ABSTRACT

Purpose: Mismatch between preoperative planning and surgical outcome in maxillofacial surgery relate to on-table replication of pre-surgical planning and predictive algorithm inaccuracy: software error was hereby decoupled from planning inaccuracy to assess a commercial software. The hypothesis was that soft tissue prediction error (1) would be minimised if the surgical procedure was replicated precisely as planned, and (2) is independent of the extent of bone repositioning.

Methods: Cone-beam computed tomography scans of sixteen Le Fort I (LFI) osteotomy patients were collected at Boston Children's Hospital. Pre and postoperative models of bone and soft tissue were constructed and the maxilla repositioning was replicated. Each model was subdivided into six regions: mouth, nose, eyes, and cheeks. Soft tissue prediction (performed using Proplan CMF - Materialise®) for each patient was compared with the relative postoperative reconstruction and error was determined. $P<0.05$ was considered significant.

Results: LFI segment repositioning was replicated within 0.70 ± 0.18 mm. The highest prediction error was found in the mouth (1.49 ± 0.77 mm) followed by the cheeks (0.98 ± 0.34 mm), nose (0.86 ± 0.23 mm), and eyes (0.76 ± 0.32). Prediction error on cheeks correlated significantly with mouth ($r = 0.63$, $p< 0.01$) and nose ($r = 0.67$, $p< 0.01$). Mouth prediction error correlated with total advancement ($r = 0.52$, $p = 0.04$).

Conclusion: ProPlan CMF is a useful outcome prediction tool, however accuracy decreases with the extent of maxillary advancement even when errors in surgical replication are minimised.

1 INTRODUCTION

Maxillary hypoplasia (MH), is a bone malformation disorder in which the upper jaw is underdeveloped, resulting in midfacial retrusion and prognathic mandibular appearance. This has been associated with cleft lip and palate (CLP) [1-4], and syndromic anomalies such as fetal alcohol syndrome [5, 6], congenital central hypoventilation syndrome [7], Pfeiffer [8, 9] Apert [10], and Crouzon syndrome [11]. MH usually manifests in more than one plane requiring three-dimensional correction of the deformity [12, 13]. Le Fort I osteotomy (LFI) which is a conventional orthognathic surgery is a common procedure to correct MH [14, 15].

Patients' primary reason to pursue correction and undergo orthognathic surgery is based on aesthetic, functional, and psychosocial concerns [16-18]. In view of this, the ability to predict postoperative facial appearance is essential and can be used for exploring treatment options, communication, and managing expectations [19, 20]. Over the past few years, the development of three-dimensional computer planning programmes has made it possible to plan particular surgical operations and predict the effect of different interventions on facial appearance [21-27]. Whilst these studies have significantly enhanced our understanding of soft and hard tissue profile, this has not yet led to the widespread use of a 3D planning software in common clinical practice due to uncertainty on the accuracy of soft tissue prediction in specific areas, for example around the lips and nose [21, 22, 28]. The prediction accuracy is dependent on the complexity of the surgery and the relationship between hard and soft tissues [29, 30]. However, soft tissue changes may not always correlate with those of the underlying skeleton [31, 32].

The surgical simulations rely on images acquired with computed tomography (CT), multi-slice computed tomography (MSCT), and cone-beam computed tomography (CBCT) [25, 27, 33]. In a review by Olivetti et al. [34], Dolphin 3D (Dolphin Imaging and Management Solutions, Chatsworth, CA, USA), and Orthoforecast were reported to provide the most accurate soft tissue predictions when compared to other commercially available software: TIOPS [35], SimPlant O&O [24], 3DMDvultus [36, 37], and Maxilim [38, 39]. A recent study by our group assessed the prediction accuracy of Dolphin and another user friendly software, ProPlan CMF (Dentsply-Sirona, York, PA, USA), by testing a range of maxillary advancement (0-7 mm) and their corresponding effect on soft tissue prediction. Results showed that the mismatch between planned and postoperative maxillary position was non-negligible when comparing predicted and postoperative soft tissue shape. ProPlan is based on a finite difference method, a relatively fast discretization approach which enables solving mathematical equations through numerical approximations [40].

Mismatch between preoperative planning and surgical outcome in maxillofacial surgery relate to on-table replication of planning and software inaccuracy. Herein, to further investigate the previously reported source of error with ProPlan, software error was decoupled from planning inaccuracy. The aim of this study was to investigate the accuracy of ProPlan CMF software in predicting the soft tissue movements in MH patients who underwent Le Fort I maxillary advancement. The hypothesis was that soft tissue prediction error would be minimised if surgical procedure was performed as planned, and the prediction error would not be associated with the extent of maxillary advancement. Pre and postoperative CBCT images were evaluated to determine the soft

tissue prediction error in a sequence of 4 steps: (1) Image acquisition, (2) surgical simulation, (3) soft tissue modelling and (4) quantitative measurement.

2 MATERIALS AND METHODS

This study was approved by the Institutional Review Board of the Center for Applied Clinical Investigation at Boston Children's Hospital (P00024296) and all patients provided consent. All procedures performed were in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. A visualization of the overall pipeline for this work is available in Figure 1

2.1 Patients

Following ethical approval, the radiology database of the Boston Children's Hospital Oral and Plastic surgery was retrospectively searched for patients with maxillary hypoplasia who underwent LF I osteotomy and maxillary repositioning between 2011-2017. From the 107 candidates, patients with a cleft, previous surgical history in the maxillofacial region, surgery in the period between LFI and post-operative scan, and incomplete CBCT scans or of insufficient quality to construct a 3D image were excluded. After applying the exclusion criteria, 16 patients with a mean age of 18.50 ± 2.13 years (range, 15-22) at the time of surgery were included. Patients' ethnicity and weight were reviewed and reported in Supplemental Table 1. All operations were performed by the same surgeon.

2.2 Image Acquisition

The CBCT scans were obtained within 2-9 months prior to surgical correction and within 11-15 months postoperatively (Supplemental Table 1). Imaging data were stored in

digital imaging and communications in medicine (DICOM) format and imported into the Mimics inPrint 3.0 (Materialise, Leuven, Belgium) to construct 3D meshes of the pre and post-op facial skeleton and the soft tissue. During the 3D construction process, all redundant objects, such as lines and tubes, were semi-automatically removed manually. Each 3D model - soft tissue and bone, preoperative and postoperative - was exported as separate stereolithography (STL) files.

2.3 Surgical Simulation

To determine the exact location of the LF1 osteotomy during surgery, the preoperative and postoperative bone 3D meshes were imported into ProPlan CMF 3.0 *(Materialise, Leuven, Belgium)* and superimposed. The preoperative bone 3D model was registered to the postoperative bone model in the maxillary arch region (Figure 2A). With the help of plates and the screws visible on the postoperative bone model, two planar cuts on the preoperative 3D bone model were performed and LFI osteotomy was replicated (Figure 2B): the preoperative bone model was split into two parts: the skull base (in yellow in figure 2B) and the osteotomised maxillary arch, which from now on will be referred to as ‘the LF I segment’ (in blue in figure 2B). A similar methodology was used in a previous publication from our group [40].

2.4 Advancement simulation

The split preoperative 3D bone model was afterwards aligned with the skull base of the postoperative bone model (Figure 2C). The LF I segment was advanced in order to achieve the relative postoperative position (Figure 2D). The total advancement inducing such repositioning was recorded. The total advancement was calculated as the

displacement of the A point: total advancement, advancement in the X, Y, Z directions, in-plane advancement in the xy and zy planes were considered.

2.5 Soft Tissue Prediction

Proplan (Materialise®) was used to perform a prediction of the post-operative appearance of the soft tissue assuming that the bone repositioning occurred according to the recorded advancement. Preoperative soft tissue and split-preoperative bone model (LF1 segment and skull base) were imported into the software. By employing the 'Soft tissue simulation tool', the recorded total advancement (as described in section 2.4) was applied the LF1 segment and the STL file of the predicted deformed soft tissue was generated. The post-advancement bone model ("simulated bone") and the predicted deformed soft tissue ("simulated soft tissue") were exported.

2.6 Measurements

The simulated bone was superimposed and aligned to the postoperative bone by means of matching selected landmarks in the 3-matic Research 13.0 software. Due to the inconsistency of the scans, eleven landmarks were selected. At least six of the eleven landmarks had to be present for the case to be included. The following landmarks were chosen: the left frontozygomatic, the right frontozygomatic, the nasion, the left zygion, the right zygion, the left orbita, the right orbita, the basion, the left hypoglossal canal, the right hypoglossal canal and the opisthion [41]. This indirectly led to the alignment of the simulated soft tissue and the postoperative soft tissue.

To ensure the region at which the comparison was performed was consistent throughout the population, the simulated and postoperative soft tissues were cropped using planar

cuts, defined by the soft tissue B-point (the deepest point on the anterior border of mandibular symphysis) and the right and left sub-auricular points (Figure 3A).

Using the MATLAB R2018a software (MathWorks, USA) the surface distance between predicted and postoperative soft tissue STL files were measured using an in-house built Matlab code based on intersecting facial landmark in six anatomical areas as follows: right eye, the left eye, the nose, the mouth, the right cheek and the left cheek (Figure 4). Surface distance colourmaps were created to visualize the areas where the prediction error was above 2mm using ParaView 5.6.1 (Kitware Inc, USA).

The simulated and postoperative bone models were imported into the Meshmixer software (Autodesk Inc., San Rafael, CA). The anterior aspect surface of the LFI segment was isolated for all the simulated and postoperative bone STL files and exported for data processing (Figure 3B). Similarly to the soft tissue, the surface distance between prescribed and postoperative LF1 segments was determined using MATLAB.

2.7 Statistical analysis

Statistical analyses were performed using SPSS (IBM SPSS Statistics for Windows, IBM Corp, Chicago, IL, USA). All data were tested for normality using the Shapiro-Wilk test. A Mann Whitney-U test was used to compare the soft tissue prediction errors in the various regions of the face. Values are presented as mean ± standard deviation. The Spearman's rank correlation coefficient (r_s) was used to assess whether the soft tissue prediction errors were correlated in different regions of the face, and also with the total advancement. A p-value <0.05 was considered statistically significant.

3 RESULTS

Sixteen MH patients with African-American (n=3), Caucasian (n=11), Hispanic (n=1) and Indian-Caucasian (n=1) ethnicity met the inclusion criteria in this study. The pre and post-op patients' weight were respectively 67.92 ± 10.96 kg (n=16) and 70.10 ± 12.44 kg (n=14 - the post-op information was not available for two patients).

All patients received an anterior advancement. The comparison between the simulated and postoperative bone, limited to the anterior aspect of the maxilla (figure 3B), showed that the LF1 osteotomy was replicated accurately, with a mean error of 0.70 ± 0.18 mm. Colour maps were produced to visualise such errors (Figure 5).

Supplemental Table 2 presents discrepancies in soft tissue responses when the predicted and postoperative soft tissue models were compared. Of all the regions, mouth was quantified with the highest amount of error (1.49 ± 0.77 mm) in comparison to cheeks (0.98 ± 0.34 mm, p=0.02), nose (0.86 ± 0.23 mm, p=0.001) and eyes (0.76 ± 0.32 mm, p=0.001). No other significant differences were found. For each patient, colour maps were produced to depict the soft tissue prediction error with the superimposition of predicted and postoperative STL files (Figure 6). No correlations were found between the post-op weights, change in the weight, and soft tissue prediction error. The prediction error in cheeks was significantly correlated with mouth (rs = 0.63, p =0.009) and nose (rs = 0.67, p =0.004). No other significant correlations were found (Supplemental Table 3). The average advancements in X, Y, and Z directions were respectively, 1.45 ± 1.02 mm, 7.06 ± 2.06 mm, and 1.23 ± 0.64 mm, with an average total advancement of 7.41 ± 2.06. The soft tissue prediction error in the mouth area was found to increase significantly with the total maxillary advancement (r_s= 0.52, p=0.04), advancement in y-direction (r_s= 0.59,

p=0.02), total in-plane displacement in xy- plane (r_s= 0.52, p=0.04) and yz-plane (r_s= 0.56, p=0.03). Patients' age was not correlated with the error in the soft tissue prediction (Supplemental Table 4).

4 DISCUSSION

Orthognathic surgery to correct skeletal deformities can nowadays be planned and predicted using a wide range of commercial software. While these seem to have reasonably good accuracy in terms of hard tissue changes, there are discrepant findings in the literature about soft tissue prediction accuracy. This study aimed to evaluate the accuracy of ProPlan CMF in predicting soft tissue responses in patients with maxillary hypoplasia who underwent an LF1 surgery assuming that the surgery unfolded exactly as planned.

In this study, the LF1 segment repositioning was successfully replicated with a mean error of 0.70 ± 0.18 mm in sixteen MH patients with no history of cleft and surgery in the maxillofacial region. A difference of a maximum 2 mm between the planned surgery and the actual surgical outcome has been proposed as clinically acceptable by several authors [26, 42-45].

The prediction errors in orthognathic surgery are associated with both planning and the surgical process [22, 23, 25-28, 40]. One of the main problems reported with planning is the reliability of the software or inaccuracy in recognising soft tissue responses in specific areas; in particular the nose and the upper lip due to their peculiar anatomy and composition [22, 23, 40]. In accordance with previous reports, our findings showed that the mouth was the most significant region of error, and there was a strong relationship between the total advancement of the maxilla and soft tissue prediction error in the same area. This might be associated with surgical osteotomies localised in the mouth region. Using SurgiCase-CMF®, Bianchi et al. [46] and Marchetti et al.[25], reported large errors

in the areas of lip and chin. It was suggested that the inaccuracies could be due to the fact that the software moves the CT data of the lips as a continuous area, while in reality, they move separately [25]. ProPlan does not require landmarks and has no manual setting for specific material properties [40]. This pre-programmed soft tissue behaviour and the movements of lips as a continuous area could have caused some of the prediction error. Differences in lip tonicity, length, posture, and mass between patients result in more inaccuracies in software that use pre-programmed fixed hard tissue to soft tissue ratios for the prediction of the soft tissue results [23, 27, 47, 48].

Prediction of soft tissue responses is more difficult than the underlying bone since soft tissue is a plastic tissue that can be transformed by changes in body weight, patient posture, age, and muscle tension [24]. Clemente et al.[49], reported that various ethnic populations also results in differences in the soft tissue to hard tissue ratios. The soft tissue prediction errors in our study were not correlated with age and patients' weight. Furthermore, ethnicity was not taken into account due to the small number of patients in each group.

Soft tissue scarring and swelling have been reported to cause variability in soft tissue responses [24] and create difficulties in the simulation procedures [25]. According to Van der Vlis M et al. [50], a significant decrease in soft tissue swelling after orthognathic surgery still occurs between 6-12 months postoperatively. Herein, the postoperative CBCT scans for all patients were obtained approximately one year after surgery (12.81 ± 1.11 months) to rule out any effects of the postoperative swelling. Error in the eye region may be due to different eyelid positions between preoperative and postoperative scans,

as well as a minor movement during the imaging session which may have caused small localised artefacts. Correlation between prediction error in the different areas (cheeks, nose, and mouth) is probably due to the connection and continuity between the different sections of the face: underestimation of tissue movement on an area reflects on the prediction accuracy of the adjoining ones.

Previous studies have assessed the long-term stability of maxillary advancement following LFI osteotomy [51]. Postoperative relapse is one of the most serious issues, which manifests as backward and upward changes of the maxillary segment [52]. In non-cleft patients with MH a 10% rate of relapse has been reported, while the corresponding rates in CLP patients was much higher, ranging between 25-50% [51, 53, 54]. Hoffman et al.[55], evaluated 45 patients who underwent one-piece LFI osteotomy with rigid fixation to advance the maxilla. They found that patients' age, gender, the degree of advancement had no effect on postoperative skeletal stability. In our study postoperative relapse was not taken into account when assessing the prediction accuracy.

In this work, in order to decouple the errors in planning and the software, the planning aspect of the surgery was reproduced by excluding as many of the presented causes of planning error as possible. Despite all the attempts to minimise the error, there are still some causes for planning errors that could not be avoided. After advancing the maxilla during the LF1 surgery, screws and plates are placed on each of the maxillary buttresses for stability [56]. Screw placements on the bone have been reported as a cause of error in chin and nose regions [28]. Although in our study patients had no operations in the maxillofacial area in the period between the LF1 surgery and the postoperative scan, the

screws used for fixation were present at the time of the post-op scans and may have contributed to the prediction error.

Previous surgical history is another factor that could cause variability in soft tissue behaviour [24]. To ensure consistency, patients were excluded if they had had other surgeries before being treated by the LF1 surgery. All patients were treated in Boston Children's hospital by the same surgeon, therefore, planning errors due to differences in operative technique were negligible and the surgical approach can be considered to be consistent across patients.

In this study, we investigated the accuracy of soft tissue predictions generated by ProPlan CMF in sixteen patients who underwent Le Fort I osteotomy. While previous studies have compared the performance of surgical prediction software by assessing either the accuracy in bone repositioning [46] or quantifying a prediction error - which is due to a combination of inaccurate replication of surgical planning and inherent software inaccuracy [25, 46, 28] - we have hereby attempted to decouple these two sources of error to assess the capability of the predictive algorithm. The results showed that perfect replication of the planning is not sufficient, and it is likely that the complex nature of the different components of facial soft tissue should be considered to improve the prediction outcome.

The main limitation in this study was the sample number, which was small (though comparable to other similar studies [40,43,45,46]) due to the strict inclusion criteria: nevertheless, the results provide meaningful statistical results thanks to the homogeneity of the population considered.

Although from a clinical point of view ProPlan CMF is a reasonable tool to predict the postoperative outcome of an LF1 surgery, its prediction capability of soft tissue changes is inherently limited as highlighted by this study. Predictions were generated using postoperative scans as guidelines and assuming the bone repositioning planning perfectly reflected the subsequent surgical procedures. Comparison between surgical planning and outcome showed that even in the best-case scenario, i.e. when surgery perfectly replicates planning, the soft tissue prediction doesn't fully match the soft tissue outcomes. The results highlighted a positive correlation between the amount of error and the amount of advancement, implying that ProPlan does not suffice when making predictions for patients with larger advancements. Thus, when ProPlan is used to make predictions for the outcome of surgery, its limitations should be taken into consideration during patient communication. There is a lack of software with the ability to perfectly predict soft tissue behaviour; developments in that field are clinically perceived to be of great value. Further research should be carried out to explore factors that can potentially affect the amount of error-sensitive areas.

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FIGURE LEGENDS

Figure 1: Study pipeline: A) Pre-op (i) and Post-op (ii) image segmentation for the creation of the pre- and post-op bone and soft tissue 3D models in Mimics InPrint 3.0®. B) Postprocessing: i) replication of the surgical osteotomy and repositioning in Meshmixer 13.0; ii) surgical prediction performed in ProPlan CMF; iii) quantification of the prediction error carried out in Matlab R2020. The dotted arrows show the 3D models used as input for each step of the postprocessing."

Figure 2: A) Alignment of the pre-operative 3d model (yellow) to the post-operative model (red) at the maxilla. Osteotomy are identified by means of plates, screws and visible sign of the surgical cuts on the post-op skull B) LF1 osteotomy planes (red dotted lines) used to create the split preoperative bone model. The skull base is portrayed in yellow and the LF1 segment in blue. C) Alignment of the split preoperative bone to the skull base of the postoperative 3D model (red). D) Movement of the LF1 segment (blue) to match the maxillary position of the postoperative model (red) while the skull base (yellow) remains in place.

~~Figure 2: 3D models of the pre-operative soft-tissue in blue (A) and the predicted soft-tissue in red (B).~~

Figure 3: A) Cropping the STL files in 3-Matic Research 13.0. The planar cuts were defined by the B-point (red) and the right and left sub-auricular points (green). B) The isolated LF1 cut (marked in dark grey) on a post-operative bone STL file.

Figure 4: The landmarks (A) used to create the six regions of the face (B). The following landmarks were used: glabella(g), left exocanthion (lex), left endocanthion (len), right exocanthion (rex), right endocanthion (ren), left zygion (lzy), right zygion (rzy), left alar crest(lac), right alar crest (rac), left cheilion (lc), right cheilion (rc) and the midlip (ml). The face was divided as follows: right eye (red), the left eye (green), the nose (yellow), the mouth (magenta), the right cheek (black) and the left cheek (blue).

Figure 5: Colour maps that illustrate the errors of the predicted LF1 cuts.

Figure 6: Colour maps that illustrate the errors of the predicted soft-tissue. Errors within a range of 0 to 2 mm were depicted as indigo. Errors within a range of 2 to 5 mm were gradually coloured green, yellow, orange, red and purple.