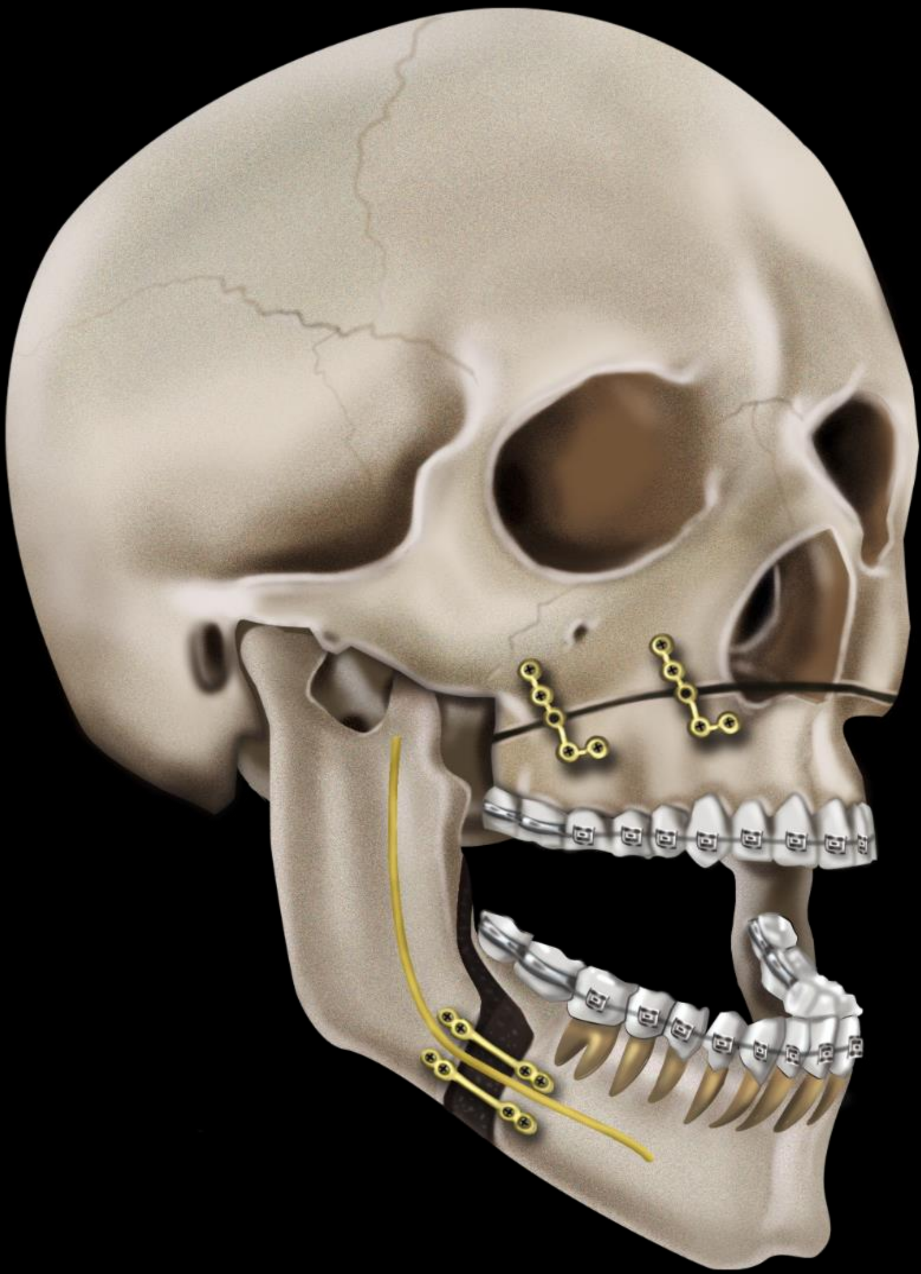
SKELETAL RELAPSE IN ORTHOGNATHIC SURGERY

A THREE-DIMENSIONAL UPDATE TO THE HIERARCHY OF SURGICAL STABILITY



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2021

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Biomedical Sciences Group
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DOCTORAL SCHOOL
BIOMEDICAL SCIENCES

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Sohaib SHUJAAT

Dissertation presented in partial fulfilment of the requirements for the degree of Doctor in Biomedical Sciences

Jury:

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SKELETALE TERUGVAL NA ORTHOGNATISCHE CHIRURGIE

EEN DRIE-DIMENSIONALE UPDATE NAAR DE HIËRARCHIE VAN CHIRURGISCHE STABILITEIT

Sohaib SHUJAAT

Proefschrift voorgedragen tot het behalen van de graad van Doctor in de Biomedische Wetenschappen

Jury:

Promotor: Prof. dr. Reinhilde JACOBS
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PREFACE

This doctoral thesis consists of 7 research articles, proceeded by a scientific introduction and concluded by a general discussion, clinical relevance and future recommendations. The research articles follow the standard scientific IMRAD structure (Introduction, Methods, Results and Discussion), and were based on the following peer-reviewed publications:

Article 1

Shaheen E, **Shujaat S**, Saeed T, Jacobs R, Politis C. Three-dimensional planning accuracy and follow-up protocol in orthognathic surgery: a validation study. *Int J Oral Maxillofac Surg.* 2019;48(1):71-76. doi:10.1016/j.ijom.2018.07.011. (shared first-authorship)

Article 2

Shujaat S, Shaheen E, Politis C, Jacobs R. Accuracy and reliability of voxel-based dento-alveolar registration (VDAR) in orthognathic surgery patients: a pilot study with two years follow-up. *Br J Oral Maxillofac Surg.* August 2020. doi:10.1016/j.bjoms.2020.08.033.

Article 3

Shujaat S, Shaheen E, Politis C, Jacobs R. Three dimensional evaluation of long-term skeletal relapse following Le Fort I maxillary advancement surgery. A 2 year follow-up study. *Int J Oral Maxillofac Surg.* (Accepted)

Article 4

Shujaat S, Shaheen E, Politis C, Jacobs R. Three dimensional evaluation of distal and proximal segments skeletal relapse following isolated mandibular advancement surgery in 100 consecutive patients. A one year follow-up study. *Int J Oral Maxillofac Surg.* (Accepted)

Article 5

Shujaat S, Shaheen E, Politis C, Jacobs R. Three dimensional pharyngeal airway space changes following isolated mandibular advancement surgery. A prospective 1-year follow-up study. J Craniomaxillofac Surg. (Under review)

Article 6

Shujaat S, Shaheen E, Novillo F, Politis C, Jacobs R. Accuracy of cone beam computed tomography–derived casts: A comparative study. J Prosthet Dent. 2021;125(1):95-102. doi:10.1016/j.prosdent.2019.11.021.

Article 7

Shujaat S, Da Costa Senior O, Shaheen E, Politis C, Jacobs R.Visual and haptic perceptibility of 3D printed skeletal models in orthognathic surgery. J Dent. (Accepted)

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Last but not least, I am thankful to my elder brother, **Usama Shujaat**, who is not with us anymore in this world (May his soul rest in peace) but I can always feel his presence, giving me the strength and energy from the heavens above to continue and finish my thesis.

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List of abbreviations

2D	Two-dimensional
3D	Three-dimensional
6DoF	Six degrees of freedom
A/P	Anterior/Posterior
AP	Acoustic pharyngometry
BMI	Body mass index
BSSO	Bilateral sagittal split osteotomy
CBCT	Cone-beam computed tomography
CCW	Counter-clockwise
CJ	Colorjet
CT	Computed tomography
CW	Clockwise
DICOM	Digital Imaging and Communications in Medicine
DLP	Digital light processing
FDM	Fused deposition modeling
I/E	Intrusion/Extrusion
L/R	Left/Right
LF I	Le Fort I
mCSA	Minimal cross-sectional area
MJ	Multijet
SLA	Stereolithography
MRI	Magnetic resonance imaging
PAS	Pharyngeal airway space
PICO	Population, intervention, comparison, and outcome
PJ	Polyjet
SLS	Selective laser sintering
STL	Standard Tessellation Language
SVD	Singular value decomposition
TMJ	Temporomandibular joint
VBR	Voxel-based registration
VDAR	Voxel-based dental arch registration

General introduction
Aims & Hypotheses

1.1 Introduction

Orthognathic surgery occupies a special position in medicine and surgery. To begin with, it is a subspecialty of two specialties: Oral and Maxillofacial Surgery and Orthodontics. Second, orthognathic surgical treatment needs the ideal combination of art and science, from the fine details of diagnosis and treatment planning to the finesse of surgical technique. Finally, unlike other common procedures in surgery, orthognathic surgery patients don't simply 'need' such treatment; they additionally 'desire' it for acquiring a combined aesthetic and functional soft and hard tissue harmony which is a life changing experience for such patients.[1]

The post-surgical and post-treatment goals of orthognathic surgery are multifold. The most common ones include, acquiring the desired dentomaxillofacial position and maintenance of the achieved dentoskeletal position, facial soft tissue and the airway space without recurrence at follow-up.[2]

1.2 Historical background of orthognathic surgery

The term orthognathic surgery, often termed as “surgical orthodontics” or “combined orthodontic-surgical correction” is derived from Greek origin, where “*orthos*” means “correct or straighten” and “*gnathos*” means “jaw”. Thereby, it can be defined as a procedure for the three-dimensional (3D) correction of the dentoskeletal deformities. The two most common orthognathic surgical procedures include Le Fort I osteotomy (LF I) and bilateral sagittal split osteotomy (BSSO).[3]

In 1859, Von Langenbeck[4] provided the first description of the maxillary LF I osteotomy for gaining access and removing nasopharyngeal polyps, followed by Wassmund in 1927[5] who used the approach for correcting mid-facial deformity. Later, pterygomaxillary suture separation with an osteotome was described by Axhausen[6] and Schuchardt.[7] In 1949, Moore and Ward[8] made further modifications to the approach. Despite the evolution of the LF I osteotomy and contribution from various surgeons, certain unpredictabilities were observed with the procedure such as , difficulty while separating the maxilla from the pterygoid plate region, bleeding and relapse. To overcome these limitations, in 1965, Obwegeser proposed the complete mobilization of the maxilla offering a tension-free stabilization which became a treatment of choice for correcting mid-facial and maxillary deformities.[9] Based on Obwegeser’s approach, LF I further underwent certain modifications to refine the approach further, however the main principle behind these alterations remained the same i.e. achieving a completely mobilized maxilla with a viable vascular pedicle and presence of a stable fixation.[10] The modern LF1 maxillary osteotomy procedure includes surgical cut made from nasal septum to the pterygomaxillary junction below the apices of roots of the maxillary teeth, allowing manipulation of the maxilla either anteroposteriorly, mediolaterally or superoinferiorly and correction of the deformity based on the functional and/or aesthetic needs of the patient (Figure 1).[11]

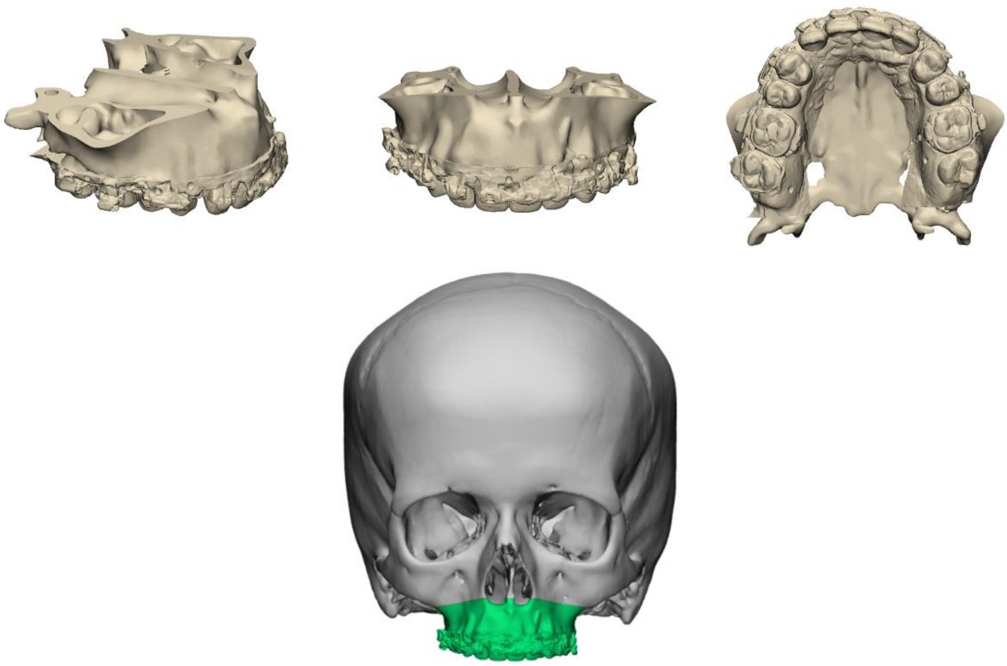


Figure 1. Modern Le Fort I osteotomy design

The BSSO procedure is one of the most common mandibular orthognathic surgical procedure performed either alone or in combination with LF I osteotomy. The first description of an intraoral stepped horizontal ramus osteotomy was reported by Karl Schuchardt in 1942, which later on modified to become the modern BSSO.[12] Thereafter, the BSSO approach underwent major modifications with the greatest developments in design accredited to Trauner and Obwegeser (1957)[13], followed by Dalpont (1961)[14],Hunsuck (1968)[15] and Epker (1977).[16] These modifications allowed decrease in complication rate which commonly included neurosensory disturbances of the lower lip and chin region, relapse, soft tissue swelling and condylar displacement. The main modifications involved positioning of the buccal osteotomy cut in a more anterior position which reduced the pterygomasseteric muscle stripping, increased cancellous bone contact and reduced post-operative complication rate. All the modifications employed “sagittally splitting” the mandibular ramal region into two bone surfaces with their cancellous parts facing each other. This splitting allowed the repositioning of the distal mandibular segment (tooth-bearing region) for correcting the mandibular asymmetry and/or retro- or proganthia by mandibular rotation, advancement or setback. Also taking care to avoid unnecessary movement of the proximal segment (condyle-bearing region) to minimize the risk of condylar sag or displacement.[17] In modern orthognathic surgery, a modification based on Hunsuck/Epker approach is mostly used by the surgeons with the only difference being the extent of the lingual split from the Obwegeser/Dal Pont approach. The lingual cut extends just posteriorly to the lingula in the former instead of the involvement of the whole ramal width, thereby, allowing reduction in soft tissue dissection and higher stability.[18] **Figure 2** illustrates the most widely used Hunsuck and Epker BSSO approach.

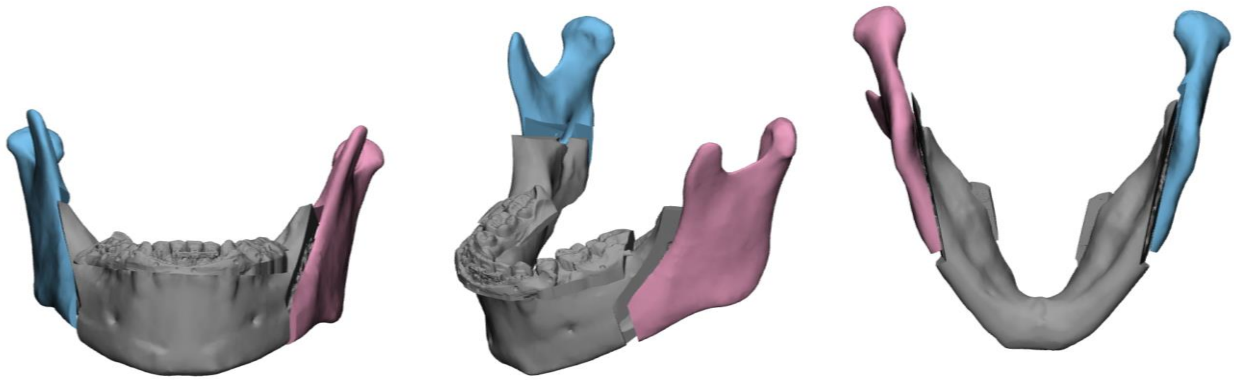


Figure 2. Hunsuck and Epker bilateral sagittal split osteotomy approach for mandibular advancement

1.3 Recurrence (Relapse)

Relapse can be defined as a failure to achieve stability or “a return to pre-operative state” which can compromise the final achieved position.[19] The opposite of relapse is *stability* which is defined as the maintenance of the hard (skeletal structures, teeth) and soft tissue (facial soft tissue, pharyngeal airway space) over a period of time. Relapse is one of the most commonly studied complication in orthognathic surgery. Its occurrence can be linked with certain factors which can either lead to early or late surgical relapse. Multiple intrinsic and extrinsic factors are also responsible for relapse at follow-up. Extrinsic factors include complications related to surgery, such as bad splits, condylar displacement and osteotomy slippage. In addition, surgeon expertise, type of surgery, surgery sequence, amount of expansion, magnitude of advancement and type of fixation are also associated with relapse where rigid fixation offers more stability compared to the historical wire fixation. The intrinsic factors include patient characteristics related to growth, body mass index, occlusion, myofunction, and temporomandibular joint conditions.[20]

1.3.1 Factors governing early relapse

1.3.1.1 Treatment planning

When considering the treatment planning of the patient, the surgeon should have a sound knowledge about the physiology and function of dentoskeletal and soft tissue structures so an appropriate surgical movement and procedure can be proposed. As an imprecise planning which disregards the limitations associated with the amount and direction of movement can contribute to early relapse.[21] For instance, patients requiring larger mandibular advancement with BSSO (>8mm or more) which crosses the physiological limit of the jaw has a tendency to relapse more compared with less amount of movement.[22] In such a scenario, concomitant application of bone graft should be opted to offer a higher stability. Additionally, during the planning phase, excessive rotation of jaws should be avoided as such to avoid the early relapse resulting from the opposing forces of the muscular sling.[23]

Attention should be paid when obtaining patients surgical records, performing virtual planning or model surgery. As any discrepancy in these steps can influence the final outcome and ultimately lead to early relapse. For instance, an inaccurate centric bite without adequate seating of the condyle in the mandibular fossa, an inaccurate facebow record, model inaccuracies and warping of the dental stone models can all influence the post-surgical stability.[24] Even though recent advancements have led to the application of various software based workflows in orthognathic surgery, care should be taken to avoid errors associated with the patients records collection as it can still influence the post-operative stability.

1.3.1.2 Intra-operative errors

One of the most common intra-operative errors which secondarily influences early relapse is the failure of appropriate seating of the condyle into the fossa. Normally, following orthognathic surgery the condyles should be seated in the fossa passively with optimal inter-maxillary fixation. Failure to achieve the required positioning can result in an unstable post-operative occlusion and condylar displacement.[25] Condylar displacement can occur with both LF I and BSSO surgery. In LF I, an improper removal of the interferences at the posterior region can lead to condylar dislocation or relapse, where the maxillomandibular complex has the tendency to rotate superiorly for correcting the mid-facial position vertically. Similarly in BSSO, proximal segment positioning without excessive flaring and condylar seating is also crucial for ensuring a stable outcome.[23]

1.3.1.3 Post-operative bone healing

Wound healing is an important factor which can inadvertently influence the stability of the jaws and results in early relapse. For instance, if a bad-split (*an unfavorable fracture of the mandible at the course of the osteotomy design*) occurs, it should be identified, fixed and stabilized appropriately. Failure to do so can result in an acute relapse due the functional and physiological adaptation of the jaw. Other wound healing abnormalities should also be considered, such as infection, malunion, non-union of the bony segments or fracture of plates, which can all lead to early relapse of dentoskeletal and soft tissue structures.[26] Thereby, requiring an additional surgery or an aggressive approach for correcting these complications.

1.3.2 Factors governing late relapse

1.3.2.1 Growth

It is the most obvious physiological process which can lead to late relapse or instability of the achieved new position of the jaws. Although, the modern orthognathic surgery planning is mostly performed at a post-pubertal stage when facial growth has been completed to avoid the likelihood of relapse due to the inadvertent catch up or lack of growth. Nevertheless, the growth potential should be kept in mind as the facial tissue continues to grow even after the age of 18 years and well beyond early adulthood. The growth at this stage is miniscule and might not lead to a clinically significant relapse, however, this factor should also be considered when evaluating relapse.[1]

1.3.2.2 Physiological adaptation

The main recipe for the long-term relapse is attributed to the physiological response brought by the change in normal anatomy via the surgeon, where the normal patient physiology overpowers the surgeon-induced physiological change. The physiological adaptations include changes in the bite force and muscular and soft tissue tension, all of which try to oppose the new achieved skeletal and dental units. For instance, the lip and tongue pressure changes after orthognathic surgery, thereby, leading to relapse or instability of the facial soft tissue and dentoskeletal structures.[27] This change in the functional matrix caused by the muscular and soft tissue tension varies with different orthognathic surgical procedures and relies majorly on the amount of movement.[28] Therefore, care should be taken during the treatment planning phase that the changes in the functional matrix are taken into consideration for minimizing its influence on the long-term stability.

1.4 Hierarchy of skeletal stability

The stability of LF1 and BSSO procedures is dependent on the direction and amount of movement. The hierarchy of stability related to orthognathic procedures can be differentiated into either post-surgical or post-treatment stability. The post-surgical stability refers to the relapse occurring during the first post-surgical year and is directly linked to the healing, orthodontic treatment and early physiological adaptations. The post-treatment stability is any relapse occurring beyond the first post-operative year and is associated with the long-term physiological adaptations.

1.4.1 Le Fort I osteotomy and skeletal relapse

LF I surgery is commonly performed alone or in combination with BSSO for the correction of maxillary vertical excess, vertical deficiency or antero-posterior deficiency by superior, inferior and/or anterior repositioning of the maxilla respectively. The relapse varies depending on the direction and magnitude of maxillary movement. LF1 superior repositioning is considered to be one of the most stable procedure post-surgically, however a study observed a post-treatment relapse of more than 2mm in approximately 20% patients, which was due to the unfavorable facial growth.[29] In studies where repositioning was performed following the completion of the adolescent growth spurt showed excellent short and long-term stability.[30] Some long-term studies have shown that the superior repositioning has a tendency to undergo relapse in around one third of the patients, where the maxilla moves slightly in a download direction. However, this relapse is clinically not noticeable as it is compensated by the bite of the patient and incisors eruption.[31] In contrast, inferior maxillary repositioning is less predictable and has a tendency to relapse in a superior direction due to the strong functional occlusal forces resulting from the mandibular teeth. Evidence suggests a relapse of more than 2mm in approximately 50% of these patients. [1,23]
To overcome the relapse, certain solutions have been proposed, such as simultaneous BSSO surgery for decreasing the occlusal forces and/or inter-positioned bone graft.[32] The LF I maxillary advancement surgery is less stable than the superior repositioning and more stable than the inferior repositioning. Its stability is largely dependent on the amount of movement.[33] In patients where advancement of 3mm or more is planned or those having visible vertical gaps have a tendency to relapse posteriorly due to either inadequate osteosynthesis or lack of osseous tissue. Therefore the application of autogenous anterior iliac bone graft or synthetic materials such as hydroxyapatite can lead to reduction in the recurrence rate.[34]

1.4.2 Bilateral sagittal split osteotomy and skeletal relapse

Mandibular osteotomy is performed for the correction of mandibular asymmetry, deficiency or excess by BSSO rotation, advancement (anterior repositioning) or setback surgery (posterior repositioning) respectively. Just like the LF I superior repositioning surgery, mandibular advancement falls in the category of highly stable procedures, demonstrating a relapse of less than 2mm in more than 90% of the cases at the end of the 1st year of surgery. However, beyond the 1st year, the mandibular length and ramal length is known to decrease owing to the condylar remodeling at a long-term interval. [33] The decreased mandibular dimensions could also be attributed to osteotomy slippage. Osteotomy slippage is a response of the para-mandibular connective tissue stretch with a low level of muscle activity, which reacts under tension against the surgical skeletal changes. [35] It involves resorptive processes at the osteotomy site, reflected by the remodeling at the gonial angle and upward vertical movement related to dimensional loss.[36,37] The mandibular relapse is positively correlated with the amount of mandibular advancement and undesirable condylar displacement during surgery.[38] The BSSO setback surgery frequently relapses towards a forward direction and has the tendency to relapse more than advancement surgery. The relapse mostly occurs due to the inadequate control of the proximal segment which might get pushed posteriorly and at follow-up the muscular forces intend to pull it back to its original position with distal segment being carried forward.[39]

1.4.3 Bimaxillary surgery and skeletal relapse

Bimaxillary surgery refers to simultaneous correction of skeletal class II or III abnormalities with a combination of LF I and BSSO (double jaw surgery). Evidence related to the rate of relapse between bimaxillary surgery and isolated jaw surgeries is controversial. As some studies suggest bimaxillary surgery to be more stable than single jaw surgery and vice versa. De Haan et al. compared the rate of relapse between isolated mandibular setback surgery and in combination with maxillary advancement surgery. They observed no significant difference between both procedures.[40] Scheuer und Höltje reported higher stability with mandibular surgery alone than bimaxillary surgery.[41] Proffit et al.[33] suggested less relapse associated with isolated mandibular advancement compared to the bimaxillary advancement, whereas Chen et al. observed no clinically significant difference between both procedures. [42] The variation is relapse exists due to multiple factors such as patient-related factors (age, sex, population group) or surgery-related factors (amount of movement, bone graft, type of fixation).

1.5 Transition from two-dimensional to three-dimensional skeletal relapse assessment

1.5.1 Why not 2D cephalometry?

Since the introduction of 2D lateral cephalometric radiography by Broadbent in 1931,[43] it has been considered as the main tool for assessing skeletal and soft tissue relapse in orthognathic surgery patients. Although it provided useful information related to relapse and has been extensively used for assessing relapse, nevertheless, the limitations associated with its application cannot be ignored, such as, errors of projection, magnification, landmark identification, linear and angular evaluation of relapse, observer variability and superimposition.[44,45] Recent technological developments have led to the replacement of conventional manual cephalometry with the utilization of computerized cephalometric prediction methods to reduce manual errors, however, the inability of the 2D images to represent the 3D anatomical structures is not sufficient as the phenomenon of relapse rather occurs in three dimensions.[46]

1.5.2 Why not 3D cephalometry?

To overcome the limitations of 2D images, they have been replaced by the 3D acquisition devices. Nowadays, the most common device utilized for assessing skeletal relapse is the cone-beam computed tomography (CBCT) which offers 3D assessment of relapse and overcomes most of the errors associated with 2D imaging. Previous studies have been carried out assessing skeletal relapse with 3D cephalometry, however, the introduction of error by adding a third dimension should be kept in mind. As 3D cephalometry also relies on manual identification of landmarks so the error of observer variability is still at hand.[47] Both of which can be a huge problem for accurately and objectively identifying the amount of relapse. Additionally, it only provides information pertaining to the landmarks displacement rather than the skeletal structure three-dimensionally so it cannot be considered a true 3D representation of relapse but a pseudo 3D assessment.

1.5.3 Why not color-coded comparison?

Some studies assessing skeletal relapse utilized color-coded comparison, where the segmented 3D skeletal structure immediately following surgery is superimposed onto that at follow-up and the outcome generated is based on color. The color represents the distances between the surfaces of two structures in the 3D space by providing the mean, median or root mean square distances, the smaller the value (close to 0) the better is the result or that is the assumption. This color coded map is useful when tracing for example changes in the bone or bone remodeling, however it fails to represent the translational and rotational direction of relapse and also it is not possible to calculate the systematic error of the approach.[48] So the clinical benefit of such a methodology is questionable as it does not provide any clinically relevant information to the surgeon on which direction the relapse occurred and thereby, the surgical approach or treatment plan cannot be improved.

1.5.4 Is six degrees of freedom the answer?

The recent advances in technology and improved algorithm designs have allowed the true 3D representation of relapse following orthognathic surgery. The six degrees of freedom (6DoF) refers to the freedom of maxillary or mandibular movement in 3D space following LF I and BSSO respectively. So instead of relying on landmarks displacement as with the cephalometry, the 6DoF takes the whole structure into consideration, by objectively measuring the amount and direction of relapse with respect to translational (mediolateral, anteroposterior, superoinferior) and clockwise/counter-clockwise (CW/CCW) rotational parameters (pitch, roll, yaw) (Figure 3).[49] This allows quantification of relapse without the introduction of human error. The 6DoF can offer a more clinically oriented explanation of the relapse and thereby improve treatment planning which is performed with the 3D planning software programs. Till now, only a few studies exist assessing the translational and rotational skeletal relapse following LFI and/or BSSO surgery.

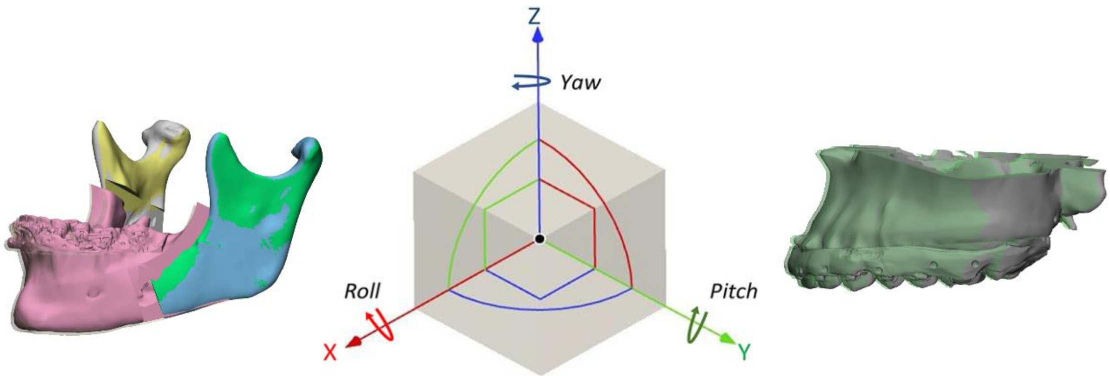
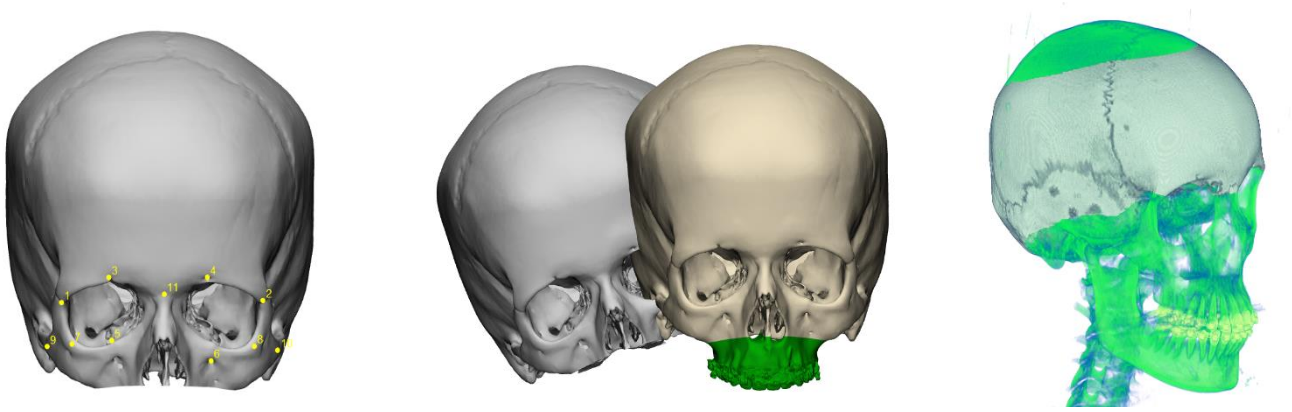


Figure 3. Six degrees of freedom (translational: ‘x’, ‘y’ and ‘z’ axis; rotational: pitch, roll, and yaw).

1.6 Images superimposition

When assessing relapse, an important step is called image superimposition or registration which is applied for superimposing two CBCT scans using a stable region of interest so relapse can be observed. The three most commonly applied registration methods in orthognathic surgery include, point-based[50], surface-based[5] and voxel-based registration (Figure 4).[52] Out of these, voxel-based registration is the most accurate and acceptable method of superimposition.[53,54] Unlike, point-based which relies on landmark identification and surface-based which is dependent on the segmentation accuracy,[55,56] voxel-based registration offers the best approach using data from the voxels of the CBCT scan for superimposition.[52] In orthognathic surgery anterior cranial based is most commonly utilized for voxel-based registration. Some studies have also suggested zygomatic arch and dentoalveolar region for the registration process with optimal reliability and accuracy.[52,57,58] Although, voxel-based registration (VBR) has been around for almost a decade, nevertheless, only a few studies are available assessing skeletal relapse for 1 year or more with both voxel-based registration based on mutual information and quantification with 6DoF.[59]



Point-based registration ***Surface-based registration*** ***Voxel-based registration***

Figure 4. Common types of image registrations methods

1.7 Evidence-based review of 3D skeletal relapse in class II patients

A review was conducted to assess skeletal mandibular relapse in Class II patients requiring BSSO advancement at a follow-up period of one or more years. The population, intervention, comparison and outcome (PICO) criteria included a skeletal class II population with particular characteristics; BSSO advancement surgery, bimaxillary surgery; the difference between immediate and post-treatment position of skeletal structures at a follow-up period of a year or more as the comparison; and 3D relapse of the skeletal structures as the outcome. Inclusion criteria involved randomized controlled trials (RCTs), prospective studies, retrospective studies, and case series with at least 10 patients, follow-up of at least 1 year with rigid internal fixation and 3D assessment of skeletal relapse, The search strategy was accomplished with medical subject headings (MeSH) and synonyms of three concepts related to orthognathic surgery (osteotomy), outcomes (relapse, recurrence), and methods of radiographic evaluation ((cone beam) computed tomography, 3D cephalometry). A combination of controlled vocabulary and free-text terms was designed and applied in the Medline database PubMed, Cochrane and Embase. Electronic databases were searched until September 2020. After the screening of titles and abstracts from 570 papers, 354 potentially eligible articles were selected. Out of these, 300 were excluded for the following reasons; case series with fewer than ten patients, literature reviews, and follow-up of less than one year. Finally, 11 articles were included for qualitative synthesis, where 6 articles assessed relapse in patients undergoing BSSO advancement and 5 articles involved bimaxillary advancement patients (Table 1).[59, 60-69]

Table 1. Patient characteristics of the included studies.

Studies	Study design	Sex		Sample size	Mean Age	Type of surgery	Class	Surgical movement	Additional surgeries
		M	F	n	years				
Carvalho et al., 2010	Prospective observational	9	18	27	30.04	BSSO	II	MA	genioplasty=9
Motta et al., 2011	Prospective observational	9	18	27	30.04	BSSO	II	MA	genioplasty=9
Goncalves et al., 2013	NR	3	7	10	31	LF I+BSSO	II	MMA	NR
Xi et al., 2015	Prospective	17	39	56	30.2	BSSO	II	MA	None
Xi et al., 2015	NR	17	39	56	29.2	BSSO	II	MA	None
Hernández-Alfaro et al., 2017	Retrospective	14	50	64	29.4	LF I+BSSO	II	MMA	genioplasty=34, maxillary segmental osteotomy= 45
Xi et al., 2017	NR	16	34	50	29.5	LF I +BSSO	II	MMA	genioplasty
Bianchi et al., 2018	Retrospective	4	8	12	31.8	LF I +BSSO	II	MMA	NR
Sun et al., 2018	Retrospective cohort	6	18	24	29.9	BSSO	II	MA	None
Liebregts et al., 2019	Retrospective cohort	33	73	106	28	LF I +BSSO	II	MMA	genioplasty=57, history of SARME= 28
Yin et al., 2020	Retrospective cohort	10	21	31	24	BSSO	II	MA	None

BSSO: bilateral sagittal split osteotomy,LF I: Le Fort I maxillary osteotomy, MMA: maxillomandibular advancement, MA: mandibular advancement

All the studies had variable methodologies, where mostly relied on either color-coded comparison [59-61,66] or 3D cephalometry with different landmark-based linear/angular evaluation methods.[62-65,67,69] Only one study reported on the relapse by assessing 6DoF (Table 2), where the authors compared relapse of bimaxillary osteotomy with either maxilla- or mandible-first approach. They found no significant difference between the skeletal relapse of both the approaches at a period of 1 year and most of the relapse was clinically insignificant (<2mm).[59]

Table 2. Methodologies of the included studies.

Studies	Post-operative data acquisition points		Total follow-up period	Structures assessed	Type of superimposition	Relapse quantitative evaluation technique
	t1	t2				
Carvalho et al., 2010	4-6 weeks	12 months	12 months	mandible	voxel-based	color-coded surface analysis
Motta et al., 2011	6 weeks	12 months	12 months	mandible	voxel-based	color-coded surface difference
Goncalves et al., 2013	5 days	12 months	12.5±1.4 months	condyles	landmark-based	color-coded surface analysis
Xi et al., 2015	1 week	12 months	12 months	mandible	voxel-based	3D cephalometric analysis
Xi et al., 2015	1 week	12 months	12 months	mandible	voxel-based	3D cephalometric analysis
Hernández-Alfaro et al., 2017	1 month	12 months	12 months	mandible	landmark-based	3D cephalometric analysis
Xi et al., 2017	1 week	24 months	24.5 months	mandible	voxel-based/ surface-based	3D cephalometric analysis
Bianchi et al., 2018	1-10 days	12 months	12.4 months	maxilla and mandible	voxel-based	color-coded surface analysis
Sun et al., 2018	6 weeks	12 months	12 months	mandible	volume-based/ Surface-based	3D cephalometric analysis/ registration vector calculation
Liebregts et al., 2019	1 week	12 months	10.2 ± 3.0 months	maxilla and mandible	voxel-based	landmark-free translational and rotational analysis
Yin et al., 2020	1 week	12 months	12 months	mandible	volume-based/ Surface-based	3D cephalometric analysis

Based on the studies evaluating relapse with structural color-coded analysis, majority of the clinically significant relapse was observed in the ramal and condylar segment in the bimaxillary surgery group compared to the isolated BSSO surgery (Table 3). The cephalometric analysis showed an overall mandibular relapse of around <1-2mm in both surgical groups. However, the review suggested a lack of a standardized 3D protocol and a scarcity of evidence related to the assessment of distal and proximal segments relapse by applying 6D0F with semi- or fully-automatic approaches for avoiding the human error associated with landmark identification and/or manual segmentation. Additionally, a high risk of bias existed, so no clear conclusions could be drawn based on the available evidence. Future studies are recommended for assessing skeletal relapse utilizing voxel-based registration and 6DoF so a more clinically oriented outcome can be generated, thereby, further allowing improvement in treatment planning.

Table 3. Relapse associated with bilateral sagittal split osteotomy (BSSO) and bimaxillary surgery based on structural superimposition.

3D structural relapse from immediate to 1year (mm)			
		BSSO	**Bimaxillary surgery**
Maxilla		-	2.7±1.2[67]
Mandibular body	**Complete Chin**	− 0.40±2.50[60]	-
Ramus	**Inferior ramus (right)**	-0.46 ± 1.55[60]	-
	Inferior ramus (left)	-0.26±1.82[60]	-
	Superior ramus (right)	-0.31±1.31[60]	-
	Superior ramus (left)	-0.13±1.35[60]	-
	Posterior ramus (right)	0.53±1.20*[60]	-
	Posterior ramus (left)	0.18±1.70[60]	-
	Right ramus	-	3.5±1.6[67]
	Left ramus	-	4.5±1.9[67]
Condyle	**Condyle (right)**	0.16±1.53	-
	Condyle (left)	0.05±1.58	-
	Right posterior surface	-	2.4±1.3[67]
	Left posterior surface	-	2.0±1.1[67]
	Right medial pole	-	2.0±1.5[67]
	Left medial pole	-	1.6±0.7[67]
	Right anterior surface	-	-
	Left anterior surface	-	-
	Right lateral pole	-	2.8±2.5[67]
	Left lateral pole	-	1.8±0.7[67]
	Right superior surface	-	2.1±1.0[67]
	Left superior surface	-	2.0±0.6[67]

* indicates statistical significance

1.8 Relationship between skeletal and pharyngeal airway space relapse

Airway occupies a central position in the maxillofacial complex, serving to perform various physiological functions such as swallowing, respiration and speech.[70] It consists of 3 main regions, naso-, oro- and hypopharynx (Figure 5).[71] The walls of the pharyngeal airway space (PAS) consist of soft tissue so its patency is dependent on the surrounding muscles contraction and tension. As the changes in skeletal morphology induced by the orthognathic surgical procedures also influence soft palate, tongue and hyoid bone position which in turn can lead to change in the PAS dimensions by either increasing or decreasing the muscular tension.[72] The change in PAS is correlated to the amount and direction of skeletal movement and relapse.[73] For instance, BSSO setback surgery is associated with a decrease in PAS dimensions which may compromise the respiratory function and can lead to obstructive sleep apnea (OSA). On the other hand, bimaxillary advancement or BSSO advancement surgery causes an increase in PAS, thereby improving the respiratory status.[74,75] Similarly LF I advancement surgery has also been known to influence the nasal airway function.[76]

Although many studies have been conducted assessing the short- and long-term stability of PAS following various orthognathic surgical procedures, however controversy exists related to its stability at follow-up and correlation with skeletal relapse for orthognathic surgical procedures.[77] Studies assessing the PAS dimensions at follow-up in patients undergoing BSSO setback have shown variable results, where some suggest complete or partial relapse of the PAS to its original dimensions due to the readaptation of the soft tissue and the achieved changes in airway are temporary, whereas, others have reported its stability over a long period of time.[78] Based on a meta-analysis performed by Christovam et al.,[79] controversy existed related to PAS stability, where in relation to BSSO advancement, some studies indicated an increase in PAS patency at short-term follow-up which sustains its dimensions at follow-up, while others suggested an initial increase with decrease over a period of time. Patients undergoing maxillary advancement with mandibular setback showed an immediate decrease in PAS and no relapse was observed at follow-up, while others suggested no change. Patients undergoing bimaxillary advancement have been reported to show an immediate widening of PAS and stability at follow-up. With respect to the correlation between skeletal and PAS relapse, some studies showed a strong positive correlation between skeletal and PAS relapse due to the influence of the supra- and infra-hyoid muscles which could have led to the PAS relapse, while others suggested a weak correlation.[80,81] The main reason for the variability in findings might have been due to different factors such as amount of movement, method of assessment and small heterogeneous datasets. Additionally numerous studies have reported on the PAS changes and relapse following bimaxillary surgery, however, only a few studies exist evaluating 3D PAS changes at a follow-up of 1 year or more following isolated BSSO surgery. [79,82,83]

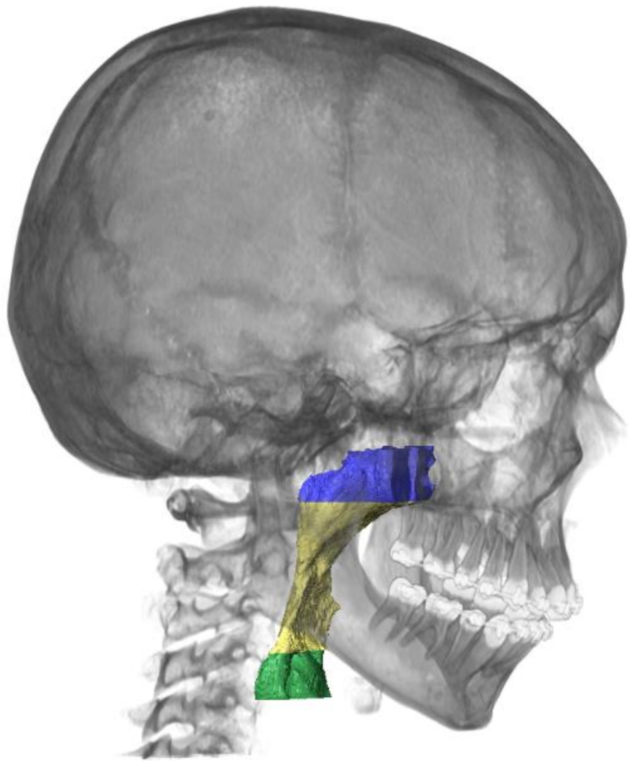


Figure 5. Anatomical sub-regions of pharyngeal airway space, blue: nasopharynx; yellow: oropharynx; green: hypopharynx.

1.9 Imaging of airway in orthognathic surgery

Conventionally, lateral cephalometry has been the standard choice for evaluating PAS changes and relapse following orthognathic surgery. The inherent limitations are the same as those mentioned beforehand for assessing skeletal relapse. Additionally, the evidence on 2D airway change has been limited by assessing relapse in the sagittal plane only without considering the three dimensions and volumetric assessment.[84] Based on these limitations, the 3D imaging devices, such as CT, CBCT, magnetic resonance imaging (MRI), nasopharyngoscopy and acoustic pharyngometry (AP) have replaced its 2D counterpart for assessing PAS changes.[85]

1.9.1 Static meeting dynamic

In orthognathic surgery, CBCT is the main imaging tool for airway assessment. Its application for the purpose of volumetric PAS and minimal cross-sectional area assessment of the airway have been widely reported and has been found to be an accurate and reliable tool.[86,87] However, one might argue that a CBCT provides a static image of a dynamic airway structure. Considering the dynamic nature, AP has been recommended to accurately measure the PAS with high reproducibility. The technique utilizes acoustic reflection and generates sound waves for dynamically measuring the PAS volume and minimal constriction area.[88]

Tsolakis et al.[89] compared the dynamic AP with CBCT for assessing pharyngeal volume and cross-sectional area and found no clinically significant difference between both the approaches with almost equivalent accuracy. Additionally, a high correlation existed with both the static and dynamic approaches. In contrast, Ananthan et al.[90] suggested CBCT to be superior to the AP, and confirmed CBCT to be the modality of choice for assessing airway size and stability. Based on these findings, even when static meets dynamic in the PAS region, the accuracy and reliability of CBCT is optimal for the purpose of diagnosis, treatment planning and follow-up of orthognathic surgical procedures. The accuracy can be further increased by standardizing CBCT acquisition protocols, patient positioning and scanning parameters.

1.10 Prevention of skeletal relapse and life-sized models

As the skeletal relapse is multifactorial and can affect the long-term aesthetic and/or functional outcomes of the orthognathic surgical procedure, so consideration should be given to certain factors which can be controlled, thereby minimizing the relapse and optimizing the surgical approaches to ensure long-term stability. Recently, remarkable advancements have been achieved in the development and application of virtual surgical planning of orthognathic surgery procedures. At the same instance, the 3D printing industry has also showed a sudden boom and has evolved in the medical industry.[91] However, little research has been carried out on the accuracy and applicability of patient-specific 3D printed skeletal models and their role in decreasing relapse.[92] The control of the early relapse is crucial for the long-term stability of a surgical procedure. For instance, early relapse is associated with either forced fixation of the BSSO leading to condylar displacement or lack of proximal segment control and visualization intra-operatively. This early relapse can in turn cause late relapse by condylar resportion.[93] Various condylar repositioning devices have been proposed which intend to increase the operating time and are technique sensitive, thereby, manual repositioning still remains the method of choice.[94] Additionally, bony interferences in both LF I and BSSO osteotomies may also casually lead to relapse.[23,95]

A patient-specific 3D printed model can overcome these risk factors to a certain extent, where the surgeon is able to visualize and simulate the surgical procedure beforehand, thereby, not only allowing a better control of the bone cutting and control of segments but also helping to reduce the operation and bleeding time.[96] Although nowadays virtual planning is being employed as the main choice for simulating orthognathic surgery, however, the visual and haptic feedback role of patient-specific models should not ignored as a modality for overcoming early relapse and also as medium for bending plates for fixation. Simulation on a 3D patient specific model can train the surgeon beforehand, allowing improved control of the bone segments intraoperatively.[93] However, the accuracy and visual and haptic feedback aspect to that of real skeletal structures is one of the least studied aspect in orthognathic surgery, which needs to be considered first before making further advances related to the realistic soft tissue and muscular replication.

1.11 Aims and Hypotheses

Orthognathic surgery is considered to be a cornerstone for surgically treating dentofacial deformities. It is associated with unwanted skeletal or soft tissue relapse over time. Based on the lack of true 3D-based prospective evidence, the overreaching aim of the PhD project was to assess 3D skeletal and PAS relapse following orthognathic surgery and to observe whether 3D printed patient-specific skeletal models can offer a realistic bone replication and visuo-haptic feedback to enable surgeons in future studies to control early relapse and optimize surgical techniques. The outcomes of this thesis can guide surgeons to plan and modify their treatment planning based on the amount and/or direction of relapse. **The general hypothesis was that skeletal and PAS changes might occur at follow-up, thereby, requiring careful treatment planning to improve the surgical outcome.**

This doctoral thesis is divided into three main parts, each with its respective objectives.

Part 1 Skeletal relapse

Most of the studies assessing skeletal relapse following LF I and BSSO surgery have either been short term, quantified two-dimensionally or by applying 3D cephalometry which are prone to human error. No standardized 3D protocol exists for objective quantification of relapse. Additionally, the studies assessing relapse only report the magnitude of relapse without considering the 6DoF. Thereby, it is important to study the magnitude as well as the direction of skeletal relapse and to gather information on the potential variables influencing the occurrence of relapse which can allow the minimization of risk and improve treatment planning.

The objectives were:

- To propose and validate a cephalometric-free semi-automatic 3D tool for the assessment of orthognathic surgery planning accuracy and short-term postoperative relapse.
- To assess the accuracy and reproducibility of the 3D tool for assessing skeletal relapse at a long-term postoperative follow-up.
- To prospectively evaluate 3D skeletal relapse of proximal and distal mandibular segments at a one year follow-up time-point after BSSO advancement surgery based on a validated semi-automatic tool and to assess the influence of patient- and surgery-related variables.
- To prospectively assess the 3D relapse of maxillary advancement with superior or inferior repositioning at a two years follow-up time-point and to investigate the influence of patient- and surgery-related variables which might influence the relapse.

The hypothesis was that:

“Skeletal changes might occur following maxillary LF I advancement surgery with superior or inferior repositioning and also after BSSO advancement surgery, thereby, leading to relapse as compared to the initial surgical outcome.”

Part 2 Pharyngeal airway space relapse

The orthognathic surgical procedures influence the PAS immediately after surgery and at follow-up. This change in PAS affects the respiratory status and sleep quality in patients. With the technological advancements, 3D volumetric assessment of PAS and its collapsibility (minimum cross-sectional area (mCSA)) has become an objective standard for assessing airway. Lack of evidence exists related to the PAS changes at a one year or more follow-up after BSSO advancement surgery and whether the airway relapse is correlated to the surgical advancement. This part provides insight into the influence of BSSO advancement surgery on the airway which should be considered during the treatment planning phase.

The objectives were:

- To three-dimensionally assess the volumetric and surface area changes of the PAS following isolated BSSO advancement surgery at a follow-up period of one year.
- To investigate the changes in collapsibility of the airway by assessing the mCSA of the PAS.

The hypothesis was that:
"The 3D volume, surface area and mCSA of PAS increases following BSSO advancement surgery and might diminish at a follow-up period of 1 year."

Part 3 3D printed models application in orthognathic surgery
3D printing plays a significant role in preoperative maxillofacial treatment planning, however lack of evidence exists in relation to its application in orthognathic surgery. This part of the thesis focuses on printing bone-like patient-specific skeletal models to allow a platform for future studies for simulating surgical procedures on accurate models offering visuo-haptic feedback to that of real bone before real surgery, thereby allowing control of factors such as bony interferences and condylar displacement which can influence short- and long-term relapse.

The objectives were:

- To evaluate the quantitative accuracy of CBCT-derived mandibular skeletal models utilizing various printing technologies.
- To analyze the visuo-haptic quality of 3D printed models derived from medical printers based on different technologies for application in orthognathic surgery.

The hypothesis was that:
"The quantitative accuracy and visuo-haptic perceptibility of 3D printed mandibular models may differ, depending on the type of medical printing technologies and materials."

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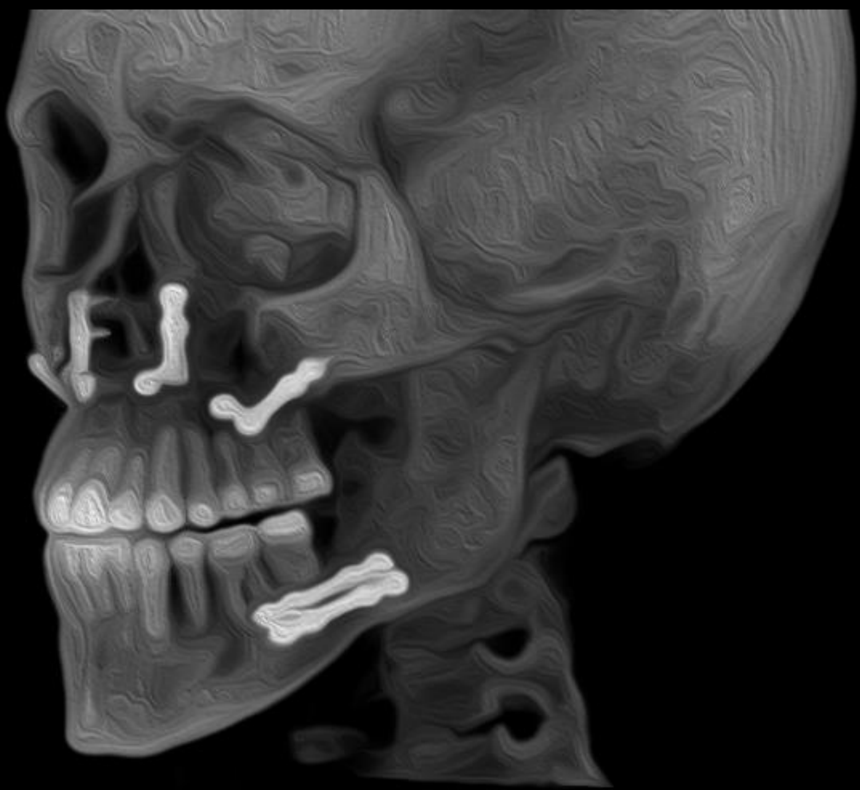
Part 1
SKELETAL RELAPSE



ARTICLE 1

Three-dimensional planning accuracy and follow-up protocol in orthognathic surgery: a validation study

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Abstract

Purpose

The purpose of the study was to propose and validate a three-dimensional (3D) tool for the assessment of orthognathic surgery planning accuracy and postoperative follow-up.

Materials and methods

A total of 15 patients (four male, 11 female; mean age 29.6 years) with skeletal class II and III, who underwent bimaxillary surgery were recruited for the study. All patients had preoperative computed tomography (CT), and cone-beam computerized tomography (CBCT) scans 1–6 weeks and 6 months postoperatively. The data was exported to a customized stepwise module developed in Amira software resulting in the error being presented as translational and rotational differences in movement between the planning and the actual outcome. To evaluate the reliability of the proposed method, intra-class correlation coefficient (ICC) was applied at a 95% confidence interval on the translational and rotational output of two observers.

Results

The inter- and intra-observer reliability were found to be high (ICC range: 0.94–0.98) with mean error of less than 0.4mm and 0.7° for translational and rotational movements for both planning accuracy and follow-up protocols.

Conclusions

The study provides a reliable, quantitative and time-efficient method for evaluating the accuracy of virtual surgical planning and postoperative follow-up.

Keywords: virtual surgical planning; orthognathic surgery; follow-up; surgical accuracy; recurrence

Introduction

Recent advances in three-dimensional (3D) technology and rapid prototyping (RP) have led to the development of objective techniques for diagnosing, treatment planning, predicting outcomes and follow-up of orthognathic surgery patients[1, 2]. This has improved the understanding of the complex 3D anatomy of the dental and craniofacial region.

Three-dimensional simulation to predict the post-surgical outcome plays a vital role in improving the actual surgical outcome and, in addition, in improving patients' quality of life by achieving suitable aesthetics and functional results[3]. Therefore, it is essential to compare the accuracy of virtual to real surgical outcome so that any undesirable results can be addressed objectively. The most important step in predicting the accuracy of post-surgical outcome is interrelated to the registration and alignment of the pre- and postoperative computed tomography (CT)/cone beam computed tomography (CBCT) scans[4].

Various methods have been proposed in the literature for comparing the accuracy of the virtual 3D planning to the actual surgical procedure[2, 4, 5, 6]. These methods can be categorized into cephalometry based or registration based. The central demerits of those suggested methods have been the human error related to cephalometric landmark placement[7], time inefficiency or the usage of multiple software for assessing the accuracy of surgical planning in orthognathic surgery[4].

Currently three accepted registration methods exist in the literature: landmark based registration (LBR)[8], surface-based registration (SBR)[9] and voxel-based registration (VBR)[10]. LBR involves a higher degree of human error relying on identification of landmarks and inter-observer variations,[7] whereas surface-based registration (SBR) is dependent on the accuracy of 3D scanned models and the quality of the segmentation from CT/CBCT scans[11]. VBR is a technique by which pre- and postoperative CT/CBCT scans of patients can be superimposed automatically based on the volumetric similarities between the two scans[10]. Hence, VBR is considered the gold standard for registration as it is regarded as the least variable method[12, 13].

Gaber et al.[14] recommended a protocol for the 3D postoperative accuracy evaluation based on their systematic review. The protocol consisted of applying VBR on the anterior cranial base for aligning and registering the two scans, hence eliminating human error related to landmark identification and placement, followed by an automated or semi-automated evaluation with translational or rotational assessment. They insisted on validating the protocol via inter- and intra-observer reliability tests.

Baan et al.[5] suggested the application of a software, OrthoGnathicAnalyser, for the translational and rotational assessment, whereas the remainder of the steps in the protocol were carried out by an additional software, Maxilim (Medicim NV, Mechelan, Belgium). Stokbro and Thygesen[4] suggested the application of two free open-source software and the protocol was time consuming as suggested by the authors.

Recent methods applied in orthognathic surgery are more focused towards the planning aspect and no 3D protocol exists for objective quantification of long-term postoperative follow-up. Relapse studies have either been based on 2D or 3D cephalometry[15, 16] carrying the risk of human error. Literature lacks evidence on the availability of a time-efficient and a solely software-based protocol for analysing the 3D movements in orthognathic surgery.

Therefore, the aims of this paper were to propose and validate a cephalometric-free semi-automatic 3D tool and protocol to compare the 3D virtual planning with the actual surgery outcome and assessment of postoperative follow-up after orthognathic surgery.

Materials and methods

Ethical Approval

This study was conducted in compliance with the World Medical Association Declaration of Helsinki on medical research. Ethical approval was obtained from the Ethical Review Board of the University Hospitals Leuven (reference number: S57587). Informed consent was not required for this retrospective study as patient-specific information was kept anonymous. The sample size was calculated using a priori power analysis in G* power 3.1, assuming 80% power at a significance level of 5%.

Patients and radiographic examination

Fifteen patients (four male, 11 female, mean age 29.6 years) with skeletal class II and III, who underwent orthodontic treatment and bimaxillary surgery (Le Fort I and bilateral sagittal split osteotomy (BSSO)) without genioplasty during the period 2015–2016, were recruited from the Department of Oral and Maxillofacial Surgery, University Hospitals Leuven, Leuven, Belgium. The inclusion criteria included patients within the age range of 18–55 years, accessibility to patients' preoperative, immediately postoperative (1–6 weeks) and 6 months postoperative CT/CBCT scans and presence of virtual surgical planning used for the fabrication of 3D-printed intermediate wafers. Exclusion criteria were previous history of oral and maxillofacial surgical intervention, presence of craniofacial anomalies such as cleft lip and/or palate, craniosynostosis, hemifacial microsomia and other syndromic diseases.

The study included a total of 45 scans (15 preoperative CT scans, 15 CBCT scans at 1–6 weeks postoperative, and 15 CBCT scans at 6 months postoperative). The details of the systems used are shown in Table 1 including one CT system and two different CBCT systems (16 scans with CBCT1 and 14 scans with CBCT2). All scans were carried out using a standardized protocol (Table 1) as described by Stratis et al.[17].

Table 1. Acquisition settings for the computed tomography/cone beam computed tomography systems.

	CT	CBCT 1	CBCT 2
System	Siemens Somatom Definition Flash	Planmeca Promax 3D Max	Newtom VGi-evo
System's origin	Siemens AG, Erlangen, Germany	Planmeca, Helsinki, Finland	Newtom, Verona, Italy
Total mAs	855	216	15.3
Potential (KV)	120	96	110
Slice thickness (mm)	0.75	0.6	0.3
Field of view FOV (mm^2)	-	230x260	240x190

CBCT, cone beam computed tomography; CT, computed tomography.

Virtual 3D planning protocol

Virtual 3D planning was performed in PROPLAN software (Materialise, Leuven, Belgium). The preoperative CT patient Digital Imaging and Communications in Medicine (DICOM) images were imported into the software where composite models of maxilla and mandible were created. The movements of the maxilla defined by the surgeon were planned to create the intermediate splint while the final splint was fabricated as described by Shaheen et al.[18]. The composite models of the maxilla in original and final positions were exported as stereolithography (STL) files to be used in the surgical accuracy-assessment protocol.

Surgical Technique

All bimaxillary surgeries were executed by the same surgical team. Surgical procedure involved maxillary Le Fort I osteotomy[19] followed by Hunsuck/Epker modification of BSSO[20, 21]. Maxilla was fixed with two L-shaped miniplates and monocortical screws on each side. In addition, BSSO fixation was carried out using two miniplates and monocortical screws transorally for each split[22].

Postoperative Assessment Protocols

Two semi-automatic protocols were developed in Amira software (version 6.3.0, Thermo Fischer Scientific, Merignac, France) in a user-friendly wizard module instructing the user at every step. The first protocol was designed for accuracy assessment of the maxilla after bimaxillary surgery by comparing the immediate postoperative scan to the preoperative virtual planning. The second protocol was intended for following up the patient 6 months, 1 year and 2 years postoperatively. Fig. 1 summarizes the flowchart of the main steps involved in both protocols.

The steps and details of the accuracy assessment protocol and the follow-up protocol, explained with the 6 months postoperative data, are described in the following subsections.

Accuracy assessment protocol

***Step 1:* Import DICOM images.** The user imported the preoperative and immediate postoperative DICOM images into the module.

***Step 2:* Cranial base registration.** The postoperative images were registered onto the preoperative anterior cranial base using rigid VBR with mutual information[23, 24, 25] as shown in Fig. 2.

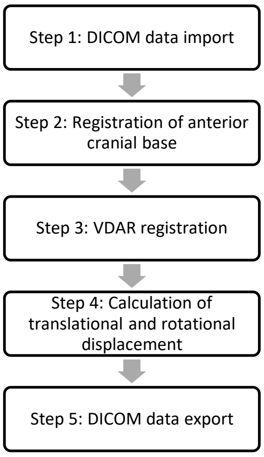

Figure 1. Protocols flowchart

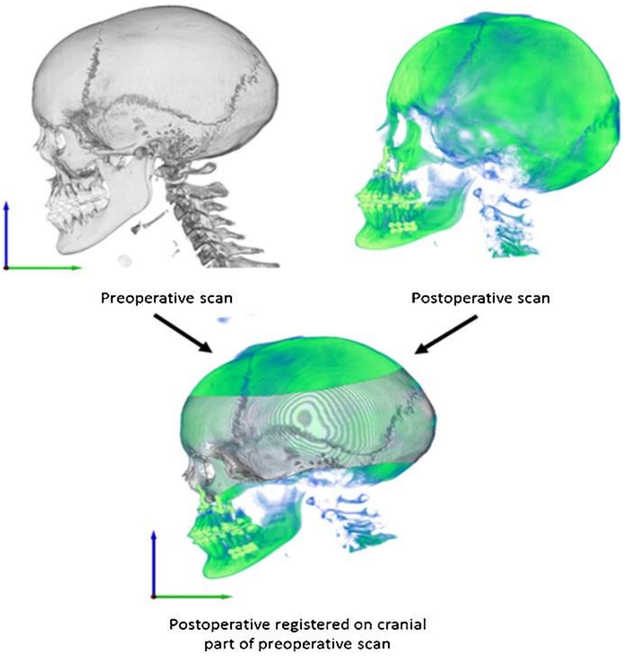

Figure 2. The postoperative scan (green) registered on the preoperative scan (grey) based on the preoperative anterior cranial base using rigid voxel-based registration.

Step 3: **Registration of the maxillary segments.** To overcome the human error associated with cephalometric landmarking, the preoperative maxillary segment was registered to the postoperative maxillary segment[5]. Maxillary segments were manually outlined on the registered postoperative model avoiding the inclusion of the titanium plates, followed by the selection of the same area in the preoperative model. The selection area from the two parts did not have to be identical as the VBR algorithm overcame this limitation (Fig. 3). The transformation matrix (TM1) acquired after the registration was used in the next step.

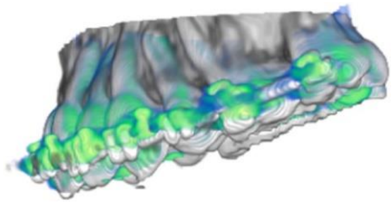

Figure 3. The preoperative maxillary segment (grey) registered on the registered postoperative maxillary segment (green) using rigid voxel-based registration.

Step 4: **Calculation of 3D translational and rotational movements.** The STL of the virtually planned maxillary segment and the preoperative maxillary segment were imported into the module (both segments were identical except for the position). The transformation matrix (TM1) obtained in the previous step was applied to the preoperative maxillary STL to reposition it to the actual achieved position.

Three landmarks were placed on the occlusal surface to construct the occlusal plane of the planned maxillary segment (midpoint of the incisal edge and mesiobuccal cusps of the first molars left and right). These landmarks represented the orientation of the maxilla in 3D coordinates. The planned maxillary segment was then superimposed on the postoperative achieved maxillary segment using SBR to obtain a new transformation matrix (TM2). This TM2 was applied on the three landmarks to reposition them to the achieved position. These six points, i.e. three points on planning object and the corresponding three points on achieved position, were further analysed using singular value decomposition (SVD) algorithm written in Python and integrated into the Amira wizard module. The output of this step was the 3D clinical error assessment of the translational and rotational movements that was represented by the six degrees of freedom. The translational movements included: left/right (L/R), anterior/posterior (A/P) and intrusion/extrusion (I/E). The rotational movements were categorized into pitch, roll and yaw. The interpretation of these parameters was previously described by Baan et al.[5].

Step 5: **Data export.** The registered postoperative images were exported and saved in DICOM format as well as the maxillary achieved segment (saved as STL) to be used in the follow-up protocol.

Follow-up protocol

The protocol included objective assessment of 6 months postoperative scans. The module involved repetition of all the steps as mentioned in the accuracy assessment protocol, except step 4, by treating the registered postoperative as the preoperative data and the follow-up as the postoperative. During step 4, the maxillary achieved segment was imported as the preoperative STL and duplicated. One copy represented the planning model and the other copy was transformed into the achieved position. The calculations were then applied to these two objects to analyse the stability of the maxillary segment in a period of 6 months. The registered follow-up images and the maxillary achieved segment were then exported as explained in step 5 of accuracy assessment.

Observers

All data were assessed by two observers. The observers included a clinical engineer with 15 years of experience and a maxillofacial surgeon with 10 years of experience. Repetition of the assessment was performed 1 month after the first session by both observers for calculating the inter- and intra-observer reliability. Time taken by both observers for applying accuracy assessment and follow-up protocol to every patient was recorded during all sessions.

Statistical Analysis

Data were analysed using MedCalc statistical software (version 12.0, Ostend, Belgium). Intra-Class Correlation Coefficient (ICC) was applied at a 95% confidence interval for assessing the inter- and intra-observer reliability of planning accuracy and follow-up (where <0.50 = poor reliability; 0.50–0.75 = moderate reliability; 0.75–0.90 = good reliability; >0.90 = excellent reliability)[26]. The mean, absolute mean and standard deviation were also calculated for all the data.

Results

Table 2 illustrates the validation of both surgical accuracy assessment and follow-up protocols via the inter- and intra-observer tests using ICC for translational and rotational movements at a 95% confidence interval. Accuracy assessment ICC showed an excellent reliability (0.97–0.98) with mean absolute differences of 0.33–0.34 mm for translational and 0.42–0.63° for rotational movements. The follow-up ICC was 0.94–0.95 with mean absolute differences of 0.25–0.30 mm and 0.31–0.39° for translational and rotational movements, respectively.

Table 2. Inter- and intra-observer intraclass correlation coefficient (ICC) results with mean absolute difference (AD) and standard deviation (SD).

	Accuracy assessment reliability				**Follow-up reliability**			
	Translational		**Rotational**		**Translational**		**Rotational**	
	ICC	**Mean AD ± SD (mm)**	**ICC**	**Mean AD ± SD (°)**	**ICC**	**Mean AD ± SD (mm)**	**ICC**	**Mean AD ± SD (°)**
Inter-observer	0.97	0.33 ± 0.36	0.97	0.42 ± 0.41	0.94	0.25 ± 0.18	0.94	0.31 ± 0.32
Intra-observer	0.98	0.34 ± 0.44	0.98	0.63 ± 1.1	0.95	0.30 ± 0.37	0.95	0.39 ± 0.44

Table 3 demonstrates the error of the surgical accuracy assessment and follow-up protocols related to translational and rotational movements of the maxilla and the time required for the specific modules for all 15 cases. The mean time for both modules was within the range of 9.4–10.9 min.

Table 3. Results of the accuracy assessment and follow-up protocols for the 15 patients.

Protocols			Translational movements (mm)			Rotational movements (°)		
		Time (minutes)	L/R	A/P	I/E	Pitch	Roll	Yaw
Accuracy assessment protocol	Mean (SD)	9.4 (2.1)	0.2 (1.0)	-0.2 (1.8)	-0.9 (1.1)	-1.2 (2.9)	0.1 (1.0)	0.2 (2.2)
			-0.3 (1.4)			-0.3 (2.2)		
	Absolute mean (SD)		0.8 (0.6)	1.2 (1.3)	1.1 (0.9)	2.3 (2.1)	0.8 (0.6)	1.6 (1.5)
			1.0 (1.0)			1.6 (1.6)		
Follow-up protocol	Mean (SD)	10.9 (3.3)	-0.1 (0.7)	-0.2 (0.8)	0.1 (0.6)	0.3 (1.4)	-0.1 (0.7)	0.0 (0.4)
			-0.1 (0.7)			0.1 (0.9)		
	Absolute mean (SD)		0.5 (0.5)	0.6 (0.5)	0.5 (0.3)	1.1 (0.8)	0.5 (0.5)	0.3 (0.2)
			0.5 (0.5)			0.7 (0.7)		

A/P, anterior/posterior; I/E, intrusion/extrusion; L/R, left/right; SD, standard deviation.

The mean indicates the direction of the error while the absolute mean quantifies the magnitude of the error. For the accuracy assessment protocol, the I/E movement was the least reliable parameter (mean = −0.9 mm; absolute mean = 1.1 mm). The overall translational error for both protocols showed a mean of ≤−0.3 mm and absolute mean of 1 mm. The overall rotational error was within 1.6°. For the follow-up protocol, the overall mean absolute error was 0.5 mm for the translational movements and 0.7° for the rotational movements, which were considered more stable compared to the accuracy-assessment protocol.

Discussion

Virtual 3D planning in orthognathic surgery has been an area of interest for the past few years. Various methods have been proposed for assessing the accuracy of virtual planning, but to date no consensus has been reached as to which method is the most reliable, user friendly and least time consuming. Literature also lacks evidence on application of a sole software for follow-up assessment. Based on Gaber et al.'s[14] recommendations, the following study was carried out to introduce a new technique for evaluating the precision of planning versus actual surgery and follow-up.

The inter and intra-observer reliability (ICC) were high for both protocols (0.94–0.98) with inter and intra mean variability of less than 0.4mm and 0.7° for translational and rotational movements, respectively. The ICC was slightly lower for the follow-up module (0.94–0.95) compared to the planning (0.97–0.98) but still both modules were found to have excellent agreement. This might have been related to the unavoidable minor teeth movement during the finishing stage of the postsurgical orthodontic treatment[27]. Nevertheless, VBR counteracted these minor dental changes as registration was based on volumetric information of the whole arch. A similar study by Baan et al.[5] exhibited an ICC of 0.97–0.99 for the maxillary region with their 3D tool OrthoGnathicAnalyser. Stokbro et al.[4] demonstrated an ICC of ≥0.99 based on only intra-observer reliability.

In the current study, a state-of-the-art stepwise module was established using a single software for validating the accuracy of planning and follow-up. The module was considered semi-automated and user friendly because it consisted of 12 steps in the form of a fully automated wizard requesting the user to either import objects or press next, apart from only four steps: highlighting the cranial base part, the pre- and postoperative maxilla and pointing to the three landmarks on the preoperative maxilla. However, the highlighting was carried out as drawing on the screen for all parts with the mouse facilitating the user interaction. The accuracy of highlighting and drawing of maxilla and cranial base was independent of operator experience as it relied on a VBR algorithm. Furthermore, literature suggests VBR to be a reliable and accurate method for anterior cranial base registration[28]. The time taken for each module was around 10min (Table 2) as compared to similar studies which either failed to provide the time duration of the assessment procedure or were considered to be time consuming[5]. The time taken for cranial base registration ranged between 1 and 5 min. Our method compared with various open-source software studies was found to be less time consuming and within the same error range[4]. Time is the least documented and most ignored factor related to the assessment methods, therefore we deemed it necessary to be addressed. The translational and rotational differences (<2 mm and <4°) in accuracy assessment and follow-up protocols were considered to be clinically insignificant[29]. These minor variations can be considered more reliable as compared to the less accurate 3D cephalometric methodologies[4]. A high-resolution STL of the maxilla was used to facilitate the placement of three landmarks on the maxillary teeth during the SBR step in accuracy assessment protocol which were deemed adequate for orienting the maxilla in 3D coordinates and reconstructing the occlusal plane. The main role of this maxillary segment STL was to avoid the human error by automatically repositioning the landmarks without user interference from one position to another, i.e. for the accuracy-assessment protocol, from preoperative position to the actual outcome position and from actual outcome position to planned position; furthermore, for the follow-up protocol, automatically repositioning landmarks from immediate postoperative position to achieved 6 months postoperative position.

All 15 cases involved in the study showed a similar range of error for follow-up irrespective of the type of CT/CBCT device and image acquisition settings used for acquiring the scan. For instance, patients having preoperative CT and postoperative CBCT showed the same amount of error when compared with patients having only CBCT scans and vice versa. This was confirmed by the excellent ICC results (≥0.94). Moreover, the mean absolute difference of inter- and intra-observer reliability for accuracy assessment (translation: ≤0.34 mm, rotation: ≤0.63°) and follow-up (translation: ≤0.30 mm, rotation: ≤0.39°) methods was found to be highly accurate, proving that the type of scan had no effect on the methods applied as no digitization was needed and the registration (VBR) was based on volumetric similarities.

This study had certain limitations. The quantitative analysis only involved the maxillary movements for validating the method, thereby, further analysis is required for assessing the application of the method in maxillary segmental osteotomy, mandibular region (BSSO) with or without genioplasty. For the follow-up module, the study was only limited to 6 months postoperative cases. We hypothesize that the above-mentioned method is applicable for long-term follow-up (up to 1- and 2-years follow-up) to check for relapse as dental changes within these periods would be minimal. However, additional studies are required to confirm this hypothesis.

Conclusions

In conclusion, the study provides a reliable, user-friendly and time-efficient method for evaluating the planning and follow-up accuracy, hence improving the standards in orthognathic surgery.

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ARTICLE 2

Accuracy and reliability of voxel-based dentoalveolar registration (VDAR) in orthognathic surgical patients: a pilot study with two years' follow-up

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Abstract

Purpose

The purpose of this study was to validate the applicability of using maxillary voxel-based dentoalveolar registration (VDAR) at long-term follow up in orthognathic surgical patients.

Materials and methods

A retrospective sample of 25 patients (skeletal class II or III) who underwent bimaxillary orthognathic surgery was recruited and divided into two groups. Group A included 15 patients (seven females, eight males, mean (SD) age 25.8 (14.4) years) with unrestored dentition and group B involved 10 patients (five females, five males, mean (SD) age: 26.2 (11.9) years) with dental restorative treatment. Postoperative cone-beam computed tomography (CBCT) scans were acquired at four time-points, one to six weeks (T1), six months (T2), one year (T3) and two years (T4). Voxel- based registration was applied using the cranial base and then complete dental segment with part of the alveolar bone at T1-T2, T1-T3 and T1-T4 time-intervals. The translational and rotational accuracy and reproducibility of the registered maxillary segment was evaluated at these three intervals by analysing the transformation matrix using singular value decomposition.

Results

All translational and rotational movements showed an excellent reliability in both groups without any significant difference. The combined translational and rotational difference was found to be within the clinically acceptable range of 2 mm and 4°.

Conclusions

The VDAR was found to be accurate and reliable to be utilised for a long-term skeletal follow-up in orthognathic surgical patients.

Keywords: orthognathic surgery; 3-D imaging; relapse; follow-up studies

Introduction

The protocols associated with three-dimensional (3D) pro- grams usually rely on a vital step known as image registration, which involves the spatial alignment of similar structures for accurately quantifying skeletal changes.[1,2] In orthognathic surgery, the most common method for registration is intrinsic in nature, which involves the registration of image datasets based on either the identification of anatomical land- marks (landmark-based), segmentation of anatomical surface models (segmentation-based), or by relying on grey level intensity of voxels (voxel-based) in serial image datasets.[1,3,4] Voxel-based registration (VBR) of cone-beam computed tomographic (CBCT) images is considered to be the most reliable and consistent intrinsic method for assessing surgical changes.[5,6] Whereas, both landmark and surface-based identification carry a higher risk of inaccuracy based on human error (linked with landmark identification and 3D model volume rendering) they are dependent on the quality and density, respectively, of the images of anatomical structures.[7] Voxel-based image registration overcomes the aforementioned limitations, as it is a fully automatic process dependent on utilising the radiopacities and radiolucencies of CBCT data for superimposition, omitting the need for land- mark placement and the application of thresholding to create a surface model.[2]

To assess skeletal changes, the anterior cranial base and a combination of anterior cranial base and foramen magnum are considered to be the most stable and reproducible anatomical structures for superimposing images acquired at different time-points following surgery.[7] For overcoming the large field of view (FOV) and increased dose factor, the zygomatic arch has also been suggested as an alternative.[8] Shaheen et al applied voxel-based registration utilising complete maxillary dentoalveolar segments for assessing short-term orthognathic surgical skeletal changes and proposed that the registration based on volumetric information of the whole dental arch with alveolar bone counteracted the minor dental changes.[9] In addition, they hypothesised that this registration could be an accurate and reproducible method for long-term follow up in orthognathic surgery. Recent evidence suggests that no validation studies have been carried out yet to assess the applicability of using voxel-based dentoalveolar registration (VDAR) to analyse long-term post-surgical skeletal changes and to observe whether this offers a clinically-acceptable degree of accuracy compared to its 2D and 3D counterparts, which are prone to human error. Therefore, the following study was conducted to validate the applicability of using maxillary VDAR in orthognathic surgical patients. The primary aim was to assess the reproducibility of VDAR and the secondary aim assessed the difference in registration at various follow-up time points.

Materials and methods

In this retrospective study, patients who had undergone bimaxillary orthognathic surgery for the correction of dento-facial deformity were recruited. The sample was selected based on previously comparable studies[10–12] and calculated using a priori power analysis in G* power 3.1, assuming 80% power at a significance level of 5%. Ethics approval was granted by the Ethics Review Board of the University Hospitals, Leuven, Belgium (reference number: S57587) and the need for informed consent was waived as patient specific information was anonymised.

All surgeries were performed by the same surgical team and included maxillary Le Fort 1 osteotomy and bilateral sagittal split osteotomy (BSSO) by the Hunsuck-Epker approach without genioplasty. Rigid internal fixation with titanium miniplates and monocortical screws was applied for fixation and stabilisation of maxillary and mandibular osteotomised segments of bone. The patients were divided into two groups to observe the influence of additional artefacts on the accuracy of the methodology . Group A included patients with unrestored normal dentition and the presence of orthodontic brackets for no longer than seven months. Group B patients additionally had a history of dental treatment such as composite/amalgam fillings, endodontic treatment, and/or crown placement during the follow-up period. The inclusion criteria involved patients with a minimum age of 16 years and the presence of postoperative CBCT scans with optimal image quality. Exclusion criteria included craniofacial syndrome, metabolic disease, previous history of orthognathic surgery or trauma. A purposive sampling strategy was employed for the recruit- ment of patients following the establishment of these criteria.

Postoperative CBCT scans were acquired at four time- points, one to six weeks (T1), six months (T2), one year (T3), and two years (T4). The scans were acquired with Planmeca ProMax® 3D Max (Planmeca Oy) and NewTom VGi evo (NewTom) using a standard CBCT scanning protocol (field of view: 230x260- 240x 140mm^2; voxel size: 0.3-0.6mm; 96-110kV).[13] A patient-specific lowest dose possible was employed for scanning with Planmeca ProMax and tube cur- rent modulation option of NewTom VGi evo was utilised to reduce the exposure to radiation. Additionally, the serial scanning of the patients included in this study was justified from a radiation protection viewpoint, as they were recruited from a dataset that had assessed condylar resorption, airway changes, and/or relapse following large amounts of surgical movement. All images were exported in Digital Imaging and Communications in Medicine (DICOM) format for further processing.

The protocol of this study was based on a previous methodology validated by Shaheen et al,[9] for assessing short-term skeletal relapse at one time interval using VDAR (Fig. 1). We utilised the same protocol to assess the long-term validity of VDAR at three instances (T1-T2, T1-T3, T1-T4) with T1 as the clinical reference standard. Fig. 1 illustrates the steps involved in the protocol. Only step three was the focus of this study with primary outcome measure evaluating VDAR reproducibility at long-term intervals and secondary outcome included the evaluation of the mean differences at different time intervals. Group A patients offered a standardised sample, therefore, avoiding potential confounding factors for demonstrating internal validity. At the same instance, external validity was performed by recruitment of group B patients to observe the generalisability of the protocol.

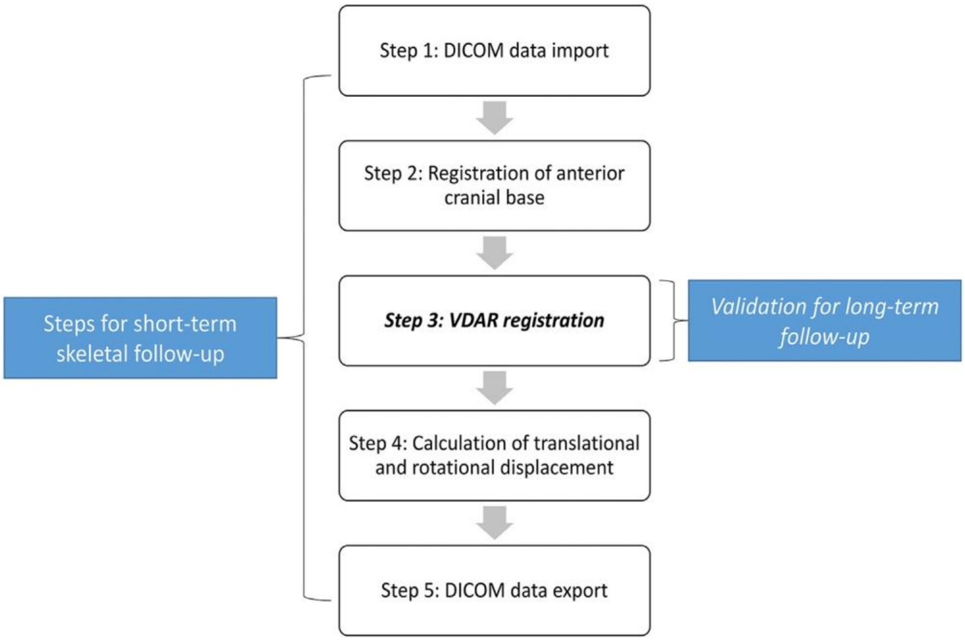

Fig. 1. Follow-up protocol flowchart.

Image registration

The CBCT scans at T1 and T2 time-points were imported into Amira software (Amira 6.5.0, FEI) and volume rendering was applied. Following anterior cranial base registration, maxillary segments were highlighted from both scans. Care was taken to avoid the inclusion of titanium plates in the extracted parts. The registration region involved the whole dental arch with all teeth and part of the alveolar bone. Also, the highlighted segments at T1 and T2 did not have to be completely identical based on the original hypothesis of this study that VBR overcomes this slight dissimilarity between the two parts. VBR with mutual information[14] was applied to superimpose T1 and T2 maxillary segments. This approach was repeated for registering scans at T1-T3 and T1-T4 time- intervals.

Translational and rotational movement assessment

The VDAR resulted into a transformation matrix which was then analysed using a singular value decomposition algorithm to retrieve the translational (x,y,z) and rotational (pitch,roll,yaw) movements for depicting the difference between the maxillary segment at T1 and T2 time-points. The same steps were repeated for assessing the difference in movement transformation from T1 to T3 and T4 time-points.

The methodology was performed blindly by two independent observers, a clinical engineer having an experience of 15 years and a maxillofacial surgeon with 10 years of experience, for validating this methodology and assessing the error associated with the maxillary segment translation and rotational movement at long-term follow up. Both observers analysed the data twice at an interval of two weeks for calculating interobserver and intraobserver reliability.

The statistical calculations were carried out utilising MedCalc Statistical Software version 12.7.8 (MedCalc Software bvba). Interobserver and intraobserver reliability was assessed by the intraclass correlation coefficient (ICC) at a 95% confidence interval (poor = <0.50, mod- erate = 0.50–0.75, good = 0.75–0.90, and excellent >0.90)[15] and a p value of less than 0.05 was considered to be statistically significant. The translational and rotational difference between scans at all time-intervals (T1-T2, T1-T3, T1-T4) was calculated and represented as mean (SD).

Results

The sample comprised 25 patients with skeletal class II or III, who underwent bimaxillary orthognathic surgery and were divided into two groups. Group A included 15 patients (seven females, eight males, mean (SD) age: 25.8 (14.4) years) with unrestored dentition and group B involved 10 patients (five females, five males, mean (SD) age: 26.2 (11.9) years) with dental restorative treatment. No patients underwent tooth extraction or implant placement during the follow-up period.

Tables 1 and 2 represent the intraobserver and inter- observer reliability in group A and B. All translational and rotational movements showed an excellent reliability between two time points. The lowest value was seen for inter- observer reliability of roll (0.9741) at T1-T4 in group A and pitch (0.9603) at T1-T2 time interval in group B. No significant difference was observed between both observers for both group A (p=0.092) and group B (p=0.354).

Table 1. Interobserver and intraobserver intraclass correlation coefficient (ICC) in group A patients.

Reliability	Post-operative time-intervals	Translational movements (ICC)				Rotational movements (ICC)			
		X	Y	Z	Combined	Pitch	Roll	Yaw	Combined
	T1-T2	1	1	1	1	0.9994	0.9969	0.9999	0.9994
Intra-observer	T1-T3	1	1	1	1	0.9997	0.9879	0.9994	0.9815
	T1-T4	1	1	1	1	0.9979	0.9772	0.9974	0.9959
	T1-T2	1	1	1	1	0.9968	0.9861	0.9961	0.9937
Inter-observer	T1-T3	1	1	0.9999	1	0.9971	0.9815	0.9980	0.9887
	T1-T4	1	1	0.9999	1	0.9816	0.9741	0.9939	0.9666

ICC: Intra-class correlation coefficient, T1: 1-6 weeks, T2: 6 months, T3: 1 year, T4: 2 years.

Table 2. Interobserver and intraobserver intraclass correlation coefficient (ICC) in group B patients.

Reliability	Post-operative time-intervals	Translational movements (ICC)				Rotational movements (ICC)			
		X	Y	Z	Combined	Pitch	Roll	Yaw	Combined
	T1-T2	0.9921	0.9997	0.9982	0.9992	0.9603	0.9918	0.9835	0.9751
Intra-observer	T1-T3	0.9952	0.9981	0.9994	0.9981	0.9957	0.9958	0.9926	0.9951
	T1-T4	0.9986	0.9997	0.9945	0.9994	0.9878	0.9783	0.9807	0.9857
	T1-T2	0.9984	0.9949	0.9958	0.9957	0.9754	0.9795	0.997	0.9775
Inter-observer	T1-T3	0.9851	0.9975	0.999	0.9977	0.9948	0.9970	0.9891	0.9945
	T1-T4	0.9982	0.9916	0.9908	0.9922	0.9815	0.9847	0.9765	0.9808

ICC: Intra-class correlation coefficient, T1: 1-6 weeks, T2: 6 months, T3: 1 year, T4: 2 years.

Table 3 shows the mean translational and rotational error of the registered dentoalveolar segments at different time-intervals in group A and B. The maximum mean difference was observed for the 'z' axis translational movement 0.67 (0.8mm) and pitch 1.09° (1.37°) at T1-T4 in group A. Group B also observed maximum mean (SD) difference for the 'z' axis translational movement 0.64 (0.51) mm and pitch 0.42 (1.30) °

at T1-T4 time-interval. The combined translational and translational error showed a mean difference of less than 0.5mm and 0.5° and no significant difference was observed between both groups (p=0.237).

Table 3. Mean (SD) translational and rotational error at registered time-intervals in group A and B patients.

Post-operative time-intervals	Translational error (mm)			Rotational error (°)		
	X	Y	Z	Pitch	Roll	Yaw
				Group A		
T1-T2	0.08±0.13	0.11±0.11	0.25±0.25	0.64±0.62	0.57±0.78	0.17±0.25
T1-T3	0.11±0.18	0.15±0.16	0.47±0.51	0.66±0.59	0.63±1.04	0.15±0.21
T1-T4	0.14±0.12	0.28±0.35	0.67±0.80	1.09±1.37	0.95±1.29	0.37±0.50
Overall difference		0.25±0.29			0.58±0.73	
				Group B		
T1-T2	0.10±0.11	0.36±0.78	0.28±0.41	0.28±0.59	0.11±0.14	0.51±0.21
T1-T3	0.15±0.78	0.35±0.43	0.05±0.35	0.23±0.41	0.03±0.08	0.17±0.07
T1-T4	0.21±0.51	0.30±0.58	0.64±0.51	0.42±1.30	0.20±0.38	0.05±0.14
Overall difference		0.27±0.50			0.22±0.37	

T1: 1-6 weeks, T2: 6 months, T3: 1 year, T4: 2 years.

Discussion

Medical image registration is a vital part of the orthognathic surgery follow-up assessment chain. The application of VBR for image registration has been widely accepted compared to it surface-based counterpart. However, little is known about the application of VBR with region-based superimposition for the assessment of the long-term skeletal relapse.[6,16-19] Therefore, the present study was conducted to evaluate the accuracy and reliability of VDAR in the maxillary region for evaluating long-term skeletal changes in orthognathic surgical patients.

Most of the studies focusing on VBR accuracy in orthognathic patients have been based on short-term follow up.[6,9,20,21] Although minimal individual orthodontic tooth movements with alveolar bone turnover are inevitable during post-surgical follow up, we found no studies that assessed whether a dentoalveolar segment could negate these movements by applying VBR to assess long-term skeletal follow-up changes in orthognathic surgical patients.

In relation to the reproducibility of the technique, the ICC for both translational and rotational movements showed an excellent interobserver and intraobserver reliability at long- term follow up. The slight decrease in rotational reliability could have been associated with the effect of scatter from orthodontic brackets in Group

A,[19] which might have been further influenced by the scatter from the dental treatment in Group B. However, no comparable evidence was found assessing the effect of scatter on the reproducibility and accuracy of image registration in orthognathic surgical patients. The ICC for translational movements in our study showed slightly more reliability than that of Koerich et al who validated using maxillary and mandibular regional superimposition.[2] As a pilot study, ours does show a possible tool for skeletal changes assessment, although future studies should try to overcome limitations of this best-possible-fit methodology.

A study by Nada et al[21] investigated the accuracy and reproducibility of VBR at follow up based on four anatomical regions in orthognathic surgical patients, such as the ante- rior cranial base, forehead, left and right zygomatic arches. According to their findings, the mean (SD) distance for anterior cranial base superimposition ranged between 0.20 (0.08) mm and 0.37 (0.16) mm and for zygomatic arches it ranged between 0.20 (0.09) mm and 0.45 (0.22) mm.[21] Lee et al utilised a dry skull and assessed the superimposition error of anterior cranial base superimposition with various head orientations and found a mean (SD) error of 0.396 (0.142) mm.[22] In comparison, our findings in the dentoalveolar region were in accordance with the aforementioned findings. However, unlike these previous studies, in which there was a potential risk of error associated with the segmentation process, we relied on a transformation matrix using singular value decomposition to represent the translational and rotational movement of the dentoalveolar segment at two intervals. Most of the evidence related to the registration in orthognathic patients relied on the anterior cranial base and provided translational error.[6,21] In contrast, we also evaluated rotational error as well. All our values were within the clinically acceptable range of 2 mm and 4°.[23] Clinically, VDAR can provide the surgeon with information related to the accuracy of planned versus achieved surgical skeletal positioning of the maxillary and mandibular skeletal structures and also the amount of relapse at follow up. Therefore, it will improve the surgical technique and lead to more accurate and stable results.

At the same instance, regional superimposition of maxillary and mandibular structures with smaller FOV have also been proposed in the literature for assessing the accuracy of bone grafts and implant placement.[24–26] Another advantage of regional superimposition has been related to the evaluation of condylar morphology as the cranial base can only provide information related to movement and relapse.[27] In orthognathic surgery, we do not advocate limiting the CBCT FOV, as cranial base registration is vital for studying skeletal movement, relapse and remodelling. We believe that VBR of the dentoalveolar region as a regional structure following cranial base registration can also provide information related to long-term skeletal relapse. At the same time, controversy exists surrounding the accuracy and reliability of utilising regional structures for superimposition.[26]

This research, however, was subjected to some limitations. Firstly, the effect of implant artefacts and tooth extraction on the error of the registration was not carried out. Secondly, the methodology was only tested for maxillary dental sub- volume, however, based on our findings it can be assumed that mandibular sub-volume would lead to findings within a clinically acceptable range. Thirdly, this methodology might not be suitable for evaluating relapse in patients treated with a surgery-first approach requiring longer postoperative orthodontic treatment. Future randomised studies should concentrate on a follow-up of more than two years to observe whether the dental sub-volume segment remains stable within the clinical acceptable range to be utilised for superimposition and for studying regional skeletal changes. Also, the influence of longer postoperative orthodontic treatment on the accuracy and reproducibility of our technique should also be considered in further studies.

Conclusions

In conclusion, VDAR superimposition was found to be accurate and reliable to be utilised for a long-term skeletal follow-up in orthognathic surgery patients. We believe that this method could be considered as a more accurate alternative compared to its 2D and 3D counterparts which are often associated with higher degree of systemic and human error.

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ARTICLE 3

Three dimensional evaluation of long-term skeletal relapse following Le Fort I maxillary advancement surgery. A 2 year follow-up study

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Abstract

Purpose

The aim of this study was to assess the relapse of Le Fort I (LF I) maxillary advancement with superior or inferior repositioning at a two years follow-up period.

Materials and methods

A total of 50 consecutive patients (Male: 24, Female: 26, Age range: 15-56 years) with skeletal class II or III who underwent bimaxillary surgery with LF I maxillary advancement in combination with either superior or inferior repositioning and BSSO advancement/setback were recruited. Pre-operative (T0), immediate (T1) and two-years post-operative (T2) cone-beam CT scans were acquired. Data were imported into a validated module for assessing the skeletal changes at T0-T1 and T1-T2 time-intervals.

Results

Patients undergoing maxillary advancement with inferior repositioning in either combination with mandibular advancement or setback showed a slightly higher relapse, however, no significant difference existed between superior and inferior repositioning. Majority of the translational and rotational movements had a relapse of less than 1mm and 1° irrespective of the surgical movement. No significant difference in relapse existed between patients with or without anterior iliac bone graft placement.

Conclusions

Relapse of both translational and rotational movements was found to be within a clinically acceptable range of 2 mm and 2°. However, a lack of superoinferior stability was observed in patients undergoing maxillary advancement with inferior repositioning as compared to superior repositioning.

Keywords: maxillary osteotomy; three-dimensional imaging; recurrence; follow-up studies; cone-beam computed tomography

Introduction

Le Fort I (LF I) maxillary osteotomy is one of the most versatile and widely accepted procedure used alone or in combination with bilateral sagittal split osteotomy (BSSO) for the correction of aesthetic and functional maxillo-mandibular disharmony[1]. Although, historically maxillary osteotomy predates till mid-1800s, Obwegeser was the first to propose a technique for completely mobilizing the maxilla offering high level of stabilization and less relapse compared to its predecessors[2,3].

The long-term success of combined orthodontic-orthognathic surgical treatment is dependent on the post-operative relapse which can compromise the operative effect. Most of the evidence focusing on long-term assessment of single-piece LF I relapse has been based on 2D cephalometry[4-6]. The limitations associated with 2D cephalometry include landmark identification error, 2D projection of 3D structures, magnification of anatomical structures and image reorientation error[7]. Similarly, 3D cephalometry has been utilized for assessing relapse, however, it is also prone to human error[8]. To overcome the human and other inherent errors associated with both 2D and 3D cephalometry, various landmark-free image registration methods and algorithms have been applied for assessing relapse and stability which counter the impact of human error. Out of these methods, voxel-based registration has been considered as the most accurate and reliable compared to its surface and point-based counterparts[9].

Some of the studies assessing maxillary relapse have attempted to assess relapse with color-coded comparison by segmenting the anatomical structures[10], however this type of comparison only allows for the assessment of magnitude without considering the six degrees of freedom (6DoF) in the 3D space. At the same instance, limited evidence is available focusing on the long-term LF I relapse utilizing both voxel-based registration and 6DoF[11]. The evidence related to long-term hierarchy of orthognathic surgery stability has been mostly based on 2D or non-standardized 3D landmark-dependent evaluation methods and a few studies are available focusing on the true long-term 3D aspect of relapse[12]. We believe that a research gap exists related to 3D long-term relapse of orthognathic surgery procedures. Therefore, the current study was conducted to assess long-term relapse of 1-piece LF I maxillary osteotomy. The primary aim was to assess the relapse of maxillary advancement with superior or inferior repositioning at a two years follow-up time-point. The secondary aim was to assess the influence of patient- and surgery-related variables which might influence the relapse.

Materials and Methods

This prospective study was conducted in compliance with the World Medical Association Declaration of Helsinki on medical research and ethical approval was obtained from the University Hospital (reference number: B322201526790). Informed consent was obtained from the patients and patient-specific information was anonymized. The sample size was calculated using a priori power analysis in G* power 3.1, assuming 80% power at a significance level of 5%. A total of 50 consecutive patients (Male: 24, Female: 26, Age range: 15-56 years) with skeletal class II or III who underwent combined orthodontic and surgical treatment for the correction of dentofacial deformities were recruited. The data was collected from a period of May 2015 till October, 2019. All patients underwent bimaxillary surgery with LF I maxillary advancement in combination with either superior (51%) or inferior repositioning (49%) and BSSO advancement (50%)/ setback (50%). The patients were operated by the same surgical team and underwent a classic maxillary osteotomy in accordance with the approach described by Bell[13] and mandibular surgery according to Hunsuck/Epker BSSO modification[14,15]. The fixation of maxillary segment was carried out with L-shaped miniplates (2.0, KLS Martin, Mühlheim, Germany) and mandibular osteotomy was fixed and stabilized using two miniplates and mono-cortical screws on each side. An autogenous bone graft was harvested from the anterior iliac crest and was interposed in visible vertical gaps following maxilla repositioning and in those patients requiring maxillary advancement of ≥3mm[16]. The inclusion criteria involved availability of pre-operative (T0), immediate 1-6 weeks after surgery (T1) and two-years post-operative (T2) CBCT scans. Patient having craniofacial syndromes, cleft lip and/or palate, history of maxillofacial trauma and multi-piece LF I were excluded.

The CBCT scans were acquired with two devices, Planmeca Promax 3D Max (Planmeca, Helsinki, Finland) and Newtom VGi-evo (Newtom, Verona, Italy) with standardized scanning parameters of 96-110 KV, 230x260-240x190 field of view (FOV) and slice thickness of 0.3-0.6mm[17]. Following acquisition of the CBCT images at T0, T1 and T2 time points, all the data were saved in a Digital Imaging and Communications in Medicine (DICOM) format.

The DICOM data was imported to a validated step-wise module created in Amira software (version 2019.3, Thermo Fischer Scientific, Merignac, France) for assessing surgical and follow-up changes by calculating the 6DoF i.e. translational and rotational movement differences between two time points[17,18]. The 6DoF refers to the freedom of the movement of a 3D anatomical structure and includes three translational and three rotational parameters for assessing the magnitude and direction of relapse. The translational magnitude and direction is defined by the x, y, z axis which refers to medial/lateral, anterior/posterior and superior/inferior movement. Meanwhile, the rotational parameters include clockwise (CW) and counter-clockwise (CCW) pitch , roll and yaw movement (Figure 1). For assessing relapse, the input data for the module consisted of T1,T2 DICOM datasets and Standard Tessellation Language (STL) file depicting the T1 maxillary LF I position. The algorithm automatically transformed the T1 STL to the T2 position and provided with the 6DoF positional change of the segment from T1 to T2 time-point as an output [18,19]. Similarly, surgical movement was assessed between T0 and T1 time-points. Figure 2A-F illustrates an example of surgical movement and relapse.

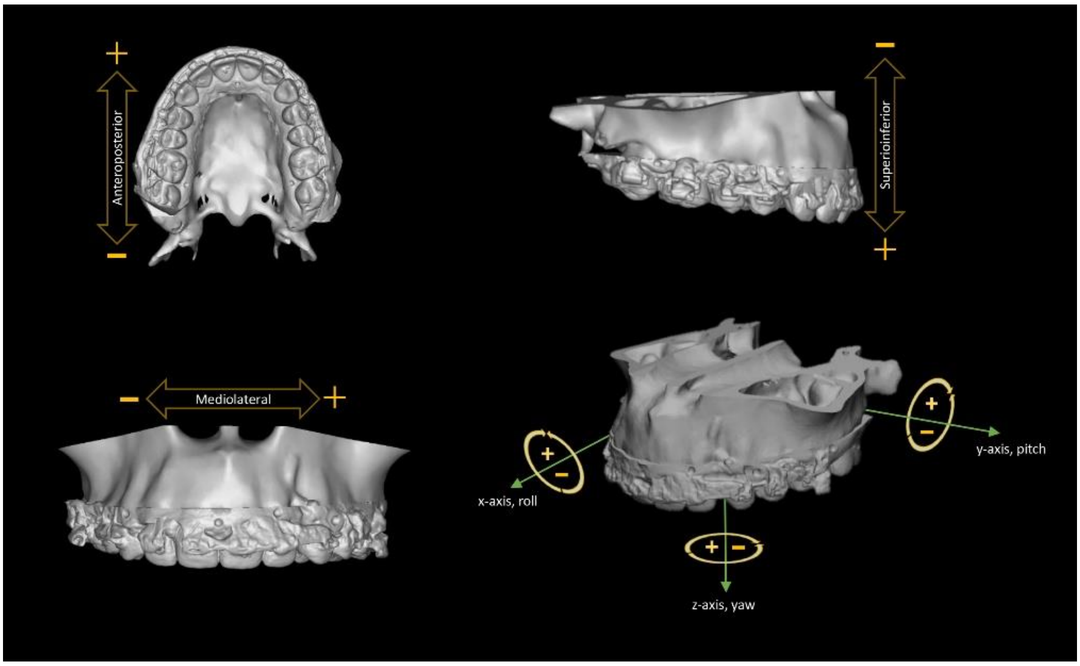

Figure 1. Illustration of six degrees of freedom, where +ve sign indicates relapse in medial, anterior, superior and counter-clockwise direction, -ve sign indicates lateral, posterior, inferior and clockwise direction

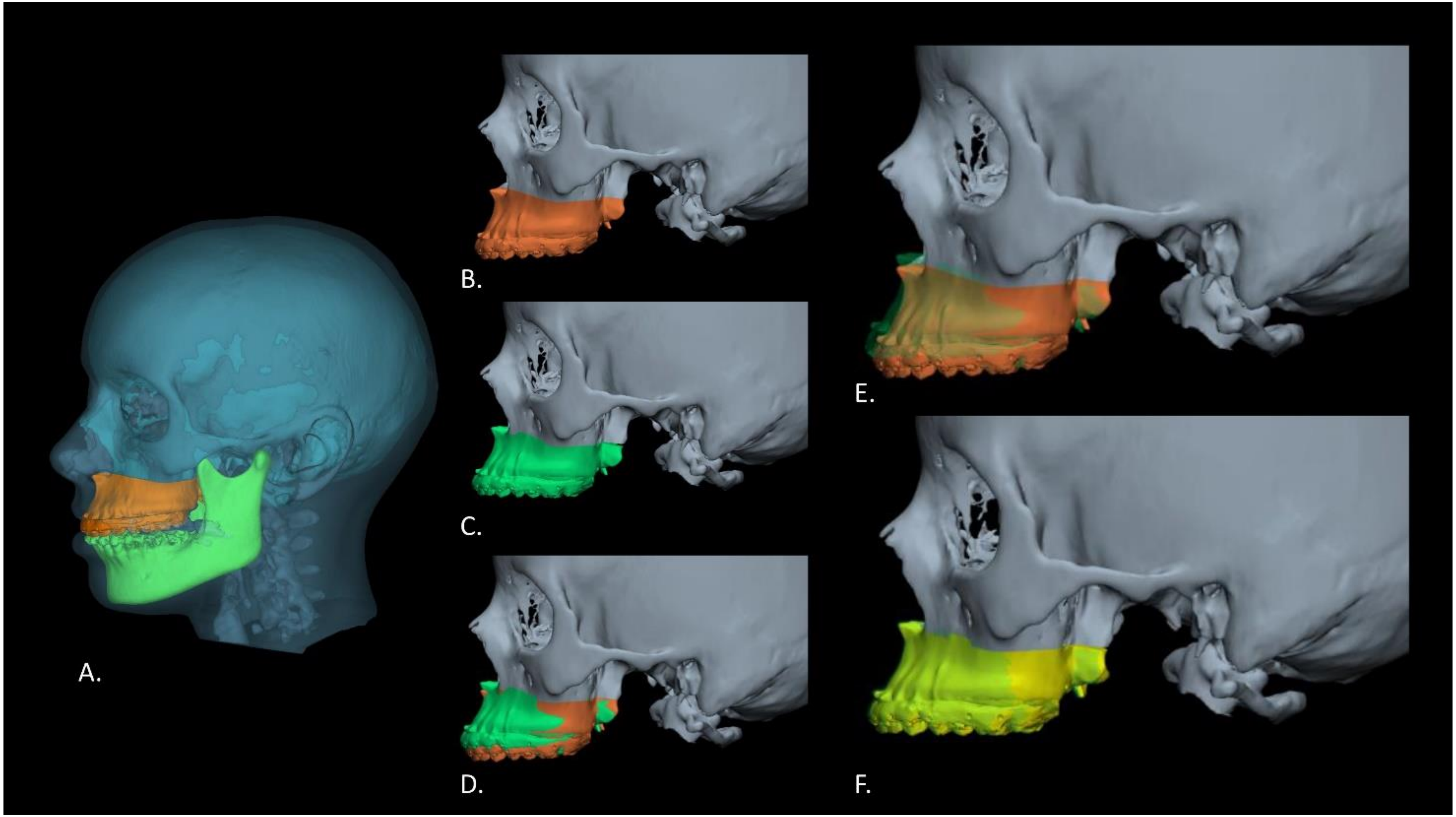

Figure 2. Three-dimensional assessment of maxillary movement and relapse. **A.** Representation of pre-operative occlusion, **B.** pre-operative maxilla position, **C.** immediate post-operative maxilla position showing maxillary advancement with superior repositioning, **D-E.** superimposed pre- and immediate post-operative data representing amount of surgical movement, **F.** superimposed immediate and two-years post-operative scans representing amount of relapse in yellow color.

Statistical Analysis

Data was analyzed using SPSS software version. The mean and standard deviation was calculated for both surgical movement (T0-T1) and relapse (T1-T2). The normality of data was assessed using Shapiro-Wilk test and Levene's test was conducted to assess equality of variances. Student’s t-test was used to determine statistical significance between movement and relapse. Analysis of variance (ANOVA) was utilized for assessing the variables, which included age, sex, amount of movement, skeletal class and bone graft. Wilcoxon test was performed for those variables that were not normally distributed around their mean value. Spearman’s correlation test was applied for assessing the correlation between amount of movement and relapse. A p value of less than 0.05 was considered significant.

Results

Overall, the patients underwent a mean maxillary advancement of 3.7±2.3mm. An anterior iliac crest bone graft was harvested and grafted in 47% of the patients, whereas 53% did not receive any graft. Table 1 describes the percentage of relapse based on the maxillary advancement with either superior or inferior repositioning. The patients undergoing maxillary advancement with inferior repositioning in either combination with mandibular advancement or setback showed the highest percentage of translational relapse of more than 2mm. Overall, the majority of the translational and rotational movements had a relapse of less than 1mm and 1° irrespective of the surgical movement.

Table 1. Percentage of relapse based on translational (mm) and rotational (degree) movements.

	Max. adv.+ superior repos.+mand. adv.			**Max. adv.+ inferior repos.+ mand. adv.**		
Direction	**Ò 1 mm**	**> 1mm - Ò 2 mm**	**> 2mm**	**Ò 1 mm**	**> 1mm - Ò 2 mm**	**> 2mm**
Mediolateral	100	0	0	75	17	8
Anteroposterior	83	17	0	83	8	8
Superoinferior	83	17	0	67	25	8
	<1°	**1-2°**	**>2°**	**<1°**	**1-2°**	**>2°**
Pitch	50	33	17	50	25	25
Roll	83	17	0	58	42	0
Yaw	100	0	0	84	8	8
	Max.adv.+ superior repos.+ mand. setback			**Max.adv.+ inferior repos.+ mand. setback**		
Direction	**Ò 1 mm**	**> 1mm - Ò 2 mm**	**> 2mm**	**Ò 1 mm**	**> 1mm - Ò 2 mm**	**> 2mm**
Mediolateral	79	7	14	83	17	0
Anteroposterior	71	21	7	83	17	0
Superoinferior	93	7	0	67	0	33
	<1°	**1-2°**	**>2°**	**<1°**	**1-2°**	**>2°**
Pitch	43	21	36	50	33	17
Roll	86	14	0	83	17	0
Yaw	86	7	7	100	0	0

max.:maxillary; mand.: mandibular; adv.:advancement; repos: repositioning

Table 2 illustrates the translational and rotational relapse associated with the x, y, z axis and pitch, roll and yaw movements. Patients undergoing maxillary advancement with inferior repositioning in combination with mandibular advancement showed the highest amount of relapse in a superior (0.86±0.85mm, p= <0.0001) and posterior direction (0.65±1.11mm, p=<0.0001) in comparison to other surgical procedures. For the rotational movements, maxillary advancement with superior repositioning and mandibular setback showed the highest relapse of pitch in a CCW direction (1.66±1.81°, p=0.0009) followed by inferior repositioning with mandibular advancement (1.39±2.47°, p=0.0012). Overall, all translational and rotational relapses were within a clinically acceptable range of 2mm and 2°. When correlating the amount of movement with relapse, a positive correlation was observed with all surgical procedures, where the highest translational and rotational correlation was seen in patients with superior repositioning with mandibular advancement (Table 3). The combined findings irrespective of the surgical procedure showed a minimal relapse with a weak to moderate correlation to the amount of movement (Table 4).

Table 2. Translational (mm) and rotational (degree) relapse related to maxillary superior and inferior repositioning.

	Max. adv.+ superior repos.+mand. adv.		**Max. adv.+ inferior repos.+ mand. adv.**	
Direction	**Movement**	**Relapse**	**Movement**	**Relapse**
Mediolateral	-0.45±0.95	-0.12±0.19	0.18±1.08	-0.22±0.96
Anteroposterior	2.97±0.93	**-0.13±1.02***	4.08±1.67	**-0.65±1.11***
Superoinferior	1.77±1.05	**0.47±0.67***	-2.53±1.49	**0.86±0.85***
Pitch	-0.95±4.57	0.65±1.54	4.37±3.48	**1.39±2.47***
Roll	1.02±2.50	-0.58±0.74	0.28±1.95	-0.11±1.10
Yaw	0.55±2.37	-0.23±0.43	0.31±1.18	0.45±0.84
	Max.adv.+ superior repos.+ mand. setback		**Max.adv.+ inferior repos.+ mand. setback**	
Direction	**Movement**	**Relapse**	**Movement**	**Relapse**
Mediolateral	-0.09±0.66	0.26±1.81	0.12±0.78	-0.23±0.67
Anteroposterior	3.71±2.26	**-0.21±2.03***	4.15±1.17	**0.23±1.01***
Superoinferior	1.16±0.94	**0.24±0.54***	-1.53±1.97	0.80±1.72
Pitch	-3.16±3.12	**1.66±1.81***	-1.48±1.82	0.87±1.20
Roll	0.01±1.11	0.30±0.88	0.88±1.68	0.32±0.61
Yaw	-0.35±1.77	-0.38±1.05	1.17±1.07	**-0.12±0.21***

max.:maxillary; mand.: mandibular; adv.:advancement; repos: repositioning, +ve sign indicates relapse in medial, anterior, superior and counter-clockwise direction, -ve sign indicates lateral, posterior, inferior and clockwise direction, *indicates statistical significance (p<0.05)

Table 3. Correlation between amount of movement and relapse related to maxillary superior and inferior repositioning.

	Max. adv.+ superior repos.+mand. adv.	Max. adv.+ inferior repos.+ mand. adv.
Direction		
Mediolateral	0.49	0.18
Anteroposterior	0.74	0.26
Superoinferior	0.43	0.06
Pitch	0.68	0.45
Roll	**0.93***	0.37
Yaw	**0.84***	0.38
	Max.adv.+ superior repos.+ mand. setback	**Max.adv.+ inferior repos.+ mand. setback**
Direction		
Mediolateral	0.22	0.09
Anteroposterior	0.20	0.32
Superoinferior	0.11	0.14
Pitch	0.39	0.35
Roll	0.12	0.49
Yaw	0.18	0.29

max.:maxillary; mand.: mandibular; adv.:advancement; repos: repositioning, +ve sign indicates relapse in medial, anterior, superior and counter-clockwise direction, -ve sign indicates lateral, posterior, inferior and clockwise direction, *indicates statistical significance ($p<0.05$)

Table 4. Combined translational (mm) and rotational (degree) movement and relapse irrespective of the surgical procedure.

Movement direction	Mean movement	Mean relapse	Significance	Correlation (r)
Mediolateral	-0.06± 0.97	-0.06 ±1.16	0.068	0.22
Anteroposterior	3.72 ±2.25	-0.22 ±1.43	0.538	**0.35**
Superoinferior	-0.2 ±2.2	0.45± 0.87	0.060	**0.33**
Pitch	-0.99±4.7	0.60± 2.23	0.075	**0.64**
Roll	0.28±1.73	0.06 ±0.89	0.633	**0.34**
Yaw	-0.13±1.92	-0.02± 0.85	0.803	0.24

+ve sign indicates relapse in medial, anterior, superior and counter-clockwise direction, -ve sign indicates lateral, posterior, inferior and clockwise direction

When subdividing the data further based on those receiving bone graft against without bone graft (Table 5, Table 6), the relapse associated with each surgical procedure was within the range of 1mm and 1° who received bone graft, apart from patients with inferior repositioning and mandibular setback which showed the highest non-significant maxillary relapse in superior direction (1.20±1.56mm, p=0.0719) with CCW pitch rotation (2.15±0.64°, p=0.3759). In relation to patients not receiving bone graft, the translational relapse for all surgical procedures was also within the range of 1mm, except patients undergoing superior repositioning with mandibular setback which showed a non-significant relapse in medial direction (1.38±2.78mm, p=0.3981). Amongst the rotational parameters, CW and CCW pitch movement relapsed the highest with all surgical procedures. No significant difference existed based on the sex of the patient (p<0.05). Additionally, no significant difference existed between patients with and without bone graft in x (p=0.2865), y (p=0.5126), z (p=0.8503) axis and with respect to pitch (p=0.4190), roll (p= 0.2338) and yaw (p= 0.9723). Similarly, when categorizing patients into young and old patients at the time of surgery as suggested by Bailey et al.[20] (young female<18yrs, young male<20yrs; old female≥18, old male≥20), no significant differences were observed.

Table 5. Translational (mm) and rotational (degree) movement and relapse in patients with interposed anterior iliac bone graft

	Max. adv.+ superior repos.+mand. adv.		**Max. adv.+ inferior repos.+ mand. adv.**	
Direction	**Movement**	**Relapse**	**Movement**	**Relapse**
Mediolateral	-0.83±0.81	-0.17±0.21	-0.07±0.90	0.00±0.50
Anteroposterior	3.53±0.32	-0.30±1.42	3.30±1.55	-0.60±0.80
Superoinferior	2.47±1.10	0.73±0.93	-1.40±2.72	0.93±1.10
Pitch	0.13±6.64	0.47±1.87	3.03±2.43	-0.63±0.46
Roll	-0.43±1.33	-0.20±0.60	-0.30±0.75	-0.10±1.45
Yaw	0.80±0.62	-0.13±0.12	1.17±0.70	0.53±1.60
	Max.adv.+ superior repos.+ mand. setback		**Max.adv.+ inferior repos.+ mand. setback**	
Direction	**Movement**	**Relapse**	**Movement**	**Relapse**
Mediolateral	-0.16±0.64	-0.37±0.48	0.00±0.71	-0.40±0.00
Anteroposterior	4.73±2.15	**0.14±1.07***	3.95±1.63	-0.05±0.92
Superoinferior	1.44±1.04	**0.09±0.57***	-3.65±2.33	1.20±1.56
Pitch	-2.47±2.47	**0.99±1.45***	-2.40±3.68	2.15±0.64
Roll	0.28±1.10	0.41±1.02	-0.90±1.98	0.60±0.99
Yaw	-0.50±2.13	-0.20±0.51	0.95±0.92	-0.10±0.14

max.:maxillary; mand.: mandibular; adv.:advancement; repos: repositioning, +ve sign indicates relapse in medial, anterior, superior and counter-clockwise direction, -ve sign indicates lateral, posterior, inferior and clockwise direction, *indicates statistical significance (p<0.05)

Table 6. Translational (mm) and rotational (degree) movement and relapse in patients without bone grafting.

	Max. adv.+ superior repos.+mand. adv.		**Max. adv.+ inferior repos.+ mand. adv.**	
Direction	**Movement**	**Relapse**	**Movement**	**Relapse**
Mediolateral	-0.35±1.34	-0.10±0.28	0.28±1.11	-0.26±1.03
Anteroposterior	1.90±0.85	0.35±0.64	2.24±1.65	**-0.66±1.16***
Superoinferior	0.80±0.28	0.20±0.28	-2.45±1.60	**0.77±0.80***
Pitch	-3.25±0.64	**1.70±0.28***	4.37±3.82	**-1.51±2.69***
Roll	3.80±2.12	-1.35±0.49	0.40±2.10	-0.12±1.00
Yaw	-0.50±4.81	0.00±0.42	0.21±1.27	0.28±0.70
	Max.adv.+ superior repos.+ mand. setback		**Max.adv.+ inferior repos.+ mand. setback**	
Direction	**Movement**	**Relapse**	**Movement**	**Relapse**
Mediolateral	0.02±0.75	1.38±2.78	0.18±0.91	-0.15±0.85
Anteroposterior	1.72±1.23	-0.84±3.22	2.25±1.99	**0.38±1.15***
Superoinferior	0.64±0.45	0.52±0.38	-0.48±0.45	-0.45±1.71
Pitch	-4.40±4.06	**2.86±1.91***	-1.03±0.43	0.23±0.79
Roll	-0.46±1.05	0.10±0.59	1.78±0.48	**0.18±0.46***
Yaw	-0.08±1.01	-0.70±1.70	1.28±1.25	-0.13±0.26

max.:maxillary; mand.: mandibular; adv.:advancement; repos: repositioning, +ve sign indicates relapse in medial, anterior, superior and counter-clockwise direction, -ve sign indicates lateral, posterior, inferior and clockwise direction, *indicates statistical significance ($p<0.05$)

Discussion

The transition from 2D to landmark-free 3D methodologies is considered to be paradigm shifting cornerstone for a better understanding of the relapse following orthognathic surgery procedures[21,22]. Therefore, the present study assessed the 3D long-term surgical relapse associated with single-piece LF I maxillary osteotomy using a landmark-free methodology.

Our findings suggested an excellent stability of the LF I maxillary osteotomy both with superior and inferior repositioning. Even though a significant relapse was detected in certain directions, nevertheless, relapse for all translational and rotational movements was found to be within a clinically acceptable range of 2mm and 2°[5,23]. The highest change was observed in a superoinferior direction. Patients undergoing advancement with superior repositioning showed more translational stability compared to inferior movement. Our findings were in accordance with other studies showing slightly higher relapse with inferior repositioning[23,24]. Relapse associated with inferior repositioning might have been attributed to the occlusal forces and that of superior repositioning to the utilization of post-operative elastics[25]. Proffit et al suggested maxillary inferior repositioning to be a highly unstable and a problematic procedure[23], however, we found its relapse to be within the clinically acceptable limits. This difference in stability in our study could have also resulted as the amount of surgical movement was larger in cases with inferior repositioning. Additionally, due to movements in multiplicity of directions and involvement of mandibular surgery, the distribution of data could have resulted in bias within our findings. Nevertheless, it should be kept in mind that even though surgery is performed according to the planning, the complete control of the maxillary movement according to the planning is difficult to achieve during surgery and is dependent on the cutting accuracy, thereby resulting in multidirectional intra-operative movements.

The relapse is dependent on various factors such as bite force, amount of movement, bone grafting and stabilization technique[26,27,28]. Numerous studies have been conducted describing the association between skeletal stability and bone grafting. Some studies suggested reduction in relapse following bone grafting, whereas, others found no significant diffference[4,28,29]. No consensus has been reached whether bone grafting provides more stability. In our study the patients with inter-positioned anterior iliac bone graft showed overall no significant influence on relapse when compared with patients who did not receive any graft. This could be attributed to the fact that the mean anterior and superoinferior movement was not large enough to assess the influence of bone grafting.

Furthermore it was observed that amongst the rotational movements, pitch showed most relapse with a higher degree of rotation in CCW direction at follow-up in patients with superior repositioning and mandibular setback which was in accordance with other findings[11]. As the CCW pitch rotation of maxilla offers a wide bony contact area, unlike CW pitch rotation which leads to delayed bone healing and might cause the maxilla to relapse in an opposite CCW direction. The rotational parameter yaw which is deemed necessary for relocating the maxilla into a symmetrical position also relapsed slightly in all surgical procedures which might have been resulted due to the difference in muscular activities of the patients, thereby influencing the return of maxilla to its original position[30]. At the same instance, it would be interesting to observe and correlate the impact of chewing and eating habits on the 3D maxillary relapse. Although all aforementioned factors somehow influenced relapse in specific directions, nevertheless, based on percentage most changes observed were less than 1mm and 1° for both translational and rotational movements. Also, based on the multi-directional movements it was difficult to conclude why a higher positive correlation was observed in certain directions. However, when observing at the combined data of all surgical procedures, only the rotational pitch movement showed a moderate positive correlation (r=0.64), whereas, a weak correlation existed for all other rotational and translational movements (r= 0.22-0.35).

The strength of the study was the long-term 3D assessment of skeletal relapse and its prospective nature. The study had certain limitations. Firstly, the sample included patients undergoing bimaxillary surgery with both mandibular advancement and setback and the multiplicity of movement could have led to a crude sample distribution and bias, therefore, further studies should be conducted by recruiting patients with isolated single-jaw surgery. Secondly, changes in the mandibular and condylar region were not evaluated. Thirdly, the mean superior and inferior repositioning was inadequate to observe the influence of larger amount of movements. Nevertheless, we provided evidence related to the long-term 3D maxillary relapse based on 6DoF which has not been clearly addressed in previous studies. Future studies should also be conducted specifying the influence of occlusal forces and muscle pull on relapse.

In conclusion, single-piece LF I maxillary advancement was found to be a highly stable procedure without any clinically significant relapse in both skeletal class II and III patients up to 2 years follow-up. Bone grafting showed no significant influence on stability. However, a lack of superoinferior stability was observed in patients undergoing maxillary advancement with inferior repositioning as compared to superior repositioning.

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ARTICLE 4

Three dimensional evaluation of distal and proximal segments skeletal relapse following isolated mandibular advancement surgery in 100 consecutive patients. A one-year follow-up study

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Abstract

Purpose

The aim of this study was to three-dimensionally evaluate skeletal relapse of proximal and distal mandibular segments following isolated bilateral sagittal split osteotomy (BSSO) advancement surgery.

Materials and methods

The study enrolled 100 consecutive patients prospectively (mean age: 25.8±11.7 years) consisting of 35 male (mean age: 24.6±11.0 years) and 65 female patients (mean age: 26.4±12.1 years) requiring mandibular advancement without genioplasty. Cone-beam computed tomographic (CBCT) scans were acquired for each patient at three time-points: preoperatively (T0), immediately 1-6 weeks after surgery (T1) and 1 year after surgery (T2). A validated tool was utilized for assessing the surgical movement and relapse.

Results

Based on percentage, majority of the distal and proximal translational and rotational movements relapsed within the range of 2 mm and 2°. The distal segment revealed a significant relapse in a posterior, inferior and CW pitch direction. Both left and right proximal segments showed a significant translational relapse in medial, posterior and superior direction. Amongst the rotational parameters, proximal segments relapsed significantly in CW pitch, CW roll and CCW yaw direction.

Conclusion

Overall, both distal and proximal bone segments showed a clinically acceptable translational and rotational stability. The proximal segments torqued towards their original position with a reduction of flaring.

Keywords: mandibular advancement; three-dimensional imaging; recurrence; follow-up studies; cone-beam computed tomography

Introduction

Mandibular advancement with bilateral sagittal split osteotomy (BSSO) is the most widely used surgical technique for the correction of mandibular retrognathism[1]. Amongst the orthognathic surgical procedures, it is considered to be a highly stable and predictable procedure based on the hierarchy of post-surgical stability[2,3]. However, like every surgical procedure, BSSO advancement is also associated with unwanted secondary effects and one of the most commonly reported side-effect of this procedure includes skeletal relapse[4].

Scientific evidence on assessing skeletal stability has been mostly based on two-dimensional (2D) or three-dimensional (3D) cephalometry, which is prone to human error and subjectivity meanwhile also lacking clinical relevance[5-9]. For that reason, semi-automatic voxel-based image superimposition and landmark-free assessment methodologies have been recently applied for assessing skeletal relapse[10,11].

Additionally, in relation to the BSSO surgery, studies assessing the positional and angular relapse of the proximal and distal mandibular segments have also mostly relied on cephalometry[8,12,13]. Currently, limited evidence exists utilizing semi-automatic methodologies with voxel-based registration for the assessment of long-term relapse following isolated BSSO advancement surgery.[14-16] Even though previous landmark based studies have found BSSO advancement to be a highly stable procedure, we believe no study exists assessing the 3D six degrees of freedom (6DoF) relapse of mandibular proximal and distal segments following isolated BSSO advancement surgery in a large homogenous group of patients. Therefore, the current study was conducted to three-dimensionally evaluate skeletal relapse of proximal and distal mandibular segments following BSSO advancement surgery in 100 consecutive patients based on a validated semi-automatic tool.

Materials and methods:

This study was in compliance with the World Medical Association Declaration of Helsinki on medical research. Ethical approval was received from the Ethical Review Board of the University Hospitals Leuven (reference number: B322201526790) and patient-specific information was anonymized. The sample size was calculated using a priori power analysis in G* power 3.1, assuming 80% power at a significance level of 5%. The prospective study enrolled 100 consecutive patients (mean age: 25.8±11.7 years) consisting of 35 male (mean age: 24.6±11.0 years) and 65 female patients (mean age: 26.4±12.1 years).

Data was collected from a period of February 2015 till December 2019. The inclusion criteria involved skeletal class II patients with mandibular deficiency requiring mandibular advancement without genioplasty. Patients with syndromic or degenerative diseases, bimaxillary surgery, previous TMJ intervention, history of maxillofacial trauma and cleft lip and palate were not included. All patient were diagnosed with mandibular retrognathism and underwent BSSO advancement without genioplasty in accordance with Hunsuck/Epker BSSO modification[17-19]. A 7mm cut-off point based on the amount of advancement was used for categorizing the patients into low and high advancement cases.

The treatment planning of all the cases was carried out utilizing a validated protocol, where Proplan CMF software (Materialise, Leuven, Belgium) was used for defining surgical movements and creating composite skeletal models and occlusal wafers[20]. Wafers were printed with the Objet Connex 350 printer (Stratasys, Eden Prairie, MN, USA).

All surgeries were performed by the same team of oral and maxillofacial surgeons. Following osteotomy and achievement of final occlusion, rigid fixation and stabilization was accomplished with two KLS-Martin mini-osteosynthesis plates (KLS Martin GmbH, Freiburg, Germany) and mono-cortical screws on both sides as suggested by Tulasne and Schendel[21]. The cone-beam computed tomographic (CBCT) scans were acquired for each patient at three time-points, preoperatively (T0), immediately after surgery (T1) and 1 year follow-up (T2). The immediate scan for 86% of the patients was carried out at an interval of 7-10 days and 14% of the scans at 40-42 days interval. The scans were carried out utilizing a standardized protocol proposed by Stratis et al[22]. (field of view: 230x260 - 240x190mm2, kV: 96-110, slice thickness: 0.3-0.6mm) with Planmeca Promax 3D Max (Planmeca, Helsinki, Finland) and Newtom VGi-evo (Newtom, Verona, Italy). All scans were saved in Digital Imaging and Communications in Medicine (DICOM) format.

A validated tool developed in Amira software (version 2019.3, Thermo Fischer Scientific, Merignac, France) was used for assessing the surgical movement and relapse.[23] First the surgical movement was assessed by importing the data at T0-T1 time-interval. The data at both T0 and T1 was imported and the two images were registered onto the anterior cranial base sub-volume which was unaffected by the surgery by applying voxel based registration with mutual information. For achieving a transformation matrix, the registered T1 data was transformed onto the T0 position by delineation of a volume of interest (VOI) in both T0 and T1. The VOI for distal segment involved dentoalveolar region[10,23,24] and for proximal segments a modified delineation of ramus was performed as proposed by Verhelst et al[25]. Later, the mandibular distal and left and right proximal segments were imported individually into the tool as stereolithography (STL) files. A singular value decomposition (SVD) algorithm was applied to the previously obtained transformation matrix to calculate the six degrees of freedom (6DoF) movement difference between T0 and T1 for all segments. The 6DoF included three translational (anteroposterior, superoinferior, mediolateral) and three rotational clockwise/counter-clockwise (CW/CCW) movements (pitch, roll, yaw) (Figure 1). The rotational CW/CCW pitch around the transverse axis refers to the brevi-gnathial/ longi-gnathial movement of the jaw, CW/CCW roll around the anteroposterior axis as right/left skeletal canting and CW/CCW yaw around the superoinferior axis as right/left laterognathia. Similar steps were repeated for assessing relapse (T1-T2). Figure 2 illustrates the superimposed DICOM images at T0-T1 and T1-T2 time-intervals. Figure 3 represents the skeletal movement and relapse based on the registered STL files of the distal and proximal segments.

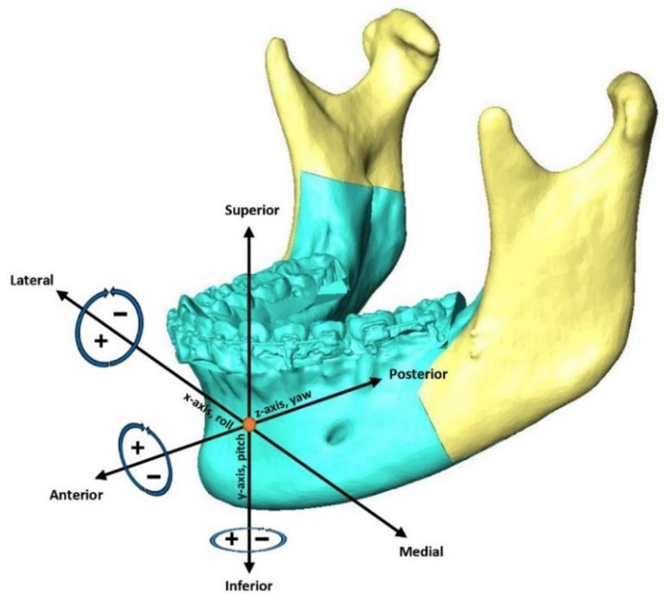

Figure 1. Representation of six degrees of freedom (6DoF), yellow color represents left and right proximal segment, blue color represents distal segment.

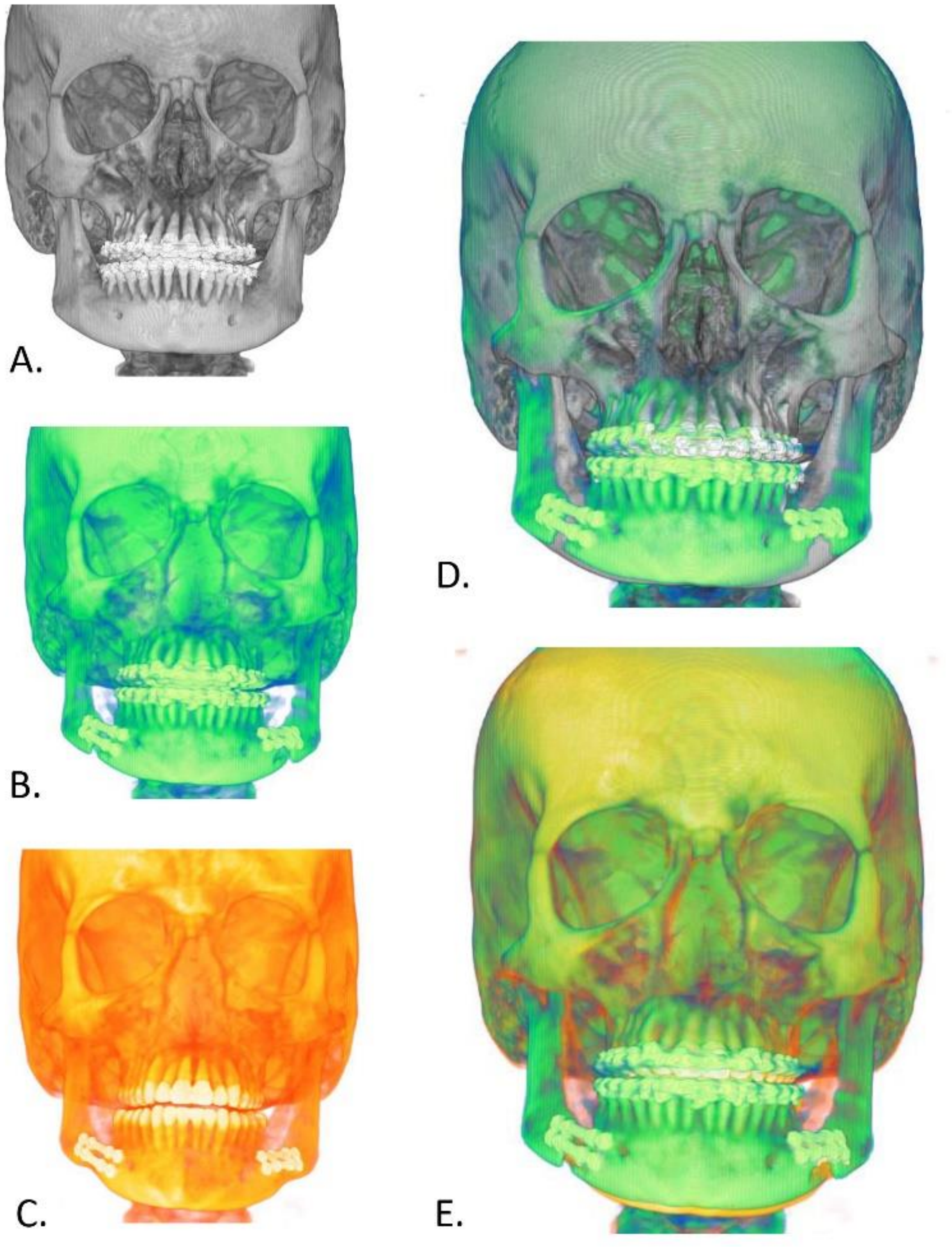

Figure 2. Voxel-based superimposition of CBCT scans using dentoalveolar region for distal segment registration and modified delineation of ramus for proximal segments , **A.** preoperative CBCT scan (T0), **B.** immediate postoperative scan (T1), **C.** 1 year follow-up scan (T2), **D.** superimposed T0 and T1, **E.** superimposed T1 and T2.

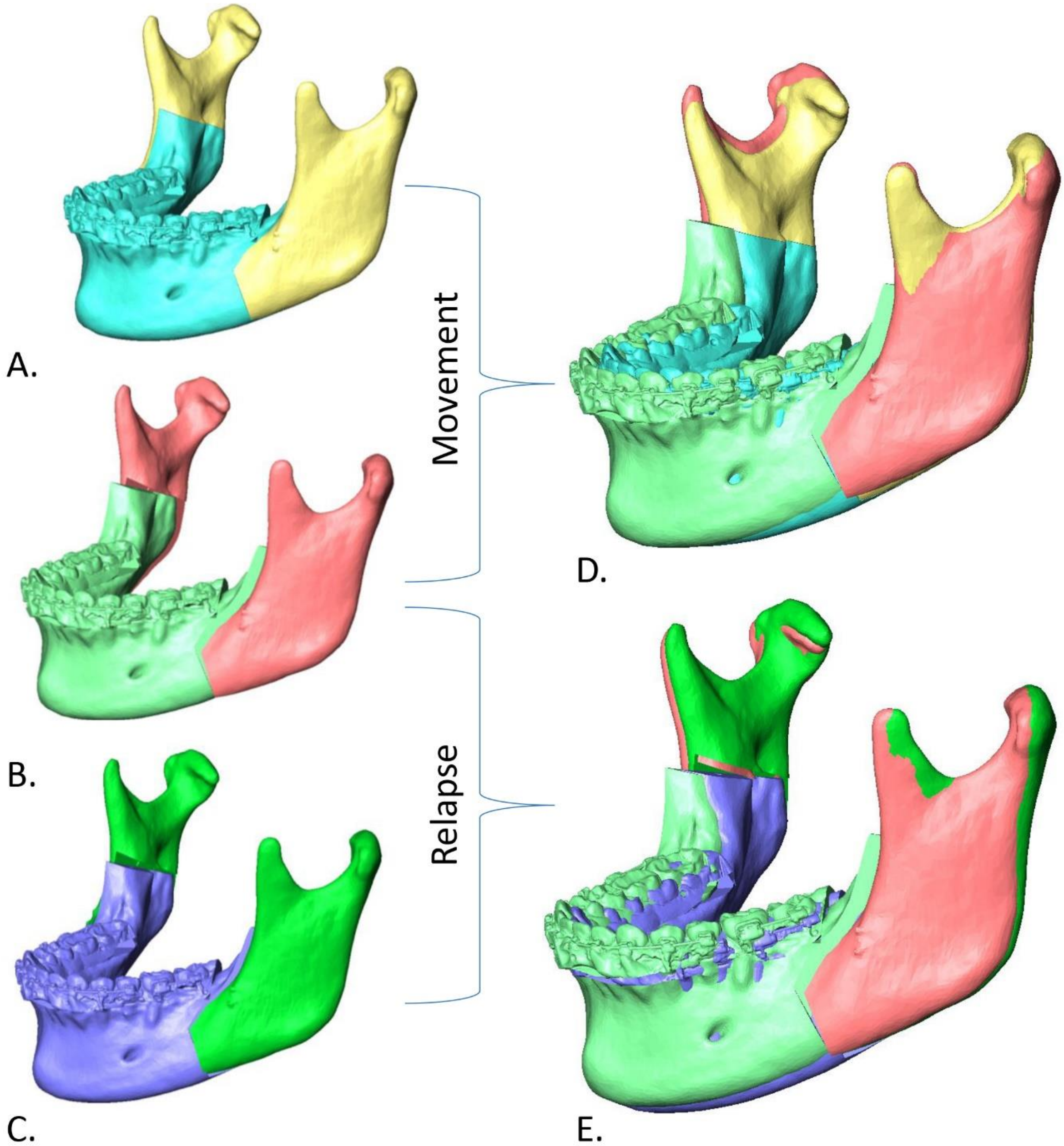

Figure 3. Illustration of the superimposed distal and proximal segments resulting from the transformation matrix for retrieval of translational and rotational parameters using singular value decomposition algorithm. **A-C.** segmented mandibular distal and proximal segments preoperatively (T0), immediately after surgery (T1) and 1 year follow-up (T2), **D.** superimposed distal and proximal segments at T0-T1 representing mandibular advancement with anterior movement of the distal segment and lateral movement of the proximal segments, **E.** superimposed distal and proximal segments at T1-T2 showing distal segment relapse in a posteroinferior direction and torquing of the proximal segments towards their original position.

Statistical analysis

The data were analyzed with a statistical software package SPSS version 21.0 for Windows (SPSS Inc, Chicago, USA). Descriptive statistics were calculated and presented as mean and standard deviation. Shapiro-Wilk test was utilized for testing the normality of the data. The significance of relapse was calculated using Student t-test. Age was analyzed with the Student's t-test and gender with Pearson's χ2 test.Spearman's correlation test was carried out to test the correlation between amount of movement and relapse. It was interpreted as negligible (0.00–0.09), weak (0.10–0.39), moderate (0.40–0.69), strong (0.70–0.89) and very strong (0.90–1.00) correlation[26].

Results

The patients underwent an average anterior mandibular advancement of 6.03±2.72mm. Based on percentage, majority of the distal and proximal translational and rotational movements relapsed within the range of 2mm and 2° (Table 1). The distal segment revealed a significant relapse in a posterior, inferior and CW pitch direction. The maximum amount of relapse for the translational movements was in a posterior direction (-1.33±1.46mm) followed by inferior direction (-1.21±2.02mm). In relation to the rotational movements maximum relapse was observed in CW pitch direction (-1.28±2.04°). A non-significant relapse of less than 0.5mm and 0.5° was associated with the rest of the movements (Table 2).

Table 1. Percentage (%) of the amount of translational and rotational relapse.

	Distal segment %			**Left proximal segment %**			**Right proximal segment %**		
Translational	**<1mm**	**1-2mm**	**>2mm**	**<1mm**	**1-2mm**	**>2mm**	**<1mm**	**1-2mm**	**>2mm**
ML	80	19	1	65	33	2	75	21	4
AP	36	36	28	50	37	13	49	32	19
SI	61	27	12	73	12	13	70	19	11
Rotational	**<1°**	**1-2°**	**>2°**	**<1°**	**1-2°**	**>2°**	**<1°**	**1-2°**	**>2°**
Pitch	40	29	31	59	21	20	57	21	22
Roll	82	16	2	65	24	11	59	25	16
Yaw	77	21	2	52	26	22	35	35	30

ML: mediolateral, AP: anteroposterior, SI: superoinferior

Table 2. Distal segment distribution, translational (mm) and rotational (degree) movement and relapse (mean ± standard deviation) associated with the mandibular advancement.

Movement direction	Distal segments (n)	Mean Movement	Mean Relapse
Medial	60	1.14±1.19	-0.14±0.74
Lateral	40	1.04±1.15	-0.24±0.89
Anterior	100	6.03±2.72	**-1.33±1.46***
Superior	37	1.30±1.49	**-1.21±2.02***
Inferior	63	1.61±1.15	0.11±1.20
CW pitch	28	1.84±2.13	-0.13±1.86
CCW pitch	72	2.81±1.89	**-1.28±2.04***
CW roll	49	0.98±0.92	-0.36±0.83
CCW roll	51	0.78±0.62	-0.20±0.71
CW yaw	45	0.97±0.96	-0.32±0.91
CCW yaw	55	1.37±1.38	0.11±0.80

-ve value in relapse indicates the opposite direction to that of movement, +ve value in relapse indicates the same direction to that movement, *****indicates statistical significance ($p<0.05$)

Both left and right proximal segments showed a significant translational relapse in medial, posterior and superior direction, with maximum relapse in a posterior direction (-1.15±1.39mm). Amongst the rotational parameters, relapse was observed in CW pitch, CW roll and CCW yaw direction. Both translational and rotational relapse were within a clinically acceptable range of 2mm and 2° (Table 3).

Table 3. Left and right proximal segments distribution, translational (mm) and rotational (degree) movement and relapse (mean ± standard deviation) associated with the mandibular advancement.

Movement direction	Left proximal segments (n)	Left proximal segment movement	Right proximal segments (n)	Right proximal segment movement	Left proximal segment relapse	Right proximal segment relapse
Medial	5	2.22±3.20	2	1.65±1.91	-0.36±0.94	-0.25±0.49
Lateral	95	1.90±1.00	98	1.99±1.07	**-0.64±3.20***	**-0.61±0.77***
Anterior	78	1.99±1.24	80	2.14±1.52	**-0.80±1.25***	**-1.15±1.39***
Posterior	22	1.65±2.63	20	1.29±1.42	0.36±1.15	0.54±1.19
Superior	73	1.34±1.13	70	1.52±1.30	0.23±1.54	0.03±1.60
Inferior	27	0.99±1.20	30	0.83±1.12	**-0.93±1.54***	**-0.81±0.97***
CW Pitch	4	0.93±0.69	3	0.33±0.15	-0.58±1.39	-0.10±0.40
CCW Pitch	96	3.94±2.01	97	4.16±2.20	**-0.79±1.52***	**-0.83±1.72***
CW Roll	8	0.83±0.71	2	2.30±0.28	-0.34±0.94	-0.95±0.49
CCW Roll	92	5.11±2.57	98	5.24±2.55	**-0.71±1.25***	**-0.72±1.17***
CW Yaw	87	4.34±2.82	88	4.58±3.02	**-1.29±1.29***	**-1.65±1.08***
CCW Yaw	13	1.22±1.11	12	1.31±1.74	0.48±1.11	0.01±1.14

-ve value in relapse indicates the opposite direction to that of movement, +ve value in relapse indicates the same direction to that movement, *****indicates statistical significance ($p<0.05$)

Table 4 illustrates the overall translational and rotational movement and relapse of distal and proximal segments. The maximum translational relapse of both distal and proximal segments was observed anteroposteriorly. In relation to the rotational relapse, distal segment showed higher pitch relapse, whereas, yaw movement relapsed more with both proximal segments.

Table 4. Overall translational (mm) and clockwise (CW)/ counter-clockwise (CCW) rotational (degree) movement and relapse of distal and proximal segments.

	Distal segment (mm)		Left proximal (mm)		Right proximal (mm)	
	Movement	**Relapse**	**Movement**	**Relapse**	**Movement**	**Relapse**
Mediolateral	0.27±1.58	0.01±0.82	1.70±1.48	**-0.59±0.79***	1.82±1.85	**-0.60±0.77***
Anteroposterior	6.03±2.72	**-1.33±1.46***	1.19±2.23	**-0.70±1.24***	1.46±2.03	**-1.03±1.37***
Superoinferior	0.54±1.90	**0.52±1.63***	0.71±1.55	**0.42±1.56***	0.82±1.64	0.27±1.48
Pitch	1.51±2.86	**-0.89±2.08***	3.75±2.19	**-0.73±1.53***	4.02±2.30	**-0.80±1.70***
Roll	0.08±1.17	-0.07±0.81	4.64±2.95	**-0.63±1.25***	5.09±2.74	**0.69±1.18***
Yaw	0.31±1.68	**0.21±0.85***	3.62±3.26	**-1.19±1.29***	3.88±3.47	**-1.45±1.21***

Distal segment, -ve value: lateral, posterior, superior, CW pitch, CW roll, CW yaw. **Distal segment, +ve value:** medial, anterior, inferior, CCW pitch, CCW roll, CCW yaw. **Left proximal segment, -ve value:** medial, anterior, inferior, CCW pitch, CCW roll, CW yaw. **Left proximal segment, +ve value:** lateral, posterior, superior, CW pitch, CW roll, CCW yaw. **Right proximal segment, -ve value:** lateral, anterior, inferior, CCW pitch, CW roll, CCW yaw. **Right proximal segment, +ve value:** medial, posterior, superior, CW pitch, CCW roll, CW yaw. *indicates statistical significance ($p<0.05$)

Age and sex of the patient had a negligible influence on the amount of relapse. When comparing the overall relapse based on the two time-point of T1 to T2, no significant difference was detected. The correlation between amount of movement and relapse showed an overall significantly weak to moderate positive relationship for both distal and proximal segments ranging between 0.30 and 0.45. The low advancement cases included 64% and high advancement consisted of 36% patients. A higher positive correlation existed in high advancement cases (r=0.30) compared to lower anterior advancement (r=0.08). The correlation was also confirmed with the higher amount of relapse in patients with high advancement, where the distal segment relapsed significantly in posterior direction (-2.17±1.27) compared to the low advancement cases (-0.87±1.35mm). Furthermore, apart from the posterior relapse of the distal segment in the high advancement cases, all translational and rotational parameters in both groups were within a clinically acceptable range of 2mm and 2° (Table 5).

Table 5. Overall translational (mm) and clockwise (CW)/ counter-clockwise (CCW) rotational (degree) movement and relapse based on the amount of anteroposterior movement.

	Low advancement					
	Distal segment		Left proximal		Right proximal	
	Movement	Relapse	Movement	Relapse	Movement	Relapse
ML	0.22±1.75	0.06±0.92	1.67±1.62	**-0.62±0.79***	1.61±2.08	**-0.67±0.83***
AP	4.59±1.96	**-0.87±1.35***	0.63±2.31	**-0.38±1.13***	0.72±1.75	**-0.58±1.13***
SP	0.34±1.77	0.54±1.21	0.96±1.65	**0.28±1.45***	0.98±1.81	**0.13±1.06***
Pitch	1.29±2.70	**-1.14±2.11***	3.39±2.20	**-0.71±1.32***	3.49±2.21	**-0.57±1.48***
Roll	0.04±1.25	-0.02±0.85	4.81±2.76	**-0.61±1.08***	5.16±2.82	**0.72±1.15***
Yaw	0.36±1.85	0.13±0.87	4.28±3.02	**-1.30±1.15***	4.29±3.47	**-1.40±1.20***

	High advancement					
	Distal segment		Left proximal		Right proximal	
	Movement	Relapse	Movement	Relapse	Movement	Relapse
ML	0.35±1.21	0.13±0.60	1.74±1.18	**-0.53±0.79***	2.19±1.26	**-0.48±0.62***
AP	8.70±1.72	**-2.17±1.27***	2.23±1.63	**-1.30±1.23***	2.83±1.80	**-1.86±1.41***
SP	0.90±2.10	0.47±2.23	0.25±1.22	0.68±1.74	0.53±1.23	0.53±2.04
Pitch	1.91±3.14	-0.43±1.97	4.42±2.04	-0.77±1.88	5.02±2.16	**-1.23±1.99***
Roll	0.16±1.02	-0.17±0.73	4.31±3.29	**-0.66±1.55***	4.95±2.62	**0.64±1.26***
Yaw	0.21±1.31	0.36±0.79	2.39±3.37	**-0.97±1.51***	3.11±3.38	**-1.55±1.24***

ML,mediolateral; AP,anteroposterior, SP,superoinferior. **Distal segment, -ve value:** lateral, posterior, superior, CW pitch, CW roll, CW yaw. **Distal segment, +ve value:** medial, anterior, inferior, CCW pitch, CCW roll, CCW yaw. **Left proximal segment, -ve value:** medial, anterior, inferior, CCW pitch, CCW roll, CW yaw. **Left proximal segment, +ve value:** lateral, posterior, superior, CW pitch, CW roll, CCW yaw. **Right proximal segment, -ve value:** lateral, anterior, inferior, CCW pitch, CW roll, CCW yaw. **Right proximal segment, +ve value:** medial, posterior, superior, CW pitch, CCW roll, CW yaw
*****indicates statistical significance ($p<0.05$)

Discussion

Despite the recent technological advancements and application of 3D software programs for assessing stability of orthognathic surgical procedure, only a few studies with a landmark-free methodology are available assessing the 3D relapse. Skeletal relapse following mandibular advancement surgery has been known to depend on the intra-operative positioning of the proximal segments, gap between proximal and distal osteotomy segments and condylar resorption[27,28]. However, little is known about the true 3D translational and rotational positional changes of the mandibular osteotomy segments immediately after surgery and at follow-up. Therefore, the aim of this study was to prospectively evaluate the skeletal relapse of the distal and proximal segments following mandibular advancement surgery at a follow-up time-point of 1 year. The reason for including patients at 1 year follow-up was to assess the post-surgical stability which includes changes till the end of 1st post-surgical year and is directly related to the post-surgical orthodontics, healing phase of the surgery and the mandibular physiological adaptation. It differs from post-treatment stability which occurs beyond first post-surgical year and is related to the long-term skeletal adaptation.[3]

Based on our findings the distal segment showed a significant translational relapse in a posterior and inferior direction. This migration at follow-up after mandibular advancement could have resulted from the supra-hyoid musculature pull back, soft tissue tension or by the adaptive changes of the proximal segment[8,16,29]. A cut-off point of 7mm has been suggested in literature for mandibular advancement with traditional BSSO to reduce skeletal relapse and opt for distraction osteogenensis for movements larger than 7mm[30]. However, these studies were based on 2D evaluation methods which have been known to be prone to error. A positive correlation existed between amount of movement and relapse in our study, which was in accordance with other studies[5,31-34]. Additionally, a higher correlation existed between the amount of movement and relapse in high advancement cases compared to the low advancement, where patients undergoing more than 7mm advancement show a clinically significant relapse of more than 2mm. Rotational movements related to the distal segment only showed a significant relapse of the CCW pitch movement in a CW direction. As the CCW rotation of distal segments results in the stretching of the soft tissue by elongation of pterygo-masseteric sling and supra-hyoid muscles, which could have acted as a contributory relapse factor[35].

The control of proximal segment is another important parameter influencing the stability of mandibular advancement surgery. An improper seating of condylar head into the fossa can lead to rotational changes in the proximal segment and cause condylar resorption[27]. We observed that the proximal segment in most of the cases translated laterally, anteriorly and superiorly with a CCW pitch, CCW roll and CW yaw immediately following surgery. However, overall this skeletal movement was minimal within the range of 2mm and 6°, confirming the control of proximal segment during surgery. Our findings also suggested a negligible to weak correlation between movement of the proximal segment and distal segment relapse. Thereby, further confirming that the distal segment relapse was minimally influenced by the proximal segments. A significant relapse of both the proximal segments in a medio-posterior and superior direction with CW rotational relapse of pitch, roll and CCW relapse of yaw was observed. This relapse could have resulted from the altered muscle orientation which tended to return both the proximal segments towards their original position[34]. As the masseter, medial pterygoid and temporalis muscles remain attached at the proximal segment, their shortening is expected at follow-up leading to relapse of the proximal segment[36,37]. Although a statistically significant relapse existed for most of the movement directions, nevertheless, overall the changes were present within a clinically acceptable range of 2mm and 2°, apart from high advancement cases where a significant posterior relapse of more than 2mm was observed. Additionally, based on percentage, none of the patients in our study had more than 4mm relapse which was consistent with the study by Proffit et al[38]. Age and sex of the patient had no significant influence on the relapse, which was in accordance with some studies[5,39]. The sex of patient did not provide any difference in relapse which might be due to the fact 65% of the patients were females and this skewness in data could have resulted in non-significant findings. Additionally, the most likely reason for not finding any significant relapse difference based on age of the patient could potentially be attributed to the limited follow-up period of one year. Further long-term follow-up could provide more information related to relapse. However, it should be kept in mind that the radiation dose is justified. So far no positional statements exist related to the justification of dose for long-term CBCT based follow-up of orthognathic surgery patients and requires attention.

The main strengths of the study included a large sample size and utilization of 3D 6DoF for assessing relapse. The study also had certain limitations. Firstly, the condylar changes were not assessed and further studies are required to assess the condylar remodeling and its influence on the proximal and distal segment relapse. Secondly, the effect of bone-graft could not be assessed as only 11% patients underwent a grafting procedure. Thirdly, only post-surgical stability was assessed, further studies should concentrate on investigating the post-treatment stability as well beyond the first post-surgical year. Fourthly, soft tissue analysis was not carried out and future studies should employ stereophotogrammetric devices to acquire facial soft tissue images at a starting time-point when postoperative edema has subsided to allow for an accurate assessment of long-term soft tissue relapse.

In conclusion, mandibular advancement surgery was found to be a stable procedure. Despite the statistically significant relapse in certain directions, both distal and proximal bone segments showed a clinically acceptable translational and rotational stability at one-year follow-up. The proximal segments torqued towards their original position with a reduction of flaring. Future investigations should focus on the post-treatment stability beyond the first post-surgical year and also comparative studies should be carried out to assess the long-term relapse associated with the conventional and surgery-first approach to help reach a better clinical decision.

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Part 2
PHARYNGEAL AIRWAY RELAPSE

ARTICLE 5
Three dimensional pharyngeal airway space changes following isolated mandibular advancement surgery. A prospective 1-year follow-up study

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Abstract

Purpose

The aim of this study was to assess the three-dimensional (3D) volume, surface area and airway constriction changes following isolated mandibular advancement at a follow-up period of one year.

Materials and methods

A total of 120 patients who underwent bilateral sagittal split osteotomy (BSSO) advancement surgery were recruited. Cone-beam computed tomography (CBCT) scans of all the patients were acquired preoperatively (T0), immediately following surgery (T1) and at one year follow-up (T2). The volume and surface area of the total airway, nasopharynx, oropharynx and hypopharynx was assessed. The minimal cross-sectional area (mCSA) of the oro-hypopharyngeal region airway was also evaluated for all time points and intervals.

Results

The total airway showed a 38% increase in volume and 13% increase in surface area from T0 to T1. The oropharyngeal region showed the maximum immediate change in airway volume and surface area. At T1-T2 follow-up, both volumetric and surface area showed a relapse of less than 7% for all sub-regions. The mCSA of the airway showed a significant increase of 71% from T0 to T1 ($p < 0.0001$), whereas a non-significant relapse was observed at T1-T2 ($p = 0.1252$).

Conclusions

The total airway volume, surface area and minimum constriction area remained stable at a follow-up period of one year.

Keywords: mandibular advancement; pharynx; three dimensional-imaging; recurrence; follow-up studies; cone-beam computed tomography

Introduction

Dentofacial deformity in skeletal class II patients is most commonly characterized by mandibular retrognathism (Fekonja *et al.*, 2018). One of the most highly stable, predictable and widely accepted surgical technique for correcting the skeletal, soft tissue and dental discrepancies in such patients involves bilateral sagittal split osteotomy (BSSO) advancement surgery (Monson, 2013). Advancement of the mandible not only protrudes the mandible into a desirable position but also influences the pharyngeal airway space (PAS) by altering the hyoid bone position and supra-, infra-hyoid and base of tongue musculature (Gale *et al.*, 2001). These anatomical changes have the tendency to increase the airway volume and dimensions by repositioning of the pharyngeal soft tissue anteriorly (Nishanth *et al.*, 2020). This increase in PAS not only improves the airway patency in obstructive sleep apnea (OSA) patients but it also improves the respiratory status and sleep quality in non-OSA patients without any breathing or respiratory disorders (Isono *et al.*, 1995).

Since the mid-1980s, numerous studies have been carried out assessing airway changes in patients undergoing mandibular advancement surgery (Bear and Priest, 1980; Al- Moraissi *et al.*, 2015). However, with the technological advancements, three-dimensional (3D) volumetric assessment of the PAS has become an objective standard method for assessing airway compared to its conventional 2D counterparts such as panoramic radiograph and lateral cephalogram (Christovam *et al.*, 2016). The 3D volumetric PAS changes following bimaxillary, single jaw advancement and/or setback surgeries has been extensively studied in obstructive sleep apnea (OSA) patients (Tan *et al.*, 2017; Gottsauner-Wolf *et al.*, 2018; An *et al.*, 2019). However, there are only a few studies concerning the 3D changes in PAS volume in skeletal class II patients following isolated mandibular advancement in non-OSA patients and how the airway changes at follow-up (Kochel *et al.*, 2013).

Apart from volumetric changes following mandibular advancement, another important parameter known as most restricted or minimum cross-sectional area (mCSA) of the PAS has been reported in literature (Shokri *et al.*, 2020). The mCSA predicts the collapsibility of the PAS and is an important parameter for assessing the airway resistance (Van Holsbeke *et al.*, 2011). Although numerous studies have assessed mCSA in patients requiring orthognathic surgery (Shokri *et al.*, 2020). Nevertheless, few studies are available focusing on the mCSA changes at follow-up utilizing CBCT in non-OSA patients treated with isolated BSSO advancement surgery (Tan *et al.*, 2017). The main limitation of studies assessing airway changes has either been related to their small sample size (Hernández-Alfaro *et al.*, 2011; Furche *et al.*, 2019) or short-term follow-up with a maximum duration of 6 months (Kochel *et al.*, 2013).

Currently, no evidence exists evaluating 3D airway changes in a large homogenous group of patients with a follow-up of 1 year or more in non-OSA patients undergoing isolated mandibular advancement. Therefore, the current study was conducted to address two aims. The first aim was to three-dimensionally assess the volumetric and surface area changes of the airway following isolated mandibular advancement at a follow-up period of one year. The second aim investigated the changes in collapsibility of the airway by assessing the mCSA of the pharyngeal airway.

Materials and methods

This study was conducted in compliance with the World Medical Association Declaration of Helsinki on medical research. Ethical approval was obtained from the Ethical Review Board of the University Hospitals Leuven (reference number: B322201526790). All patient-specific information was anonymized. The sample size was calculated using a priori power analysis in G* power 3.1, assuming 80% power at a significance level of 5%.

A total of 120 patients were recruited prospectively, consisting of 40 male and 80 female patients having a mean age of 26.0±12.2 and a follow-up period of 12.0±2.6 months. Data was collected from a period of August 2014 till March 2020. Patients undergoing isolated mandibular advancement surgery and having a craniocervical angle (N∠S∠Ba) of less than 5° for overcoming the variation in head position (Furche *et al.*, 2019) were included in the study. Exclusion criteria involved patients with craniofacial anomalies, syndromic disorders, OSA, previous history of trauma or any other orthognathic surgery procedure such as Le Fort I or genioplasty. All surgeries were performed by the same surgical team and involved BSSO advancement based on Hunsuck/Epker modification with transoral rigid internal fixation of the osteotomized segment with two miniplates and monocortical screws on each side (Hunsuck, 1968; Epker, 1977; Tulasne *et al.*, 1989; Politis *et al.*, 2018). Cone-beam computed tomography (CBCT) scans of all the patients were acquired preoperatively (T0), immediately following surgery at an interval of 1-6 weeks (T1) and at one year follow-up (T2). All scans were acquired using a standardized scanning protocol (Stratis *et al.*, 2017) and patients were in a relaxed and upright position with the Frankfort Horizontal (FH) plane parallel to the floor. Two CBCT devices were utilized for acquiring the scans, Promax 3D Max (Planmeca, Helsinki, Finland) and Newtom VGi-evo (Cefla, Imola, Italy). Scanning parameters were set at 230 x 260 to 240 x 190 mm^2 field of views, 96-110kV and a slice thickness of 0.3-0.6mm. Following CBCT acquisition, all scans were exported in DICOM (Digital Imaging and Communications in Medicine) format. T0 images were re-oriented and adjusted to the FH plane where required.

Voxel-based registration was applied utilizing the anterior cranial base for superimposition T1 and T2 scans onto the T0 scan using Amira software (version 2019.3, Thermo Fischer Scientific, Merignac, France). Following image registration, all data was imported to ProPlan CMF 3.0 (Materialise, Leuven, Belgium), where segmentation of airway was performed with the initial threshold setting between -1024 to -500 Hounsfield units (HU) with manual adjusted in cases where a proper depiction of the airway was not observed. Following segmentation, planes were reconstructed for dividing the PAS into the following anatomical regions: nasophayrnx, oropharynx, hypopharynx and complete PAS. The division of sub-regions was performed based on previously validated anatomical and technical limits (Guijarro-Martínez and Swennen, 2013) (Figure 1).

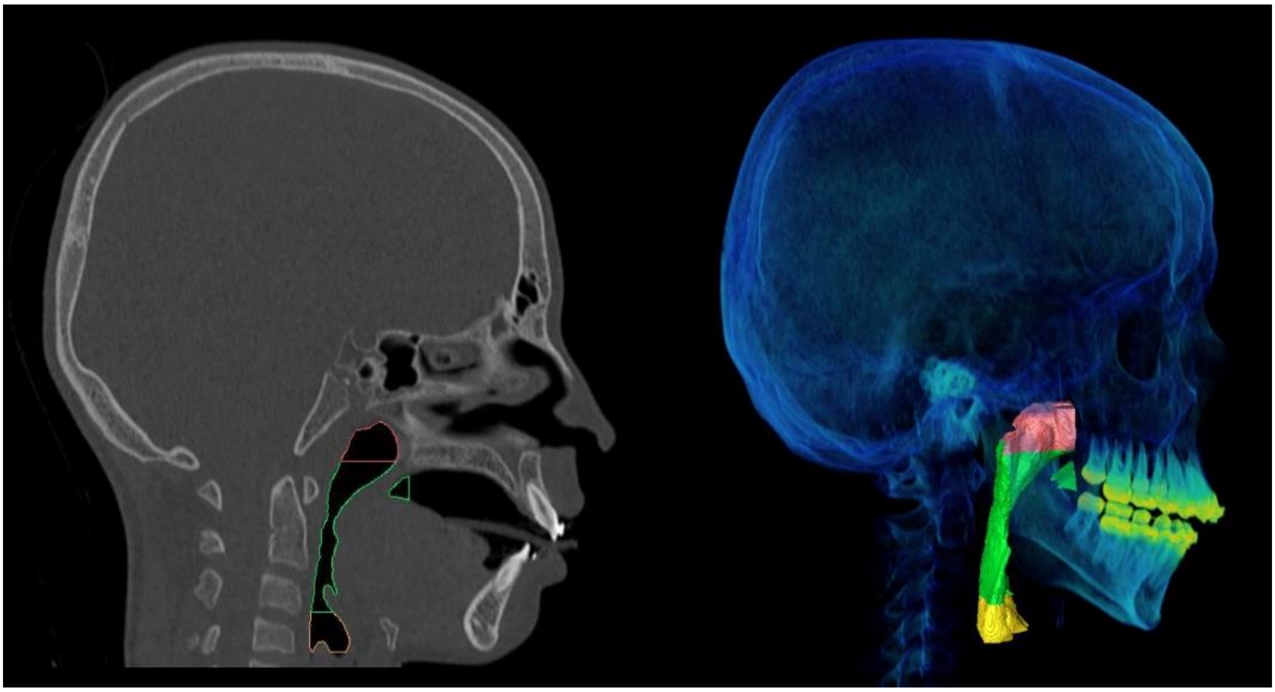

Figure 1. Pharyngeal airway space sub-regions division with posterior nasal spine (PNS) as the anterior vertical limit and pharyngeal soft tissue contour as the posterior limit. Red color indicates nasopharyngeal region extending from root of clivus superiorly to PNS inferiorly, green color indicates oropharyngeal area extending from PNS superiorly to anterior–inferior point of the body of third cervical vertebrae (C3ai) inferiorly, yellow color indicates hypopharyngeal region extending from C3ai superiorly to anterior–inferior point of the body of fourth cervical vertebrae inferiorly (C4ai).

The volume and surface area of the segmented structures were then calculated. The DICOM dataset was then imported to InVivo Anatomage software (Anatomage, San Jose, CA, USA) for determining the mCSA of the complete airway. It was defined as the minimal cross-sectional area along the airway axially extending from the posterior nasal spine superiorly till the anterior–inferior point of the body of the fourth cervical vertebrae inferiorly. The software automatically detected and calculated the mCSA (Figure 2). Validity and reliability of the software for calculating mCSA has been previously reported (Torres *et al.*, 2020).

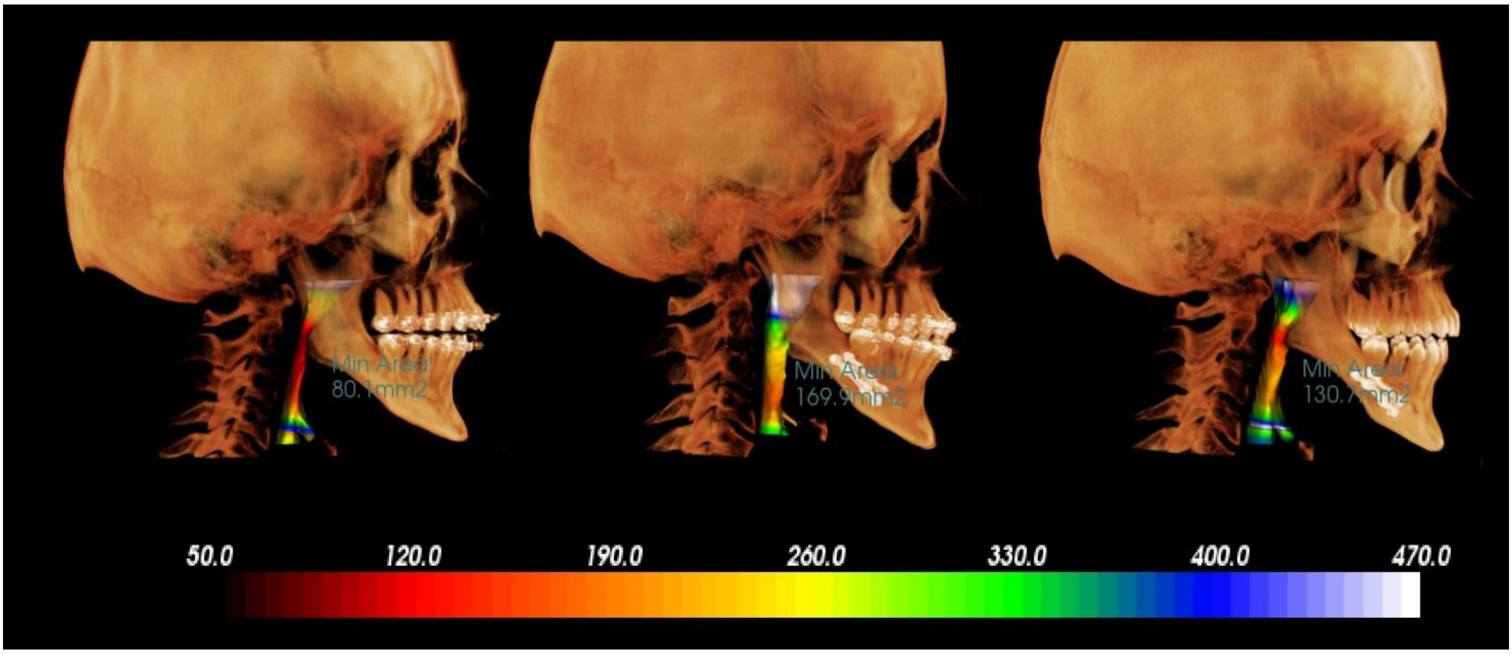

Figure 2. Illustration of minimum cross-sectional area changes following mandibular advancement surgery A. before surgery, B. 2 weeks following surgery, C. 1 year after surgery.

Statistical analysis

Data were analyzed with MedCalc Statistical Software version 19.2 (MedCalc Software Ltd, Ostend, Belgium). Descriptive statistics including percentage, mean and standard deviation were calculated for all the data. Normality of data was assessed with Shapiro–Wilk test. For normal distributed data t-test was utilized to determine the change in PAS parameters from T0 to T1 and T1 to T2. Wilcoxon signed-rank test was applied for data with non-parametric distribution. Spearman correlation coefficient was applied for assessing the relationship between amount of advancement and mCSA change immediately after surgery and at follow-up. Statistical significance was set at 0.05 for all parameters.

Results

Patients underwent a mean mandibular body advancement of 5.7±2.3mm anteriorly and a relapse of -1.2±1.2mm posteriorly. No significant difference was observed in relation to the cranio-cervical angle ($p>0.062$), thereby confirming the stability of head position. Table 1 describes the mean and percentage of change for volume, surface area and mCSA at T0-T1 and T1-T2 time-intervals. The total airway showed a 38% increase in total airway volume and 13% increase in surface area from T0 to T1. The oropharyngeal region showed the maximum change in airway volume and surface area, followed by hypopharynx and nasopharynx. The surgery immediately led to a significant increase in total airway volume and surface area ($p< 0.0001$) from T0 to T1. When divided into sub-regions, most of the significant volumetric changes occurred in the oropharyngeal region followed by nasophraynx ($p< 0.0001$). No significant volumetric changes were seen in the hypopharyngeal region immediately following surgery ($p=0.948$).
At T1-T2 follow-up, both volumetric and surface area showed a relapse of less than 7% for all sub-regions, where the total airway volume decreased by 5% and the surface area increased by 3%. Amongst the volumetric measurements, only the total airway volume ($p=0.004$) and oropharyngeal sub-region ($p=0.004$) showed a significant decrease. No significant changes in surface area were observed at follow-up, with both

total airway and all sub-regions showing an increase in surface area. According to Table 1 and Figure 3, the mCSA of the airway showed a significant increase of 71% from T0 to T1 (p< 0.0001), whereas a non-significant relapse in opposite direction was observed at T1-T2 (-15%, p=0.125).

Table 1. Change in airway volume, surface area and minimum cross-sectional area (mCSA).

Pharyngeal airway space	T0 (mean ± SD)	T1 (mean ± SD)	T2 (mean ± SD)	Relative change % (T0-T1)	Significance (T0-T1)	Relative change % (T1-T2)	Significance (T1-T2)
Volume (mm³)							
Total airway	21194.14 ± 5113.33	28617.26 ± 8032.89	26556.54 ± 8055.54	38%	< 0.0001	-5%	0.004
Nasopharynx	5437.92 ± 2175.23	5919.18 ± 2101.36	5812.14 ± 2249.14	14%	< 0.0001	-2%	0.2094
Oropharynx	14773.96 ± 4813.27	21908.69 ± 6828.23	20136.73 ± 6680.5043	59%	< 0.0001	-4%	0.0035
Hypopharynx	3243.95 ± 1330.66	3259.58 ± 1624.11	3529.96 ± 2024.87	21%	0.9482	2%	0.2958
Surface area (mm²)							
Total airway	10869.39 ± 2148.63	12095.80 ± 2476.5	12273.99 ± 2884.84	13%	< 0.0001	3%	0.4460
Nasopharynx	3081.18 ± 821.31	3158.71 ± 804.38	3249.71 ± 868.29	5%	0.1483	4%	0.0560
Oropharynx	6771.97 ± 1713.87	7939.60 ± 1881.65	8008.57 ± 2010.05	22%	< 0.0001	4%	0.7258
Hypopharynx	1925.02 ± 657.01	1875.73 ± 674.8	1947.94 ± 763.86	8%	0.6428	6%	0.4556
mCSA (mm²)							
	98.07 ± 47.59	182.29 ± 93.90	167.48 ± 78.96	71%	< 0.0001	-15%	0.0783

T0: before surgery, T1: immediately after surgery, T2: one-year follow-up , SD: standard deviation, %: percentage

-ve percentage indicates decrease, +ve percentage indicates increase

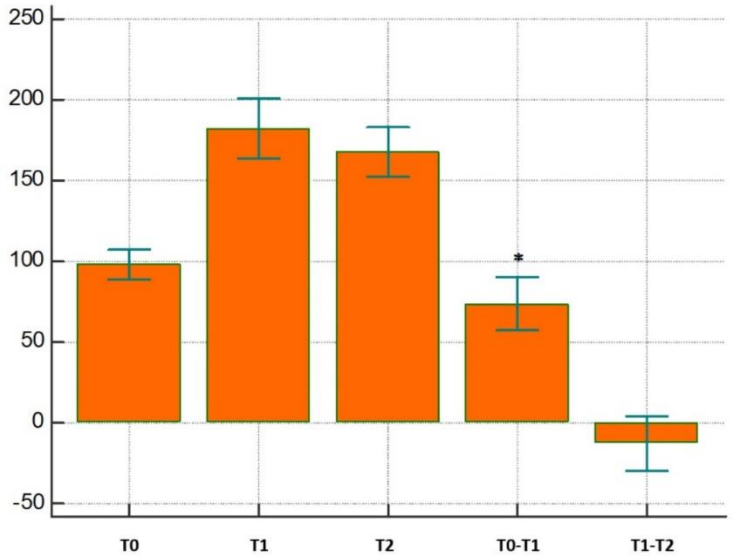

Figure 3. Minimum cross-sectional area (mm²) at (T0) before surgery, (T1) immediately after surgery, (T2) one-year follow-up, T0 to T1 and T1 to T2 time-intervals. ***represents statistical significance ($p<0.05$)

The immediate changes in airway mCSA showed a significantly weak correlation with the amount of advancement ($r=0.25$, $p<0.0049$) (Figure 4). Both, the total PAS and anatomical sub-regions showed a negligible to weak correlation with amount of movement and relapse (Table 2). No age- and sex-related differences were observed for all the parameters.

Table 2. Correlation between pharyngeal airway space and skeletal movement and relapse.

	Movement correlation		**Relapse correlation**	
		Volume		
	T0-T1	Significance	T1-T2	Significance
Total airway	0.16	0.1026	0.03	0.7524
Nasopharynx	-0.19	**0.0395***	0.10	0.2891
Oropharynx	0.32	**0.0004***	0.01	0.9276
Hypopharynx	0.06	0.5441	0.19	**0.0383***
		Surface area		
	T0-T1	Significance	T1-T2	Significance
Total airway	0.15	0.914	0.00	0.9746
Nasopharynx	-0.23	0.1385	-0.04	0.6381
Oropharynx	0.29	0.5025	-0.09	0.3144
Hypopharynx	0.05	0.279	0.15	0.1043
		minimum cross-sectional area		
	T0-T1	Significance	T1-T2	Significance
	0.25	**0.0049***	0.13	0.1921

T0: before surgery, T1: immediately after surgery, T2: one-year follow-up

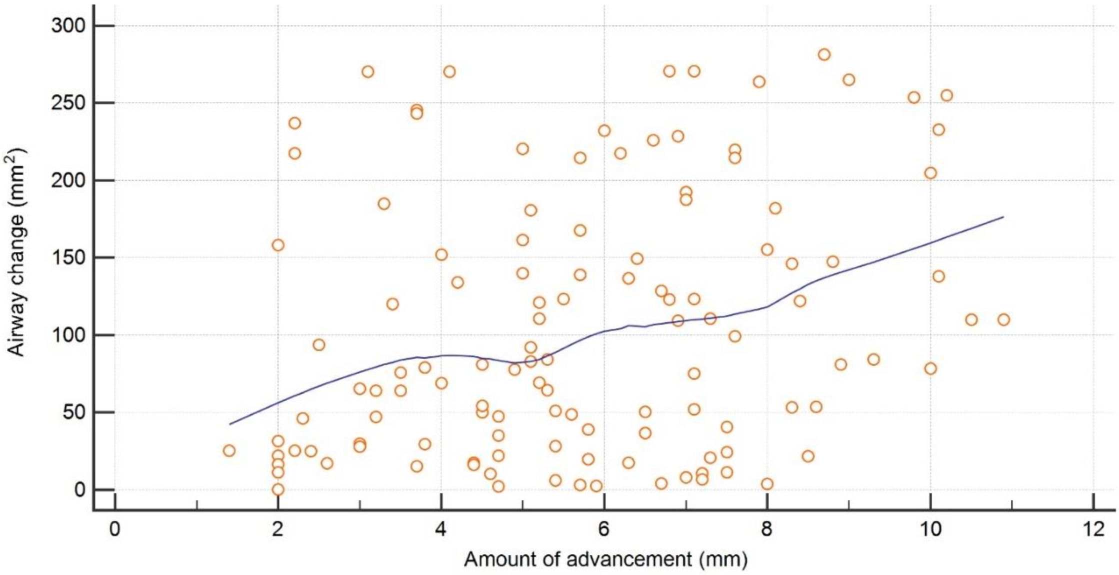

Figure 4. Correlation between amount of mandibular advancement and minimum cross-sectional area

Discussion

The present study was conducted to address volumetric, surface area and mCSA changes immediately after surgery and at 1 year follow-up in a large homogenous group of non-OSA patients following isolated BSSO advancement surgery. The main goal of this study was to provide evidence related to the airway changes in non-OSA patients which currently lacks in literature.

Our findings suggested a significant increase of the total PAS and mCSA immediately following surgery. The most likely explanation for this change could be related to the anatomical changes achieved by the BSSO advancement, where the most prominent change include the elevation of the hyoid bone during surgery with supero-anterior movement due to the conjoint response of supra- and infra-hyoid muscles and change in tongue position (Battagel *et al.*, 1998). The oro- and hypopharyngeal region showed the highest change in volume immediately after surgery. This could be attributed to the stretching of the genioglossus and geniohyoid muscles which originate from the mental spine and are responsible for protruding the tongue and hyoid bone anteriorly (Tsuiki *et al.*, 2007). These muscles increase the soft tissue tension of the oro/hypopharyngeal region, thereby leading to expansion of the PAS. Additionally, mandibular advancement also puts tension on the palatoglossus muscle which arises from the soft palate and attaches to the side of the tongue (Achilleos *et al.*, 2000; Nishanth *et al.*, 2020), thereby resulting in a further change of the oropharyngeal region. Mandibular advancement further influences the pharyngeal dilators by changing their tone. and when combined with hyoid bone movement and stretching of the associated muscle attachments this might have led to increased hypopharyngeal patency and resistance (Tsuiki *et al.*, 2007). At the same instance, nasopharynx also showed a significant increase in volume. It seems surprising that mandibular advancement led to the increase in nasopharyngeal region even without any maxillary intervention. A possible explanation for this could be related to the tension transmitted to the soft palate and posterior wall of the pharynx through the palatopharyngeal muscles (Isono *et al.*, 1995; Poon *et al.*, 2008). However changes in the nasopharyngeal area were minimal, potentially related to the dorsocranial anatomy limiting nasopharyngeal movement (Kochel *et al.*, 2013). Additionally, a negligible to weak correlation existed between the PAS changes and skeletal changes at both immediate and follow-up time-points. Thereby, also confirming that the skeletal relapse had a minimal influence on the PAS volume and dimensions. As no studies were found correlating skeletal movement and relapse with PAS changes in isolated mandibular advancement cases at follow-up in non-OSA patients, so a comparison with similar literature was not possible. Nevertheless, AlSaty *et al.*,(2020) also did not find any correlation between skeletal relapse and change in airway space following maxillomandibular advancement with and without genial tubercle advancement.

The significant immediate increase in the airway dimensions and mCSA immediately after surgery was consistent with other studies (Hernández-Alfaro *et al.*, 2011; Valladares-Neto *et al.*, 2013; Kochel *et al.*, 2013; Nishanth *et al.*, 2020). A variation in the percentage of change existed when compared with these studies which could have resulted due to the mean amount of movement and heterogeneity of data based on sample size and landmarks utilized for segmenting airway sub-regions. Additionally, based on the correlation analysis, some patients had a little while others had more change in mCSA with the same amount of advancement immediately after surgery. Thereby confirming that at an individual patient level change in mCSA cannot be predicted based on the amount of advancement. These inconsistencies in mCSA could have resulted due to the breathing movements, tongue positioning, post-operative edema, and variability in soft tissue compensation following new skeletal positioning (Kochel *et al.*, 2013; Al-Moraissi *et al.*, 2015; Nishanth *et al.*, 2020). We also believe that the amount of rotational skeletal movement and waxbite thickness could have also attributed to the mCSA variability amongst the patients requiring a same amount of advancement.

At follow-up, a significant decrease of the total airway volume was observed, where the oropharyngeal region showed maximal change. Even though mandibular advancement has been known to be a stable procedure, skeletal relapse of the distal segment is still observed in a posterior direction at follow-up. This posterior relapse is associated with recoiling of the hyoid musculature which exerts force in a posterior direction, thereby acting as a precipitating factor for causing the oropharyngeal airway to relapse (Carlson *et al.*, 1987). Our findings were consistent with another study which showed a decrease in total airway volume of approximately 4% at long-term follow-up which was comparable to the 5% change seen in this study (Kochar *et al.*, 2019). Volumetric and surface relapse of the total airway and its sub-regions were within the range of -2% to 6% which confirmed that the airway remained clinically stable at follow-up. Although certain sub-regions showed statistically significant relapse at follow-up, nevertheless, overall changes at one-year time-point were clinically insignificant.

The mCSA was also evaluated in this study, which is considered an important parameter as it influences resistance to the airflow. Instead of assessing constriction in each segment separately, mCSA was assessed for the complete oro/hypopharyngeal airway. We believe that by doing so it provides more clinical relevant information about how the constriction changes for the complete airway instead of focusing on the segments separately for mandibular advancement surgery (Christovam *et al.*, 2016). A 71% increase in mCSA was observed immediately following surgery which then showed a non-significant relapse of -15% at long-term follow-up. This again confirms that mandibular advancement surgery influences the complete palatoglossohyoid muscle and ligament system, thereby not just increasing the volume but also the cross-sectional area (Kochel *et al.*, 2013). The increase in mCSA has been associated with the tension produced by stretching of the suprahyoid and velopharyngeal muscles (Fairburn *et al.*, 2005; Kuna *et al.*, 2008). These muscles intend to go back to their original position which could explain the decrease in mCSA at follow-up. Nevertheless all parameters showed clinically insignificant changes at follow-up.

The study had certain limitations. Firstly, the breathing movements during the CBCT scan acquisition were not controlled. Secondly, the tongue movement was also not controlled at all the time-points. In the midst of these limitations, we believe that our study provides a clinically relevant update on airway changes in non-OSA patients undergoing isolated mandibular advancement. Further comparative studies should be conducted to assess PAS follow-up changes following isolated BSSO advancement surgery in both OSA and non-OSA patients.

In conclusion, isolated mandibular advancement led to a significant immediate increase in the total airway volume, surface area and minimum constriction area. All changes remained stable at a long-term follow-up. Based on our findings, BSSO advancement surgery could be regarded as a stable procedure for widening of the PAS with maintenance of the positive space at follow-up.

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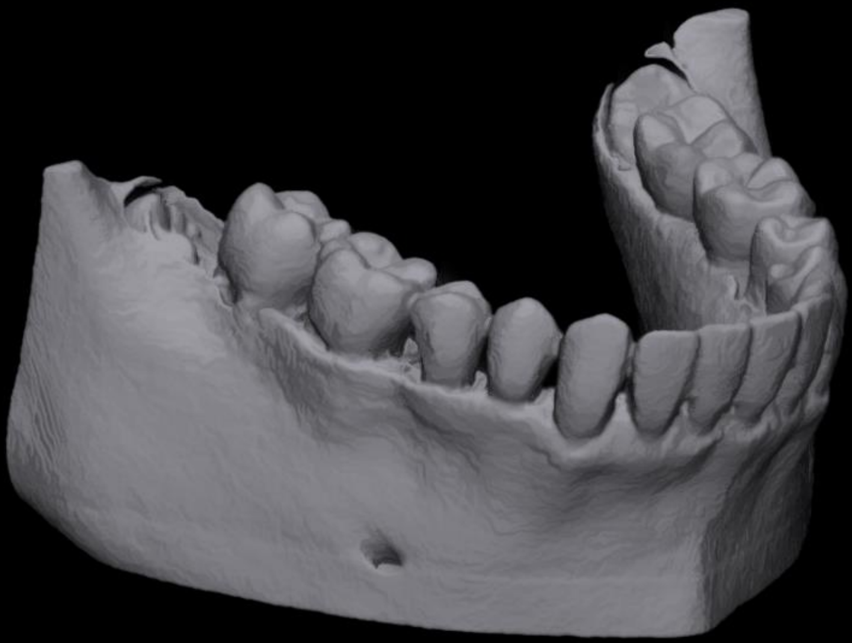
Part 3
LIFE-SIZED 3D PRINTED SKELETAL MODELLING



ARTICLE 6

Accuracy of cone beam computed tomography-derived casts: A comparative study

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Abstract

Statement of problem

The accuracy of the external surface and internal trabecular architecture of large cone beam computed tomography (CBCT)-derived dentomaxillofacial anatomic casts has not yet been thoroughly investigated.

Purpose

The purpose of this comparative study was to evaluate the quantitative accuracy of CBCT- derived mandibular casts by applying an innovative land-mark free methodology.

Material and methods

Following inclusion and exclusion criteria, a CBCT scan of an 18-year-old woman was acquired. The mandible was segmented and isolated from the data set. The segmented mandible included depiction of the cortical surface, trabecular architecture, erupted teeth, and impacted third molars with incomplete root formation. Fifteen mandibular casts were fabricated by using multijet (MJ=4), digital light processing (DLP=4), stereolithography (SLA=2), fused deposition modeling (FDM=2), colorjet (CJ=2), and selective laser sintering (LS=1)-based high-quality medical commercial and office printers. Each printed cast was scanned and superimposed onto the original mandible, and the error of the complete mandible and individual surfaces were assessed with a color-coded map.

Results

When the overall combined error associated with complete casts based on printing technology were compared, MJ showed the least error (0.6 ±0.7 mm). FDM technology (2.2 ±3.4 mm) had the highest overall absolute error. No significant difference was observed when both individual surfaces and the complete mandible were compared.

Conclusions

Overall, casts replicated the skeletal and dental anatomic surfaces well. However, shortcomings were observed in relation to depicting trabecular architecture.

Introduction

Recent advances in 3D printing, also known as additive rapid prototyping, and modeling has revolutionized medicine and dentistry.[1] Three-dimensional printing together with digital imaging including intraoral scanning, cone beam computed tomography (CBCT), and magnetic resonance imaging has been used for fabricating 3D printed casts or biomodels,[2] a generic term for biomedical prototypes defined as the replication of anatomic structures into a 3D physical model.[3] A benefit of such casts is the interaction with the patient's anatomy that adds information for diagnosis, treatment planning, and clinical training.[4, 5, 6] The introduction of such biomodels and virtual planning has improved the communication between radiologists and surgeons.[7,8] Additive manufacturing and rapid prototyping technologies and processes have been used for making such casts with multiple layer by layer deposition of printing material, which stack up to form the 3D object.[9] These include stereolithography (SLA), fused deposition modeling (FDM), selective laser sintering (SLS), selective laser melting, polyjet (PJ), and electronic beam melting.[3,9,10] In addition to the technology-based classification of 3D printers, the process of printing can be classified as liquid-based, solid-based, or powder-based materials.[11]

Studies evaluating the surface accuracy of 3D-printed skeletal casts with accurate representation of anatomic structures are sparse. Most of the studies assessing the accuracy of such casts used landmarks with intraobserver and interobserver error.[12, 13, 14, 15] The authors are unaware of studies on the accuracy of the surfaces using the internal trabecular architecture of large CBCT-derived dentomaxillofacial anatomic casts. Therefore, the current study was conducted to evaluate the quantitative accuracy of CBCT-derived mandibular casts by applying an innovative landmark-free methodology. The null hypothesis was that no significant differences would be found related to the accuracy of different casts.

Material and methods

This research was carried out in compliance with the World Medical Association Declaration of Helsinki on medical research. The study was approved by the Ethical Review Board of the University Hospitals Leuven, Belgium (reference number: S57587) for collecting and using patient imaging data. Informed consent was not required as patient-specific information was anonymized.

A CBCT scan was acquired of an 18-year-old woman referred to the Department of Restorative Dentistry for evaluation of traumatized maxillary central incisors. Scanning was performed with a CBCT device (Newtom VGi evo; NewTom Inc), operating at 110 kV with a slice thickness of 0.15 mm and 11×10 cm field of view. Inclusion criteria involved a good quality image, presence of the entire mandible, normal cortical bone, dense trabecular architecture, and impacted mandibular third molars with incomplete root formation. The exclusion criteria were the presence of any pathological condition, restorations, and artifacts in the mandibular region. The image was exported in Digital Imaging and Communications in Medicine (DICOM) format for further processing.

The DICOM data were imported to a 3D-segmentation software program (Mimics inPrint; Materialise), where a combination of automatic and manual thresholding was applied to segment and isolate the mandible from the CBCT volume. A cutting plane was applied at the inferior border of the mandible to expose the trabecular architecture and at the posterior border to expose the roots of the impacted third molars (Fig. 1). The segmented anatomic structures in the definitive standard tessellation language (STL) file of the mandible depicted the cortical surface, trabecular architecture, erupted teeth, and impacted third molars with incomplete root formation.

A.

B.

C.

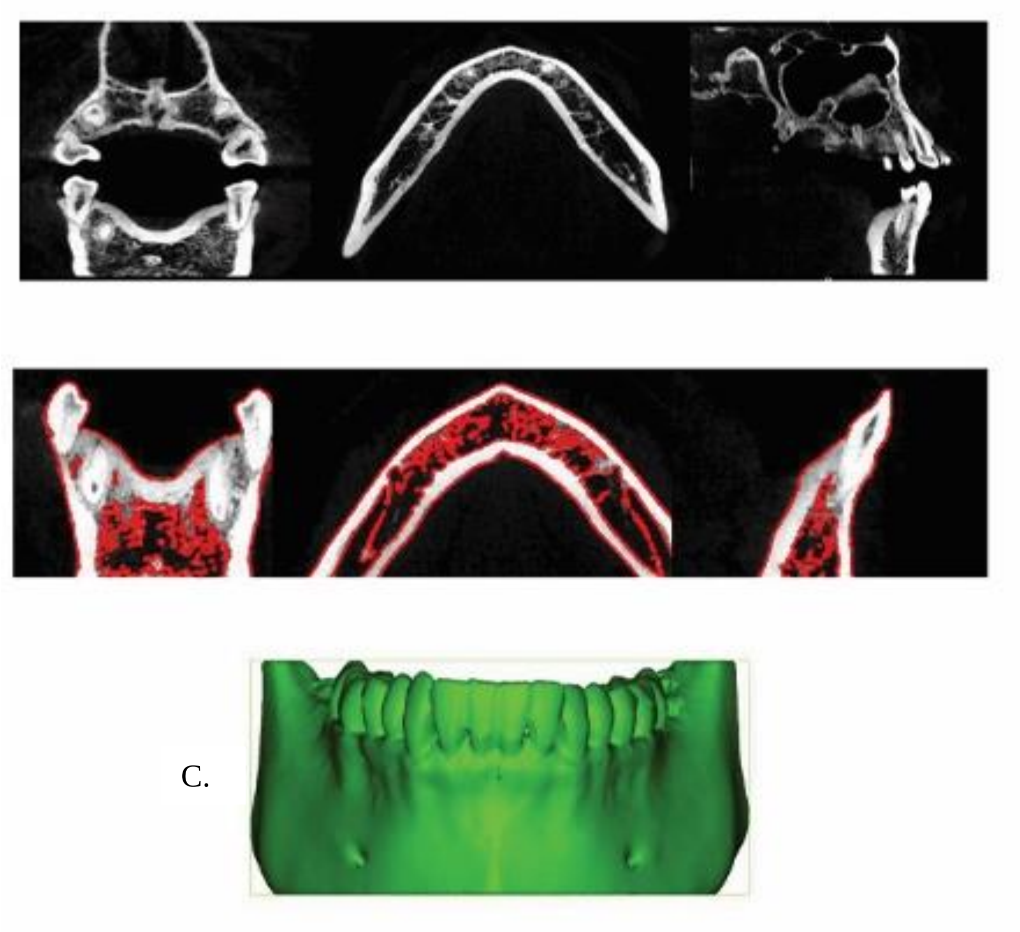

Figure 1. Reconstruction of cone beam computed tomography-derived mandibular cast A, CBCT dataset, B. combination of manual and automatic thresholding applied to the mandibular region. C, segmented mandible.

Fifteen mandibular casts were fabricated from the original STL by using multijet (MJ=4), digital light processing (DLP=4), stereolithography (SLA=2), fused deposition modeling (FDM=2), colorjet (CJ=2), and selective laser sintering (LS=1) based high-quality medical commercial and in-office printers. A combination of various printers, materials, and layer resolutions were used to generate anatomic replicas of the mandible (Table 1).

Table 1. Specifications of the printed models

Serial No. of Casts	Technology (Total Casts Printed)	Printer	Material	Layer Resolution (μm)
1 2 3 4	MJ (n=4)	MJP 2500 MJP 2500 Objet 350 Objet 350	M2R-WT M2R-CL Verowhite Veroclear	32 32 30 30
5 6 7 8	DLP (n=4)	Rapidshape D90 II UV XL P30 Moonray S P4 mini XL	Dreve model P30 shera sand Green dental model resin ABS Tough	38 50 50 35
9 10	SLA (n=2)	ProX800 Form 2	Accura ABS White (SL7810) Standard Gray resin	25 25
11 12	FDM (n=2)	In-House 1 In-House 2	Ossofill Polywood	30 30
13 14	CJ (n=2)	ProjetPro660	Visijet PXL 1 Visijet PXL 2	100 200
15	LS (n=1)	In-House 3	Polyamide PA 12	120

CJ, colorjet; DLP, digital light processing; FDM, fused deposition modeling; LS, selective laser sintering; MJ, multijet; SLA, stereolithography.

After postprocessing, each cast was scanned with the Newtom VGi-evo CBCT device (high resolution, kV=110, slice thickness=0.125 mm, field of view = 10×5 cm) (Fig. 2) and segmented following the same protocol as that for the original mandibular STL by applying thresholding to create an STL file for each cast.

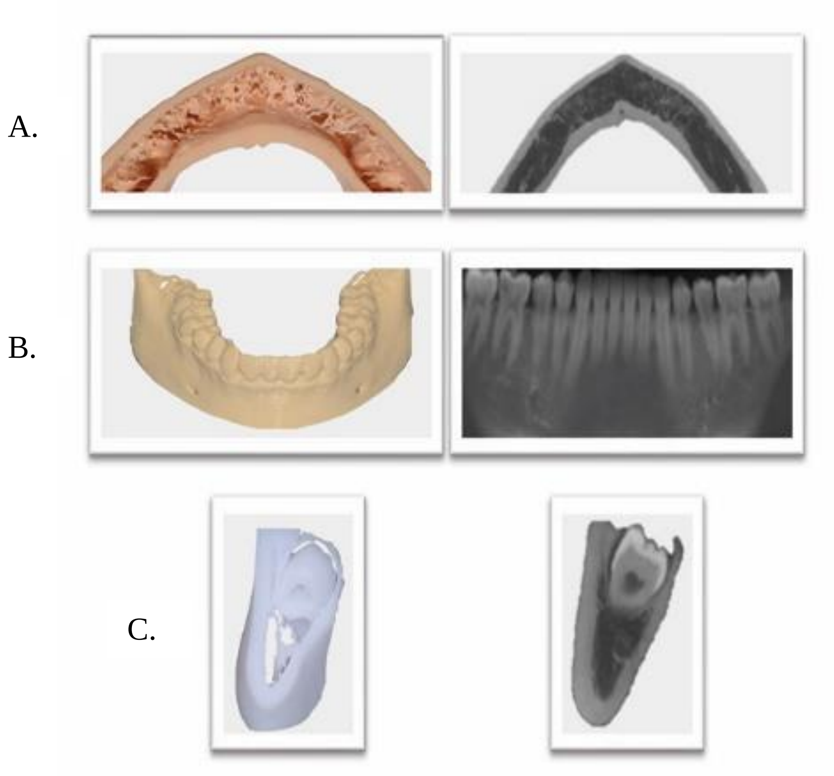

Figure 2. Three-dimensional printed model corresponding to the CBCT image. A, inferior view, B. frontal view. C, posterior view

Each printed cast from the STL file was superimposed onto the original DICOM file of the mandible by applying a rigid voxel-based registration algorithm with mutual information[16] in an image processing software program (Amira; FEI). This superimposition oriented the printed cast in the same 3D coordinates as those of the original STL file for an accurate comparison of the anatomic structures (Fig. 3). The transformed position of the STL file after superimposition was then exported.

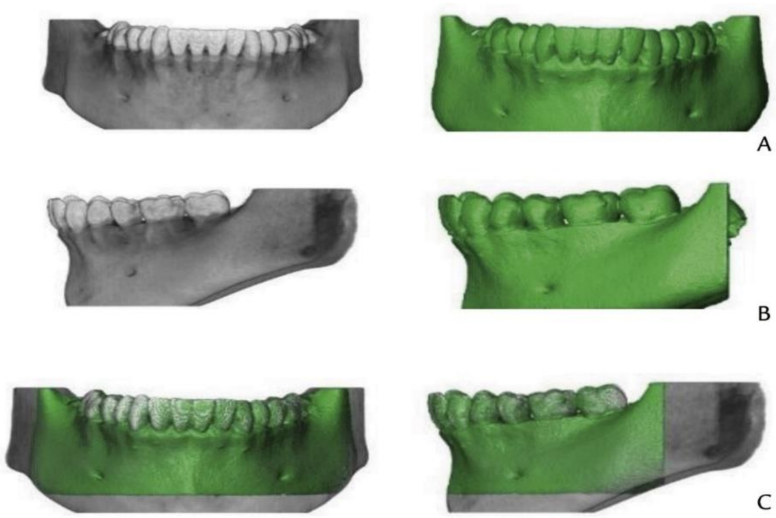

Figure 3. Steps of image registration. A, Volume editing of original DICOM data to isolate mandible followed by volume rendering. B, Volume rendering of STL file of printed casts. C, Voxel-based registration superimposing printed cast on original CBCT reference. CBCT, cone beam computed tomography; DICOM, Digital Imaging and Communications in Medicine; STL, standard tessellation language.

Both the original and transformed printed casts from the STL files were imported to a 3D modeling software program (3-matic; Materialise) for surface extraction and comparison. Both the original and printed mandibular cast STL files were divided into 6 separate anatomic regions (buccal and lingual surface, trabecular surface, erupted teeth, and impacted left and right third molars) to evaluate the printing error of each surface individually (Fig. 4).

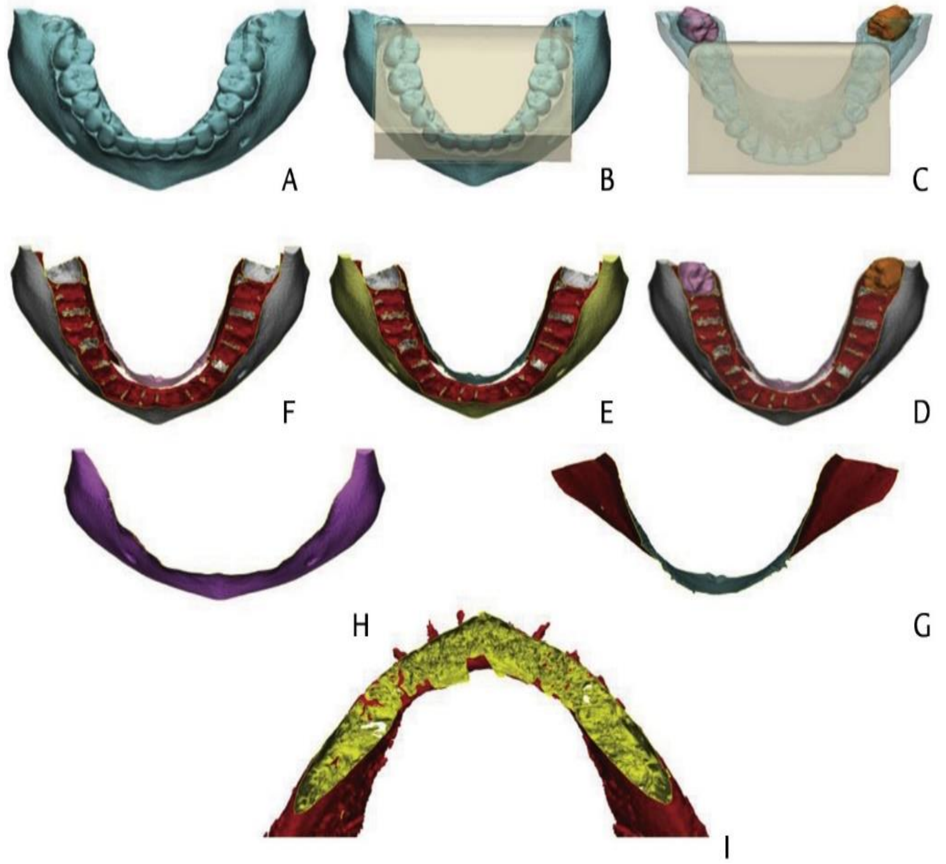

Figure 4. Surface extraction procedure. A, 3D virtual printed cast. B, Erupted tooth container. C, Impacted left and right third molar containers. D, Subtraction of erupted teeth. E, Subtraction of third molars. F, Bone container following shape of surface. G-I, Extraction of buccal, lingual, and trabecular surface.

Both the complete mandible and extracted surfaces (buccal, lingual, trabecular, erupted teeth, impacted third molars) of the 3D printed cast were superimposed with those of the original CBCT-derived reference STL file individually. A part comparison with a color-coded map was carried out to evaluate the absolute mean difference (mm) between the complete mandible and each surface of the printed and original STL file (Fig. 5).

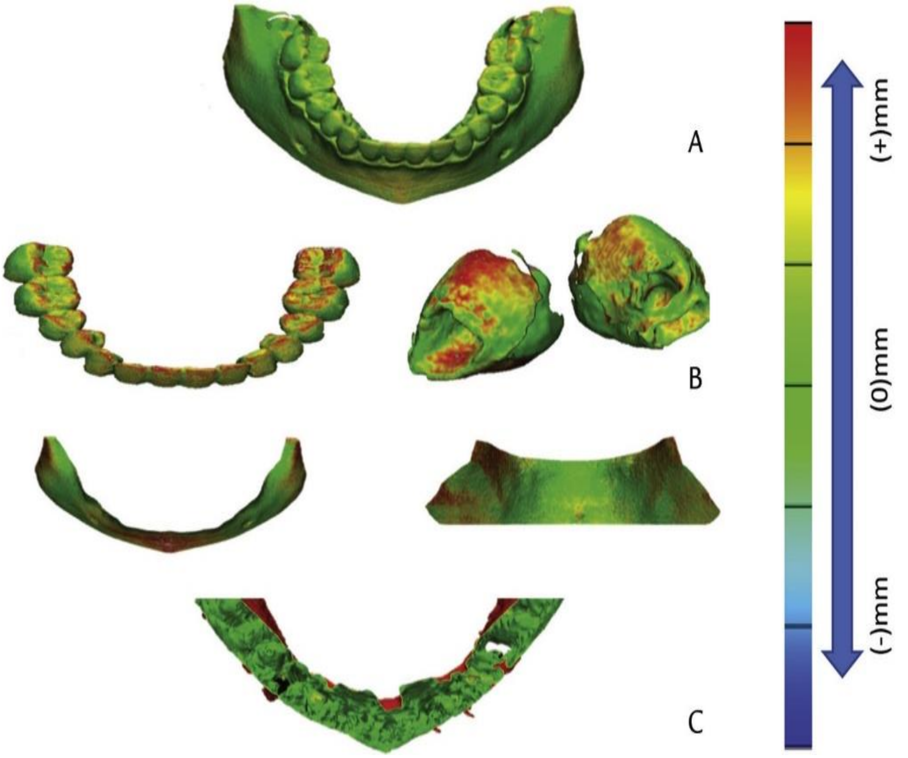

Figure 5. Part comparison analysis of superimposed original and cast STL file. A, Superimposed complete mandible. B, Color-coded difference between original and printed teeth. C, Buccal, lingual, and trabecular surface error comparison. STL, standard tessellation language.

Two observers (S.S., F.N.), a medical engineer with an experience of 1 year and a maxillofacial with an experience of over 10 years performed the assessment twice blindly and repeated the observations at an interval of 2 weeks to calculate the interobserver and intraobserver reliability. Data were analyzed with a statistical software program (MedCalc 16.4.2; MedCalc Software bvba). To assess interobserver and intraobserver reliability, the intraclass correlation coefficient was applied at a 95% confidence level (where <0.50=poor reliability; 0.50–0.75=moderate reliability; 0.75–0.90=good reliability; >0.90=excellent reliability).[17] The absolute mean difference and standard deviation were calculated to observe the difference between the original and printed casts. A nonpaired *t* test was performed to compare the objective error of the printed casts. The *P* values were corrected following the Sidak test for multiple comparisons[18] (α=.05).

Results

The objective assessment revealed excellent interobserver (0.98, *P*=.82) and intraobserver (0.99, *P*=1.00) reliability based on intraclass correlation coefficient without a significant difference among observers. Figure 6 illustrates the error of casts in relation to teeth. Cast 1 and 2 printed with MJ technology showed the least amount of error (0.06 ±0.04 mm) was associated with both erupted and impacted teeth compared with the original STL file, whereas cast 11 (FDM) showed the highest discrepancy was associated with erupted teeth (0.70 ±0.74 mm), impacted left (0.61 ±0.74 mm), and right third molars (0.55 ±0.68 mm).

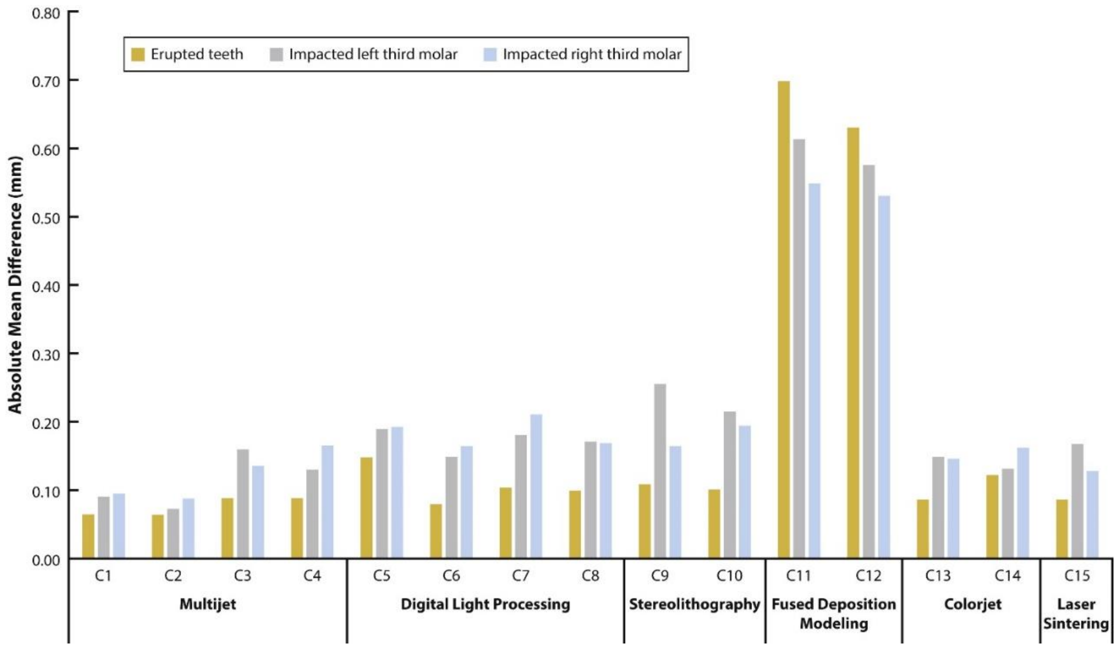

Figure 6. Absolute mean difference (mm) of tooth comparison between original virtual model and cast. C, Cast. Refer to Table 1, serial no. of models for cast specifications.

Figure 7 illustrates the error of casts related to replicating buccal, lingual, and trabecular surfaces. The lingual cortical surface of cast 9 (SLA) showed the least amount of error (0.04 ±0.04 mm), followed by cast 15 (LS: 0.05 ±0.04 mm), 1 (MJ: 0.06 ±0.04 mm), and 2 (MJ 0.06 ±0.05 mm). Cast 5 (DLP) showed the highest lingual surface error (0.15 ±0.12 mm). The buccal cortical surface was most accurately represented by cast 15 (LS; 0.05 ±0.06 mm), and the highest difference was observed for cast 5 (SLA) (0.15 ±0.13 mm). The trabecular surface replication of cast 2 (MJ) had the least absolute mean error (0.08 ±0.07 mm), and the highest error was associated with cast 11 (FDM: 0.43 ±0.64 mm).

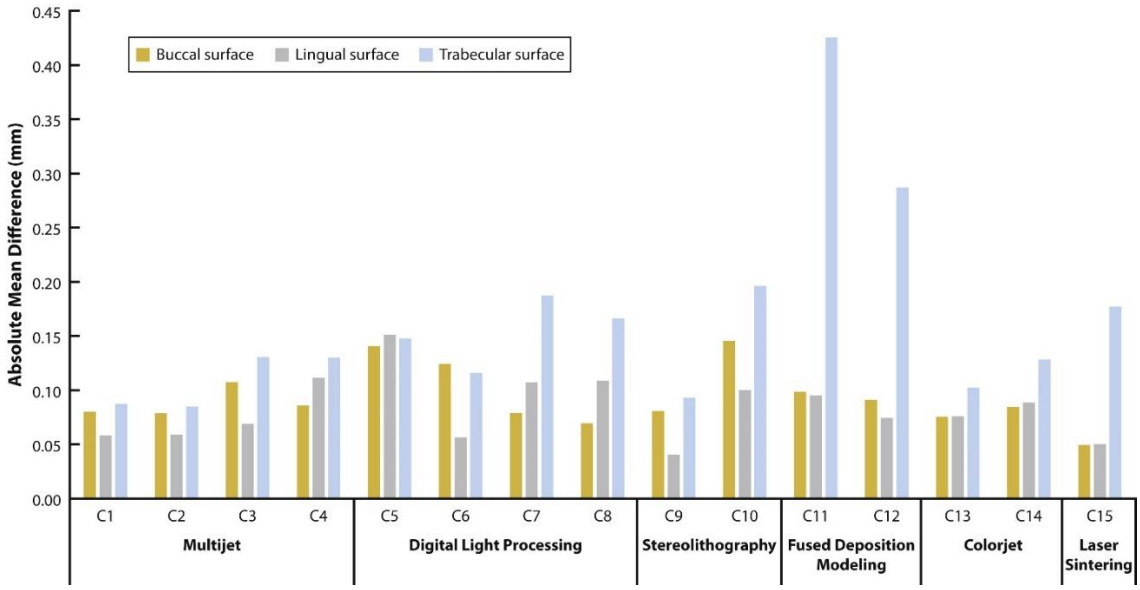

Figure 7. Absolute mean difference (mm) of buccal, lingual, and trabecular surface comparison between original virtual model and cast. C, Cast. Refer to Table 1, serial no. of models for cast specifications.

When the overall combined error associated with the complete casts based on printing technology was compared, MJ showed the least error (0.6 ±0.71 mm), followed by CJ (0.67 ±0.68 mm), LS (0.67 ±0.68 mm), DLP (0.82 ±0.78 mm), and SLA (0.96 ±1.2 mm). The FDM technology (2.2 ±3.43 mm) had the highest overall absolute mean difference. However, no significant difference was observed when both individual surfaces (P=1.00), and the complete mandibular cast (P≥.99) based on technology were compared.

Discussion

The results of the present study showed no significant difference between the individual surfaces and complete mandibular casts. Therefore, the null hypothesis was accepted.

Three-dimensional printed casts play a significant role in preoperative treatment planning by providing a replica of the actual craniofacial skeletal tissue and the shaping of medical devices such as fixation plates before surgery, thus enabling surgeons to familiarize themselves with patient-specific anatomy, especially in patients with atypical anatomy.[5] Additionally, practicing prosthodontic and craniomaxillofacial surgery simulations on such casts can reduce operating time and blood loss. These casts can also provide novel teaching and tools for training dental and oral and maxillofacial residents.[6]

In the present study, 6 printing technologies (MJ, DLP, SLA, FDM, CJ, and LS) were used to construct 15 mandibular casts with a combination of materials and layer resolutions to observe how precisely the anatomic structures were printed. An innovative concept of segmenting different anatomic surfaces was used to improve the accuracy and reliability of the comparison of the original with the printed cast. The methodology was independent of the observer experience as shown by the excellent observers reliability. The findings revealed that all technologies, except the FDM-based casts, accurately represented tooth morphology and were within a clinically acceptable range of 0.25 mm.[19] However, this range was defined based on linear measurements by comparing conventional maxillary and mandibular plaster models with printed casts, and the authors are unaware of evidence for an acceptable 3-dimensional accuracy range for a cast compared with the anatomic structure. Although, no statistically significant difference was observed related to all surfaces of casts, the impact of these small differences on clinical significance is unknown.

In the present study, certain inaccuracies were also observed with both FDM-based polywood and ossofill casts. The cast acquired with the polywood material had porosities on the tooth surfaces, whereas the ossofill (polylactic acid) cast imperfectly represented the cuspal and incisal surface morphology. Furthermore, both were unable to print fine trabecular structures, possibly because of warping deformation and shrinkage during thermoplastic cooling.[20] Recent evidence has been consistent with the findings in the present study, also showing that FDM technology is inadequate for printing fine structures with reduced dimensional accuracy.[21,22]

Buccal and lingual cortical surfaces were found to be accurately depicted in all casts; however, the least amount of error was achieved with SLA and LS casts for the lingual and buccal surfaces. PJ (multijet, colorjet) and LS technology materials had the lowest overall error. However, trabecular structures were more accurately printed with the MJ printers, which was consistent with findings from a previous study reporting the high-dimensional accuracy of LS and the better anatomic reproducibility of PJ technology.[23] As the finishing of PJ-based casts only required pressurized water for removing the support material, the postprocessing error was reduced, unlike LS, in which airborne-particle abrasion might have caused surface wear in trabecular regions.[10]

The outcomes of the present study also suggested that the accuracy of casts depended more on the combination of type of printer technology and material, rather than layer resolution. However, further studies are required to test the effect of layer resolution on the accuracy of printing casts. Also, the error associated with various CBCT devices and protocols for acquiring volumetric data and their effect on the printing accuracy should be addressed in future research. To overcome the error related to CBCT devices, the application of an accurate industrial scanner to evaluate the accuracy of printed dentomaxillofacial structures, especially trabecular architecture, and printing them separately without the need to construct a complete patient-specific cast is recommended.

The study had limitations, including that the segmentation process based on the thresholding of CBCT data required manual delineation, which was both time consuming and subjective. Further research is required to develop CBCT-friendly segmentation algorithms to allow for the detailed and accurate replication of patient-specific anatomy. Additionally, the postprocessing of casts might have introduced errors, especially for thin trabecular surfaces; therefore, improvements are required in printing technologies and materials with optimal layer resolution.

Conclusions

Based on the findings of this comparative study, the following conclusions were drawn:

1. Overall, 3D printed casts were able to replicate skeletal and dental anatomic surfaces well, although some casts showed shortcomings in relation to depicting trabecular architecture.

2. MJ technology with Visijet M2R material was found to be the most accurate combination for replicating mandibular anatomic structures.

3. The mechanical properties of these casts need to be assessed for the purpose of drilling bone and performing dentomaxillofacial surgeries with the same tactile perceptibility as that of real bone.

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ARTICLE 7

Visual and haptic perceptibility of 3D printed skeletal models in orthognathic surgery

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Abstract

Purpose

To assess the anatomical and tactile quality of 3D printed models derived from medical printers for application in orthognathic surgery.

Materials and methods

A CBCT-scan of an 18 years old female patient was acquired with NewTom VGi evo (NewTom, Verona, Italy). Thereafter, mandibular bone was segmented and isolated from the scan using Mimics inPrint 2.0 software (Materialise NV, Leuven, Belgium). Six printers with different technologies were utilized for printing skeletal models, which included stereolithography (ProX800, 3D Systems, Rock Hill, SC, USA), digital light processing (Perfactory 4 mini XL, Envisiontec, Dearborn, MI, USA), fused deposition modeling (uPrint SE, Stratasys, Eden Prairie, MI, US) , colorjet (ProJet CJP 660Pro, 3D Systems, Rock Hill, SC, USA), multijet (Objet Connex 350, Stratasys, Eden Prairie, MN, USA) and selective laser sintering (EOSINT P700, EOS GmbH, Munich, Germany). A questionnaire was designed, where 22 maxillofacial residents scored whether the printed models were able to mimic bone color, texture and anatomy. Five maxillofacial surgeons performed bone cutting with screw insertion/removal to assess the tactile perceptibility.

Results

In relation to texture and cortical and medullary anatomy replication, Perfactory 4 mini XL printer showed the highest mean score, whereas, Objet Connex 350 scored highest for color replication. The haptic feedback for cutting and screw insertion/removal varied for each printer, however, overall it was found to be highest for ProX800, whereas, EOSINT P700 was found to be least favorable.

Conclusions

The digital light processing based Perfactory 4 mini XL printer offered the most acceptable anatomical model, whereas, deficiencies existed for the replication of haptic feedback to that of real bone with each printer.

Clinical significance

The study outcomes provide pearls and pitfalls of 3D printed models utilizing various printers and technologies. There is a need for research on multi-material printing as such to improve the haptic feedback of skeletal models and render the models more human bone-like to improve surgical planning and clinical training.

Keywords: 3-D printing; mandible; orthognathic surgical procedures; visual perception; touch perception

Introduction

Three-dimensional (3D) printing, also known as additive manufacturing (AM), is constantly evolving in the dentomaxillofacial field for patient-specific skeletal models. The AM process has replaced its subtractive counterpart by offering an improved surface resolution, higher strength, capability of printing complex geometries and production of less waste material [1].The most commonly utilized AM technologies for printing patient-specific skeletal models include fused deposition modelling (FDM), stereolithography (SLA), multijet (MJ), selective laser sintering (SLS), digital light processing (DLP) and binder/color jetting (BJ/CJ) in combination with various materials such as metals, resins and ceramics [2] All AM printing processes undergo three steps for converting a virtual object into a physical structure i.e. modelling, printing and post-processing and the 3D object is printed by the sequential deposition of material in a layer-by-layer pattern [3]. The 3D printed models have been widely utilized in the dentomaxillofacial field for training residents to understand anatomy/pathology and also for performing dental and surgical procedures [4,5]. Most models used for clinical teaching are ready-made standard models which fail to reflect a clinical scenario. To overcome this limitation, various studies have proposed printing of patient-specific 3D models utilizing different printing technologies. However most of these have been related to conservative and prosthetic procedures, cleft repair, bone grafting, sinus lift and extraction of teeth [6,7]. There is lack of evidence related to the utilization of models for performing orthognathic surgery and also which printing technology offers improved anatomical replication and tactile perceptibility for performing surgery [8,9]. Although, the quantitative accuracy and anatomical and haptic quality of the skeletal models has been widely reported in cranio-maxillofacial surgery [[10,11,12,13]]. However, to our knowledge no study is available comparing the visual and haptic perceptibility of 3D printed skeletal models utilizing multiple commercial medical printers offering bone-like printing properties with different technologies to serve planning, training and research applications in orthognathic surgery.

Therefore, the aim of this study was to analyze the anatomical and tactile quality of 3D printed models derived from medical printers based on different technologies for application in orthognathic surgery.

Material and methods

This research was carried out in compliance with the World Medical Association Declaration of Helsinki on medical research. The study was approved by the Ethical Review Board of the University Hospitals Leuven, Belgium (reference number: S57587).

Data acquisition

A maxillofacial cone-beam computed tomographic (CBCT) scan of an 18 years old female patient was acquired from the orthognathic surgery patient's database. The patient was scanned with NewTom VGi evo (NewTom, Verona, Italy) utilizing a standardized protocol and the scanning parameters involved 110 kV, 11×10 cm field of view and a slice thickness of 0.15mm. Following image acquisition, the patient CBCT dataset was saved in Digital Imaging and Communications in Medicine (DICOM) format. The DICOM data was imported into Mimics inPrint 2.0 (Materialise NV, Leuven, Belgium) for segmenting and isolating the mandible from the rest of the scan. The mandibular model was then saved in standard tessellation language (STL) format for the purpose of 3D printing.

3D printed models

A total of six different technology-based printers (SLA, DLP, FDM, CJ, MJ and SLS) were utilized for printing models offering bone-like color and material properties based on the company's recommendations. Table 1 summarizes the major features of the printers [[14,15,16,17,18,19]] and Table 2 provides an overview of the post-cured mechanical properties of the materials used for printing [[20,21,22,23,24]], apart from the FDM-technology based material which was an in-house variant of polylactic acid (PLA) and no further information was provided by the manufacturer.

Table 1. Main features of the printers utilized for printing the mandibular model.

Printer name	Manufacturer	Tech.	Printing process	Slicing software	Layer res.	Support used	Post-processing
ProX800	3D Systems, Rock Hill, SC, USA	SLA	VP	3D Sprint	0.025	Same as printing material	tripropylene glycol methyl ether and IPA bath, hand-rinsing, compressed air, sanding
Perfactory 4 mini XL	Envisiontec, Dearborn, MI, USA	DLP	VP	One Rapid Prototype	0.035	No support	IPA bath, compressed air
uPrint SE	Stratasys, Eden Prairie, MI, US	FDM	ME	CatalystEX	0.1	Soluble support material (SR-30, Stratasys)	water-based detergent solution, compressed air, sanding
ProJet CJP 660Pro	3D Systems, Rock Hill, SC, USA	CJ	BJ	3D Sprint	0.1	No support	acrylate sulfate bath, soft air brush, compressed air
Objet Connex 350	Stratasys, Eden Prairie, MN, USA	MJ	MJ	Objet Studio	0.03	soluble support material (SUP705, Stratasys)	high pressure waterjet, IPA bath
EOSINT P700	EOS GmbH, Munich, Germany	SLS	PBF	RP Tools	0.12	No support	compressed air and sanding

VP: Vat photopolymerization, ME: Material extrusion, BJ: Binder jetting, MJ: Material jetting, PBF: Powder bed fusion

Table 2. Post-cured mechanical properties of the materials used to print the mandibular model.

Commercial name	**Accura ABS White (SL 7810)**	**ABS Tough**	**VisiJet PXL**	**Verowhite**	**PA 2200 - Polyamide 12**
Manufacturer	**3D Systems, Rock Hill, SC, USA**	**EnvisionTec GmbH, Gladbeck, Germany**	**3D Systems, Rock Hill, SC, USA**	**Stratasys, Eden Prairie, MN, USA**	**EOS GmbH, Munich, Germany**
Tensile Strength (MPa)	46-48	75	26.4	50 – 65	48
Tensile Modulus (MPa)	2290-2400	4420	12560	2,000 – 3,000	1650
Elongation at Break (%)	8-14	3.50	0.21	10 – 25	18
Flexural Strength (MPa)	74-76	93	44.1	75 – 110	-
Flexural Modulus (MPa)	2040-2120	2520	10680	2,200 – 3,200	1500
Impact Strength (J/m, Kj/m²)	24-47 J/m	16.5 J/m	-	-	53 Kj/m²
Hardness, Shore D	86	86	-	83 – 86	75
General description	plastic-like liquid resin	plastic-like liquid resin	gypsum-like composite powder	acrylic-like liquid resin	polyamide nylon-like powder

Stereolithography

The SLA printer was an industrial-grade ProX800 (3D Systems, Rock Hill, SC, USA) offering a build envelope capacity of 650 x 750 x 550 mm, minimum layer thickness of 0.03mm and XY accuracy of 0.001mm. The material used for printing was Accura ABS White (SL 7810, 3D Systems), a rigid and tough acrylonitrile butadiene styrene (ABS) plastic-like resin. The prepared STL was imported to a software (3D Sprint, 3D Systems) for optimizing the printing parameters and a layer resolution of 0.025 was selected. The resin was cured by an ultraviolet (UV) laser through vat photopolymerization process and the printer used top-down configuration i.e. according to gravity for construction of each individual layer till the mandible was printed. The top-down architecture allowed fast printing as no separation of the print from the build plate was required following each layer deposition. Support structures were removed manually using a putty knife. The post-processing involved tripropylene glycol methyl ether and isopropyl alcohol (IPA) bath, and hand-rinsing with brush and IPA. Compressed air was used to blow dry the model from inside. Thereafter, the model was placed into ProCure 750 (3D Systems) for the final curing. Sand paper was used to smoothen out the model (Figure 1A).

Digital light processing

The DLP printer was Perfactory 4 mini XL (EnvisionTec GmbH, Gladbeck, Germany) with a build volume of 115 × 72 × 230 mm, minimum layer thickness of 0.02mm and XY accuracy of 0.03mm. The printing material was ABS Tough (EnvisionTec GmbH), which was also like an ABS plastic-like resin. The slicing software, Envision One Rapid Prototype (EnvisionTec) was used to upload the file to the printer with a layer resolution of 0.035. The software automatically aligned the flat surface of the model with the platform without the need for support structures. This printer also exploited the vat photopolymerization process similar to that of the ProX800 printer and also the printing architecture was top-down. However, the Perfactory 4 mini XL technology differed to ProX800 as the liquid resin hardened with the combination of a light source and a projector. The printer used mask projection for the process of photopolymerization and once the model was cured, it was peeled off from the platform. Excess resin was removed using IPA bath and compressed air (Figure 1B).

Fused deposition modeling

The FDM printer was uPrint SE (Stratasys, Eden Prairie, Minnesota, US) with a maximum build size of 203 × 152 × 152 mm, minimum layer thickness of 0.25 mm and filament diameter of 1.75 mm. The printing material was an in-house variant of a PLA-based plastic material. No details of the printing materials properties were provided by the manufacturer. The slicing software utilized for printing order was CatalystEX 4.4 (Stratasys) and a layer resolution of 0.1 was selected. The printer utilized the extrusion technology and it functioned by extruding strings of PLA in successive rows (horizontal layering) for forming the model. The support material (SR-30, Stratasys) was soluble in nature and was removed by immersing the model in a basket of WaveWash™ support cleaning system (Stratasys) which automatically dissolved the supports using a water-based detergent solution (Ecoworks™ cleaning agent, Stratasys), leaving behind only the insoluble PLA model. Later small fragments of the support material were removed by blowing air and sanding was applied (Figure 1C).

ColorJet

The CJ printer included ProJet CJP 660Pro (3D Systems, Rock Hill, SC, USA) with a build volume of 254 x 381 x 203 mm, minimum layer thickness of 0.1mm and XY accuracy of 0.1mm. The chosen material was Visijet PXL core (3D Systems) which was a gypsum like composite powder and according to the manufacturer the material was composed of 80-90% calcium sulfate hemihydrate. The binder used for binding the material was VisiJet PXL Clear (ZB63, 3D Systems). The digital slicing program consisted of 3D Sprint (3D Systems) without any support structures as the powder supported the material during the printing process and a layer resolution of 0.1 was selected. The printer applied binder jetting technology and functioned by layer by layer printing process and spreading of the powder material layers on the platform. Followed by deposition of binding agent for bonding the material through inkjet nozzle. The build platform moved downwards following binding of each layer till the model was printed. At post-processing unbounded core material was removed using a soft air brush, blow air and model was bathed in acrylate sulfate bath (Figure 1D).

Multijet

The printer was a polyjet Objet Connex 350 (Stratasys, Eden Prairie, MN, USA) with a maximum build size of 340 × 340 × 200 mm, minimum layer thickness of 0.02 mm and an accuracy of 0.1-0.3 mm. The thermoplastic material was a photosensitive polymer liquid known as Verowhite (Stratasys). The slicing program for optimizing the printing properties was Objet Studio software (Stratasys) and the layer resolution was 0.03. The printing process consisted of jetting layers of the acrylic-based photopolymer onto the build tray delivered via a polyjet and instantly curing by a UV light tube situated in the printer head. After curing each layer the platform submerged at a depth corresponding to the thickness of the first layer, thereby allowing each layer to be covered by the polymerized resin. Following printing of the model, post-processing involved removal of the soluble resin-based support material (SUP705, Stratasys) using a high pressure waterjet station (Stratasys) and an IPA bath (Figure 1E).

Selective laser sintering

The printer was EOSINT P700 (EOS GmbH, Munich, Germany) with a build volume of 700 x 380 x 580 mm and minimum layer thickness of 0.1mm. The material utilized was PA 2200 - Polyamide 12 (EOS GmbH) which was a fine polyamide powder-based material, also commonly known as nylon. The model was sliced with EOS RP Tools (EOS GmbH) and sent to PSW 3.1 (EOS GmbH) for defining the processing and laser parameters with a model layer resolution of 0.12. The printer functioned by spreading a layer of the heated material on a build platform and the layers were sintered and fused with two 50 W CO_2 lasers. The platform kept lowering at a set distance following sintering of each layer till the complete model was printed. No support structures were needed as the unfused material supported the model. The post-processing involved removal of the powder from the printed structure using compressed air and sanding for a smooth finish (Figure 1F).

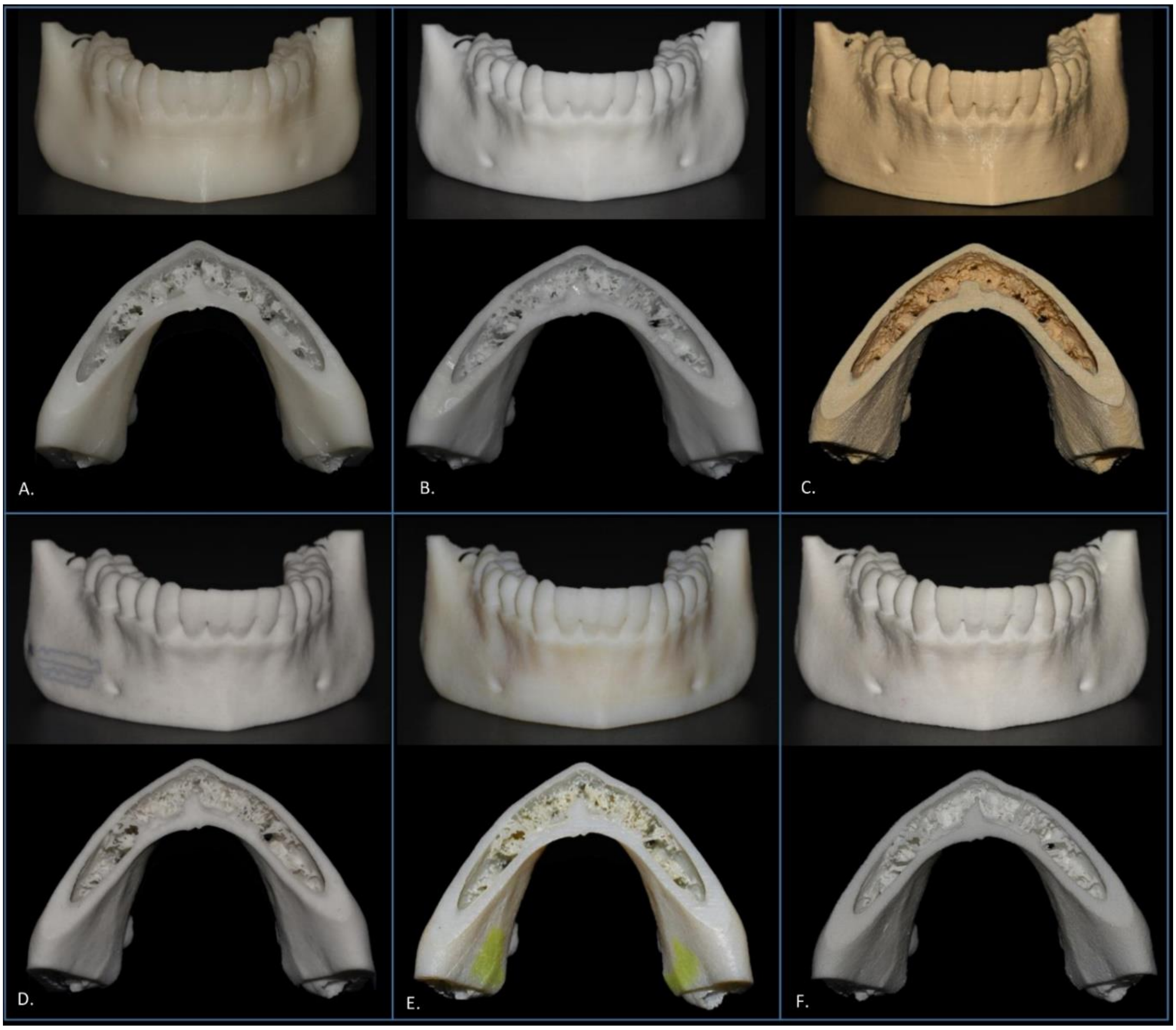

Figure 1. Frontal and inferior view of the printed models, A. ProX800 (stereolithography), B. Perfactory 4 mini XL (digital light processing), C. uPrint SE (fused deposition modeling), D. ProJet CJP 660Pro (colorjet), E. Objet Connex 350 (multijet), F. EOSINT P700 (selective laser sintering)

Outcome variables

Following acquisition of printed models, a questionnaire was designed for observing the anatomical replication and tactile perceptibility of the printed models. Questions were divided into two parts, where the first part consisted of anatomy-related questions and second part involved surgery-related questions. Each question was answered based on a Likert scale ranging from 1 to 5 (where, 1= strongly disagree, 2= disagree, 3= neutral/ undecided, 4= agree, 5= strongly agree) (Table 3). The contents of the questionnaire were validated based on two experts review and later pre-tested by allowing 6 observers to fill the anatomy-related questions and 2 observers filled the surgery-related questions twice at an interval of 1 week.

Table 3. Questionnaire for evaluating anatomical replication and tactile perceptibility.

Question no.	Questionnaire	Strongly disagree 1	Disagree 2	Neutral 3	Agree 4	Strongly Agree 5
Anatomy-related questions						
1	Does the 3D printed model feel like real bone to touch?					
2	Does the 3D model visually look like real bone in colour?					
3	Does the cortical bone follow the anatomy as that of the original 3D image					
4	Does the medullary bone follow the same anatomy as the original 3D image?					
Surgery-related questions						
5	Was the tactile perception and resistance of osteotomy cuts equal to that of real bone					
6	Was the tactile perception and resistance of drilling bone for screw placement equal to that of real bone					
7	Was the tactile perception and resistance of screw placement equal to that of real bone					
8	Was the tactile perception and resistance of screw removal equal to that of real bone					

A total of 22 senior residents experienced in oral and maxillofacial surgery and 3D imaging were recruited to score the anatomy-related question. All participants were trained and calibrated beforehand, which involved providing each observer with clear instructions on how to answer the questionnaire. Additionally, training was provided on both the 3D virtual image and the printed model to identify the anatomical structures. Apart from identifying the cortical and medullary bone surfaces, the observers were also trained and calibrated to identify dentoalveolar bone, anterior mental protuberance, posterior mental spines, lingual foramen, mental foramen, anterior oblique line, mylohyoid line and sub-mandibular fossa region. The scoring was carried out by comparing the models physically to the original 3D STL displayed on a computer screen (Dell® U2415b UltraSharp 24" Widescreen LCD) (Figure 2), except for the texture and color perception of the printed model to that of real bone, which was evaluated based on the clinical experience of the observers.

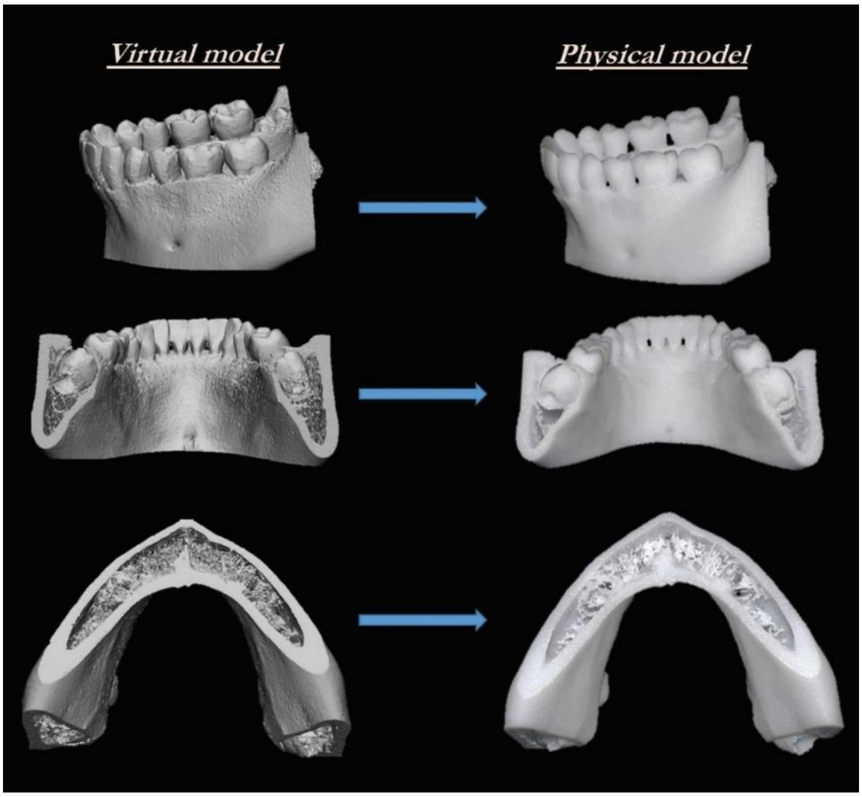

Figure 2. Anatomical comparison of virtual with physical model

Five maxillofacial surgeons with a minimum experience of 4 years performed model surgery and answered the surgery-related questions. Model surgery consisted of performing bone cutting with buccal and sagittal cuts using a short side cutting Lindemann burr (1.4 × 5 mm)   and later on fixation was carried out with two 4-hole straight 1mm titanium miniplates and eight 2.0 × 5.0 mm monocortical locking screws (KLS-Martin GmbH, Freiburg, Germany) on a stable platform. For conducting the surgery, a 3D template was designed to keep the placement of cuts standardized between observers (Figure 3).

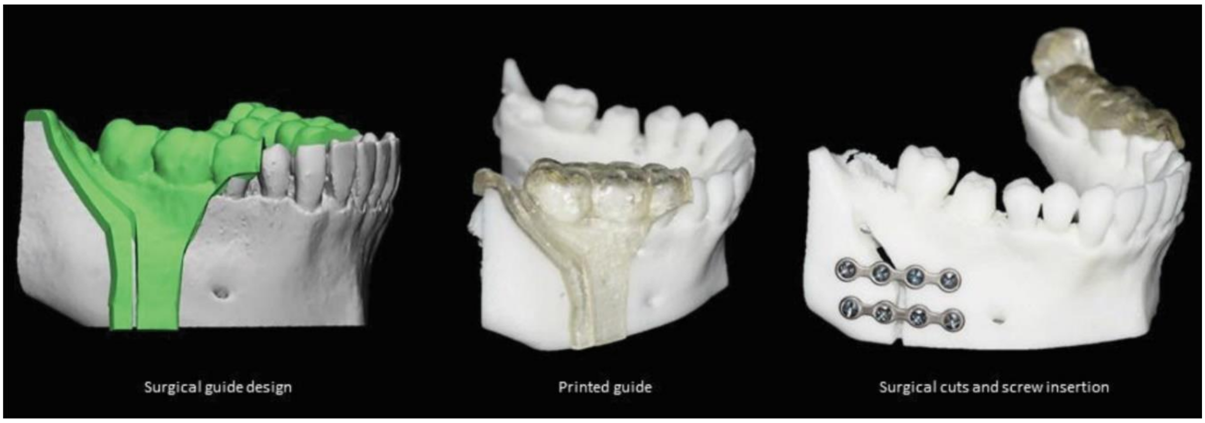

Figure 3. Template guided partial bilateral sagittal split osteotomy model surgery with buccal and sagittal cuts and fixation with miniplates and screws.

Statistical evaluation

Data were analyzed using MedCalc for Windows, version 19.4 (MedCalc Software, Ostend, Belgium). Mean scores were calculated for all the model's parameters. Kruskal-Wallis test followed with pairwise multiple comparisons were conducted with Bonferroni correction to compare the six printers. A p value of 0.05 was considered as statistically significant.

Results

In relation to anatomy-related questions, touch perception of Perfactory 4 mini XL showed the highest mean score and lowest scoring was observed for the uPrint SE printer. The Perfactory 4 mini XL based model showed a significantly higher score for touch perception to that of real bone compared to the ProX800, uPrint SE and ProJet CJP 660Pro . The visual appearance of models based on color was highest for Objet Connex 350 using Verowhite and Perfactory 4 mini XL with ABS tough material. The lowest visual replication was observed for uPrint SE based mandibular models using an in-house variant of PLA. All models showed a significantly higher score when compared with the uPrint SE based model. Similarly, the cortical bone was replicated the best with Perfactory 4 mini XL, ProJet CJP 660Pro and Objet Connex 350 printer without any significant difference and lowest score was observed with the uPrint SE printer. The medullary replication with Perfactory 4 mini XL had a significantly higher score when compared with other technologies and lowest score was seen with uPrint SE**.** (Figure 4, Table 4).

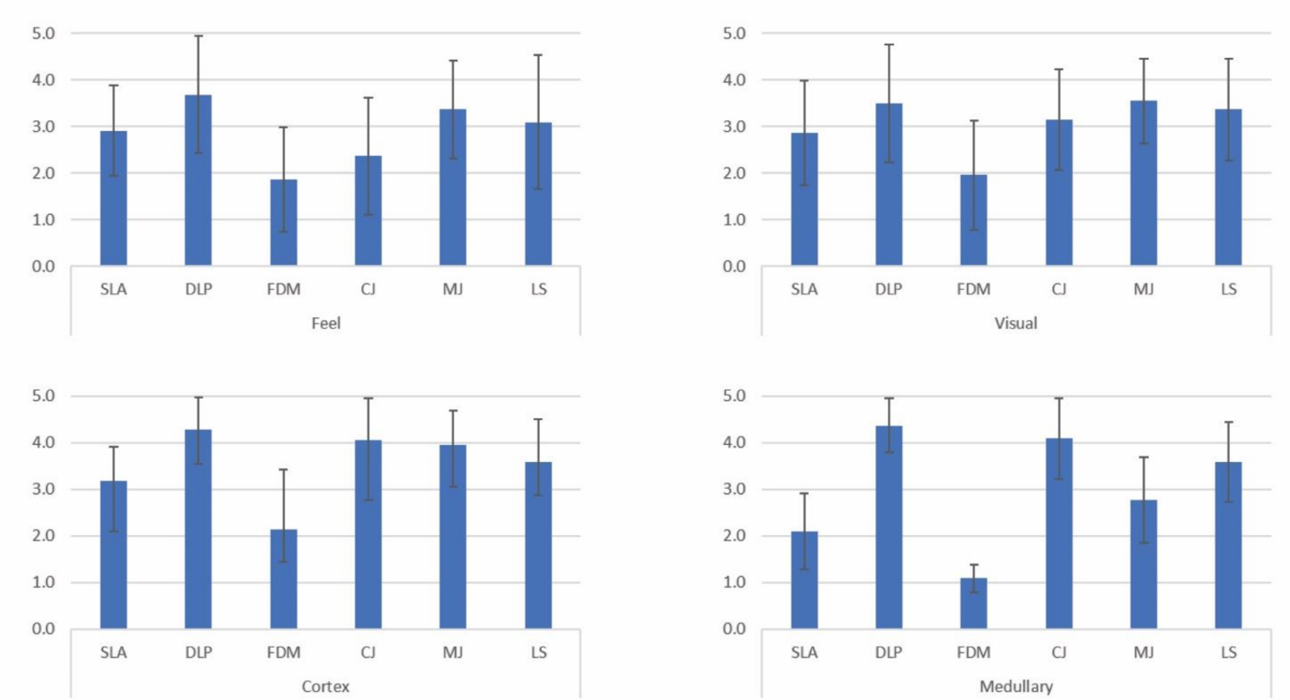

Figure 4. Mean score ± standard deviation of the anatomy-related questions based on printing technology

ProX800*: stereolithography (SLA),* Perfactory 4 mini XL*: digital light processing (DLP),* uPrint SE*: fused deposition modeling (FDM),* ProJet CJP 660Pro*: colorjet (CJ),* Objet Connex 350*: multijet (MJ),* EOSINT P700*: selective laser sintering (SLS)*

Table 4. Pair-wise comparison with Bonferroni correction (significance) of anatomy-related questions based on printing technology.

Technology comparison	Feel	Visual	Cortex	Medullary
SLA-DLP	**0.014***	0.074	**<0.001***	**<0.001***
SLA-FDM	**0.002***	**0.011***	**<0.001***	**<0.001***
SLA-CJ	0.076	0.509	**<0.001***	**<0.001***
SLA-MJ	0.132	**0.044***	**0.002***	**0.023***
SLA-SLS	0.529	0.141	0.153	**<0.001***
DLP-FDM	**<0.001***	**<0.001***	**<0.001***	**<0.001***
DLP-CJ	**0.001***	0.229	0.412	0.341
DLP-MJ	0.231	0.901	0.119	**<0.001***
DLP-SLS	0.156	0.613	**0.013***	**0.001***
FDM-CJ	0.158	**0.002***	**<0.001***	**<0.001***
FDM-MJ	**<0.001***	**<0.001***	**<0.001***	**<0.001***
FDM-SLS	**0.005***	**<0.001***	**<0.001***	**<0.001***
CJ-MJ	**0.006***	0.166	0.457	**<0.001***
CJ-SLS	0.078	0.404	0.066	0.05753
MJ-SLS	0.592	0.645	0.158	**0.003***

ProX800: stereolithography (SLA), Perfactory 4 mini XL: digital light processing (DLP), uPrint SE: fused deposition modeling (FDM), ProJet CJP 660Pro: colorjet (CJ), Objet Connex 350: multijet (MJ), EOSINT P700: selective laser sintering (SLS)

Based on the surgery-related questions, the tactile perception and resistance of osteotomy cuts to that of real bone was highest for ProJet CJP 660Pro based models. Apart from Objet Connex 350 and Perfactory 4 mini XL , all other technologies showed a significantly lower score for osteotomy when compared with ProJet CJP 660Pro. The tactile sensation of drilling for screw insertion was highest for Objet Connex 350 model followed by ProX800 and Perfactory 4 mini XL . Only EOSINT P700 printer showed a significantly lower score when compared with other technologies. The screw insertion and removal score was highest for ProX800 whereas it was found to be lowest for uPrint SE (Figure 5, Table 5). Overall, Perfactory 4 mini XL was able to well replicate the mandibular bone anatomy, whereas, surgery scoring was found to be highest for ProX800 based models followed by Objet Connex 350 and Perfactory 4 mini XL. The uPrint SE printer showed the least scoring for anatomical questions, whereas, EOSINT P700 was found to be least favorable for performing model surgery.

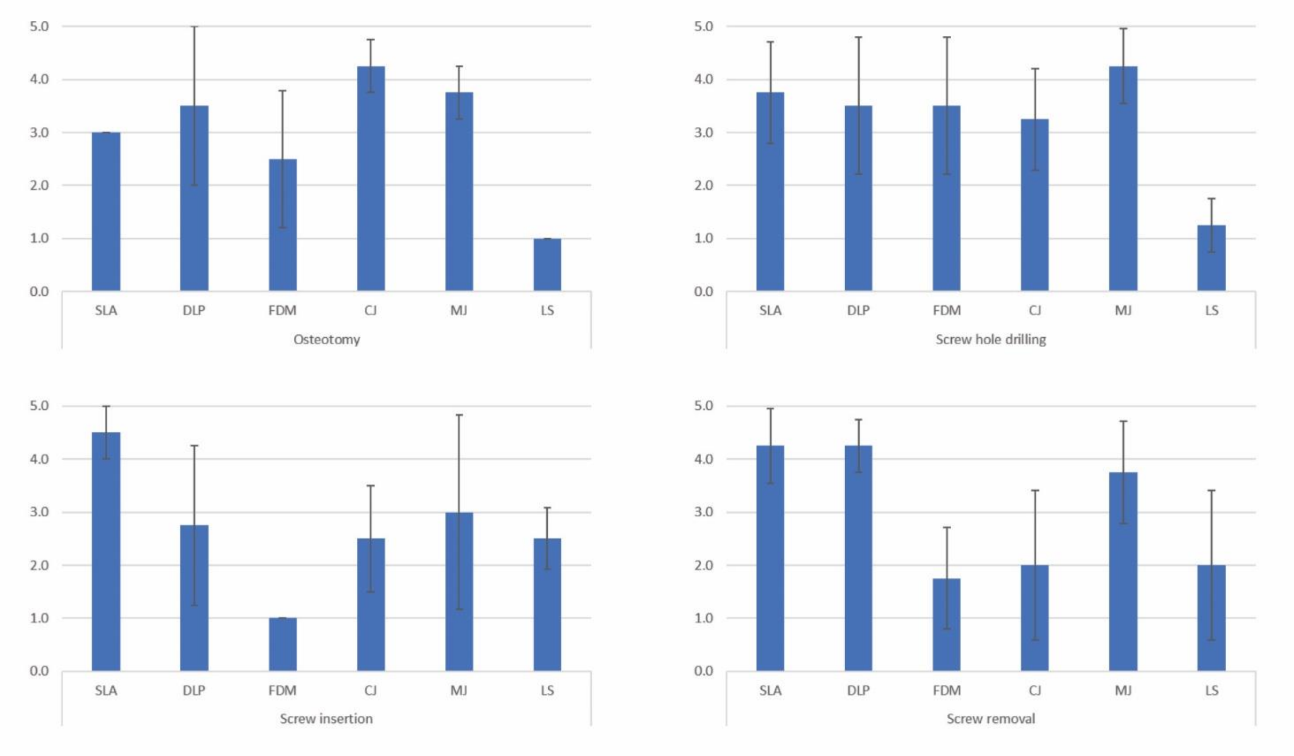

Figure 5. Mean score ± standard deviation of the surgery-related questions based on printing technology
ProX800*: stereolithography (SLA),* Perfactory 4 mini XL*: digital light processing (DLP),* uPrint SE*: fused deposition modeling (FDM),* ProJet CJP 660Pro*: colorjet (CJ),* Objet Connex 350*: multijet (MJ),* EOSINT P700*: laser sintering (SLS)*

Table 5. Pair-wise comparison with Bonferroni correction (significance) of surgery-related questions based on printing technology.

Technology comparison	Osteotomy	Screw hole drilling	Screw insertion	Screw removal
SLA-DLP	0.505	0.764	0.126	0.874
SLA-FDM	0.508	0.764	**0.012***	**0.027***
SLA-CJ	**0.011***	0.543	**0.016***	0.056
SLA-MJ	**0.040***	0.445	0.224	0.445
SLA-SLS	**0.008***	**0.017***	**0.017***	0.056
DLP-FDM	0.377	1	**0.011***	**0.017***
DLP-CJ	0.761	0.764	0.761	**0.044***
DLP-MJ	0.880	0.368	1	0.349
DLP-SLS	**0.045***	**0.025***	0.738	**0.044***
FDM-CJ	**0.045***	0.764	**0.040***	0.877
FDM-MJ	0.121	0.368	**0.047***	**0.037***
FDM-SLS	**0.047***	**0.025***	**0.012***	0.877
CJ-MJ	0.185	0.177	0.655	0.105
CJ-SLS	**0.011***	**0.024***	0.738	1
MJ-SLS	**0.011***	**0.017***	0.766	0.105

ProX800*: stereolithography (SLA),* Perfactory 4 mini XL*: digital light processing (DLP),* uPrint SE*: fused deposition modeling (FDM),* ProJet CJP 660Pro*: colorjet (CJ),* Objet Connex 350*: multijet (MJ),* EOSINT P700*: selective laser sintering (SLS)*

Discussion

The utilization of 3D printed models has gained a significant traction in oral and maxillofacial surgery. Although, currently the training in orthognathic surgery primarily relies on either practicing on cadavers or gaining experience directly on patients. Nevertheless, with the advancements in technology, 3D printed training models are constantly being incorporated into the simulation-based clinical training programs for the dental and maxillofacial residents [13]. Various technologies are being employed for printing a replica of skeletal structures [25]. In addition to the anatomical accuracy, the visual and tactile feedback of these models is also important for their implementation in clinical training. Therefore, current study was conducted to observe which printer offered the most optimal mandibular bone model from an anatomical and haptic perspective.

In relation to feeling the texture of the printed models to that of real bone, Perfactory 4 mini XL offered the most highest score, closely followed by Objet Connex 350 and EOSINT P700, whereas, the least scoring was observed for uPrint SE, ProJet CJP 660Pro and ProX800. The main reason for this decreased texture scoring with uPrint SE and ProX800 printers was based on the fact that both models invariably showed layer steps following printing which could have influenced the texture of the models. The stepping effect has been known to be a disadvantage with some of the SLA and FDM printers due to the layered manufacturing process [[26,27,28,29]], which was also seen with the printers included in this study. On the contrary, DLP printers also have been known to show stepped layers owing to the phenomenon of layer-by-layer production, however, Perfactory 4 mini XL printer used in this study led to a smooth finish. To overcome this stepping effect certain commercial solutions could be utilized which either cover or melt the outer surface to make it smoother [30]. The ProJet CJP 660Pro based model's texture was negatively influenced by the printing material (Visijet PXL), which had gypsum like properties and thereby it is not an ideal choice for printing based on its inherent composition where texture close to that of real bone is a requirement [31]. In contrast to the aforementioned printers, Perfactory 4 mini XL, Objet Connex 350 and EOSINT P700 all had a smooth finish without the visibility of the stepping effect. However, based on our findings no printer and material utilized in this study was able to optimally mimic the texture to that of a real human bone. Similarly, all printing materials offered moderate replication within the similar range based on color, apart from FDM (uPrint SE) which was due to the contrasting beige color of the material, nevertheless, none of the materials offered true color replica to that of real bone. The color of a model is an important factor as it can influence both the anatomical teaching and surgery experience. From an educational perspective, although addition of different colors deviating from the native anatomy might be visually attractive to a naked eye, however, a false color might lead to recall error as the residents or trainees would expect to see the same color while performing surgery [32]. Previously, Mcmillan et al. [33] printed temporal bone models for simulating surgical dissection and concluded that the darker colored models which failed to represent a realistic bone color negatively affected the performance of observers during surgical drilling.

Apart from ProX800 and uPrint SE, all other printers offered a good replication of the cortical bone with the best scoring in favor of Perfactory 4 mini XL. Although DLP is a variant of SLA with the only difference being the polymerization process, where ProX800 used a laser for polymerization and Perfactory 4 mini XL polymerized by light. However, ProX800 offered less scoring for anatomical replication which might be due to the longer postpolymerization process compared to the Perfactory 4 mini XL technology [34]. This can lead to distortions in the model, thereby affecting the anatomical quality of the printed model. The EOS P700 based models showed a slightly lower score for anatomical replication which could have been caused by a superficial wear following sandblasting at the post-processing step [35]. The uPrint SE printer received lowest scoring for all anatomical parameters, as some FDM based printed models have rigid edges, which require additional finishing method, for instance hand sanding which can lead to inconsistent and crude finishing of a model [36]. Thereby, not only it can lead to a decreased tactile perception but also affect the anatomical replication due to the poor surface quality and voids formation within the printed mandible as observed in this study [37]. Another reason for the abnormal finish of the uPrint SE based model might have been due to the presence of mesh errors and inverted normals seen in the slicing software due to the trabecular structures which the manufacturer was unable to fix, thereby, this could have further contributed to printing errors and coarse finish. Objet Connex 350 provided optimal cortical bone replication, however trabecular replication received a low score which might have resulted due to the breakdown of the structures during post-processing with waterjet due to the high fragility of structures printed with MJ printers [38]. However both Perfactory 4 mini XL and ProJet CJP 660Pro offered good replication of trabecular bone as no high pressure water-jetting was required to clean the model.

Currently no objective method exists to optimally quantify haptic feedback of a surgeon while performing surgery, therefore a questionnaire was created to assess the feedback. The haptic quality of all models varied for each step. Our findings suggested that ProJet CJP 660Pro with gypsum like material offered the highest scoring for performing osteotomy cuts whereas a low scoring was seen for drilling holes, screw insertion and removal. In contrast, Favier et al. [12] performed endoscopic skull base surgery using calcium sulfate hemihydrate with a BJ technology and found it to be optimal for the purpose of drilling. This variability in our findings could be attributed to the fact that the mechanical properties of the mandible differs from that of a skull base. EOSINT P700 was the least favorable for performing surgery, which might be due to the nylon-like materials mechanical properties that failed to offer a realistic feeling. Haffner et al. [39], also found nylon to be least reliable for performing mastoidectomy procedure. The authors also suggested PLA and ABS to be more reliable options, Our findings were partially in accordance with their study as ABS based models printed with ProX800 and and Perfactory 4 mini XL offered higher scoring, however, we found PLA-based model less reliable which might have been due to the printers inability to replicate the model with trabecular structures efficiently. The combined scoring of ProX800, Objet Connex 350 and Perfactory 4 mini XL models was ≥4 which could make them slightly more suitable models for performing surgical procedure in the mandibular region. Whereas, ProJet CJP 660Pro, uPrint SE and EOS P700 models with the specified materials received the lowest scoring cannot be considered optimal for performing model surgery. The control of certain printing parameters such as, in-fill pattern and percentage, print shell, orientation of the model and appropriate material selection might allow production of a model mimicking a real bone structure [40]. As the haptic feedback not only relies on the technology and printer settings but also on the material characteristics such as elastic modulus and tensile strength [7]. However, these parameters were not controlled in the study as the models were provided based on manufacturer based settings which could replicate a bone-like model.

Although various studies have been performed related to the application of different technologies for performing cranio-maxillofacial surgery [[41,42,43]].[19-21] Nevertheless, no studies were found comparing the aforementioned printer or technology for performing osteotomy with plate and screw placement in the mandibular region. Therefore, it was not possible to compare this haptic aspect of these models with already present evidence. Nevertheless, our findings may allow future printing related studies to further optimize the printing and post-processing process and material selection by considering the deficiencies discussed in this paper, as such to allow printing of a model which not only provides an anatomical replica but also haptic feedback to that of real bone.

The study had certain limitations. Firstly, complete mandible with condylar region was not printed and lingual cut was not performed, thereby, complete mobilization of the mandibular body was not achieved. Secondly, the deficiencies in models could have resulted at either the printing or post-processing stage of the printing pipeline, which we failed to evaluate. Thirdly, no clinical standard of real bone was utilized for comparing the anatomical and surgery-related parameters which could have led to bias. Fourthly, trueness and precision of the models was not evaluated. Further studies should consider utilizing fresh-frozen cadaveric or patient-specific intra-operative data as a clinical standard for comparison of anatomic and haptic feedback of different printing technologies. Finally, the study relied on subjective evaluation of the models by a small number of surgeons. As this might have created some bias, further studies should also focus on devising an objective method to assess haptic feedback for a larger number of observers. However, in the midst of these limitations, our study provided evidence on anatomical and haptic replication of bone with different printers which is relevant from both educational and clinical perspective. Future studies should also concentrate on the biocompatibility and mechanical properties of different technologies and materials enabling their application in cases requiring bone transplant.

Conclusion

Overall, the DLP technology based Perfactory 4 mini XL printer with ABS-like resin offered the most acceptable anatomical model. Although variability existed with each step of the surgery, nevertheless, SLA-based ProX800 printer with ABS-like material provided the most acceptable model for simulating model surgery. None of the printers and materials were able to provide an optimal model from a combined anatomical and surgery perspective. Thus, further research on multi-material printing is required as such to improve the haptic feedback of skeletal models and render the models texture and color more human bone-like.

Clinical relevance

Our findings provide evidence on the anatomical and haptic quality 3D models with various printers which may allow to guide physicians and trainees to select a certain printer and material depending on the task at hand for improving surgical planning and clinical training.

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General discussion, conclusions and future perspectives

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General discussion

Orthognathic surgery combined with orthodontic treatment is widely accepted as the treatment of choice for the correction of the dento-maxillofacial deformities by repositioning the maxilla, mandible and/or chin in a desirable position.[1] It not only corrects the facial soft/hard tissue profile but also influences the breathing status of the patients by allowing change in the airway space.[2] The two of the most common procedures performed in orthognathic surgery consist of LF I and BSSO advancement surgery. Considering the improvement in surgical techniques, advancements in software programs and replacement of 2D imaging with 3D CBCT acquisition devices, one of the least studied complication three-dimensionally consists of skeletal relapse. Relapse has been known to be one of the most common complication since the conception of orthognathic surgery.[3] Various surgical modifications and fixation techniques have improved the stability status of the surgical procedures, however, lack of evidence exists related to the true 3D objective quantification of post-surgical and post-treatment relapse.[4-6] The question related to the 3D late relapse which covers changes at 1 year and beyond still needs to be answered. As this might allow surgeons to get familiarized with the amount and/or direction of relapse, which might guide them to make a patient-specific treatment plan accordingly.

The main objectives of this doctoral thesis were to provide clear view on the 3D translational and rotational skeletal relapse following LF I maxillary advancement with superior or inferior repositioning and isolated BSSO advancement surgery, relapse of PAS following BSSO advancement and to identify possible patient- and surgery- related risk factors. In addition, application of 3D printed models in orthognathic surgery were discussed, which might act as a platform for future studies where simulation of surgery on accurate and visuo-haptically oriented skeletal models can allow control of early relapse by simulating surgery and also modification of surgical techniques. In this article, the main results are discussed and the methodological flaws are critically debated.

The first and ideal step would be to develop a tool for assessing 3D skeletal relapse, thereby allowing surgeons to objectively observe the translational and rotational relapse of the maxilla and mandible following LF I and BSSO advancement surgery respectively. Therefore, **in article 1**, we investigated the reliability and time-efficiency of a semi-automatic protocol allowing landmark-free translational and rotational assessment of the skeletal relapse using VDAR at a follow-up period of 6 months irrespective of the observer's experience. Based on the intraclass correlation coefficient, the follow-up protocol showed excellent inter and intra-observer reliability ranging between 0.94-0.95 and the mean absolute observer variability within the range of 0.3mm and 0.4° for the translational and rotational parameters respectively. Similarly, the overall mean error associated with the follow-up protocol was -0.1±0.7mm and 0.1±0.9° for the translational and rotational error. The error might have resulted due to the inevitable minor movement of teeth occurring at the post-surgical orthodontic phase or due to the presence of noise/artefacts within the CBCT scans.[7] However the algorithm based on voxel-based registration counteracted most of the minor changes by allowing registration based on the complete region of interest rather than relying on isolated information of separate regions of the arch or landmarks. When considering the repeatability of multiple measurements based on Bland-Altman plots, the mean difference for all translational and rotational errors was close to zero, thereby, confirming presence of no systematic differences or heteroscedasticity which was also in accordance with previous studies.[8,9] Other methodologies which rely on 3D cephalometry are prone to human error and the reliability of these protocols is questionable and dependent on observers experience, where the manual landmark identification error can range between 0.3 to 2.8mm and offer a difference of more than 1mm for

23% of the repeated measurements .[10,11] At the same instance, methodologies involving surface to surface distance interpretation is also troublesome as it's not possible to evaluate systematic error and it oversimplifies the complex surgical changes by providing only an absolute distance measurement.[12] In contrast, our proposed method overcame the aforementioned limitations associated with observer experience, cephalometry and segmentation, where both the observers irrespective of their field and experience were found to be reliable. Clinically, the reliability of the protocol is vital for its universal application in assessing relapse and making patient-specific treatment plan independent of the observer's level of experience. As the algorithm of our protocol was written in Python and then integrated into the Amira software, similarly same methodology can be applied with other registration softwares which allow integration of the coding such as Dolphin 3D (Dolphin Imaging & Management Solutions, Chatsworth, CA, USA), Ondemand3D (CyberMed, Seoul, Korea) and Maxilim software (Medicim NV, Mechelen, Belgium) and 3D Slicer (open-source software, www.slicer.org). At the same instance, the time consumption of these software programs also needs to be tested. The proposed protocol not only enabled a reliable quantification of the translational assessment of the skeletal relapse, but also the rotational relapse which has been reported only by a few studies.[13] Additionally, the time required for assessing relapse was around 10 minutes, unlike previous studies which were either time-consuming or required multiple software programs.[9,14]
On the basis of these findings, we hypothesized that the similar methodology would also be beneficial for assessing long-term skeletal relapse. **In article 2**, we validated the applicability of using VDAR at both short- and long-term follow-up time-interval from immediately following surgery till the time-points of 6 months, 1 year and 2 year. As the previous studies validating voxel-based registration based on different regions of interests, only considered the short-term error of their methodologies without assessing if these will still be applicable at a long-term level. [14-16] Additionally, for assessing the role of artefacts on the VDAR registration, we divided the patients into 2 groups, where group 1 offered unrestored dentition at follow-up time-points, the patients in group 2 underwent restorative treatment at follow-up time points. The protocol showed an excellent inter-and intra-observer reliability in both groups of patients ranging between 0.96 to 1.00 with the mean overall difference of less than 0.5mm and 0.5° for both translational and rotational parameters. Our findings were comparable with studies utilizing other regions for superimposition, such as, zygomatic arches, forehead and anterior cranial base.[14,17] At the same instance, the reproducibility of VDAR was higher in comparison to Koerich et al. study[18], which utilized different regions of interest in maxillary and mandibular skeletal region for superimposition. Also, unlike previous studies which only provided translational error, we provided the rotational error as well.[14,15] Although a slight amount of error existed, however in comparison to previous studies we applied no cephalometric landmarks or relied on the segmentation, thereby overcoming the human error associated with it. As previously suggested, the error might have been associated with the minor teeth movement at follow-up or image noise, same holds true for skeletal structures based superimposition as well which also continuously undergo physiological remodelling at follow-up. However all these changes are not clinically relevant as the degree of error was quite small and similar to the previous article, the repeatability of the measurements was close to zero with a high reliability. Owing to the independence from the human factor, VDAR offered a reliable technique for assessing skeletal relapse. The clinical implication of VDAR for both short- and long-term relapse assessment can improve the surgical technique by providing an accurate and reliable assessment of skeletal relapse.
Following validation of VDAR, it could be opted for assessing skeletal relapse. Therefore, **in article 3**, we applied VDAR for prospectively assessing long-term skeletal relapse of patients undergoing LF I maxillary

advancement with superior or inferior repositioning and investigated the influence of patient- and surgery related variables. The findings of this study suggested excellent stability of LF I with both superior or inferior repositioning. Nevertheless, the patients who underwent advancement with inferior repositioning showed slightly more relapse in a posterior and superior direction which was in accordance with other studies.[6] The reason for this superior relapse could have associated to the forces offered by the occlusion, post-operative elastics and the tension produced by the soft tissue and musculature, which have been known to be the contributory factors leading to skeletal instability. [19,20] The present study suggested that the percentage of patients undergoing inferior repositioning showed the highest translational relapse in combination with either mandibular advancement or setback. Nevertheless, the majority of the patients relapsed well within the range of 1mm and 1° following LF I advancement with both inferior and superior repositioning irrespective of the direction of the mandibular surgery. These findings were in contrast to the hierarchy of stability by Profitt et al.[6] where inferior repositioning was suggested to be a problematic procedure with higher relapse. The disagreement with the proposed hierarchy could be due to the fact that their findings were based on 2D evaluations which are prone to error. Secondly, owing to the small amount of movement for repositioning might have provided improved stability for the majority of the cases. Additionally, another important factor to consider is the utilization of bone graft for increasing the stability of LF I surgery. No consensus has been reached, as either some studies show its effectiveness for reducing relapse, while others suggested no significant difference in relapse with or without bone graft.[21-23] Meanwhile, the findings of the current study suggested no significant influence of the bone graft, which could be attributed to fact that the anterior advancement and superoinferior translational repositioning was not large enough to cause significant tension of the muscular and/or soft tissue which later on recoil to cause relapse. As for the rotational parameters, the pitch of the maxillary segment relapsed the highest in a CCW direction following initial movement in the CW direction. Also amongst all the translational and rotational parameters, the pitch rotation showed the highest positive correlation between the amount of movement and relapse. The reason could be related to the fact that the CW pitch movement rotates the maxilla away from the osteotomy line which creates a wider gap taking longer to heal, thereby learning to a relapse in CCW direction.[24] Overall, all patient-and surgery related factors such as age, sex, graft and skeletal class showed a clinically acceptable relapse without any significant difference, further confirming LF I to be a stable procedure based on these factors. However, certain directions of movement showed more relapse than others, thereby, providing surgeons with the ability to alter the treatment plan and improve the decision-making process when considering the multiplicity of movements.

In article 4, the 3D skeletal relapse of the proximal and distal segments were assessed in 100 consecutive patients at a period of 1 year following isolated BSSO advancement and patient- and surgery related factors were also investigated. The previous evidence mostly focused on the 3D condylar changes or 2D relapse, therefore, the following study was a step forward for better understanding the true 3D relapse of the isolated BSSO advancement surgery. The distal segment significantly relapsed in a posteroinferior direction. This migration of the distal segment at follow-up could be attributed to the pull-back of the supra-hyoid musculature, soft tissue tension or the adaptation of the proximal segment.[25-27] Previous studies have suggested a cut-off point of 7mm for the distal segment advancement which offers higher stability compared to larger movements and have recommended to opt for distraction osteogenesis beyond the 7mm point. [28] However, this limit was based on 2D methodologies which are prone to error and do not offer a detailed 3D information of the translational and rotational parameters. Therefore, in this study we also attempted to confirm this point. Overall, a positive correlation existed irrespective of the amount of movement which was in accordance with other studies.[29-33] Based on the 7mm cut-off point, the patients undergoing >7mm advancement showed a slightly higher correlation than that of ≤7mm between the amount of movement and relapse, nevertheless, we could not observe a strong correlation. At the same instance, the patients undergoing >7mm advancement showed a clinically significant relapse of the distal segment. Thereby, suggesting that the treatment planning should be altered to counter the relapse, however these findings should be confirmed in future studies due to the less number of patients in the high advancement group. As for the rotational parameters of the distal segment, only CCW pitch movement showed a significantly higher relapse in a CW direction. This relapse could have been due to the fact that the CCW pitch movement causes the pterygo-masseteric sling and supra-hyoid muscles to elongate which produces tension in the regional soft tissue, thereby leading to a physiological recoil of the segment towards its original position.[34] One of the key factors influencing the stability of the BSSO advancement surgery is the control of the proximal segments. If the proximal segment is not controlled and moved beyond the physiological limit, it can lead to condylar resorption and in return relapse of the distal segment.[35] Our findings suggested a minimal movement of the proximal segment from both the translational and rotational perspective confirming its control immediately following surgery. At follow-up, it relapsed back due to the tension produced from the altered muscular orientation in a medio-posterior and superior direction and rotated in a CW pitch, CW roll and CCW yaw direction, confirming its relapse to the original position. The main contributory musculature responsible for proximal segment relapse include masseter, medial pterygoid and temporalis muscles which observe shortening at follow-up leading to relapse.[36,37] As for the age and sex of the patient, no significant differences were observed which was also consistent with other studies. The main limitation associated with the study included failure to assess condylar changes or remodeling and soft tissue relapse and their influence on skeletal relapse. Future studies should focus on these aspects as well to provide a better understanding behind the physiology of relapse.

There has been a lack of prospective evidence related to the airway changes which occur following isolated BSSO advancement surgery in a large homogenous group of patients and whether the skeletal relapse is correlated with the airway changes at a follow-up period of 1 year or more. Therefore **in article 5**, we aimed to three-dimensionally evaluate the volume, surface area and minimum cross-sectional area (mCSA) of pharyngeal airway space (PAS) at a follow-up of 1 year following isolated BSSO advancement surgery and investigated the relationship between skeletal and airway movement and relapse. Based on our findings, an increase in all airway parameters was observed immediately after surgery. This could be attributed to the supero-anterior movement of the hyoid bone and stretching of the supra- and infra-hyoid musculature following mandibular advancement.[38] The immediate changes were more prominent in the oro- and hypo-phayngeal region showing maximal expansion with increased volume and surface area. This might have occurred due to the tension produced in the genioglossus and geniohyoid muscles originating from the mental spine and pharyngeal dilators.[39] Additionally palatoglossus muscle stretch could have further expanded the orophryngeal region.[40] Even though no maxillary intervention was performed, still a minimal increase in naso-pharyngeal airway dimensions was observed. As BSSO advancement also has the ability to put tension onto the soft palate region and posterior pharyngeal region though the stretching of the palatopharyngeal muscles, which could explain the change in naso-pharyngeal dimensions.[2,41] At follow-up of 1 year, the total PAS showed a minimal relapse of only 4% which was also consistent with the findings of Kochar et al.[42] where the authors applied acoustic pharyngometry for assessing airway relapse following

mandibular advancement at a time-point of 1 year . Additionally when dividing the PAS into naso-, oro- and hypophayrngeal regions, the volume and surface area showed a minimal relapse between the range of -2 to 6%, confirming the stability of PAS following BSSO advancement.
As for the mCSA, its increase varied with every patient independent of the amount of movement, as patients with the same amount of movement showed different amount of mCSA increase confirming that prediction of mCSA increase following the same magnitude of advancement is not possible. The increase in mCSA has been associated with the tension produced in the suprahyoid and velopharyngeal musculature,[43,44] which at the time-point of 1year intended to return to its original position and resulted in a non-significant relapse of -15%. Additionally when correlating our findings with that of the amount of skeletal movement and relapse, a negligible to weak correlation existed for all PAS parameters which was in accordance to the available evidence.[45] We found BSSO to be a stable procedure for expanding and maintaining the PAS at follow-up, thereby, it can act as an excellent stable option for obstructive sleep apnea patients without the concern of it relapsing. Our findings might have been slightly biased as the tongue, swallowing and breathing movements were not controlled, however a large sample size might have overcome the existing bias. At the same instance, owing to the airway's dynamic nature, future CBCT acquisition protocols should be standardized for airway capture and with the current advances in CBCT devices offering faster acquisition time, the control of these parameters would become systematically practicable in near future. As for the choice of software, no standard has been established. Apart from Invivo Anatomage, multiple alternative software programs exist in the market allowing volumetric and mCSA analysis such as Romexis software (Planmeca, Helsinki, Finland), Dolphin 3D, Ondemand3D and Mimics Research (Materialise, Leuven, Belgium). The choice of the software application mainly depends on its availability and the operator's discretion. However, we recommend testing the reliability and accuracy of these software programs even if these have been validated before, as the CBCT acquisition parameters might influence the outcome.

As observed in the previous articles, the late skeletal relapse varies with different procedures, with some having higher relapse than others. One may hypothesize that controlling early relapse factors can further stabilize the maxillary and/or mandibular osteotomized segments. If a real-life sized patient-specific skeletal model offering accuracy and quality to that real bone can be modelled, then it can allow simulating the surgical procedure and figuring out some of the risk factors of relapse. For instance, when performing orthognathic surgery on a model, bony interferences and movement of the proximal segment can be visualized and corrected in a simulation, thereby, improving the skeletal stability. Considering these factors and to lay a platform for future research, **in article 6,** we first opted to observe the quantitative accuracy of skeletal models using state-of-the-art medical printers with different printing technologies. Based on our findings, the multijet (MJ) was the best for replicating trabecular structures which was consistent with a previous study showing better anatomical reproducibility compared to other technologies.[46] The fused deposition modelling (FDM) technology based models showed the most error for printing fine trabecular structures, which might have resulted due to the warping deformation and shrinkage of the material at the stage of thermoplastic cooling phase.[47] Our findings were consistent with other studies which also showed inadequacy of FDM printers for printing fine structures.[48,49] As for the selective laser sintering (SLS), post-processing with airborne-particle abrasion might have led to the wearing of the trabecular structures.[50] At the same instance, none of the printers was able to offer a completely accurate replication of the trabecular structures. Although all models showed an accurate depiction of buccal and lingual cortical surfaces, nevertheless, multijet (MJ), colorjet (CJ) and SLS showed the highest overall accuracy.

Even though the quantitative accuracy of models is important from the aspect of plate bending or surgical guide manufacturing in orthognathic surgery, however it is still unknown whether these models can offer maxillofacial surgeons with a replica of patients skeletal structures for optimally performing model surgery as that on a real patient, thereby allowing a more controlled osteotomy intra-operatively with a less chance of inaccurate skeletal repositioning and early relapse. **In article 7**, we assessed the anatomical and tactile perceptibility of high-end 3D printed skeletal models to observe whether the latest medical printers which commercially offer bone-like printing properties for simulating skeletal surgical procedures could be applied in orthognathic surgery. A questionnaire was designed to assess the anatomical quality and surgical feedback of the models for performing bone osteotomy in the mandibular region. In relation to texture to that of real bone, it was either influenced by the technology or the material. The DLP printer offered the highest score for replicating texture due to its smoother bone-like finish compared to other printing technologies, whereas, SLA and DLP based models showed the least scoring due to the presence of stepping effect which has been a known disadvantage of some of these technology-based printers.[51-54] As for the CJ-based model, the gypsum-like material failed to produce the texture to that of real bone. At the same instance, none of the printers with different technologies and materials were well able to replicate the texture. For the cortical replication, all models showed good replication except SLA and FDM- based models, which might have occurred due to the longer postpolymerization process of SLA printer which can distort the model and stepping effect observed with the FDM-based model.[55-57] Unlike MJ printer which uses high-water pressure for post-processing that can lead to fracturing of the fine structures, the trabecular structure was best replicated with DLP and CJ- based models as these models were processed using alcohol bath and compressed air only.

The haptic feedback of the models varied for all the steps i.e. tactile sensation of performing osteotomy, drilling for screw insertion, screw insertion and screw removal. Based on our findings, CJ printer with gypsum-like material offered the best scoring for performing osteotomy cuts and a low scoring for drilling holes. A variability was observed when compared with another study which performed endoscopic skull base surgery using the same material and found the same material optimal for drilling.[58] This can be explained as the mechanical properties of skull differs from that of a mandible and the printer was unable to replicate an optimal haptic feedback for drilling. When considering the comparison based on the material, the nylon-like material was least favorable for the surgical simulation, whereas, acrylonitrile butadiene styrene (ABS) based model offered an optimal haptic feedback. This was in accordance with another study that also found properties of nylon to be unreliable for performing mastoidectomy and improved haptic feedback with ABS-like material.[59] Overall, SLA, MJ and DLP models offered the most optimal haptic feedback. Although studies have already been carried out in the fields of sinus lift/implantology and some other craniomaxillofacial surgery procedures[60], a lack of evidence exists performing orthognathic surgery utilizing different technologies. The findings within this study might allow further optimization of the printing process to enable replication of an anatomical and haptic bone model to be utilized for various applications in orthognathic surgery, with the main future applications being the simulation of surgical procedure to observe patient-specific and surgery-related early risk factors leading to relapse and also for modifying already present surgical techniques.

Conclusions

Following conclusions can be drawn from the thesis,

- Voxel-based dental arch regional registration following anterior cranial base registration offers an accurate, reliable and time-efficient approach for assessing skeletal relapse at both short- and long term follow-up following conventional LF I and BSSO surgery. It is a more accurate alternative as compared to other 2D and 3D counterparts where the landmark detection and threshold selection for segmentation are influenced by the human factor.
- Single piece LF I maxillary advancement with either superior or inferior repositioning in both skeletal class II and III patients offer high post-treatment skeletal stability, however superior impaction is more stable compared to the inferior repositioning at a long-term follow-up.
- Isolated BSSO advancement surgery offers optimal post-surgical translational and rotational skeletal stability at a period of 1 year, however, once the magnitude of anterior advancement of the distal segment is increased, the relapse in posterior direction also increases. As for the proximal segments, they intend to revert back to their original position and a reduction in flaring is observed.
- Isolated BSSO advancement causes a significant increase in the airway volume, surface area and constriction area, where maximum expansion is observed in the oro-pharyngeal region immediately following surgery. The expanded airway remained stable at the follow-up time-point of 1 year, thereby, BSSO advancement can be regarded as a stable procedure when widening of the airway volume and surface area is required such as in obstructive sleep apnea patients.
- Advancements in 3D printing technology have led to achieve a quantitatively accurate model for the replication of cortical bone, however, still the ability of the medical printers is not up to par for printing trabecular architecture. At the same instance, shortcomings are present for printing a patient-specific skeletal model offering color and texture to that of real bone. As for the haptic feedback for performing orthognathic surgery, limitations also exist for the medical printers. Further studies in improving the anatomical and surgical quality of the skeletal models may allow their application in a better understanding and refinement of the various surgical techniques by simulating on models before performing real surgery, enabling to guide the surgeon to help in decision-making where surgery-related early relapse factors can be controlled and the treatment planning can be further optimized.

Clinical relevance

The findings of the current PhD project provides oral and maxillofacial surgeons with the information related to the true 3D skeletal relapse which has been lacking in the literature. Clinically the protocol validated in this study based on voxel-based registration of the dental arch can not only assess translational and rotational relapse but also improve surgical technique by providing accuracy of the achieved skeletal repositioning versus planned ones. The relapse evidence collected in the thesis can guide surgeons in making patient-specific treatment plans and can further improve the decision-making process. For instance patients undergoing inferior LF I maxillary repositioning or larger magnitude of BSSO advancement are more prone to higher degree of relapse, thereby, considering the translational and rotational relapse of the maxillary and mandibular segments mentioned in the thesis can guide the surgeons to adjust the planning accordingly which can further improve the surgical outcome. Also, if isolated BSSO advancement is planned with the secondary objective being the improvement of the airway collapsibility so better airway resistance can be offered. In such a scenario, it should be kept in mind that it is difficult to predict the minimal cross-sectional airway area change just based on the amount of mandibular advancement, as patients with the same amount of movement showed variable change in the cross-sectional area.

Additionally, based on the findings of the thesis, skeletal relapse is prone to happen at 1-2 years of follow-up. So controlling certain surgery-specific early relapse risk factors should be considered such as condylar displacement, cutting accuracy or premature bone contact areas. We laid a platform on the accuracy and visuo-haptic feedback of patient-specific skeletal models which can act as a base for future research in simulating realistic orthognathic surgery. We are still not at the peak of technological advancements where 3D printers can replicate a real bone from both anatomical and haptic perspective. However, looking at the positive side, these models do offer some amount of replication to be considered for simulating surgery, modifying current surgical approaches and creating new ones.

Future recommendations

- With the technological advancements and also 3D imaging becoming a norm in orthognathic surgery, facial soft tissue and dental changes, condylar remodelling/resorption, occlusal and muscular forces, physiological changes, type of fixation and their relationship with skeletal relapse should be assessed to help clinicians reach a better clinical decision.
- An improved understanding of the difference between bone relapse and remodeling is also crucial to observe whether a relationship exists between the two entities. The relapse refers to the positional displacement of the skeletal structure at follow-up and future studies should focus on assessing these displacements utilizing the 6DoF methodology proposed in this thesis to reach a better clinical decision. Furthermore, bone remodeling which refers to adaptation of the bone due to the coordinated actions of osteoclasts and osteoblasts, should be assessed to observe whether a correlation exists between remodeling and relapse. For the evaluation of bone remodeling, 3D shape and volumetric analysis of the skeletal structures should be performed.
- The post-operative soft tissue should be analysed using stereophotogrammetric acquisition devices with a standardized protocol, starting from a time-point when the soft tissue edema has subsided.
- The role of the adaptation of surgical techniques (muscle de-attachment, periosteal elevation) or changes in the choice of osteotomies (mono- or bimaxillary intervention or axis of rotation) on surgical relapse should be evaluated.
- The influence of surgical relapse on patients' perception and quality of life should also be studied.
- The findings in this thesis may allow future comparative studies to observe which surgical technique offers higher post-surgical or treatment stability and allow refinement of the current surgical techniques by simulation on 3D printed life-sized models.
- The role of different ethnic groups and facial types on relapse should also be studied, thereby, allowing a patient-specific treatment planning rather than a conventional plan for all patients.
- The influence of different types of fixation techniques on the long-term 3D stability of orthognathic surgery procedures needs to be investigated.
- The hierarchy of surgical stability and predictability of different orthognathic procedures needs to be revisited and revised based on the 3D methodologies.

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Summary

Orthognathic surgery is considered to be a cornerstone for surgically treating dentofacial deformities. It is associated with unwanted skeletal or soft tissue relapse over time. The evidence related to hierarchy of orthognathic surgery stability has been mostly based on 2D or non-standardized evaluation methods. The 2D assessment of skeletal change has almost become obsolete as it provides limited subjective information of 3D maxillofacial structures which can influence treatment planning and post-surgical outcome evaluation.[4] Similarly, cone-beam computed tomography (CBCT) based 3D cephalometry also poses the issue of human error. Recently, remarkable advancements have been achieved in the development of 3D software programs allowing assessment of the true 3D translational and rotational skeletal relapse. At the same instance, the 3D printing industry has also shown a sudden boom and has evolved in the medical industry. We believe that a research gap exists related to the true 3D aspect of relapse following orthognathic surgery procedures. Based on the lack of prospective 3D-based evidence, the overreaching aim of the PhD project was twofold: 1. To assess 3D skeletal and pharyngeal airway space relapse following orthognathic surgery and, 2. To observe whether 3D printed patient-specific skeletal models can offer a realistic replication to enable surgeons in future studies to control certain risk factors of early skeletal relapse optimally. The outcomes of this thesis can further guide surgeons to plan and modify their treatment strategy according to a more patient-specific approach.

In **Articles 1-2**, we aimed to validate a methodology for assessing skeletal relapse following orthognathic surgery at a short- and long-term follow-up period. The methodology utilized a landmark-free CBCT-based translational and rotational assessment of relapse to overcome the limitations associated with already present 2D and 3D landmark-based protocols. Additionally voxel-based registration was applied for the superimposition of scans. The methodology was found to be reliable, user-friendly and time-efficient for evaluating relapse, hence allowing to improve the standards in orthognathic surgery.

Subsequently, in **Article 3**, we utilized the validated tool for assessing skeletal relapse in 50 patients undergoing single-piece Le Fort I (LF I) maxillary advancement with superior or inferior repositioning at a two years follow-up period. LF I maxillary advancement was found to be a highly stable procedure without any clinically significant relapse in both skeletal class II and III patients up to 2 years follow-up. Bone grafting showed no significant influence on stability. However, a lack of superoinferior stability was observed in patients undergoing maxillary advancement with inferior repositioning as compared to superior repositioning.

In **Article 4**, the skeletal relapse of distal and proximal segments was assessed following isolated bilateral sagittal split osteotomy (BSSO) advancement surgery in 100 consecutive patients. The distal segment revealed a significant relapse in posterior, inferior and CW pitch directions. The proximal segments torqued towards their original position with a reduction of flaring. Overall, both distal and

proximal bone segments showed a clinically acceptable translational and rotational stability. However, larger advancements showed a higher amount of relapse in a posterior direction which crossed the clinical acceptable limit of 2mm. Thereby, these relapses should be included in the treatment planning phase so a patient-specific plan could be designed allowing a further improvement of the decision-making process.

Subsequently in **Article 5**, we aimed to three-dimensionally evaluate the volume, surface area and minimum cross-sectional area (mCSA) of pharyngeal airway space (PAS) at a follow-up of 1 year following isolated BSSO advancement surgery and investigated the relationship between skeletal and airway relapse. Both volumetric and surface area showed a relapse of less than 7% for all sub-regions of the airway, whereas, mCSA showed a non-significant relapse of -15% at long-term follow-up. Based on our findings, BSSO advancement surgery could be regarded as a stable procedure for widening of the PAS with maintenance of the positive space at follow-up.

In **Articles 6 and 7** we aimed to assess the accuracy and visuo-haptic feedback of 3D patient-specific skeletal models for performing orthognathic surgery. The models were generated from medical printers utilizing different technology which offered bone-like printing properties. All models showed an accurate depiction of buccal and lingual cortical surfaces, whereas, shortcomings were observed for replicating the trabecular structures. At the same instance, deficiencies were observed for printing a patient-specific skeletal model offering color and texture to that of real bone. As for the haptic feedback for performing BSSO surgery, none of the printers was able to offer a realistic osteotomy procedure simulation. These two articles laid a platform for future studies for improving the anatomical and surgical simulation quality of the skeletal models, printing parameters and material selection. This in turn might allow a better understanding and refinement of the various surgical techniques and offer surgeons a realistic approach to observe certain relapse factors such as bony interferences and condylar displacement beforehand for improving the surgical stability.

The findings of this doctoral thesis showed that 3D assessment of relapse and patient-specific 3D modelling may allow a more careful treatment planning allowing to further improve the surgical outcome and enhance the decision-making process.

Samenvatting

Orthognatische chirurgie wordt beschouwd als een hoeksteen voor de chirurgische behandeling van dentofaciale misvormingen. Het wordt geassocieerd met een ongewenste terugval van het skelet of de weke delen in de loop van de tijd. Het bewijs met betrekking tot de hiërarchie van de stabiliteit van orthognatische chirurgie is grotendeels gebaseerd op 2D of niet-gestandaardiseerde evaluatiemethoden. De 2D-beoordeling van skeletale veranderingen is bijna achterhaald omdat het meer subjectieve en onvolledige informatie biedt over ruimtelijke maxillofaciale structuren, die behandelplanning en postoperatieve uitkomstevaluatie kunnen beïnvloeden. Maar zelfs bij 3D-cefalometrie blijven menselijke inschattingsfouten mogelijk. Recente vooruitgang bij de ontwikkeling van 3D-software maken het mogelijk om het werkelijke 3D translationele en roterende skeletaal recidief te beoordelen. Tegelijkertijd heeft de 3D-printtechnologie een hoge vlucht gekend met uitgebreide toepassingen in de medische industrie. Wij zijn van mening dat er tot op heden te weinig evidentie is om het werkelijke 3D-aspect van orthognatische recidief te beoordelen. Bij gebrek aan prospectieve , op 3D-gebaseerde evidentie, was het overkoepelende doel van het doctoraatsproject om 3D-recidief van skeletale en faryngeale luchtwegruimte na orthognatische chirurgie te beoordelen. Daarnaast werd getracht om te observeren of 3D-geprinte patiënt-specifieke skeletmodellen een realistische replicatie kunnen bieden om chirurgen in staat te stellen in toekomstige studies om bepaalde risicofactoren van vroege skeletale terugval optimaal te controleren. De resultaten van dit proefschrift kunnen voor chirurgen een hulp betekenen bij het plannen en aanpassen van hun behandelplanning.
In **artikel 1 en 2** werd de methodologie gevalideerd voor het beoordelen van skeletaal recidief na orthognatische chirurgie bij zowel korte als lange termijn follow-up. De methodologie maakte gebruik van een landmark-vrije CBCT-gebaseerde translationele en roterende beoordeling van recidief om zo de beperkingen te overwinnen van bestaande 2D- en 3D-landmark-gebaseerde protocollen. Daarnaast werd op voxel-gebaseerde registratie toegepast voor de superpositie van scans. De methodologie bleek betrouwbaar, gebruiksvriendelijk en tijdbesparend voor evaluatie van recidief en aldus optimalisatie van orthognatische chirurgie.
Vervolgens hebben we in **artikel 3** de gevalideerde tool gebruikt voor het beoordelen van skeletaal recidief bij 50 patiënten die een eendelige Le Fort I (LF I) maxillaire voorwaartse verplaatsing van de bovenkaak ondergingen (met superieure of inferieure herpositionering) en zulks na een follow-up periode van twee jaar. LF I maxillaire voorwaartse verplaatsing bleek een zeer stabiele procedure te zijn zonder enig klinisch significant recidief bij zowel skeletale klasse II als III patiënten tot 2 jaar follow-up. Bottransplantatie had geen significante invloed op de stabiliteit. Een gebrek aan stabiliteit werd waargenomen bij patiënten die een voorwaartse verplaatsing van de bovenkaak ondergingen met benedenwaartse herpositionering, in vergelijking met bovenwaartse herpositionering.
In **artikel 4** werd de terugval van het skelet van distale en proximale segmenten beoordeeld na geïsoleerde bilaterale sagittale splijtingsosteotomie (BSSO) voorwaartse verplaatsing bij 100 consecutieve patiënten. Het distale segment vertoonde een significante terugval in een posterieure, inferieure en benedenwaartse

richting. De proximale segmenten werden naar hun oorspronkelijke positie gedraaid met een afname van de divergentie. Over het algemeen vertoonden zowel distale als proximale botsegmenten een klinisch aanvaardbare translatie- en rotationele stabiliteit. Bij grotere voorwaartse bewegingen was er echter een grotere mate van terugval in posterieure richting die de klinisch aanvaardbare limiet van 2 mm overschreed. In de behandelplanningsfase moet met deze recidieven rekening worden gehouden, zodat een patiënt-specifiek plan kan worden opgesteld met betere besluitvorming.
In **artikel 5**, hebben we ons vervolgens gericht op een driedimensionale evaluatie van volume, oppervlak en de minimale dwarsdoorsnede (mCSA) van de pharyngeale luchtwegruimte (PAS) bij een follow-up van 1 jaar na geïsoleerde BSSO-ingreep met voorwaartse verplaatsing van de onderkaak. Tegelijk onderzochten we de relatie tussen skeletaal recidief en winst in dimensie ter hoogte van de luchtweg. Zowel het volume als het oppervlak vertoonden een terugval van minder dan 7% voor alle subregio's van de luchtwegen, terwijl mCSA een niet-significante terugval van -15% vertoonde bij langdurige follow-up. Op basis van onze bevindingen kan BSSO-ingreep met voorwaartse verplaatsing van de onderkaak worden beschouwd als een stabiele procedure voor het verbreden van de PAS met behoud van de positieve ruimte bij follow-up.
De verdere **artikel 6 en 7** hadden als doel een platform te vormen voor toekomstige studies ter verbetering van de anatomische en chirurgische simulatiekwaliteit van de skeletmodellen, afdrukparameters en materiaalkeuze. Daartoe hebben we ons gericht op het beoordelen van de nauwkeurigheid en visuo-haptische feedback van 3D patiënt-specifieke skeletmodellen voor het uitvoeren van orthognatische chirurgie. De modellen werden gegenereerd met medische printers gebruikmakend van verschillende technologieën die botachtige afdrukeigenschappen bieden. Alle modellen vertoonden een nauwkeurige weergave van buccale en linguale botplaat, terwijl tekortkomingen werden waargenomen bij het repliceren van de trabeculaire botstructuren. Tegelijkertijd werden tekortkomingen waargenomen bij het afdrukken van een patiënt-specifiek skeletmodel dat kleur en textuur aan zou moeten bieden van echt bot. Wat betreft de haptische feedback voor het uitvoeren van BSSO-chirurgie, was geen van de printers in staat om een realistische simulatie van de osteotomieprocedure te bieden. Deze bevindingen laten toe de verschillende chirurgische technieken te verfijnen en chirurgen een realistische benadering te bieden om bepaalde recidief uitlokkende factoren zoals botinterferenties en condylaire verplaatsing vooraf te observeren en te simuleren in een 3D-omgeving om zo te trachten de chirurgische stabiliteit te verbeteren.
De bevindingen van dit proefschrift tonen aan dat 3D-beoordeling van recidief en patiënt-specifieke 3D-modellering een meer zorgvuldige aanpak van de behandelplanning mogelijk maken in de hoop zo de planning én het chirurgische resultaat te verbeteren.

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PERSONAL CONTRIBUTIONS

The author, Sohaib Shujaat, devised the projects, the main conceptual ideas, collected patients clinical and radiological data, performed the experiments, analysed data and took the lead in writing the (peer-reviewed) manuscripts with scientific support from his promoter Prof. dr. Reinhilde Jacobs and co-promoters, Prof. Constantinus Politis and Dr. Eman Shaheen. Sohaib Shujaat is the first author of all of the thesis articles and corresponding research papers, except for Article 1, of which he is the second author. The project in Article 1 and was conceived before he started his PhD at the OMFS-IMPATH Research Group and later on was transferred and adapted to his PhD topic at the stage of data collection.

CONFLICTS OF INTEREST

The author, Sohaib Shujaat, has no conflicts of interest to declare with respect to publication of this work.

CURRICULUM VITAE

Sohaib Shujaat was born on November 29th, 1985. In 2008, he achieved his degree in Bachelor of Dental Surgery (B.D.S) from Lahore Medical and Dental College, Lahore, Pakistan. After his graduation, he worked as an Internee in all clinical departments of Dentistry at Lahore Medical and Dental College, Lahore, Pakistan. He obtained his “Master of Science” (MSc. Dent Sci) degree in Oral and Maxillofacial Surgery (360 credits) with merit from Glasgow Dental School and Hospital, University of Glasgow, Glasgow, United Kingdom. During his Masters, he worked on 4-dimensional facial soft tissue changes in oncology patients. From March 2013 till September 2017, he worked as a Lecturer in the Department of Oral and Maxillofacial Surgery and Course Director of Internal Medicine and Comprehensive Patient Management for dental students at Imam AbdulRahman Bin Faisal University (Formerly University of Dammam), Dammam, Kingdom of Saudi Arabia. At the same instance, he served as a Specialist (Registrar) in the Department of Oral and Maxillofacial Surgery, King Fahd Hospital of the University. He worked as a Medical (Scientific) Editor, Substitute Lecturer in Postgraduate advanced medical imaging; hot topics medical imaging II course, and a Mentor for Master and PhD students at KU/UZ Leuven, Belgium (2017-2021). He was a PhD researcher in the OMFS-IMPATH research group from September 2017 till June 2021 with Prof. dr. Reinhilde Jacobs as his scientific promoter (Department Imaging and Pathology, Faculty of Medicine, KU Leuven). His research topic for PhD was focused towards the three-dimensional (3D) relapse in orthognathic surgery patients and latest advancements in 3D printing.

List of Publications

Publications part of the PhD thesis:

*Shaheen E, **Shujaat S**, Saeed T, Jacobs R, Politis C. Three-dimensional planning accuracy and follow-up protocol in orthognathic surgery: a validation study. International Journal of Oral and Maxillofacial Surgery . 2019 Jan 1;48(1):71-6. (shared first-authorship)*

***Shujaat S**, Shaheen E, Politis C, Jacobs R. Accuracy and reliability of voxel-based dento-alveolar registration (VDAR) in orthognathic surgery patients: a pilot study with two years follow-up. British Journal of Oral and Maxillofacial Surgery. 2020 Aug 19.*

***Shujaat S**, Shaheen E, Politis C, Jacobs R. Three dimensional evaluation of long-term skeletal relapse following Le Fort I maxillary advancement surgery. A 2 year follow-up study. International Journal of Oral and Maxillofacial Surgery. 2021 (accepted)*

***Shujaat S**, Shaheen E, Politis C, Jacobs R. Three dimensional evaluation of distal and proximal segments skeletal relapse following isolated mandibular advancement surgery in 100 consecutive patients. A one-year follow-up study. International Journal of Oral and Maxillofacial Surgery. 2021 (accepted)*

***Shujaat S**, Shaheen E, Novillo F, Politis C, Jacobs R. Accuracy of cone beam computed tomography–derived casts: A comparative study. The Journal of Prosthetic Dentistry. 2021 Jan 1;125(1):95-102.*

***Shujaat S**, Da Costa Senior O, Shaheen E, Politis C, Jacobs R. Visual and haptic perceptibility of 3D printed skeletal models in orthognathic surgery. J Dent. (Accepted)*

Other publications in the field

1. **Shujaat S**, Jazil O, Willems H, Van Gerven A, Shaheen E, Politis C, Jacobs R. Automatic segmentation of the pharyngeal airway space with convolutional neural network. J Dent 2021.
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Contributions to (inter)national conferences

28-01-2021- *Accuracy of cone beam computed tomography-derived casts*, Symposium on 3D Printing in Medicine, Germany (Oral presentation)

17-12-2020- *3D printing workflow. Is AI the missing link?*, 3D Printing in Medicine Symposium, Ankara University, Ankara, Turkey (Oral presentation)

03-10-2019- *Quantitative accuracy of cone-beam computerised tomography (CBCT) derived biomodels*, International Digital Dentistry Society World Congress, Baden Baden, Germany (Poster)

22-08-2019- *Can CBCT-derived biomodels replicate skeletal anatomy accurately?* A comparative study, 22nd International Congress of Dentomaxillofacial Radiology, Philadelphia, USA (Oral presentation)

30-01-2019- *3D bone-like printing*, 3D Medical Printing Conference, Maastricht, Netherlands (Oral presentation)

06-09-2014- *4D imaging for the diagnosis and management of oro-facial deformities*, 5th Triennial International Congress of the ADT Foundation, Beijing, China (Poster)

15-11-2013- *The feasibility of applying three-dimensional motion imaging in head and neck oncology patients. A pilot study*, 3D User Group Meeting, British Orthodontic society, London, UK (Oral presentation)

23-10-2013- *The clinical application of three-dimensional motion capture (4D): A novel approach to quantify the dynamics of facial animations*, 21st International Conference on Oral and Maxillofacial Surgery (ICOMS), Barcelona, Spain (Oral presentation)

25-10-2012- *Four dimensional imaging in head and neck oncology patients*, Scottish Oral and Maxillofacial Surgery Meeting (SOMS), Royal College of Physicians, Edinburgh, UK (Oral presentation)

31-03-2012-*Three dimensional (3D) motion analysis of facial expressions in oral cancer patients: A pilot study*, Second 3D Bologna International Symposium and Workshop, Bologna, Italy (Poster)

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Orthognathic surgery is considered to be a cornerstone for surgically treating dentofacial deformities. It is associated with unwanted relapse over time. The evidence related to hierarchy of orthognathic surgery stability has been mostly based on 2D methodologies and lack of true 3D-based prospective evidence exists. This doctoral thesis aimed to assess the 3D skeletal and pharyngeal airway space relapse following orthognathic surgery and to observe whether 3D printed patient-specific skeletal models can offer a realistic bone replication. The outcomes of this thesis could allow a more careful treatment planning and application of patient-specific skeletal models could act as an *in vitro* surgical medium to control the early relapse risk factors and improve classical surgical techniques.

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