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

Short title: DOES SEQUENCING AFFECT SURGICAL ACCURACY?

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Abstract

Introduction: 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.

Methods: The investigators performed a retrospective investigation on a cohort compiled from 3 published, retrospective studies. The sample was composed of patients treated at Radboud University Nijmegen Medical Center from 2010 to 2014 and Odense University Hospital from 2011 to 2015. The inclusion criterion was bimaxillary surgery without maxillary segmentation. The exclusion criterion was the 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 counter clockwise (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 females, mean age 28 years). Operating on the mandible first significantly influenced maxillary positioning and placed the maxilla 1.5 mm posterior and with 1.4 degrees of CCW rotation compared to virtual surgical planning. The surgical sequence interaction with maxillary rotation showed similar surgical accuracy between maxilla-first with clockwise rotation and mandible-first with CCW rotation. Inferior maxillary repositioning resulted in the maxilla being placed 1.7 mm (maxilla-first) and 2.0 mm (mandible-first) posterior to the planned position.
Conclusion: Surgical accuracy was significantly influenced by the 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.
Introduction

At present, the surgeon’s preference dictates whether the mandible or maxillary 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 semi-adjustable articulators\(^2\text{--}^5\). With 3-dimensional (3D) virtual surgical planning (VSP), the old dogmas must be reevaluated as previous strengths and weaknesses may no longer be relevant\(^6\text{,}^7\). Surgeons may 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. Thereby, the desired maxillary position may 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\(^2\text{--}^4\text{,}^8\text{,}^9\). In theory, the surgical splint design should provide advantages with regard to sequencing the mandible or maxilla first, depending on the rotation of the maxilla-mandibular-complex. Clockwise (CW) rotation is believed to be more accurate using the maxilla-first approach, while counter clockwise (CCW) rotation should be more accurate using the mandible-first approach\(^4\text{,}^5\). However, only 3 studies have compared the 2 sequences in large cohort studies, and none have evaluated how CW or CCW rotation influence the clinical outcome when the mandible or maxilla is sequenced first\(^1\text{,}^10\text{--}^12\).

Unstable procedures such as inferior maxillary repositioning also affect the clinical outcome, and may cause the maxilla to be placed 1 to 2 mm posterior to the planned position\(^13\text{,}^14\). 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 surgical accuracy of sequencing the mandible or maxilla first in inferior maxillary repositioning$^{16}$.

While 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 fixed reference pin may 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 planned compared with use of 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 seeks to address the following research questions:

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

To address the research questions, the authors implemented a retrospective study using the combined clinical data from 3 published, retrospective studies\textsuperscript{10,19,20}. The cohorts were derived from populations of patients treated in the Department of Oral and Maxillofacial Surgery, Radboud University Nijmegen Medical Center (Nijmegen, the Netherlands), and in the Department of Oral and Maxillofacial Surgery, Odense University Hospital (Odense, Denmark). The studies could be combined because the data were measured by comparable protocols; however, the cohorts’ inclusion and exclusion criteria differed between the studies. Study 1 (Nijmegen) analyzed 116 consecutive patients treated with bimaxillary procedures without maxillary segmentation from 2010 to 2014\textsuperscript{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\textsuperscript{19}. Study 3 (Odense) analyzed 20 consecutive patients treated with inferior maxillary repositioning, mono- or bimaxillary procedure from 2013 to 2015\textsuperscript{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 the virtual surgical plan in the dataset. This study was exempt from ethical approval due to its retrospective nature. Participants and data were treated in accordance with the Declaration of Helsinki.

VARIABLES
The primary outcome variable was the difference between the planned and the obtained surgical repositioning of the maxilla. The primary predictor variable was the 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, sex.

VIRTUAL SURGICAL PLANNING AND ORTHOGNATHIC SURGERY

Cone beam computed tomography (CBCT) scans were 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, the VSP was performed in house using Maxilim-software (Medicim NV, Mechelen, Belgium); in Odense, VSP was performed in collaboration with 3D systems (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 following 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 assure that the preoperative conditions agreed with the VSP. The vertical height was controlled by calipers,
measuring from a bony anchored nasion reference pin (Nijmegen) or from the right medial canthal ligament (Odense). The mandible was bilaterally fixated by 3 bicortical screws (Biomet 2.0, Zimmer corp., Warsaw, IN, USA) (Odense) or 1 miniplate fixated by 4 monocortical screws (Champy 2.0, KLS Martin, Tuttlingen, Germany) (Nijmegen). The maxilla was fixated by 4 miniplates: in Nijmegen, 1.5 KLS Martin (KLS Martin, Tuttlingen, Germany), and in Odense, 2.0 Biomet (Zimmer corp., Warsaw, IN, USA). Local reposition 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 2010–12 to operating on the maxilla first in 2013–14. In the Odense cohort, the mandible was always operated on first.

OUTCOME MEASUREMENTS

Measurements were performed according to previously validated software algorithms: The OrthoGnathicAnalyser (Nijmegen)\textsuperscript{21} and a semi-automatic algorithm using 3D Slicer (Odense)\textsuperscript{22}. Both 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 (UCI). 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 centroid point was calculated as the mean of 3 dental reference points: the top of the mesiobuccal cusp on the first molar on each side (M6R and M6L) and the UCI\textsuperscript{23,24}. A positive yaw moved UCI to the left relative to the C point. A positive pitch moved UCI superior to the C point. A positive roll moved M6R superior to the C point (Fig. 1).

STATISTICS

Data were analyzed using STATA 15.1 (STATA Corp Lt, College Station, TX, USA). The descriptive variables were analyzed by chi-squared test, one-way ANOVA analysis 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 3 axes in the same patient. Therefore, the data were treated as clustered to allow for fixed and random effects both within and between the patients. A linear mixed model was built by treating the outcome in 3 axes as repeated measurements within the same patient, and therefore, they were all influenced by the patient’s response to the confounding and hypothesis-generating variables. All hypotheses generating variables and confounding variable were included in the final model. Thereby, the linear mixed model analysis could be performed to accommodate the multilevel analysis of the individuals and simultaneously adjusting for the confounding variables. If the mixed model regression was significant for predictor variables, the data were further explored; differences within groups were analyzed by Student’s 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 $P \leq 0.05$. Clinical significance was defined by the authors as differences in mean of more than 1 mm and...
rotations of more than 2 degrees, which indicates consistent unidirectional inaccuracies that are large enough to be addressed clinically by the surgeons.
Results

Of the 166 patients considered for this study, data in 145 patients could be included (Fig. 2). The total sample size was 145 participants, with 68% females and 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 significantly between the 2 study centers. The planned pitch was more negative in the maxilla-first group, and more CCW rotation of the maxilla was planned in this group.

Incorporating all 3 hypotheses into 1 global, statistical model revealed that both surgical sequencing and inferior maxillary repositioning significantly influenced surgical accuracy (Table 2). The mixed model regression showed the VSP had a significant 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 15–34% of the difference in surgical accuracy (Appendix 1). 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 significant correlation in the mixed model regression (Appendix 2). Both surgical sequencing and inferior maxillary repositioning significantly influenced surgical accuracy, but counter clockwise rotation did not significantly influence surgical accuracy. However, to further analyze the influence on surgical accuracy all 3 hypothesis variables were further explored.
Testing the primary hypothesis, there was a significant difference between maxilla-first and mandible-first sequencing along the right and anterior axis and a difference in pitch as well (Table 3). Operating on the mandible first placed the maxilla posterior with an 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 mm to 2.6 mm. The posterior positioning in the mandible-first sequencing 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). The CCW rotation in maxilla-first sequencing positioned the maxilla 1.3 mm anterior to the planned position. In contrast, the 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 significantly influenced surgical accuracy. In inferior maxillary repositioning, the maxilla was positioned 1.7 mm (maxilla-first) to 2.0 mm (mandible-first) posterior to the planned position, which was statistically significant, regardless of whether the mandible or 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, while the mandible-first placed the maxilla 0.9 mm posterior to the
planned position. The difference between the 2 sequences in superior maxillary repositioning was statistically significant.

The interaction between the 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**

Finally, the vertical surgical accuracy was not influenced by using the medial canthal ligament (Odense) compared with using an external fixed reference pin (Nijmegen).

Comparing the planned, obtained and surgical accuracy in the vertical axes showed no significant difference between the 2 methods (Table 6). Visualizing the surgical accuracy for each patient according to planned vertical reposition showed that the medial canthal ligament group was nested within the external fixed reference pin group (Figure 6, appendix 3). 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) The overall surgical accuracy was affected by the maxillary/mandibular sequencing. The maxilla-first sequencing was centered closer around the planned reposition than the mandibular-first, while the mandible-first approach resulted in significant 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 significantly influenced by the sequencing. However, the procedures appeared to be more accurate for CCW rotation when the mandible was operated on first and for CW rotations 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 significant difference in vertical accuracy using the medial canthal ligament compared with 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, since 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 in the preoperative scan, the condyles will reposition into centric relation when the patient is under general anesthesia, thereby, changing the position of the mandible. If the maxilla is positioned against the unoperated mandible, an incorrect seating during the preoperative
scan may cause the maxilla to be placed posterior to the planned position\textsuperscript{24}. But the clinical
data did not support all the 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/CCW rotation of the maxilla-mandibular-complex or superior/inferior
maxillary repositioning was performed.

\textbf{Maxillary rotation}

Rotation of the maxilla-mandibular-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\textsuperscript{4,5}. Choosing
the maxilla-first sequence in association with CCW rotation placed the maxilla significantly
anterior to the planned position, while 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, this difference in surgical accuracy should
be addressed in the VSP to achieve the desired maxillary position.

\textbf{Inferior maxillary repositioning}

Inferior maxillary repositioning is known to be 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) to 2.0 mm (mandible-first) 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, additional maxillary advancement could be beneficial to the patient and should be considered in the final VSP.

Adjusting the virtual surgical plan

Adjusting for the discrepancies between VSP and clinical outcome should be performed for either CW/CCW rotation or inferior maxillary reposition but not for both. As these discrepancies stem from the same cohort, adjusting for both rotation or inferior reposition would adjust the patient’s discrepancy twice. The interaction between the sequencing, rotation and inferior maxillary repositioning could not be further analyzed in this study as only 3 patients were operated on using inferior maxillary repositioning, CCW rotation and maxilla-first sequence. Thus, surgeons must choose to adjust the VSP according to either 

Possible explanations for the posterior maxillary position

The mechanisms that caused this posterior maxillary position were not evaluated, as 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 reposition, the maxilla was placed posteriorly independent of whether the mandible or maxilla was operated on first. Furthermore, the
superior maxillary repositioning was placed more anteriorly compared to the inferior maxillary repositioning.

The authors believe that the posterior position in inferior maxillary repositioning may be caused by immediate relapse either intraoperatively due to additional compression of the temporomandibular joint or postoperatively due to settling of the osteosynthesis material during the subsequent Le Fort 1 operation. Furthermore, in superior maxillary repositioning, the maxilla may 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, while the maxilla will be positioned anterior to the mandibular position when the mandible is operated on first. However, we 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. This study’s result of 0.3 mm difference between the planned and obtained outcome was in accordance with the findings in 2D lateral cephalometric tracings and was considered well within the acceptable limits. Likewise, visualizing each patient’s vertical
surgical accuracy, plotted against the planned reposition, showed the medial canthal
ligament patients matched outcomes in the external reference pin patients. 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)\(^\text{10}\), only 2 retrospective cohort studies have
previously evaluated the surgical accuracy in the maxilla-first versus the mandible-first
approach\(^\text{11,12}\). Both studies were planned with plaster cast models in a semi-adjustable
articulator, and the outcome was evaluated on lateral cephalometric tracings. Salmen et
al.\(^\text{11}\) found a difference between the groups \((N = 16 \text{ patients/group})\) in the vertical direction
but not in the horizontal direction\(^\text{11}\). 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 significant. 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 significant. In contrast, this study found a significant
horizontal difference between the sequences, while there was no significant vertical
difference. The study by Ritto et al.\(^\text{12}\) found no significant 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 \((N = 20 \text{ patients/group})\). Thus, the results from this
study do not reflect the results found in the literature. The difference between this study’s
results and the literature may have several causes. The surgery was planned using VSP,
which enables accurate placement of the condylar positioning along with accurate occlusal plane re-creation. The outcome was measured in 3D with improved measurement tools with a reproducibility of less than 0.3 mm\textsuperscript{21,22}, while the measurement reproducibility for cephalometric tracing was between 0.46 to 1.68 mm\textsuperscript{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**

There remains a number of limitations and unanswered questions regarding the potential benefits of sequencing the mandible first. This study focuses 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 since 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. Thereby, 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 may not be evaluated sufficiently by CBCT scans but may be addressed more accurately by intraoral scans of the postoperative occlusion instead.

Future studies may wish to address whether interactions occurred between inferior maxillary repositioning and CCW rotation. There may also exist a threshold with which the benefit of the appropriate sequence becomes more obvious. In this study, the inferior reposition and CCW rotation were only measured overall, including both minor and major repositions in one outcome, without interactions and detailed subgroup analysis. Combining
additional future studies into a larger cohort analysis may 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 may mask potential benefits of the appropriate sequencing in bimaxillary procedures.

Finally, this study relies on 3D printed splints to position the moving segments. Although computer-aided designed and manufactured splints accurately fit and reposition the moving segments, the looseness of the TMJ may affect the surgical accuracy and position of the segments. 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 may improve the surgical accuracy. However, the clinical benefit of waferless maxillary positioning must also 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 the subgroup of patients treated with inferior maxillary repositioning was positioned posterior to the planned position in both the mandible-first and the maxilla-first approach. This posterior discrepancy should be addressed by additional advancement in the VSP to position the maxilla closer to the planned position. Thus, both sequences may
achieve closer adherence to the desired maxillary position by adjusting the VSP to include
the effects on surgical accuracy.
Acknowledgement

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Competing interests: None.

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


# Table 1. DESCRIPTIVE COHORT ANALYSIS

<table>
<thead>
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<th></th>
<th>Nijmegen Mx first</th>
<th>Nijmegen Md first</th>
<th>Odense Md first</th>
<th>( P ) Value(^*)</th>
<th>( P ) Value(^$)</th>
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<td>.459</td>
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<tr>
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<td>16-55</td>
<td>18-64</td>
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**Test of hypotheses**

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<th>Mandible-first sequence</th>
<th>CCW rotation</th>
<th>Inferior maxillary reposition</th>
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<tr>
<td></td>
<td>30</td>
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</tbody>
</table>

\( P \) Value\(^*\): ANOVA evaluation between all 3 groups.

\( P \) Value\(^\$\): Student’s \( t \)-test between Mandible-first and Maxilla-first groups.

**Planned Maxillary translation:**

<table>
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<th>Right</th>
<th>Anterior</th>
<th>Superior</th>
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<td>(-0.58 (1.12))</td>
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<td>(0.22 (2.49))</td>
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**Planned Maxillary rotation:**

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<th>Pitch</th>
<th>Roll</th>
<th>Yaw</th>
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<td>(0.31 (2.07))</td>
<td>(-0.07 (1.49))</td>
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<tr>
<td></td>
<td>(0.39 (5.99))</td>
<td>(0.07 (1.99))</td>
<td>(-0.14 (1.42))</td>
</tr>
<tr>
<td></td>
<td>(1.57 (4.31))</td>
<td>(0.12 (1.72))</td>
<td>(0.10 (1.63))</td>
</tr>
</tbody>
</table>

\( P \) Value\(^*\): ANOVA evaluation between all 3 groups.

Abbreviations: Md, Mandible. Mx, Maxilla. Yr, years. CCW, counter clockwise rotation.

**Note:** Translation and rotation measurements are presented as mean (standard deviations).

\* ANOVA evaluation between all 3 groups.

\$ Student’s \( t \)-test between Mandible-first and Maxilla-first groups.
**Table 2. MIXED LINEAR REGRESSION ANALYSIS OF INTERNAL CORRELATION AND CONFOUNDING VARIABLES**

<table>
<thead>
<tr>
<th>Interaction with planned movement:</th>
<th>β</th>
<th>P Value</th>
<th>95% Confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior (baseline)</td>
<td>.14</td>
<td>.002</td>
<td>.05 - .23</td>
</tr>
<tr>
<td>Superior (addition to baseline)</td>
<td>-.34</td>
<td>.000</td>
<td>-.50 - -.19</td>
</tr>
<tr>
<td>Right (addition to baseline)</td>
<td>.06</td>
<td>.628</td>
<td>-.17 - .28</td>
</tr>
</tbody>
</table>

**Test of hypotheses**

<table>
<thead>
<tr>
<th>Test of hypotheses</th>
<th>β</th>
<th>P Value</th>
<th>95% Confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maxilla-first</td>
<td>.57</td>
<td>.003</td>
<td>.19 - .95</td>
</tr>
<tr>
<td>Inferior maxillary repositioning</td>
<td>-.98</td>
<td>.000</td>
<td>-.87 - -.55</td>
</tr>
<tr>
<td>CCW rotation</td>
<td>.31</td>
<td>.127</td>
<td>-.09 - .70</td>
</tr>
</tbody>
</table>

| Age (yr)                          | -.01| .108   | -.03 - .00              |
| Female gender                     | -.10| .606   | -.49 - .28              |

| Constant                          | -.46| .106   | -1.03 - .10             |
| SD (constant)                     | 2x10^{-13}| 3x10^{-15} | 1x10^{-11} |
| SD (residual)                     | 1.84|         | 1.73 - 1.97            |

Abbreviations: Yr, years. SD, standard deviation.

Note: The outcome measurement for mixed model regression was the difference between planned and obtained movement.
### Table 3. OVERALL DIFFERENCE BETWEEN PLANNED AND OBTAINED SURGICAL REPOSITIONING

<table>
<thead>
<tr>
<th>Linear Maxillary difference</th>
<th>Mandible-first (N=88)</th>
<th>Maxilla-first (N=57)</th>
<th>P Value$^*$</th>
<th>P Value$^5$</th>
<th>Md-Mx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right</td>
<td>Mean</td>
<td>SD</td>
<td>P Value*</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Right</td>
<td>0.42 (1.65)</td>
<td>.019</td>
<td>-0.17 (1.31)</td>
<td>0.341</td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>-1.49 (2.01)</td>
<td>.000</td>
<td>-0.35 (2.65)</td>
<td>0.327</td>
<td></td>
</tr>
<tr>
<td>Superior</td>
<td>-0.22 (1.76)</td>
<td>.242</td>
<td>0.32 (2.07)</td>
<td>0.253</td>
<td></td>
</tr>
<tr>
<td>Rotational Maxillary difference</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pitch</td>
<td>1.42 (2.86)</td>
<td>.000</td>
<td>-0.25 (2.90)</td>
<td>0.415</td>
<td></td>
</tr>
<tr>
<td>Roll</td>
<td>-0.54 (1.24)</td>
<td>.002</td>
<td>-0.15 (1.40)</td>
<td>0.329</td>
<td></td>
</tr>
<tr>
<td>Yaw</td>
<td>0.12 (1.52)</td>
<td>.543</td>
<td>-0.19 (1.57)</td>
<td>0.258</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: SD, standard deviation.

* Student’s 1-sample independent t-test.

$^5$ Student’s 2-sample independent t-test of the difference between the maxilla-first or mandible-first group.
Table 4. THE SURGICAL SEQUENCE INTERACTION WITH MAXILLARY ROTATION

<table>
<thead>
<tr>
<th>Linear distance (mm)</th>
<th>N</th>
<th>Mandible-first</th>
<th>N</th>
<th>Maxilla-first</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clockwise rotation (CW):</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>38</td>
<td>0.39 (1.37)</td>
<td>38</td>
<td>0.05 (0.99)</td>
<td>.222</td>
</tr>
<tr>
<td>Anterior</td>
<td></td>
<td>-1.93 (1.85)</td>
<td></td>
<td>-1.18 (2.35)</td>
<td>.127</td>
</tr>
<tr>
<td>Superior</td>
<td></td>
<td>-0.60 (1.58)</td>
<td></td>
<td>0.31 (2.04)</td>
<td><strong>.035</strong></td>
</tr>
<tr>
<td><strong>Counter clockwise rotation (CCW):</strong></td>
<td>50</td>
<td></td>
<td>19</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td></td>
<td>0.45 (1.85)</td>
<td></td>
<td>-0.59 (1.74)</td>
<td><strong>.037</strong></td>
</tr>
<tr>
<td>Anterior</td>
<td></td>
<td>-1.16 (2.09)</td>
<td></td>
<td>1.33 (2.45)</td>
<td><strong>.000</strong></td>
</tr>
<tr>
<td>Superior</td>
<td></td>
<td>0.06 (1.84)</td>
<td></td>
<td>0.34 (2.18)</td>
<td>.602</td>
</tr>
</tbody>
</table>

* Student’s two sample independent t-test.

Note: Translation and rotation measurements are presented as mean (standard deviations).

Abbreviations: SD, standard deviation.
Table 5. THE SURGICAL SEQUENCE INTERACTION WITH SUPERIOR/INFERIOR MAXILLARY REPOSITIONING

<table>
<thead>
<tr>
<th>Linear distance (mm)</th>
<th>N</th>
<th>Mandible-first</th>
<th>N</th>
<th>Maxilla-first</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superior maxillary reposition</td>
<td>43</td>
<td>24</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td></td>
<td>0.32 (1.63)</td>
<td></td>
<td>−0.54 (1.64)</td>
<td>.041</td>
</tr>
<tr>
<td>Anterior</td>
<td></td>
<td>−0.93 (1.93)</td>
<td></td>
<td>1.45 (2.77)</td>
<td>.000</td>
</tr>
<tr>
<td>Superior</td>
<td></td>
<td>−0.34 (2.10)</td>
<td></td>
<td>0.53 (2.17)</td>
<td>.114</td>
</tr>
<tr>
<td>Inferior maxillary reposition</td>
<td>45</td>
<td>33</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td></td>
<td>0.52 (1.69)</td>
<td></td>
<td>0.11 (0.95)</td>
<td>.211</td>
</tr>
<tr>
<td>Anterior</td>
<td></td>
<td>−2.03 (1.96)</td>
<td></td>
<td>−1.65 (1.60)</td>
<td>.370</td>
</tr>
<tr>
<td>Superior</td>
<td></td>
<td>−0.11 (1.36)</td>
<td></td>
<td>0.16 (2.01)</td>
<td>.484</td>
</tr>
</tbody>
</table>

* Student’s two sample independent t-test.

Note: Translation and rotation measurements are presented as mean (standard deviations).

Abbreviations: SD, standard deviation.
Table 6. SURGICAL ACCURACY IN VERTICAL DIMENSION USING EXTERNAL REFERENCE PIN AND MEDIAL CANTHAL LIGAMENT

<table>
<thead>
<tr>
<th>Vertical measurements</th>
<th>Reference pin (N=58)</th>
<th>Canthal ligament (N=30)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Planned</td>
<td>–0.13 (2.92)</td>
<td>0.22 (2.49)</td>
<td>.561</td>
</tr>
<tr>
<td>Obtained</td>
<td>–0.31 (3.22)</td>
<td>–0.08 (2.31)</td>
<td>.701</td>
</tr>
<tr>
<td>Difference</td>
<td>–0.18 (1.83)</td>
<td>–0.30 (1.64)</td>
<td>.759</td>
</tr>
</tbody>
</table>

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 by the mandible-first approach.

Abbreviation: Ext ref pin, external reference pin. SD, standard deviation.

*Student’s two sample independent t-test.
**Figure legends**

**FIGURE 1.** Rotation of the maxilla. **A:** A positive pitch moved the upper central incisor cranially. **B:** A positive roll moved the right first molar cranially. **C:** A positive yaw moved the upper central incisor to the left.
Figure 2. Inclusion and exclusion criteria for combined cohort.
**FIGURE 3.** Distance between planned and obtained maxillary reposition between procedures and study centers. Surgical accuracy according to center and maxillary/mandible first sequencing. The main difference was seen along the anterior axis; maxilla-first showed larger variance, while mandible-first in the Nijmegen study showed a median of ~2 mm.

Abbreviations: Md: Mandible. Mx: Maxilla.
**FIGURE 4.** Correlation between surgical accuracy and virtual surgical planned reposition along the anterior axis (fitted line – Mandible-first, $y = -0.47x +0.28$; Coefficient of determination, $R^2 = 0.32$) (fitted line – Maxilla-first, $y = -0.61x +2.08$; Coefficient of determination, $R^2 = 0.15$). The planned maxillary advancement showed a moderate correlation with surgical accuracy along the anterior axis, accounting for 15% to 32% of the deviation in surgical accuracy.

Abbreviations: CI, confidence interval.
**FIGURE 5.** Correlation between surgical accuracy and virtual surgical planned reposition along the superior axis (fitted line – Mandible-first, \( y = -0.14x - 0.22 \); Coefficient of determination, \( R^2 = 0.06 \)) (fitted line – Maxilla-first, \( y = 0.05x + 0.33 \); Coefficient of determination, \( R^2 = 0.005 \)). The correlation between planned superior/inferior repositioning showed a very weak correlation with surgical accuracy in the vertical dimension, therefore 95% confidence intervals were not added to the graph.
FIGURE 6. Vertical accuracy along the superior axis between the 2 centers in mandible-first procedures. Using the medial canthal ligament (Odense) showed an overall close alignment with the vertical surgical accuracy using the current golden standard of an external reference pins (Nijmegen), except in 2 patients with large inferior repositioning.