and maxilla derived from orthognathic surgical patients. The study population was composed of all consecutive patients treated with inferior maxillary repositioning at the Department of Oral and Maxillofacial Surgery, Odense University Hospital, Odense, Denmark, from 2013 to 2015. The same population of patients was involved in a study evaluating surgical accuracy in inferior maxillary repositioning.[12] To be included in the study, the surgical treatment must have been planned using 3D virtual surgical planning software and preoperative and postoperative cone beam computed tomography (CBCT) scans must have been obtained. Patients were excluded if the surgeon deviated from the virtual surgical plan during surgery. Participants were treated according to the Helsinki Declaration (October 2000). The study was exempt from ethical review by the institutional review board. Participation was voluntary, and all participants provided written consent before inclusion in the study.

VARIABLES

When the surgical accuracy of PSP plates in vitro was quantified, the primary outcome was the mean maxillary reposition measured at 3 dental reference points along each of the 3 axes: right, anterior, and superior. The primary predictor variable was the comparison between the obtained maxillary reposition and the planned maxillary reposition. The following patient-specific categorical variables were recorded: gender, age, occlusion, and planned surgical repositioning (single-maxillary or bimaxillary procedure, maxillary or mandibular advancement).

When the in vitro results were compared with the patients' actual surgical outcomes, the outcome was the difference between the planned reposition and the obtained reposition, measured as the mean of the 3 dental reference points along each of the 3 axes. The primary predictor was the comparison between the in vitro surgical accuracy and the obtained surgical outcome after orthognathic surgery. The confounding variables were identical in the 2 cohorts, and therefore, the comparison was treated as pair-wise measurements in a single cohort.

VIRTUAL SURGICAL PLANNING

Virtual surgical planning was performed by a maxillofacial surgeon and a 3D Systems (Rock Hill, SC) engineer using Dolphin 3D surgery software (Dolphin

Imaging & Management Solutions, Chatsworth, CA). The virtual surgical plan was performed using the preoperative CBCT scan taken around 6 weeks preoperatively and a laser surface scan (3-Shape A/S, Copenhagen, Denmark) of the cast dental models manufactured by the orthodontist. The CBCT scan was performed on a NewTom 3G scanner (NewTom, Verona, Italy) with standard settings (field of view, 20 cm $\times$ 20 cm; 110 kV).

MANUFACTURING OF PSP PLATES

Biomedical designers and engineers at 3D Systems designed and manufactured the surgical guide according to the planned osteotomy and drill holes for the PSP plates (Figs 1, 2). The surgical guide was designed to optimize bone anchorage at screw placement, and the guide was fitted with occlusal support to ensure the osteotomy was placed at the planned level. The surgical guide was manufactured from resin by stereolithographic additive processing. The PSP plates were designed according to the movement of the maxilla with connections spanning the osteotomy (Figs 3, 4). The plates were designed with 11 screw holes: 6 superior and 5 inferior to the osteotomy. The PSP plates were manufactured using direct metal printing and post-processed by smoothing the screw holes to maximize adaptation between plates and screws.

IN VITRO SURGERY

All in vitro surgical procedures were performed by the same surgeon in a clinical setting. Initially, the model was scanned using the NewTom 3G scanner with standard patient settings as mentioned earlier. Then, the osteotomy guide was fixed to the dentition around the canine and first molar bilaterally. The holes were drilled according to the prespecified locations in the guide. The osteotomy was performed at the predetermined level using an oscillating saw. After down-

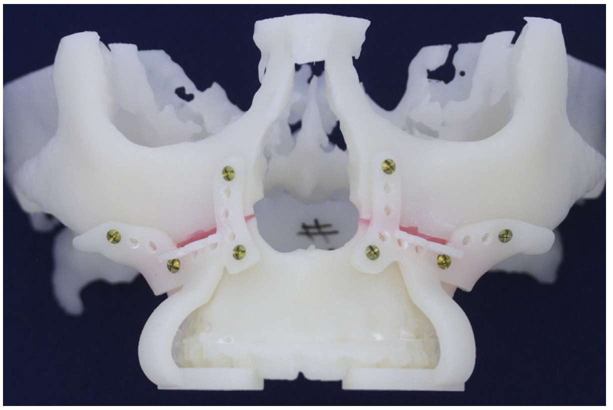

FIGURE 2. In vitro testing of osteotomy and drill guide. The drill guide is mounted with occlusal support to ensure that the osteotomy is placed at the planned level. The osteotomy is accentuated with pink wax.

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fracture of the maxilla and adaptation of the PSP plates, all models showed interference at the edge of the osteotomy in the dental segment (Fig 5). This interference was removed by rounding the upper 2 mm of the osteotomy edge with a pear-shaped hard metal burr. The PSP plates were then repositioned and fixated with 5-mm screws (Biomet 2.0 systems; Zimmer Biomet, Warsaw, IN) and controlled for adaptation to the model surface. Finally, the operated model was scanned again using standard patient settings.

DATA COLLECTION METHOD IN VITRO

The in vitro outcome was measured using a standardized semiautomatic algorithm to align the preoperative and postoperative model and position dental reference points. The 3D analysis was performed using ITK-SNAP and 3D Slicer. The complete guide for the surface-based assessment is presented in Appendix 1.

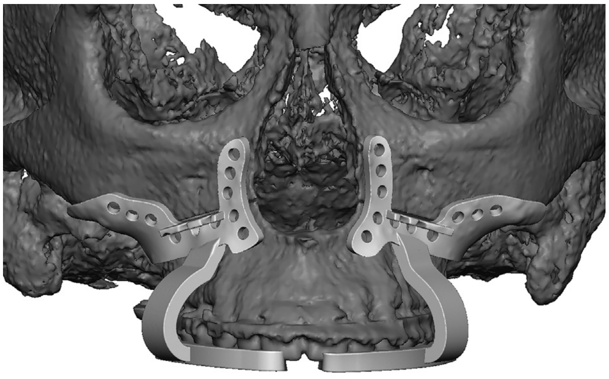

FIGURE 1. Computer-assisted designed osteotomy and drill guide.

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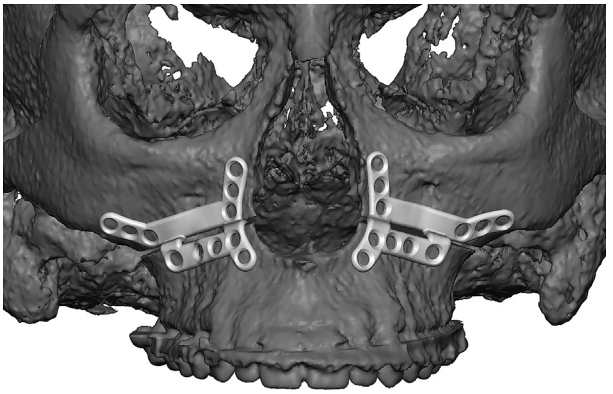

FIGURE 3. Computer-assisted designed patient-specific plates.

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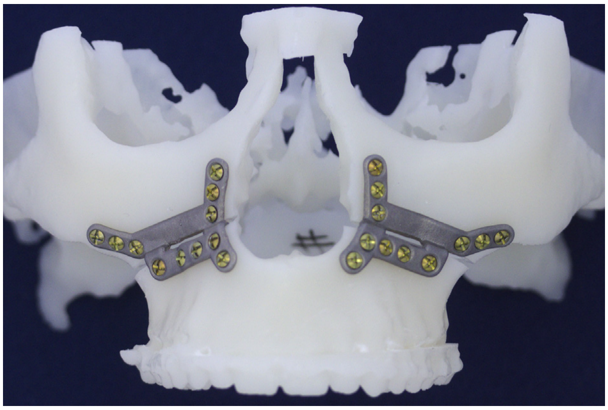

FIGURE 4. In vitro testing of patient-specific plates. The plates are mounted in prespecified drill holes to reposition the maxillary dental segment according to the virtual surgical plan.

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The preoperative model scan was aligned with the patient scan in the natural head position by aligning models of the cranial base and zygomatic arches in the 2 scans. Then, the postoperative model scan was aligned with the preoperative model scan at the cranial base. Dental reference points were inserted manually on the preoperative scan. To position the reference points identically on the postoperative scan, a copy of the preoperative maxilla was aligned with the postoperative maxilla, along with a copy of the reference points. This method was adapted from the method previously validated by us.[13]

The dental reference points were inserted at the midpoint of the incisor edge and the mesiobuccal cusps of the first molars bilaterally. The midmolar point between the first molar reference points was calculated for rotational measurements. The distance between the preoperative and postoperative reference points was measured along the 3 axes: right, anterior, and superior. The relative difference was interpreted as a measure of surgical accuracy. The absolute difference was calculated as a measure of variance to compare the results with previous findings. The clinical significance level was set at 2 mm, as proposed by previous studies of both 2-dimensional and 3D evaluations.[14-16]

Rotations were measured in degrees around each axis. The rotations were measured from the central midmolar point to a dental reference point: A positive yaw moved the incisors to the left, a positive pitch moved the central incisors superiorly, and a positive roll moved the right first molar superiorly. The clinical significance level was set at 4° for rotational measurements because differences greater than 4° can be detected by 90% of patients.[17]

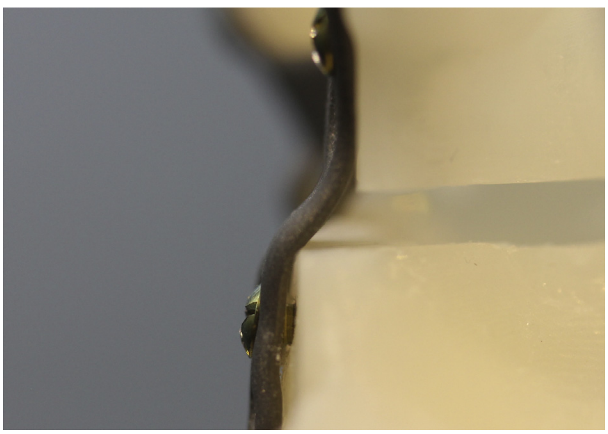

FIGURE 5. Interference between edge of osteotomy and patient-specific plate. The patient-specific plate is positioned without rounding of the osteotomy edge. The interference impedes proper positioning of the plate and may result in unintentional changes to the planned repositioning.

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DATA COLLECTION OF PATIENTS' ORTHOGNATHIC SURGICAL OUTCOMES

The in vitro results were compared with the patients' actual outcomes after orthognathic surgery. The bimaxillary surgical procedures were planned using a mandible-first approach. The maxilla was fixated by 4 L-shaped Biomet plate 2.0 systems (Zimmer Biomet). Postoperative outcomes were evaluated on CBCT scans 1 week after surgery. Analysis of the obtained surgical accuracy was performed according to the semiautomatic approach described by Stokbro and Thygesen.[13]

STATISTICS

The data were analyzed using Stata software (version 14.2; StataCorp, College Station, TX) and are presented as means and standard deviations. Normality of distribution was visualized by box plots and analyzed by the Shapiro-Wilk test. The difference between planned and obtained maxillary repositioning was analyzed by the Student t test for 1 sample. Mixed-model regression was used to accommodate multivariate analysis of the linear surgical accuracy along the 3 axes while controlling for confounding variables and evaluating their influence on statistical significance. Calculating power for future randomized clinical trials was performed by a 2-sample mean comparison and equal variances with 80% power. The significance level in all tests was defined as $P = .05$. The clinical significance level was set at 2 mm for linear measurements and 4° for rotational measurements.[14,17]

Results

The 20 patients included in this study were representative of the general orthognathic surgical population at our hospital, with 40% of patients being women and with a mean age of 28 years (range, 18 to 64 years). In addition to inferior maxillary repositioning, 95% received advancement of the maxilla (Table 1).

During model surgery, the osteotomy edges had to be reduced to achieve a close fit between the plates and the model surface. If the edge was not rounded, the plates could not adapt to the model surface, exposing approximately 1 screw thread (Fig 5). This could have caused error in repositioning the dental segment and may have had a systematic influence on the maxillary repositioning if not corrected.

Quantifying the surgical accuracy of PSP plates in vitro, we considered the measurements normally distributed despite 1 outlier along the right axis (0.85 mm). The Shapiro-Wilk test showed $P > .05$: right, $P = .058$; anterior, $P = .655$; and superior, $P = .999$. Assessment of surgical accuracy showed a difference between the planned surgical outcome and the obtained surgical outcome in model surgery along both the anterior and superior axes (Table 2). This difference indicated that the maxilla was systematically positioned 0.5 mm anterior ($P = .003$) and 0.3 mm inferior ($P = .002$) to the planned position. The relative difference was statistically significantly different from 0 mm, but the difference was not considered clinically relevant.

The rotational difference was statistically significant in pitch and roll, but the mean difference was not considered clinically different from the planned rotations (Table 2). The greatest difference from planned rotation was found in pitch, 4.0°, bordering the clinical threshold. Yaw and roll were well within the clinical threshold, −1.3° and 2.6°, respectively. The mixed-model regression analysis showed a significant correlation with surgical accuracy along the axes, indicating a correlation in the distance the maxilla was placed anterior, inferior, and slightly to the left (Table 3). No confounding factors significantly influenced the outcome—not even the magnitude of the planned reposition. Adjusting for the confounding variables did not influence the significance of the linear measurements (Table 4).

In comparing the in vitro surgical procedure with the obtained surgical outcome, the absolute difference between planned and obtained maxillary repositions showed less variance in vitro along all 3 axes (Table 5). Comparing each patient's surgical outcome with the in vitro results showed that in 11 patients, the obtained surgical outcome positioned the maxilla slightly closer to the planned position than did the PSP plates: right in 3, anterior in 5, and superior in 6. However, the orthognathic surgical procedures also produced outcomes above the 2-mm clinical threshold: anterior in 6 and superior in 4. The largest absolute difference using PSP plates in vitro was 1.46 mm.

Calculating power for a prospective randomized controlled study from the presented comparison between in vitro results and obtained surgical outcomes, we determined that the number of study participants needed is as follows: right, n = 19; anterior, n = 15; and superior, n = 17 (power = 80%, significance level = .05). This power calculation must be adjusted to account for the difference between in vitro results and what can be obtained with the actual surgical performance.

Table 1. DESCRIPTIVE COHORT ANALYSIS

	Data
Descriptive data	
Participants, N	20
Female gender, n	8
Age, yr	
Mean	28
Range	18-64
Occlusion (Angle classification), n	
Neutral (Angle Class I)	6
Distal (Angle Class II)	6
Mesial (Angle Class III)	8
Surgery, n	
Maxillary advancement	19
Additional mandibular surgery	13
Mandibular advancement	10
Mandibular setback	6

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Discussion

This study aimed to *1)* quantify the surgical accuracy of PSP plates in vitro and *2)* compare the results with the patients' actual surgical outcomes to evaluate to what extent the surgical accuracy could be improved. Quantifying the accuracy of PSP plates in vitro showed that a difference existed between the planned and obtained repositions despite favorable in vitro conditions. The maxilla was placed 0.5 mm anterior and 0.3 mm inferior to the planned position, which was statistically significant but not clinically relevant. Furthermore, these deviations were consistently in favor of a stable postoperative result, as overcorrection in inferior and anterior maxillary repositioning will probably be reduced owing to the relapse that is expected to occur over time.[11,18]

Table 2. LINEAR AND ROTATIONAL SURGICAL ACCURACY IN MAXILLARY REPOSITION OBTAINED IN MODEL SURGERY RELATIVE TO CORRESPONDING AXIS

	Mean Difference (SD)			
	Planned	Obtained	Relative Difference	*P* Value*
Linear distance, mm				
Right	0.06 (0.77)	0.15 (0.77)	0.08 (0.25)	.174
Anterior	2.93 (1.99)	3.42 (2.03)	0.48 (0.57)	.001†
Superior	−1.75 (0.85)	−2.02 (0.87)	−0.29 (0.30)	<.001†
Rotation distance, °				
Yaw	1.01 (1.48)	0.79 (1.67)	−0.22 (0.59)	.111
Pitch	−0.79 (3.32)	0.55 (3.24)	1.33 (1.46)	.001†
Roll	0.02 (1.21)	0.41 (1.02)	0.40 (0.80)	.037†

Abbreviation: SD, standard deviation.
* Student 1-sample *t* test.
† Statistically significant.

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When we compared the PSP plates with the in vitro results, the PSP plates tested in vitro showed potential for improving the surgical outcome.

Our study showed that the edge of the osteotomy in the dental segment required adjustment to secure the optimal fit of the PSP plates. The reason for interference between the plates and the osteotomy edge was retrospectively analyzed. The plates were designed with a slight bevel to decrease stress, producing an overlap of approximately 1 mm of the model. Thus, care must be taken in both design and adaptation of the plates to avoid interference that may affect the planned maxillary repositioning.

These results are comparable with those of a similar in vitro study evaluating surgical accuracy in 9 models printed from patient scans.[19] The surgical accuracy was less than 0.2 mm from our results (absolute measurements of 0.39 ± 0.30 mm for right, 0.81 ± 0.54 mm for anterior, and 0.44 ± 0.33 mm for superior). However, various directional changes

Table 3. MIXED-MODEL REGRESSION

			95% Confidence Interval	
	β	*P* Value	Lower Limit	Upper Limit
Internal correlation with anterior axis				
Superior	-0.88	.002*	-1.42	-0.33
Right	-0.46	.012*	-0.82	-0.10
Interaction with planned movement				
Anterior (baseline)	-0.02	.652	-0.12	0.07
Superior (addition to baseline)	-0.00	.966	-0.23	0.22
Right (addition to baseline)	-0.00	.965	-0.25	0.24
Female gender	-0.05	.640	-0.25	0.16
Age	-0.00	.318	-0.01	0.00
Occlusion (Angle classification)				
Distal (Angle Class II)	-0.13	.354	-0.41	0.15
Mesial (Angle Class III)	-0.06	.658	-0.34	0.22
Surgery				
Bimaxillary surgery	0.20	.193	-0.10	0.50
Constant	0.63	.004*	0.21	1.06
SD between patients	2×10^{-8}		2×10^{-13}	2×10^{-3}
SD within patients	0.38		0.32	0.45

Abbreviation: SD, standard deviation.
Note: Measurements for mixed-model regression are the difference between planned and obtained movements.
* Statistically significant.

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Table 4. LINEAR MEASUREMENTS ADJUSTED FOR CONFOUNDING VARIABLES

			95% Confidence Interval, mm	
Axes	Mean Difference, mm	*P* Value*	Lower Limit	Upper Limit
Right	0.08	.350	−0.09	0.25
Anterior	0.48	<.001†	0.31	0.65
Superior	−0.29	.001†	−0.45	−0.12

* Predictive margins with fixed proportions from mixed-model analysis. The test incorporates all covariates and evaluates whether the obtained movement is statistically different from the planned movement.
† Statistically significant.

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were planned in patients included in the study without a control group.

The clinical implementation of PSP plates showed a surgical precision resembling the results found in vitro.[6,7] Heufelder et al[6] used PSP plates in 22 patients and found surgical accuracy in absolute measurements within 0.1 mm of our results (absolute differences of 0.30 mm for right, 0.72 mm for anterior, and 0.33 mm for superior). Likewise, Li et al[7] used PSP plates in 10 patients and found surgical accuracy with a mean difference and standard deviation comparable with our results (relative value ± standard deviation of −0.18 ± 0.35 mm for mediolateral, −0.54 ± 0.53 mm for anteroposterior, and 0.33 ± 0.53 mm for superoinferior). Because both studies evaluated changes at 3 dental reference points, the results were directly comparable with our study. However, the included patient cohorts were inhomogeneous, with variable directional repositioning, and the studies included no control group. The additional 5 clinical studies of PSP plates all reported a high degree of surgical accuracy; however, the results were evaluated as surface-to-surface distances and could not be compared with our findings.[1-5]

Positioning the maxilla without an intermediate splint may eliminate an essential cause of error in orthognathic surgery. During the preoperative CBCT scan, the condyle must still be placed in centric relation to the fossa to ensure the intermediate splint transfer of the planned surgical movement. If the condyle is not properly seated in the scan, the position of the mandible will change once the patient is under general anesthesia.[20] Therefore, the mandibular position in reality may differ from the virtual surgical plan, which could alter the direction of the surgical repositioning. Hsu et al[21] reported on 3 patients in whom the surgical outcome differed by more than 4 mm from the planned position in bimaxillary surgery with treatment by a maxilla-first approach. A post hoc analysis showed the condyle was not seated in centric relation to the fossa during the preoperative scan. Sequencing the mandible first in bimaxillary surgery should eliminate this problem because the condyles are seated in centric relation before the maxilla is positioned.[20] However, Liebregts et al[22] found that the maxilla-first approach still resulted in positioning closer to the planned position, overall, compared with the mandible-first approach. By positioning the maxilla first without an intermediate splint, any errors in the centric relation during the CBCT scan become irrelevant during the maxillary positioning. Then, the mandible can be positioned in final occlusion with the condyles seated in centric relation to ensure the obtained movement is consistent with the planned movement.

The major limitation of our study is the in vitro conditions in which the surgical accuracy was evaluated. The in vitro study lacks the presence of soft tissue, which may interfere with the maxillary positioning during surgery or affect the stability of the obtained repositioning after surgery. During surgery, the surgical accuracy may be affected by interference from the

Table 5. ABSOLUTE DIFFERENCE BETWEEN PLANNED AND OBTAINED MAXILLARY POSITIONS IN ORTHOGNATHIC SURGERY AND MODEL SURGERY

	Absolute Difference, Mean (SD)		
	Model Surgery	Orthognathic Surgery	*P* Value*
Linear difference, mm			
Right	0.18 (0.19)	0.57 (0.54)	.004†
Anterior	0.61 (0.42)	1.49 (1.06)	.005†
Superior	0.35 (0.23)	1.05 (0.94)	.006†
Rotational difference, °			
Yaw	0.50 (0.38)	0.89 (0.80)	.052
Pitch	1.66 (1.05)	1.77 (1.42)	.794
Roll	0.60 (0.65)	0.94 (0.51)	.096

Abbreviation: SD, standard deviation.
* Student 1-sample *t* test.
† Statistically significant.

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buccal fat pads and the nasal septum, as well as that due to restricted surgical access. After surgery, immediate relapse may occur before the first CBCT scan at 1-week follow-up. Immediate relapse can be caused by the pull of the pharyngeal muscles, stretching of the masticatory muscles, nightly bruxism, and the position of the mandibular condyle within the glenoid fossa, which may cause posterior and superior displacement of the dental segment.[8,10] These limitations could not be avoided in the in vitro study models; therefore, the results obtained in orthognathic surgery may be biased by larger outliers or systematically affected by interference or immediate relapse. However, when the results with the surgical outcomes are compared with those in previous studies, the results align well without large outliers or differences.

The results from case series and in vitro studies cannot replace the clinical findings from randomized clinical trials, and the findings in this study should be used to ensure future RCTs are properly powered to detect differences in surgical accuracy if such differences exist. We plan to implement a prospective RCT to evaluate whether the PSP plates also improve surgical accuracy clinically.

In summary, the PSP plates positioned the maxilla in the planned position without clinically relevant differences. Care must be taken to inspect for interference between the osteotomy edge and the patient-specific plates to avoid displacement of the planned maxillary repositioning.

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Appendix 1
Guide to Quantify Surgical Repositioning in Printed Models

The algorithm for analyzing surgical repositioning in printed models used free software: ITK-SNAP and 3D Slicer. The algorithm used surface registration instead of voxel-based registration because there is no difference in voxel intensity throughout the printed model. Otherwise, the method follows the same steps as previously described.[13]

STEP 1: SEGMENTING SCAN

The scans were exported in DICOM (Digital Imaging and Communications in Medicine) format and imported into 3D Slicer. By use of the value threshold, the model was segmented. The threshold was set at −900 Hounsfield units, with −950 Hounsfield units being the threshold for air in the NewTom CBCT scanner. The labeled segmentation was exported into ITK-SNAP in GIPL (Guys Image Processing Lab) format along with the scan. In ITK-SNAP, the model was separated into 4 segments: zygomatic arches, cranial base, dentition, and midface/plated maxilla. The preoperative scan of the patient was previously segmented, so the zygomatic arches were simply labeled. All scans and labels were exported into 3D Slicer again.

STEP 2: REORIENTING MODEL TO NATURAL HEAD POSITION

The preoperative patient scan was reoriented according to the virtual surgical planning setup. The virtual surgical planning setup reorientation was provided by 3D Systems, which performed the planning session. The preoperative patient scan and labeled zygomatic arches were reoriented using the "transform" application. The labels of the zygomatic arches in all scans were used to create 3D models. The 3D models were created by the "model maker" application. The scan of the preoperative model's zygomatic arches was aligned with the preoperative patient scan's zygomatic arches. Alignment was performed with "CMF Registration > Surface registration." The patient's zygomatic arches were set as fixed, and the model's zygomatic arches were set as moving. The settings were as follows: "Rigidbody," absolute values, with 2000 iterations, 200 landmarks, and a 0.021-mm maximum distance.

The postoperative model was aligned with the preoperative model at both the cranial base and zygomatic arches. Models of the cranial base and zygomatic arches were created using "model maker." The models of the cranial base and zygomatic arches were merged by "merge models." Then, the postoperative model (moving) was aligned with the preoperative model (fixed) using "CMF registration > Surface models." The settings were the same as those previously mentioned.

STEP 3: PLACING REFERENCE POINTS IN PREOPERATIVE MODEL

Reference points were placed on the 3D preoperative model using "create-and-place fiducial." They were placed at the mesiobuccal cusps of the first molars and the middle of the incisors' edge of the 2 central incisors. The reference points were positioned on the 3D model using the "Q3DM" application. The midpoint of the central incisors was calculated automatically using "Define middle points between 2 landmarks." The midmolar point also was calculated between the first molars.

STEP 4: REFERENCE POINTS IN POSTOPERATIVE MODEL

The postoperative model's reference points must be placed identically to those of the preoperative model. Therefore, a copy of the preoperative model with reference points is aligned with the postoperative model. A copy is created by saving and reloading the preoperative dental model along with the reference points. The copied reference points must be renamed in "markups" to quantify the distance in step 5. The dental segment of the preoperative model is aligned with the postoperative model using "surface-based registration." The reference points are moved using "transform" according to the "output transform" from the surface-based registration. Thereby, the reference points in the postoperative model are placed identically to those in the preoperative model.

STEP 5: DISTANCE AND ANGLES BETWEEN PREOPERATIVE AND POSTOPERATIVE REFERENCE POINTS

The distance between the corresponding reference points is calculated using the "Q3DM" application. The rotational movements are calculated from the midmolar point to the incisor for pitch and yaw, whereas roll is calculated from the midmolar point to the left first molar. The distance and angles are exported as Excel files (Microsoft, Redmond, WA).

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Patient-specific 3D printed plates improve stability of Le Fort 1 osteotomies in vitro

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ABSTRACT

Purpose: Selective laser melting used to manufacture patient-specific 3D-printed (PSP) plates is a delicate process, which may introduce weakened areas in the plates, with risk of fracture. This in vitro study's purpose was to test the ability of PSP plates to stabilize Le Fort I osteotomies compared with manually adapted stock plates. The study's objectives were to measure the force needed to compress the osteotomy and evaluate whether the PSP plates would break during compression.
Materials and methods: This controlled in vitro study evaluated the maxillary stability using the clinical data from 7 patients. The virtually planned maxillary reposition was 3D-printed in 2 copies, and the osteotomy gap was fixated by either PSP plates or stock plates. The models were compressed until the Le Fort I osteotomy gap was eliminated. The primary outcome was the force needed to compress the model. The primary predictor variable was a comparison between PSP and stock plates. Secondary outcome measurements were the slope of elastic modulus, yield point, and force needed for 2 mm compression. Statistical testing was performed by Wilcoxon signed-rank test with significance level at $P \leq 0.05$.
Results: The PSP plates performed better than stock plates in all outcome measurements. None of the plates broke during compression despite forces of more than 4000 N. The first point of failure in PSP plates was the first screw cranial to the osteotomy. In comparison, the first point of failure in stock plates was in the plates' bend at the osteotomy.
Conclusion: In this in vitro setup, the Le Fort I osteotomies fixated with PSP plates were more stable than the osteotomies fixated with conventional stock plates. No adverse effects occurred during testing of PSP plates; thus, PSP plates seem to be a safe alternative to stock plates and may even be preferable.

1. Introduction

Patient-specific 3D-printed (PSP) plates are matched to the patient's unique bony contour, and they are designed to incorporate the virtual surgically planned repositioning of the maxilla. The PSP plates can be used in combination with osteotomy and drill guides to position the maxilla with a high degree of surgical accuracy without the need for intermaxillary splints (Gander et al., 2015; Heufelder et al., 2017; Stokbro et al., 2018). Despite PSP plates being commercially available for clinical implementation (Gander et al., 2015; Mazzoni et al., 2015; Brunso et al., 2016; Kraeima et al., 2016; Suojanen et al., 2016; Heufelder et al., 2017; Li et al., 2017), no one has evaluated the mechanical properties of PSP plates for orthognathic surgery.

Manufacturing PSP plates is an advanced process involving metal-on-metal apposition at high temperatures. Metal-on-metal apposition can be performed by selective laser melting (SLM), where a laser beam is used to sinter layers of metal powder to bind the metal together in 3D additive manufactured plates. Printed

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metal plates are more rigid than conventional plates, but if not handled correctly, the manufacturing process may introduce areas with reduced resistance to fracture (Liu et al., 2014; Szykiedans and Credo, 2016). Therefore, the authors were concerned as to whether the plates would break in patients with excessive bite force, such as in nightly bruxism.

In vitro testing of plates is usually performed on solid blocks of polyurethane (Lauria et al., 2016) or polyurethane models with thick bony walls (Araujo et al., 2001; Esen et al., 2016); however, this does not reflect the variable anatomical differences encountered in patients with growth deviations of the jaws. Therefore, this study was performed on duplicate sets of models printed from patients' 3D scans to simulate clinical conditions in orthognathic patients. Thereby, the performance could be directly compared between PSP plates and manually adapted stock plates.

The primary purpose of this study was to test the ability of PSP plates to withstand compression, compared to manually adapted stock plates on printed models derived from patients previously treated with inferior maxillary repositioning. The secondary purpose was to evaluate whether PSP plates would break during compression. The authors hypothesized that PSP plates would be more stable, but were unsure whether some of the plates might break under excessive pressure. This study measures the force needed to compress the model segments until the osteotomy gap was eliminated and to describe the first point of failure or breakage in both PSP and stock plates.

2. Material and methods

To test the study hypothesis, the authors implemented a prospective, controlled in vitro study on 3D models printed from patients' virtual surgical plans. These plans were obtained from a published study evaluating the precision of patient-specific plates in inferior maxillary repositioning (Stokbro and Thygesen, 2018; Stokbro et al., 2018). Power calculations were performed based on the first study (force at 2 mm: PSP plates − stock plates = 1413 N) calculated with twice the normal standard deviation for manually bended plates (100 N) (Lauria et al., 2016); with a significance level of 0.05 and power of 80%, the participant number was calculated to 2 sets of models. To adequately test and describe the clinical behavior of the PSP plates, data from 7 participants were enrolled. The participants with the largest osteotomy gaps were selected for inclusion in the study. Participants were treated according to the Declaration of Helsinki (October 2000). The study was exempt from ethical review by the institutional review board.

2.1. Study setup

Two identical 3D models were created from the midface of the 7 orthognathic patients.

The midface from the inferior orbital margin to the enamel–cementum junction of the teeth was recreated from the virtual surgical plan, exported from Dolphin 3D surgery (Dolphin Imaging and Management, Chatsworth, CA). The independent STL models were appended in Autodesk MeshMixer (Autodesk Inc., San Rafael, CA) to fixate the osteotomy gap and planned reposition of the dental segments. A disc was added to the midface to ensure that the right and left side would not move independently, and to calibrate the model height at 46 mm in all models.

The midface models were printed by fused deposition modeling using Stratasys uPrint (Stratasys Ltd., Eden Prairie, MN), with standard print settings: 0.254 mm layer height, sparse filled, high density models and smart support material. Models were printed in acrylonitrile-butadiene-styrene (ABS) material with soluble support material. The midface models were printed in a supine position to enable plate adaptation with the models still fixed by support material. Thereby, the PSP plates and the conventional plates were adapted to identical clinical situations. After the plates were adapted, the holes were predrilled and the support material dissolved, which created 2 independently moveable parts separated by the osteotomy gap. The PSP plates were mounted and fixated by 5 mm Biomet 2-0 screws (Zimmer Biomet Corp., Warsaw, IN) in the predrilled holes. The conventional plates were mounted and fixated by 5-mm screws, 2.0 Leibinger system (Stryker-Leibinger, Freiburg, Germany) (Fig. 1).

The PSP plates used for testing were manufactured by biomedical designers and engineers at 3D systems (3D systems, Rock Hill, SC). The PSP plates were designed with 11 screw holes: 6 superior and 5 inferior to the osteotomy. The plates were designed with 3 connections across the osteotomy gap, each with a thickness of 1.2 mm and a width of 5.2 mm. The PSP plates were manufactured in Ti64Al4V material by direct metal printing and post-processed by smoothing the surface and countersinking the screwhead to maximize adaptation between plate and screws. The control group was bilaterally fitted with 2 Leibinger 2.0 stock plates (Stryker-Leibinger, Freiburg, Germany), manufactured in grade 2 titanium. The intermediate section, spanning across the osteotomy gap, had a thickness of 1.0 mm and width of 2.4 mm. All plates were manually adapted by the same investigator. Careful measurements and markings were used to avoid the need for repeated or excessive bending of the plates during adaptation. The conventional plates were chosen with the smallest separator in the intermediate section without placing the bend directly in the screw hole.

Compression testing was performed in a Zwick Roell Z050 testing machine (Zwick Roell, Ulm, Germany). The lower compression plate was a fixed plane, and the upper compression plate was secured with a ball joint able to rotate freely, thereby allowing for asymmetrical deformation. Compression was performed with a preload of 50 N, after which compression force and displacement were recorded. Testing was performed by compressing the model 2 mm per minute, while recording the force needed to compress the model. The test was terminated when the plates failed or the osteotomy gap had completely disappeared.

2.1.1. Variables and measurements

The primary outcome measurement was the force needed to compress the model. The primary predictor variable was a comparison between PSP plates and the stock plates. Secondary outcomes were the elastic modulus of the combined setup (model, screws, and plates), along with the force at the yield point and force needed to compress the model 2 mm. Since all measurements were compared on identical sets of models, no other confounding variables were evaluated.

All tests were plotted with the compression in millimeters along the x-axis and force (Newton) needed to compress the model along the y-axis. The yield point was calculated as a 0.2% offset from the E-modulus along the displacement axis; because all models were printed at 46 mm height, this was rounded up to 0.1 mm offset.

2.1.2. Statistical analysis

Analysis of the data was performed by STATA 15.0 (STATA Corp., College Station, TX).

Measurements were treated as non-parametric measurements because of the limited number of observations. All measurements were presented by a median and range. The slope of the elastic modulus was calculated by linear regression of the steepest slope on the graphs. Comparison of outcome was performed using Wilcoxon signed-rank test. The statistical significance level was set at $P \leq 0.05$.

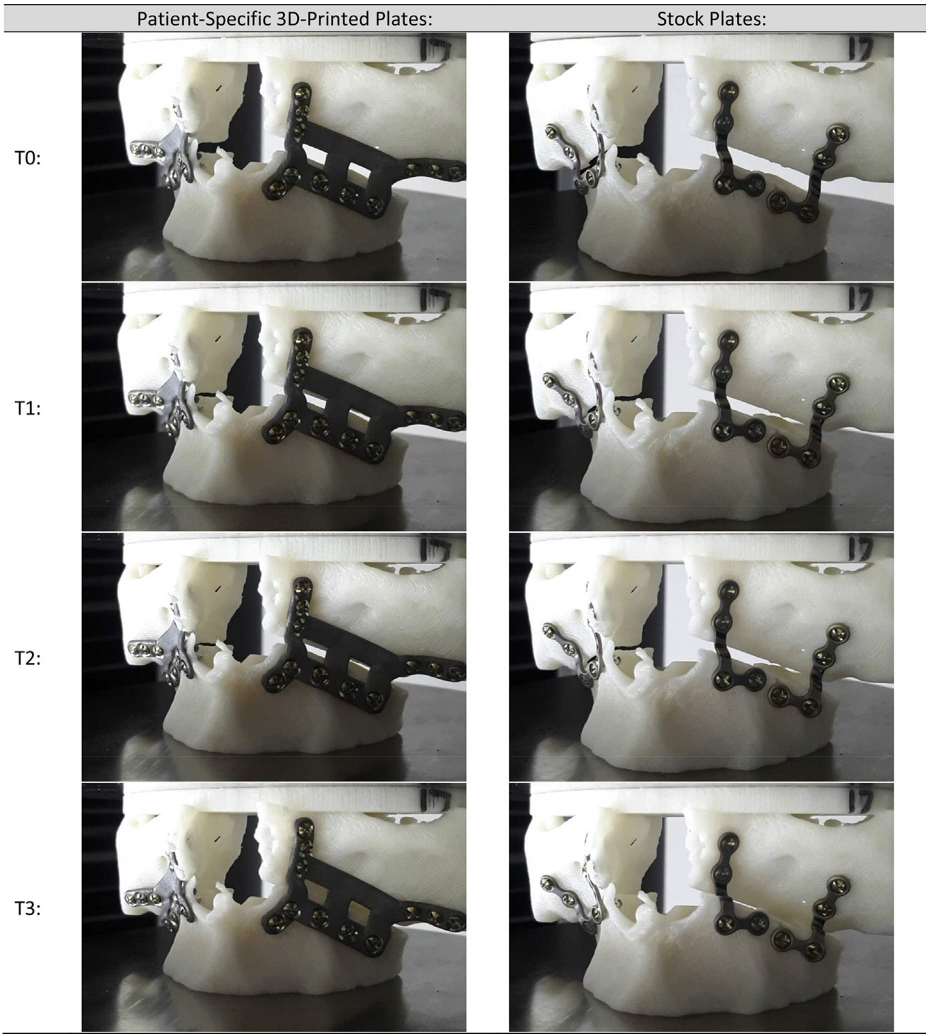

Fig. 1. Phases during test 5. T0: Pretest before load. T1: Preload of 50 N. T2: Yield point; PSP plate 2708 N, stock plate 576 N. T3: Compression with elimination of osteotomy gap: PSP plate 3034 N, stock plate 1071 N.

3. Results

The planned maxillary repositions all included down grafts and advancements of 1.0–6.9 mm (Table 1). Two patients were planned with asymmetric repositioning with more than 1 mm difference between the right and left osteotomy gaps.

Table 1
Descriptive cohort analysis.

Test	Maxillary reposition			Osteotomy gap				Conventional plate size			
	Advance	Inferior	Asymmetry	Right		Left		Right		Left	
	(mm)	(mm)		Z	P	P	Z	Z	P	P	Z
1	2.9	−2.9		2.5	2.5	2.5	2.5	M	M	M	M
2	3.5	−3.1		3.3	3.4	2.8	2.7	L	L	L	L
3	3.7	−2.5		2.4	2.3	2.5	2.9	M	L	L	M
4	1.0	−3.6		4.4	2.5	2.9	5.1	M	M	M	M
5	6.9	−2.6	Yes	2.2	2.1	1.6	3.2	M	M	L	L
6	1.0	−2.1		1.7	2.6	2.2	1.2	R	M	M	R
7	3.4	−3.1	Yes	0.8	2.0	3.2	2.9	M	L	L	M

Z = zygomatic buttress; P = piriform rim; L = long intermediate section; M = medium intermediate section; R = regular intermediate section.

Overall, the PSP plates performed better than the conventional plates (Fig. 2). In all instances, the PSP plates resisted more force before the osteotomy gap was eliminated and needed more force to compress the models 2 mm (Tables 2 and 3). Likewise, the PSP plates had higher elastic modulus and higher yield points in six of the tests. Despite forces of more than 4000 N, none of the PSP plates broke during compression.

Qualitative analysis of the plates revealed a shift in the first point of failure when PSP plates were tested (Fig. 1). Following the yield point, the first point of failure in stock plates was in the plates' bend closest to the dental segment. The first point of failure in PSP plates was loosening of the screws and/or fracture in the anatomic model. During the preloading of 50 N, the screws would settle and rotate slightly away from the osteotomy (T1). Then, force was applied during the elastic phase of the compression until the yield point (T2). During the elastic phase, the model would be slightly compressed, but without breakage or damage. After the yield point, the models would break at the screw points or the screws would become loose (T3). The first screw cranially to the osteotomy was the first point of failure. The investigators were surprised by how much the osteotomy gap was compressed in some models during the preload of 50 N.

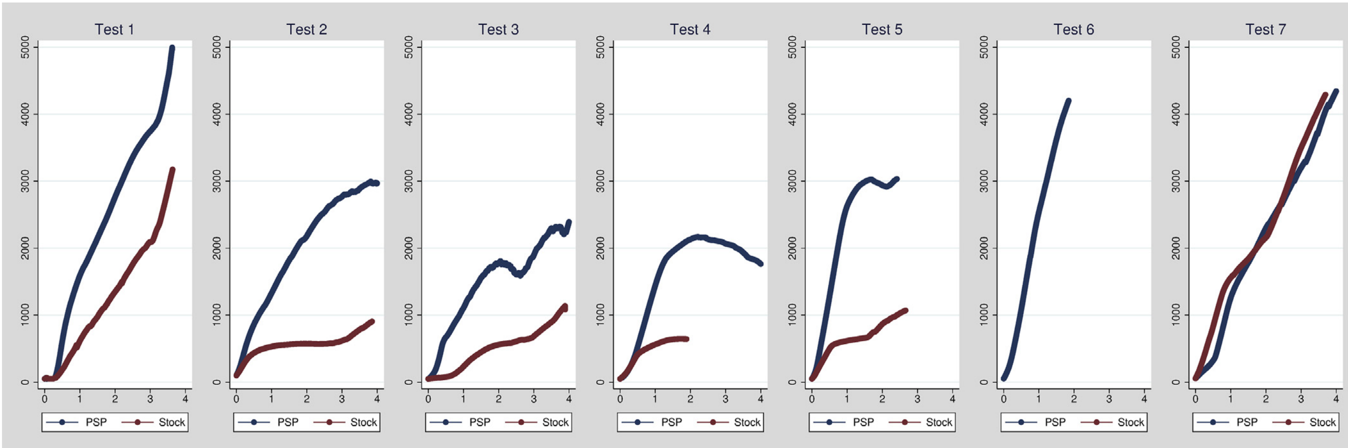

Fig. 2. Compression forces for plate displacement. Force (N) needed to compress the model is measured along the *y*-axis. Compression (mm) of the osteotomy gap is measured along the *x*-axis). Each test corresponds to one patient's midface, printed in duplicate model sets, and the osteotomy gap was fixated by either PSP plates or stock plates. In test 6, the osteotomy gap fixated with stock plates was compressed completely during the preload of 50 N. PSP = patient-specific 3D-printed plates. Stock = manually adapted stock plates.

Table 2
Force needed to eliminate the osteotomy gap.

	Median	(Range)	*P* value[a]
Patient-specific plates	3047	(1171–4966)	
Conventional plates	1133	(50–4292)	
Difference	1318	(146–2002)	0.018

[a] Wilcoxon signed-rank test.

The outliers in the conventional test groups showed large variation. In test 6, the conventional plates yielded during the initial preloading, and the osteotomy gap was compressed at 50 N. Likewise, in test 1, the posterior plates yielded during the preload, while the anterior plates still supported the osteotomy gap. In test 7, the osteotomy gap was asymmetrical and the right side was compressed during the preload, prior to the left. The details of each test and additional clinical photos are supplied in Appendix 1, along with photos of each plate's performance during each of the test phases T1 to T3.

4. Discussion

This study primarily tested the ability of PSP plates to withstand compression compared to manually adapted stock plates, on printed models derived from patients previously treated with inferior maxillary repositioning. Secondarily, the study evaluated whether PSP plates would break during compression. The study showed that PSP plates were stiffer with higher yield points than conventional plates. The first point of failure in stock plates was in the plates' bend closest to the dental segment. The first point of failure in PSP plates was screw loosening, primarily the first screw in the cranial part of the model. None of the PSP plates fractured despite compression forces of up to 4000 N.

No other study has evaluated the maximum forces needed to compress and deform PSP plates in orthognathic surgery. A study of orthopedic PSP plates, evaluating 3.5 mm anterior clavicle plates, found two to three times greater mechanical properties of PSP plates compared with stock plates (bending stiffness, bending strength, and bending structural stiffness) (Liu et al., 2014). Although a straight 3.5 orthopedic plate does not correspond to a bent 2.0 orthognathic plate, the mechanical properties of printed plates compared with stock plates seem similar between the two studies. However, it cannot be concluded from this study that PSP plates are more rigid than conventional, stock plates, as the dimensions and design of the plates differed significantly between the plates.

The mechanical properties of conventional stock plates have been tested in vitro and are better understood. Manually adapted stock plates are reported to fail between 534 and 1145 N (8 mm linear advancement) (Araujo et al., 2001), which matched the yield point in this study's control group. In vitro tests with a cleft palate found that 2 L plates bilaterally would yield after compression of more than 210 N (7 mm advancement, 3 mm osteotomy gap) (Esen et al., 2016). Stock plates yield points were also correlated with the degree of maxillary advancement, and an occlusal force of 250 N was above the yield point in 6 and 9 mm linear advancement (Huang et al., 2016). In this study, no correlation was seen between advancement and yield point; however, multiple confounding factors may have masked such a correlation.

There may be several reasons for the increased strength in PSP plates: the printed metal is stiffer, and since the plates do not need manual adaptation, the plates could be printed as a 1-piece, tripod-curved plate with connections twice as wide as the stock plates.

Table 3
Testing difference between patient-specific 3D-printed plates and manually adapted stock plates.

	Patient-specific plates		Stock plates		*P* value[a]
	Median	(range)	Median	(Range)	
2-mm Displacement (N)	2299	(1779–4318)	637	(559–3205)	0.028
E-modulus (N/mm)	2119	(922–3042)	828	(487–2254)	0.018
Yield point (E + 0.1 mm)	1518	(759–3376)	538	(444–2416)	0.018

N = Newton; E = elastic.
[a] Wilcoxon signed-rank test.

Furthermore, the number of screws increased from 16 to 22, and the screws were placed in maximum bone thickness by design. Especially the number of screws and the placement in maximum bone thickness are critical factors because these are considered to be the first points of failure in PSP plates. A screw's pull-out strength increases by 250 N per millimeter of maxillary cortical bone thickness in 2.0 screws (Shelton and Loukota, 1996). To increase stability at the first point of failure, additional fixation could be obtained by either an additional screw or a larger screw diameter cranial to the osteotomy (Nagasao et al., 2007; Shelton and Loukota, 1996).

Screw pull-out strength in orthognathic patients may be greater than in the in-vitro test. In finite element modeling, the elastic modulus of 3D printed ABS is 1.35 GPa (Poisson ratio 0.33) (Huang et al., 2016), while the elastic modulus of bone is 1.85–14.8 GPa (cancellous–cortical, Poisson ratio 0.30) (Erkmen et al., 2009). Because pull-out strength is greater in bone than in ABS, this study may have underestimated the in vivo strength of the PSP plates. Increased pull-out strength should affect only the group fixated by PSP plates because the conventional stock plates yielded in the plates without screw loosening. Increased screw pull-out strength should increase the overall stability in patients in whom the osteotomy gap is fixated by PSP plates. This increased resistance is probably of no clinical importance, because the forces used in the test far exceeded clinical occlusal forces, even in patients with nightly bruxism (8–900 N) (Nishigawa et al., 2001). However, this study evaluated only linear increasing compression and does not represent the physiological complexity of masticatory forces in chewing and bruxism. Therefore, the results should be interpreted with some restriction, as the masticatory forces may lead to different results from the forces applied in this study.

The limitation of this study is the test setup, which combines the strengths and weaknesses of the plates, screws, and model. Therefore, the elastic modulus does not reflect a single material, but the combined setup with interaction among plates, screws, and model. Thus, the results are presented as load force and are not converted into standardized Young's modulus or mechanical stress loads. However, this study setup may represent the dynamics of orthognathic surgery more closely, where the first point of failure is the crucial event. Therefore, we considered it an important observation that the first point of failure shifted from within the plates to the first screws above the osteotomy and at higher yield points.

The strength of this study is the direct comparison between conventional plates and PSP plates under clinically simulated conditions. This study provides qualitative and quantitative analysis of the first point of failure, the yield point, and the pressure needed to deflect the plates 2 mm. This information is clinically useful in evaluating the cost–benefit trade-off of new plates under challenging, clinical conditions. The clinical perspectives of PSP plates should be kept in mind during the clinical decision process in which the individual patient's clinical challenges are considered. The PSP plates should be advantageous when additional support is needed (i.e., inferior repositions, large advancements, or segmental procedures) or in challenging biological conditions (i.e., eggshell-thin maxillary bone). Thus, this study supports clinical implementation of PSP plates in selected patients.

5. Conclusion

In this in vitro setup, the Le Fort I osteotomies fixated with custom-designed PSP plates were more stable than the Le Fort I osteotomies fixated with conventional stock plates. No adverse effects occurred during testing of PSP plates; thus, PSP plates seem to be a safe alternative to stock plates and may even be preferable due to the possibility of designing increased mechanical strength in the plates.

Conflicts of interest

The authors declare that they have no conflicts of interest in regards to this work.

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This study was supported by grants from the Region of Southern Denmark (16/13511) and the University of Southern Denmark. The patient-specific 3D-printed plates were provided by 3D Systems at a reduced cost, covering the manufacturing expenses of the plates. 3D Systems did not influence the setup, test, analysis, or interpretation of the study in any way. All materials were provided and paid for by the Department of Oral and Maxillofacial Surgery, Odense University Hospital, Denmark.

Ethical approval

This study was exempt from ethical approval due to the retrospective nature of the study without direct involvement or influence on patients.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcms.2018.12.015.

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