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Orbital change following Le Fort III advancement in syndromic craniosynostosis: Quantitative evaluation of orbital volume, infra-orbital rim and globe position

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A B S T R A C T

Patients with syndromic craniosynostosis suffering from shallow orbits due to midface hypoplasia can be treated with a Le Fort III advancement osteotomy. This study evaluates the influence of Le Fort III advancement on orbital volume, position of the infra-orbital rim and globe.

In pre- and post-operative CT-scans of 18 syndromic craniosynostosis patients, segmentation of the left and right orbit was performed and the infra-orbital rim and globe were marked. By superimposing the pre- and post-operative scans and by creating a reference coordinate system, movements of the infra-orbital rim and globe were assessed.

Orbital volume increased significantly, by 27.2% for the left and 28.4% for the right orbit. Significant anterior movements of the left infra-orbital rim of 12.0 mm (SD 4.2) and right infra-orbital rim of 12.8 mm (SD 4.9) were demonstrated. Significant medial movements of 1.7 mm (SD 2.2) of the left globe and 1.5 mm (SD 1.9) of the right globe were demonstrated. There was a significant correlation between anterior infra-orbital rim movement and the increase in orbital volume.

Significant orbital volume increase has been demonstrated following Le Fort III advancement. The position of the infra-orbital rim was moved forward significantly, whereas the globe position remained relatively unaffected.

1. Introduction

Syndromic craniosynostosis (SCS), severe obstructive sleep apnea (OSA), raised intracranial pressure (ICP) and globe (sub) luxation, are absolute indications for surgical treatment. In these cases, Le Fort (LF) III or monobloc advancement is often performed at a young age (Marchac et al., 1994).

Subluxation of the globe threatens the eye, causing exposure keratitis, mechanical lagophthalmos, corneal ulcers and a risk of impaired vision and even eye-loss (Cruz et al., 2007; Khong et al., 2006). SCS patients often have small orbital volumes compared to non-syndromal patients (Cooper, 1985). Clinically, midface advancement is likely to increase the orbital volume by advancement of the infra-orbital rim and to reduce associated pathology (Cedars et al., 1999; Cruz et al., 2007; Ortiz-Monasterio et al., 1978). Fitzgerald et al. investigated globe movement after monobloc advancement by using computed tomography (CT) scan data (Fitzgerald O'Connor et al., 2009). They found significant forward movement of the globe after monobloc distraction.

There have been no studies concerning the influence of LF III advancement on orbital volume and the position of the infra-orbital rim and globe. Since the osteotomy lines are made through the lateral orbital wall, standard Hertel measurements cannot be used. The purpose of this retrospective study was to measure the influence of LF III advancement on the orbital volume, infra-orbital rim and globe position using CT-scan data.

2. Materials and methods

2.1. Patients

All SCS patients who underwent LF III advancement in the Erasmus University Medical Center between 2003 and 2009 were

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evaluated. Patients were included when the pre- and post-operative CT-scans were available for analysis.

2.2. CT-scans

The CT-scans were carried out in a supine position using the same scanner (Emotion 6, Siemens, Munich, Germany) and had a slice thickness of 1.25 mm. Sedation, was used when indicated.

2.3. Surgical procedure

Via a coronal approach the frontotemporal skull, lateral orbital region, nasal region, zygomatic arch and body were exposed. Osteotomies, following the LF III – Tessier III design (Fig. 1), were made through the frontozygomatic suture, floor of the orbit, and the nasal bone, using a reciprocating saw and osteotomes. A cephalo-osteotome was used to separate the vomer and ethmoid from the cranial base in the midline. The pterygomaxillary junction was separated either from the coronal approach or through a gingivobuccal access. Rowe's forceps were used to mobilize the Le Fort III segment. In a conventional LF III osteotomy the midface segment was advanced as much as needed and fixated using osteosynthesis plates and screws. In a LF III distraction osteogenesis (DO) case the internal or external distractors were applied and tested before suturing of the wounds. After distraction and consolidation, the distractors were removed.

2.4. LF III distraction protocol

All patients were hospitalized for 7 days regardless of age. For 24 h after surgery the patients stayed in the intensive care unit. DO was initiated after 1 week. The rate of distraction was 1 mm/day in two daily activations. The duration of DO depended on the desired advancement. During the distraction period, vector modifications took place when necessary in patients treated with an external distractor. In all patients there was a consolidation period of 3 months after distraction. Post-surgically, all patients were seen in an outpatient clinic.

2.5. Data-analysis

2.5.1. Orbital volume

The software program MevisLab (Version 2.0, Mevis Medical Solutions AG, Bremen) was used to import and analyze the CT-scans by means of a custom-designed tool. On each sagittal slice of the CT-scan, the boundaries of each orbit were manually outlined resulting in a left and right orbital mask. To facilitate the segmentation, a threshold of 400 Hounsfield Units for bony structures was used. In all slices, the anterior boundary was defined as a straight line from the most antero-superior point of the infra-orbital rim to the most antero-inferior point of the supra-orbital rim. The medial, lateral, superior and inferior boundaries were dictated by the bony structures of the orbit. When there were bony interruptions (e.g. orbital foramina), a perpendicular straight line was drawn between the nearest bony boundaries (Fig. 2). In all patients, the volume of the orbital masks was computed pre- and post-operatively for both the left and right orbit.

2.5.2. Infra-orbital rim and globe movement

The same software program was used to measure infra-orbital rim and globe movement. In order to be able to quantify the movement of structures independent of the position of the patient in the CT-scan, three reference planes were defined in the pre-treatment scan. First a horizontal plane (Fig. 3) was defined using the most lateral points of the left and right lateral semicircular

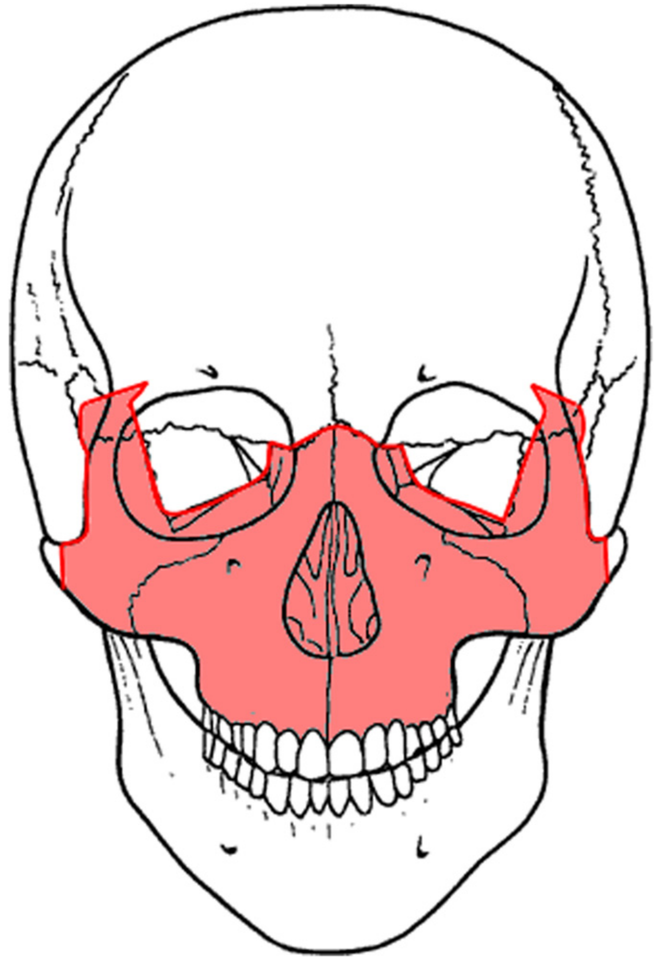

Fig. 1. Schematic drawing of osteotomy lines according to Le Fort III – Tessier III design as used in the patient cohort.

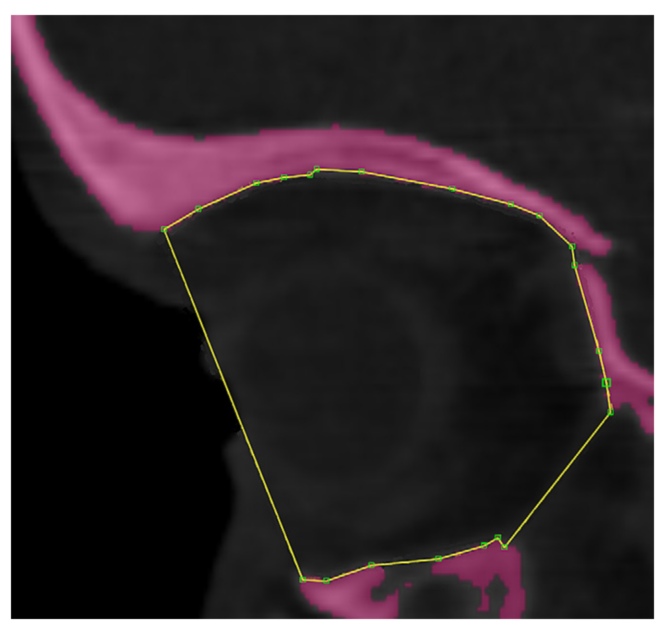

Fig. 2. The anterior boundary defined as a straight line from the most antero-cranial point of the infra-orbital rim to the most antero-caudal point of the supra-orbital rim is depicted in a sagittal CT-slice. Furthermore, bony interruptions of the orbit are evident. A perpendicular straight line was manually drawn between the most nearby bony boundaries.

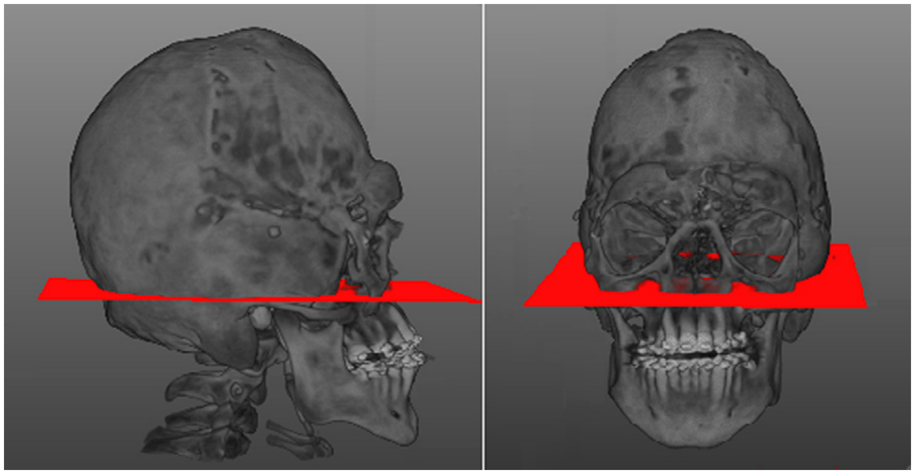

Fig. 3. Three-dimensional reconstruction of the bony skull of one of the subjects in sagittal and frontal view, visualizing the horizontal plane (red) created by means of the three reference points.

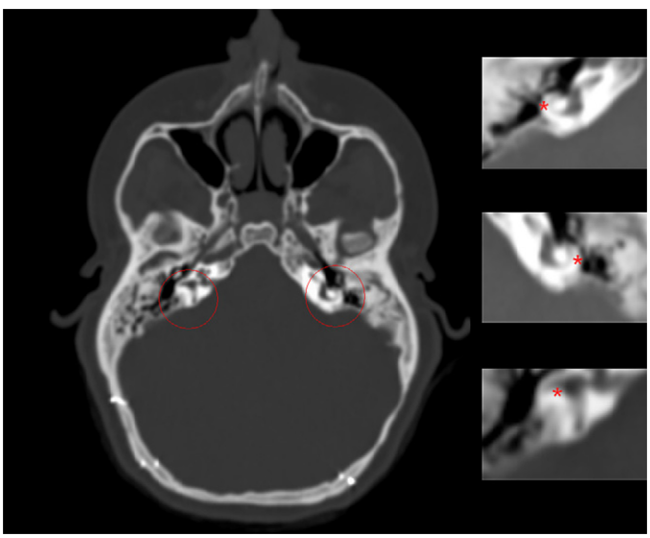

Fig. 4. Axial slice of one of the patients in which the anatomical localization of the lateral semicircular canals (LSCC) is visualized (red circles). In the depicted slice, only the left LSCC can be fully visualized; the right LSCC is only partial visible. A detailed view of the right LSCC is depicted on the right in the uppermost figure. In the middle figure the left LSCC is detailed. The red asterisks in these figures represent the most lateral points of the LSCC. In the undermost figure the most anterior part of the right LSCC is detailed (red asterisk).

canal (LSCC) and the most anterior point of the right LSCC as reference points (Fig. 4). The transverse plane was defined by the left and right LSCC and orientated perpendicular to the horizontal plane. The sagittal plane was orientated perpendicular to the horizontal and transversal plane. By translating the planes to the center of the hypophysis (S) a coordinate system was created in which S was defined to be (0,0,0) expressed in *x*-, *y*- and *z*-coordinates.

By precisely superimposing the post-operative scan over the preoperative scan in sagittal, transverse and axial orientations, the best match was found and saved (Fig. 5). The reference planes defined in the pre-treatment scans were used in the post-treatment scans. To be able to compare the movement of the infra-orbital rim and globe pre- and post-treatment, two landmarks were defined in each orbit, being the most anterior point of the infra-orbital rim and the center of the eye-globe. By comparing the *x*-, *y*- and *z*-coordinates of these points pre- and post-operatively, the movement of these landmarks in three dimensions could be analyzed.

To evaluate the influence of LF III advancement on the orbital volume, the infra-orbital rim and the anterior movements of the globe were compared pre- and post-operatively.

All measurements were performed by one observer. To determine the reproducibility of our analysis method, a second observer independently performed all measurements in five randomly selected patients of the study-group.

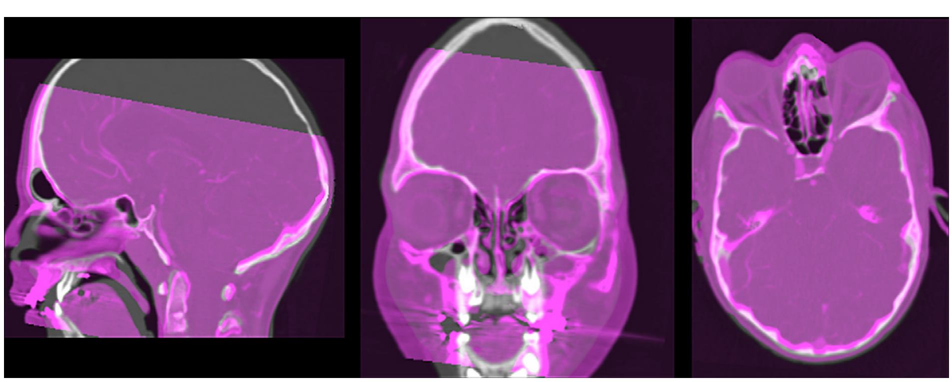

Fig. 5. Example of a CT-scan of one of the subjects in sagittal, transverse and axial view. In grey the preoperative scan is visualized; in pink the post-operative scan is depicted. Manually, the post-operative scan was superimposed over the preoperative scan. The best match was found and saved and used for analysis.

2.5.3. *Statistical analysis*

SPSS for Windows XP (Version 15.0, SPSS Inc., Chicago, USA) was used to analyze the data. Using the intra-class correlation-coefficient (ICC) the inter-observer reliability was calculated. The pre- and post-operative CT data were analyzed by means of the paired samples *t*-test. A *p*-value of <0.05 (two-tailed) was considered to be statistically significant. A correlative statistical analysis using Spearman's correlation-coefficient (r_s) was performed for the orbital volume increase and anterior infra-orbital rim movement.

3. Results

3.1. *Reliability*

The inter-observer agreement with respect to the orbital volume measurements was good (ICC 0.9). For the globe and infra-orbital rim movement the inter-observer agreements were also good, with the ICC ranging from 0.86 to 0.98.

3.2. *Patients*

A summary of the patient data is provided in Table 1. Of a total of 27 patients operated on between 2003 and 2009, 18 SCS patients were included (nine females and nine males) along with Crouzon (four females, five males), Apert (five females, two males) and Pfeiffer syndromes (two males). Absolute indications for LF III advancement in this study-group were OSA (four patients) and threatened eyes (four patients). All 18 patients had relative indications due to severe midfacial hypoplasia and associated class III malocclusion. Seventeen patients underwent Le Fort III DO with external (15 patients) or internal distractors (two patients). One patient underwent a conventional LF III osteotomy. The average age at the time of LF III advancement was 14.7 years (standard deviation (SD) 4.7 years). The average time-interval between LF III advancement and the preoperative CT-scan was 7.8 months (SD 7.7 months). Post-operatively, this time-interval was 7.2 months (SD 4.8 months).

3.3. *Orbital volume*

The average preoperative orbital volume for the left orbit was 25.7 cm^3 (SD 3.0) and post-operatively it was 32.6 cm^3 (SD 4.4). The average orbital volume for the right orbit was 25.5 cm^3 (SD 2.7) preoperatively and 32.6 cm^3 (SD 3.6) post-operatively. After LF III advancement, the orbital volume increased significantly ($p < 0.001$) at 27.2% for the left orbit and 28.4% for the right orbit. There was no statistically significant difference between the preoperative ($p = 0.56$) and post-operative left and right orbital volume ($p = 0.955$).

3.4. *Infra-orbital rim and globe movement*

The data are summarized in Table 2. On each side, the anterior ($p < 0.001$) and the medial movement (left, $p = 0.031$; right $p = 0.014$) of the infra-orbital rim were statistically significant. For the globes, only the medial movement was statistically significant (left, $p = 0.005$; right, $p = 0.004$). There were no statistically significant differences between the left and right globe measurements and left and right infra-orbital rim movement ($p > 0.05$). A significant difference between the pre- and post-operative anterior position of the globe and infra-orbital rim was demonstrated (Fig. 6).

Table 1
Patient data.

patient number	Sex	Syndrome	Indication	Intervention	Age at time of surgery (years)
1	Male	Apert	OSA	LF III external DO	16
2	Female	Apert	Midface hypoplasia	LF III external DO	20.1
3	Female	Apert	Midface hypoplasia	LF III external DO	15.1
4	Male	Apert	Exorbitism	LF III external DO	18.3
5	Female	Apert	Midface hypoplasia	LF III external DO	19.2
6	Female	Apert	Midface hypoplasia	Conventional LF III	24.3
7	Female	Apert	Midface hypoplasia	LF III external DO	13.8
8	Female	Crouzon	Exorbitism	LF III external DO	16.8
9	Female	Crouzon	OSA	LF III internal DO	16.3
10	Male	Crouzon	OSA	LF III external DO	13.4
11	Male	Crouzon	Midface hypoplasia	LF III external DO	13.6
12	Male	Crouzon	Exorbitism	LF III external DO	8.2
13	Female	Crouzon	Midface hypoplasia	LF III external DO	18.8
14	Female	Crouzon	OSA	LF III external DO	9.5
15	Male	Crouzon	Midface hypoplasia	LF III external DO	10.6
16	Male	Crouzon	Midface hypoplasia	LF III internal DO	8.9
17	Male	Pfeiffer	Midface hypoplasia	LF III external DO	14.1
18	Male	Pfeiffer	Exorbitism	LF III external DO	7.4

Table 2
Globe and infra-orbital rim movement in the study-group. Significant movements were marked with an asterisk (*). Mean and standard deviation (SD) are depicted.

	Medial movement mean (SD) in mm	Anterior movement mean (SD) in mm	Caudal movement mean (SD) in mm
Left globe	1.7* (2.2)	0.6 (1.8)	0.8 (3.0)
Right globe	1.5* (1.9)	0.8 (2.5)	1.0* (2.2)
Left rim	1.5* (2.8)	12.0* (4.2)	0.5 (5.2)
Right rim	1.6* (2.5)	12.8* (4.9)	0.7 (3.8)

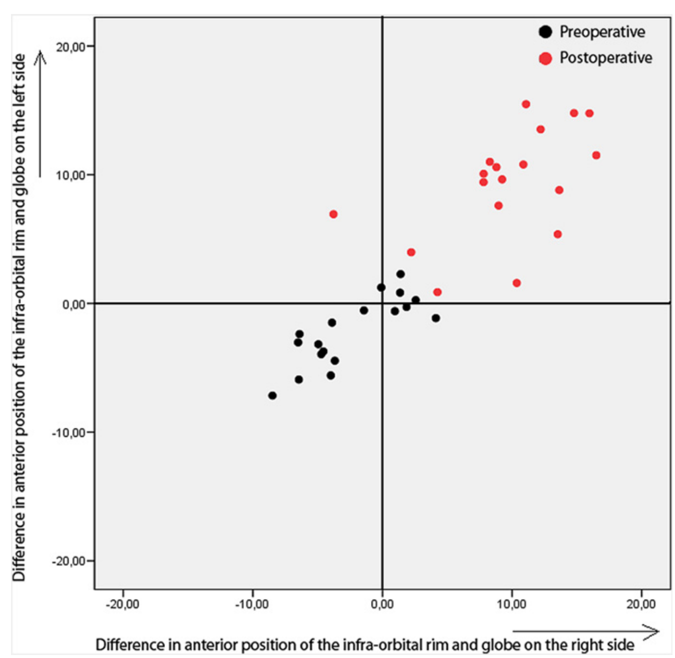

Fig. 6. Scatterplot representing the difference in the anterior position of the infra-orbital rim and globe on the right side (*x*-axis) and the difference in the anterior position of the infra-orbital rim and globe on the left side (*y*-axis). The black dots represent the preoperative data and the red dots represent the post-operative data. Statistical analysis showed a significant difference between the pre- and post-operative position of the infra-orbital rim and globe.

3.5. Correlation between orbital volume and globe movement

There was a statistically significant correlation between the anterior infra-orbital rim movement and the orbital volume gain (left: $r_s = 0.498$ and $p = 0.035$; right: $r_s = 0.642$ and $p = 0.018$).

4. Discussion

Orbital volume measurements are frequently reported with regard to enophthalmos and orbital trauma. Since 1985 different orbital volume measuring techniques have been described using three-dimensional (3D) computed tomography (CT) imaging (Bentley et al., 2002; Bite et al., 1985; Carr et al., 1992; Cooper, 1985; Fan et al., 2003; Furuta, 2001; Koppel et al., 2003; Manson et al., 1986; Schuknecht et al., 1996). A number of studies have shown a strong correlation of these measurements with skull measurements (Acer et al., 2009; Cooper, 1985; Deveci et al., 2000). Although accurate, these methods require much time and expertise and the techniques are based on estimation (Cooper, 1985; Deveci et al., 2000; Koppel et al., 2003). Since the anatomical boundaries of the bony orbit are complex, manual segmentation of datasets is necessary. Because the intrinsic anatomy of the orbit is distorted due to syndromal factors and previous surgical intervention, assumptions need to be made about the anatomical boundaries by the observer. Therefore the anterior boundary of the orbits needs to be defined. Although some studies have defined the anterior limit by a line joining the zygomaticofrontal processes (Charteris et al., 1993; Whitehouse et al., 1994), we choose to define the anterior boundary of the bony orbit as a straight line from the most antero-superior point of the infra-orbital rim to the most antero-inferior point of the supra-orbital rim in every (sagittal) CT-slice. Strict definitions were formulated concerning bony interruptions of the orbit. The ICC of our measurements showed that the chosen method was highly reproducible.

To the best of our knowledge, orbital volume changes after LF III advancement have not yet been evaluated in SCS patients. Bentley et al. investigated orbital volume changes of SCS patients not older than 36 months after fronto-orbital advancement, using semi-automatic segmentation comparable to our technique (Bentley et al., 2002). Numerous studies have reported a wide range of normal values of orbital volumes, which ranged from 21 ml to 30 ml. On average orbital volumes tend to be somewhat higher in males than in females (Deveci et al., 2000; Furuta, 2001; Koppel et al., 2003; Kwon et al., 2010; Manson et al., 1986; Schuknecht et al., 1996). Consistent with the findings of Bentley et al., normal orbital volumes were found preoperatively. After LF III advancement a significant orbital volume gain was found of 27.8%.

Considering the above findings, the infra-orbital rim and globe movements were analyzed. Several studies have measured globe position in healthy persons, SCS patients, Graves patients or patients with ophthalmic problems (Chen et al., 2008; Lee et al., 2001; Ozgen and Ariyurek, 1998; Sheikh et al., 2007). Usually in these studies a line was drawn between the most anterior points of the lateral orbital rims, using an axial CT-slice at midglobe level. To determine globe position, the perpendicular distance from the inter-zygomatic line to the posterior margin of the globe was measured pre- and post-operatively. Some miscalculations are likely to occur as this two-dimensional method does not account for differences in head position. The lateral orbital rim in SCS patients is osteotomized during LF III advancement and is therefore not suitable as a reference point.

We developed a three-dimensional (3D) method to be able to evaluate globe and infra-orbital rim position in three dimensions. The LSCCs were chosen to create a horizontal plane in vestibular orientation (VO) with reliable reproducibility. The LSCC of the inner ear has a constant relation to gravity and is unaffected by abnormal or asymmetric growth and disease (Vinchon et al., 2007). In the skulls of SCS patients, the horizontal plane in VO provides a complete set of three-dimensional directions. This VO allows precise measurements using 3D-CT-scans in SCS patients with an asymmetric skull-shape and anatomical anomalies of the skull base which renders standard landmarks and reference lines unsuitable. To compare the outcomes of the infra-orbital rim and globe movements between patients irrespective of the position of the head in the CT-scanner, three reference planes were created.

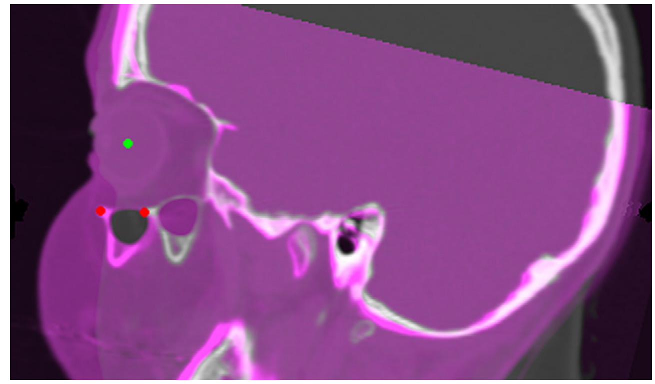

Fig. 7. Sagittal slice of the CT-scan of one of the subjects. Both the pre- (gray colored) and post-operative (pink colored) CT-scans are depicted. The red dots mark the most anterior point of the infra-orbital rim pre- and post-operatively. The green dot marks the center of the globe.

To the best of our knowledge, there have been no reports concerning the evaluation of infra-orbital rim and globe position after LF III advancement using a 3D-CT method. One study observed globe movement in SCS patients after monobloc advancement. Fitzgerald et al. measured globe movement by using several anatomical landmarks and a reference frame. However, the construction of the reference frame from the landmarks is not clear, and therefore the results are difficult to interpret. Fitzgerald et al. reported a forward movement of the bony structures and both globes (Fitzgerald O'Connor et al., 2009). We found a statistically significant anterior and medial movement of the infra-orbital rim, whereas the globe remained in almost the same position despite a slight medial movement. In both our study and in the study of Fitzgerald et al., no clinical evaluation of the eye was performed. Considering the significant anterior movement of the globe as observed by Fitzgerald et al the optical nerve is stretched in a non-physiological manner.

To evaluate the influence of LF III advancement on the shallow orbits, a significant positive correlation between the orbital volume gain and anterior movement of the infra-orbital rim was observed. Furthermore, a significant difference between the pre- and post-operative anterior position of the infra-orbital rim and globe was demonstrated, as illustrated in Fig. 6. Preoperatively, the globe is situated anterior of the infra-orbital rim while post-operatively the globe is situated posterior of the infra-orbital rim (Fig. 7). Together, these results provide insight into the effect of LF III advancement on the increase of orbital volume following LF III advancement.

The use of 3D visualization in diagnosis and treatment planning in craniofacial surgery is increasing and is now considered to be superior to two-dimensional imaging, as has been shown by the development of 3D cephalometry (Kamiishi et al., 2007; Olszewski et al., 2010). However, a recent report in this journal has shown that 3D digitization is not without disadvantages (Ozsoy et al., 2009).

Concerning orbital surgery, a recent article has shown that using 3D virtual models, physical models can be created with a degree of accuracy which can be used to shape a titanium mesh to successfully match and bridge an orbital floor fracture (Kozakiewicz et al., 2009).

The method we used in this report gives a realistic insight into the orbital changes after LF III advancement. However, thinner CT-slices may enhance accuracy. The standard treatment protocol should include a pre-and post-operative CT-scan at a fixed/standardized time-interval as superimposing pre- and post-operative CT-scans will be more accurate when there is less growth between the scans. Future research will focus on 3D visualization and quantification of the changes after LF III advancement on both skeletal and soft tissue level. The reference frame we have described may be useful as a tool for preoperative planning and post-operative evaluation of the degree of LF III advancement.

5. Conclusion

This study demonstrates a significant orbital volume gain and anterior movement of the infra-orbital rim following LF III advancement. The position of the globe was relatively unchanged.

Conflict of interest

There are no relations that could be construed as a conflict of interest.

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