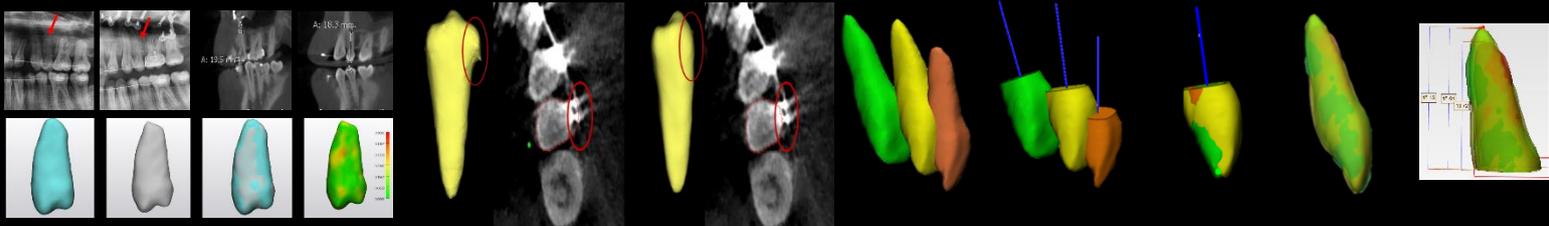


THREE-DIMENSIONAL EVALUATION OF ROOT RESORPTION AFTER MAXILLARY ORTHOGNATHIC SURGERY

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

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DRIEDIMENSIONALE EVALUATIE VAN WORTELRESORPTIE NA MAXILLAIRE ORTHOGNATISCHE CHIRURGIE

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Proefschrift voorgedragen tot het
behalen van de graad van Doctor in
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Preface

This doctoral thesis consists of 2 parts preceded by a general introduction and concluded by a general discussion and conclusion. The research articles follow the standard scientific IMRD structure (Introduction, Methods, Results and Discussion), and were based on the following peer-reviewed publications:

- **General Introduction, Aims and Hypotheses**

- **Part 1: Technical**

Article 1

Alqahtani KA, Shaheen E, Morgan N, Shujaat S, Politis C, Jacobs R. Impact of orthognathic surgery on root resorption: A systematic review. *J Stomatol Oral Maxillofac Surg.* 2022;123(5):e260-e267. doi:10.1016/j.jormas.2022.04.010

Article 2

Shaheen E, Leite A, **Alqahtani KA**, Smolders A, van Gerven A, Willems H, et al. A novel deep learning system for multi-class tooth segmentation and classification on cone-beam computed-tomography. A validation study. *J Dent.* 2021;115:103865. doi:10.1016/j.jdent.2021.103865

Article 3

Alqahtani KA, Jacobs R, Smolders A, Van Gerven A, Willems H, Shujaat S, Shaheen E. Deep convolutional neural network-based automated segmentation and classification of teeth with orthodontic brackets on cone-beam computed-tomographic images: a validation study. *Eur J Orthod.* 2023;45(2):169-174. doi:10.1093/ejo/cjac047

Article 4

Alqahtani KA, Jacobs R, Shujaat S, Politis C, Shaheen E. Automated three-dimensional quantification of I root changes following combined orthodontic-orthognathic surgical treatment. A validation study. *J Stomatol Oral Maxillofac Surg*, 2022,ISSN 2468-7855,https://doi.org/10.1016/j.jormas.2022.09.010.

- **Part 2: Clinical**

- Article 5**

- Alqahtani KA**, Shaheen E, Politis C, Jacobs R. Three-dimensional (3D) assessment of volumetric and morphological root changes after Le Fort I osteotomy. *Int J Oral Maxillofac Surg.* (Under-review)

- Article 6**

- Alqahtani KA**, Shaheen E, Oliver Da Costa Senior, Politis C, Jacobs R. Three-dimensional (3D) assessment of volumetric and morphological root changes after multi-pieces Le Fort I osteotomy. *J Craniomaxillofac Surg.* (Under-review)

- Article 7**

- Alqahtani KA**, Jacobs R, Oliver Da Costa Senior, Politis C, Shaheen E. Recommendations to minimize tooth root remodeling in patients undergoing maxillary osteotomies. *Scientific reports.* (Under-review)

- **General discussion, conclusions and future perspectives**

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‘No two things have been combined better than knowledge and patience’

Prophet Muhammad (peace be upon him)

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List of abbreviations

2D	Two-Dimensional
2-pieces	Two-pieces
3D	Three-Dimensional
3-pieces	Three-pieces
AI	Artificial Intelligence
APV	Apical Part Volume
BSSO	Bilateral Sagittal Split Osteotomy
CBCT	Cone-Beam Computed Tomography
CT	Computed Tomography
CNN	Convolutional Neural Network
CPV	Coronal Part Volume
DICOM	Digital Imaging and Communications in Medicine
DSC	Dice Similarity Coefficient
EIR	External Inflammatory Resorption
ECR	External Cervical Resorption
ERR	External Replacement Resorption
IIRR	Internal Inflammatory Root Resorption
FoV	Field of View
HD	Hausdorff distance
ICC	Intraclass Correlation Coefficient
LF I	Le Fort I
IoU	Intersection over Union
LORTHOG	Leuven Orthognathic data
MP-LFI	Multi-Pieces Le Fort I
MPV	Middle Part Volume
OP-LFI	One-Piece Le Fort I
RCT	Randomized Controlled Trials
RE	Root Remodeling

ReLU	Rectified Linear Unit
RL	Root Length
RoI	Region of Interest
RS	Root Resorption
ROBINS-I	Risk Of Bias In-randomized Studies-of Interventions
RoB 2 tool	Revised tool for Risk of Bias in randomized trials
STL	Standard Tessellation Language
SARPE	Surgical Assisted Rapid Palatal Expansion
SARME	Surgical Assisted Rapid Maxillary Expansion
TRV	Total Root Volume

General Introduction, Aims & Hypotheses

1. Orthognathic surgery

Orthognathic surgery involves various clinical techniques aimed at correcting jaw deformities and improving facial aesthetics and function (1,2). These techniques include Le Fort I osteotomy, bilateral sagittal split osteotomy (BSSO), and surgical assisted rapid palatal expansion (SARPE) (3,4). Le Fort I osteotomy involves a horizontal cut above the upper teeth to allow moving the entire maxilla forward, backward, or sideways to correct upper jaw deformities such as an open bite, crossbite, or significant protrusion (5). BSSO, on the other hand, is a technique used to address lower jaw deformities, where vertical cuts are made on both sides of the mandible, allowing the jaw to be displaced forward, backward or rotational movements. This technique is often used to treat protruded mandibles, or a significantly retruded lower jaw (6). SARPE is a type of orthognathic surgery that is used to correct narrow upper jaw. During the SARPE procedure, the surgeon makes midline cuts in the bone of the palate and inserts a small device (called a palatal expander) that is attached to the teeth or the bone (7). The device is activated by turning a screw several times a day, which pushes the two halves of the jawbone apart, creating new bone in the gap and resulting in a wider upper jaw. This process typically takes 1-2 weeks, and the patient is closely monitored by the surgical team throughout the process.

Orthognathic surgery is typically used in cases with skeletal malocclusion where traditional orthodontic methods are insufficient to correct the discrepancy (8). It is a complex surgical procedure that requires careful planning and execution by an experienced oral and maxillofacial surgeon, and it is usually performed in combination with orthodontic treatment to achieve the best results. The choice of surgical techniques depends on the patient's specific needs and goals, and it is important that the surgeon discusses with the patient the potential risks and benefits of each clinically possible technique and carefully consider all options before making a decision (9).

2. Complications of orthognathic surgery

Orthognathic surgery, while a beneficial treatment option for correcting facial and dental abnormalities, carries the potential risk of various complications. These complications may include infection, bleeding, nerve injury, temporomandibular joint disorders, and malocclusion. Additionally, there is a possibility of relapse or insufficient correction of the skeletal deformity (10–13). Another potential concern is root remodeling and resorption, where the roots of teeth may undergo changes or resorb as a result of the surgical procedure (14–17). It is important to

consider these potential complications and address them appropriately during the treatment planning and post-operative care to ensure optimal outcomes for the patients.

3. Root remodeling

Tooth root remodeling is a complex physiological process that occurs in response to various orthodontic and orthognathic forces (18,19). It involves bone resorption and formation around the root surface, causing changes to the shape, size, and structure of the root. Root remodeling is a normal physiological response to tooth movement, allowing teeth to adapt to changes in occlusal forces and maintain proper alignment within the dental arch. However, in some cases, the remodeling process can progress to root resorption, which involves the irreversible loss of root structure (20).

4. Root resorption

Root resorption can occur due to excessive forces, trauma, or other factors, and can lead to undesirable consequences such as tooth mobility, root shortening, and even tooth loss (20,21). In recent years, the field of orthodontics has seen significant advancements in understanding the intricate interplay between bone remodeling and root resorption. Bone remodeling, a dynamic and complex physiological process, plays a pivotal role in adapting the skeletal structure to various mechanical forces and functional demands. This phenomenon involves a finely tuned balance between bone resorption by osteoclasts and bone formation by osteoblasts, allowing for the continuous renewal and adaptation of the bone tissue. Importantly, this remodeling process extends its influence beyond the immediate skeletal response, also interacting with neighboring structures like dental roots (19,20). The mechanisms underlying the conversion from root remodeling to root resorption are not yet fully understood, but it is thought to involve a complex interplay of genetic, cellular, and mechanical factors (22,23).

5. Root changes after orthognathic surgery

Root remodeling and resorption following orthognathic surgery can be influenced by various factors. The type of surgical procedure, including the magnitude and direction of maxillary advancement or expansion, can impact root remodeling (10,15,24). Patient-related factors such as age and gender can also play a role (25,26).

Some studies have suggested that orthognathic surgery can also contribute to root resorption, particularly in the teeth located in close proximity to the surgical site (27–29). During the surgical procedure, blood vessels in the surrounding tissues may be disrupted, leading to a

reduction in blood supply to the affected teeth (30–33). This reduced blood flow can result in cellular damage and inflammation, which may increase the risk of root resorption (34–36). Additionally, this may be due to the mechanical forces applied to the roots during the surgery, or as a result of the changes in occlusion and bite that occur after the surgery.

Accurate quantification and understanding the relationship between root remodeling and factors that may have an impact is crucial in clinical orthodontics and orthognathic surgery. It allows for proper treatment planning, monitoring, and management to minimize the risk of root resorption and achieve optimal treatment outcomes for patients. Therefore, further research and investigation into the complex interplay of factors involved in root remodeling and resorption are essential to improve our understanding and clinical management of these processes.

6. Root assessment methods

In the past, various subjective or linear methods have been used to assess root changes in orthodontics and orthognathic surgeries using two-dimensional (2D) and three-dimensional (3D) imaging techniques (37–40). These methods involve measurements and evaluations based on visual inspection or linear measurements of root length. In 2D imaging, such as periapical or panoramic radiographs, root resorption is often visually estimated from the radiographic images. However, these methods are subjective and may have limitations in accurately quantifying root changes due to variations in radiographic magnification, distortion and angulation (15,41–44).

Linear measurements are typically conducted by manually measuring the length of the root from the apex to the cervical margin on radiographs (41). The extent of root resorption is then determined by comparing the measurements before and after orthodontic treatment or other interventions. However, there are several limitations associated with linear measurements in root resorption assessment. One of the main limitations is the potential for measurement errors due to variations in radiographic magnification, image distortion, and subjective estimation of root length. Additionally, linear measurements do not provide information about the volumetric changes in root structure, such as root volume or surface area, which is important in quantifying the severity of root resorption or remodeling (40,45,46).

Volumetric assessment has emerged as a valuable tool in orthodontic research for evaluating root resorption and remodeling, providing a more comprehensive and accurate assessment of root changes compared to subjective or traditional linear measurements.

Despite the progress made in this field, there are still challenges that need to be addressed, such as the validation of 3D methods, standardization of protocols, and optimization for different

patient populations. However, the growing interest and ongoing research in this area indicate the potential for fully automated and objective 3D protocol to become a valuable tool in evaluating root changes after orthodontic and/or orthognathic surgery, providing more accurate and reliable assessments in the future.

7. Artificial intelligence in dentistry

Artificial intelligence (AI) in dentistry is an emerging field that combines the power of advanced technologies and dental expertise to improve dental care and diagnosis. It involves the application of various AI techniques, such as machine learning, deep learning, and natural language processing, to assist dental practitioners (47–49).

One of the primary applications of AI in dentistry is in image analysis. Dentists often use radiographic imaging, such as X-rays and cone-beam computed-tomography (CBCT) scans, to diagnose dental conditions. AI algorithms can analyze these images to identify potential issues like tooth decay, periodontal disease, or abnormalities in bone structure. This can assist dentists in making accurate diagnoses and designing appropriate treatment plans (49).

Teeth segmentation is a task in dental image analysis that involves separating the individual teeth from a patient scan. Accurate teeth segmentation is essential for various dental applications, including diagnosis, treatment planning, orthodontics, and prosthodontics.

Teeth segmentation is an active area of research, and advancements in computer vision and machine learning techniques continue to improve the accuracy and efficiency of this important task in dental image analysis. It's worth noting that teeth segmentation can still be a challenging task due to variations in dental anatomy, image quality, and the presence of artefacts such as fillings, orthodontic brackets or implants.

Segmentation techniques of the teeth can be broadly categorized into three types: manual, semi-automatic, and fully automatic.

7.1 Manual segmentation:

Manual teeth segmentation involves a series of image processing steps to identify and extract teeth from dental images. These steps may include pre-processing, thresholding, morphological operations, edge detection, region growing, and contour analysis. These techniques heavily rely on defining specific rules and thresholds based on image characteristics to extract teeth regions. While these methods can work well in certain cases, they might be time consuming and limited by complex dental variations, overlapping teeth, and varying image quality (50).

7.2 Semi-automatic segmentation:

Semi-automatic techniques can be combined with manual segmentation method to develop hybrid approaches for teeth segmentation. These approaches leverage the strengths of both AI and conventional algorithms, providing improved accuracy and flexibility. For instance, AI models can be used to detect potential tooth regions or initial segmentation contours, which can then be refined using manual adjustments (51).

7.3 Fully automatic segmentation:

Fully automatic segmentation using convolutional neural networks (CNNs), has shown great promise in (mandible, mandibular canal, pharyngeal airway space) segmentation(52–54). CNNs are trained using large amounts of labeled data, allowing them to learn complex features and patterns automatically. These models take dental images as input and output pixel-level segmentation masks, which highlight the boundaries or regions.

8. Aims and hypotheses

The majority of studies assessing root changes following maxillary orthognathic surgery in conjunction with orthodontic treatment have been either short-term or two dimensionally assessed, which is prone to human error. There is no standard 3D protocol for objectively quantifying root changes.

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

Part 1: Technical

Article 1.

Aims: This systematic review aimed to evaluate the influence of orthognathic surgery on root resorption.

Hypothesis:

Orthognathic surgery may have an effect on root resorption.

Article 2.

Aims: To propose and validate an automatic multiclass artificial intelligence-based tool for accurate and efficient segmentation and classification of teeth without brackets on CBCT images.

Hypothesis:

The tool might allow automatic, fast and accurate segmentation of normal teeth.

Article 3.

Aims: To propose and validate an automatic multiclass AI-based tool for accurate and efficient segmentation and classification of teeth with brackets from CBCT images.

Hypothesis:

The tool might allow automatic, fast and accurate segmentation of teeth with brackets artefacts.

Article 4.

Aims: To develop a fully automated 3D protocol to evaluate root changes.

Hypothesis:

The protocol might allow 3D, automated and accurate assessment of root changes at a long-term follow-up in maxillary orthognathic patients.

Part 2: Clinical

Article 5.

Aims: To assess the volume, length and morphological root changes of upper teeth following one-piece Le Fort I (OP-LFI) osteotomy.

Hypothesis:

- OP-LFI osteotomy combined with orthodontic treatment may have more effect on root changes than only orthodontic treatment.
- Age, gender and amount of maxillary advancement may correlate with root remodeling.

Article 6.

Aims: To assess the volume, length and morphological root changes of upper teeth of patients who underwent multi pieces Le Fort I (MP-LFI) osteotomy.

Hypothesis:

We hypothesize that MP-LFI osteotomy may induce more pronounced root changes than OP-LFI osteotomy, anticipate potential correlations between root remodeling and age, gender, and maxillary advancement, and propose that three-pieces Le Fort I (3P-LFI) could elicit more significant root changes compared to two-pieces Le Fort I (2P-LFI) osteotomy.

Article 7.

Aims: To provide recommendations of the potential root resorption/remodeling that can occur following different types of maxillary orthognathic osteotomies.

Hypothesis:

These recommendations can serve as a valuable resource for surgeons in estimating and managing root remodeling and resorption associated with different maxillary surgical techniques.

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Part 1: Technical

ARTICLE 1: Impact of orthognathic surgery on root resorption: a systematic review.

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Abstract

Objectives: This systematic review was performed to assess the potential influence of orthognathic surgery on root resorption (RS). **Methods:** An electronic search was conducted using PubMed, Web of Science, Cochrane Central and Embase for articles published up to April 2022. Following inclusion and exclusion criteria, a total of six articles were selected that reported on RS following orthognathic surgery. Risk of bias assessment was performed according to the ROBINS-1 and ROB-2 tools. **Results:** The design of five studies was retrospective and one randomized clinical trial was included, with a follow-up period ranging between six months and ten years. The assessment methodologies mostly relied on two-dimensional imaging modalities where only one study used cone-beam computed-tomography (CBCT) for objective quantification via linear measurements. The percentage of teeth affected by RS varied between approximately 1 and 36%, where surgically assisted rapid palatal expansion (SARPE) and Le Fort I osteotomy showed the highest percentage of RS followed by bilateral sagittal split osteotomy.

Conclusions: The present data tend to indicate that specific orthognathic procedures such as SARPE and Le Fort I osteotomy may induce or reinforce RS. Yet, considering lack of evidence related to objective quantification of RS following orthodontic and/or orthognathic treatment, further CBCT-based prospective studies are required for an improved understanding of RS following different surgical procedures.

Keywords: Root resorption; orthognathic surgery; systematic review.

1. Introduction

Root resorption (RS) is a pathologic process which leads to the breakdown and loss of hard dental tissue due to the clastic activities. It can be broadly classified as either internal or external resorption depending on the locality of resorption pertaining to the root surface (1). External resorption primarily occurs at the root's external surface at the level of cementum overlying dentine, whereas resorption occurring at the predentine lined surface of the root canal or pulp chamber is referred to as internal resorption. Based on the clinical and pathological classification as proposed by Andreasen, external resorption can be further sub-divided into three types: external inflammatory resorption (EIR), external cervical resorption (ECR) and external replacement resorption (ERR). Whereas, clinically only one type of internal resorption exists known as internal inflammatory root resorption (IIRR) (2). The main causes of RS include, trauma, infection, endodontic treatment and certain systemic diseases such as, hyperparathyroidism, Gaucher's disease, Paget's disease and Turner's syndrome (3-5,6,7).

In the literature, RS following orthodontic treatment has been widely reported. It mostly occurs externally at the apical third level. Lupi et al. reported that 73% of the patients who underwent orthodontic treatment showed external apical root resorption at follow-up (8). Even though the influence of orthodontic therapy on RS has been extensively reported, little is known about the potential occurrence of RS following orthognathic surgical procedures with or without orthodontic treatment (3).

The most common orthognathic surgical procedures performed alone or in combination with orthodontic therapy for the correction of dentofacial deformities include, Le Fort I osteotomy (LF I), bilateral sagittal split osteotomy (BSSO) and surgically-assisted rapid palatal expansion (SARPE) (9-13). One of the post-surgical complications associated with these osteotomies is either the temporary or permanent damage of the dental blood supply even if the surgical procedure is carefully planned, thereby, resulting in RS (14). Although the risk of RS following orthognathic surgical procedures has been assumed to be higher compared to the conventional orthodontic treatment (15), the post-surgical damage to the dental apical blood supply and its impact on RS cannot be ignored. To elucidate the problem on RS after orthognathic surgical procedures, the aim of the present systematic review was to assess the influence of orthognathic surgical treatment on RS at follow-up.

2. Material and methods

A search protocol was registered at PROSPERO (International prospective register of systematic reviews (Reference number: CRD42018118952). The PRISMA guidelines (Preferred Reporting Items for Systematic Reviews) were followed to ensure the transparency and comprehensiveness of the review. The "PICO" (patient, intervention, comparison and outcomes) was formulated as follows:

P: Patients (18-65 years) with skeletal class I, II or III.

I: Orthognathic surgery (LF I osteotomy, BSSO, surgical assisted palatal expansion).

C: RS difference between baseline (pre-treatment/ immediately post-operatively) or control group (only orthodontic treatment) and post-treatment.

O: Mean linear, volumetric measurements, and/or percentage difference of RS.

2.1 Search strategy

An electronic literature search was conducted using PubMed (ncbi.nlm.nih.gov), WOS (webscience.org), Cochrane (cochrane.org) and Embase (embase.com) up to April 2022. The search strategy consisted of a combination of controlled terms (Mesh and Emtree terms, respectively) and keywords. The complete search strategy is provided in Appendix 1. A grey literature search was conducted through ProQuest, Google Scholar, Open Thesis, World Cat Dissertations and Open Grey to avoid potential selection bias. Following completion of the main and grey literature search, a detailed hand-search of cross-references from original articles and reviews was performed for identifying additional studies which could not be retrieved from the electronic databases. The identified articles were imported into Endnote X9 software (Thomson Reuters, Philadelphia, PA, USA) to remove duplicates.

Electronic databases were searched with the recommended MEDLINE and EMBASE filters to identify prospective studies, randomized controlled trials (RCT) and retrospective studies. The search was narrowed to studies only written in English. The full text of relevant articles was obtained according to the inclusion and exclusion criteria as described in Table 1. The inclusion criteria involved clinical studies that assessed and measured root resorption following orthognathic surgery with or without orthodontic treatment using different imaging modalities. Exclusion

criteria consisted of non-English language studies, animal studies, case reports, systematic reviews and patients with syndromic diseases.

Table 1. Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none"> -Human studies -In vivo or in vitro studies using radiographic phantoms -Patients undergoing orthognathic surgery alone or in combination with orthodontic therapy -Availability of pre- and post-operative radiological follow-up -Cohort studies -Randomized controlled studies -Non-randomized controlled studies -Case-control studies -English language 	<ul style="list-style-type: none"> -Animal studies -Abstracts without available full text articles. -Patients undergoing orthodontic treatment only. -Case reports -Systematic reviews. -Craniofacial anomalies include cleft lip and/or cleft palate, craniosynostosis, hemi facial microsomia, Gorlin-Goltz Syndrome, and Apert’s and Crouzon Syndrome.

2.2 Study selection

Two reviewers (KA and NM) independently reviewed the titles and abstracts of all records. Subsequently, full text of the studies deemed eligible for inclusion were obtained. Any disagreement was resolved by discussion between the two reviewers. When consensus could not be reached, a third expert reviewer (RJ) was consulted.

2.3 Data extraction and analysis

Relevant data were extracted independently by the two reviewers (KA and NM), for performing a descriptive synthesis. If no consensus could be reached, a third experienced reviewer (RJ) was consulted.

The corresponding authors of included articles were contacted for further information and provision of missing data. The extracted items included: patient demographics, study

characteristics, methodological analysis and numerical presentation of outcomes based on the percentage of teeth with resorption from the total number of examined teeth.

2.4 Risk of bias assessment

The risk of bias for non-randomized studies was assessed using ROBINS-I tool(16), where it was subdivided into seven categories and each category was graded as either low, moderate, serious, critical risk of bias or no information. Thereafter, the overall risk of bias was concluded for each study. The risk of bias for RCT was evaluated using the RoB-2 revised tool (17). An overall risk of bias was decided based on the evaluation of the subcategories. The qualitative evaluation of the methodology was carried out by two reviewers (KA and NM) independently. Any discrepancy was resolved by discussion.

3. Results

3.1 Search results

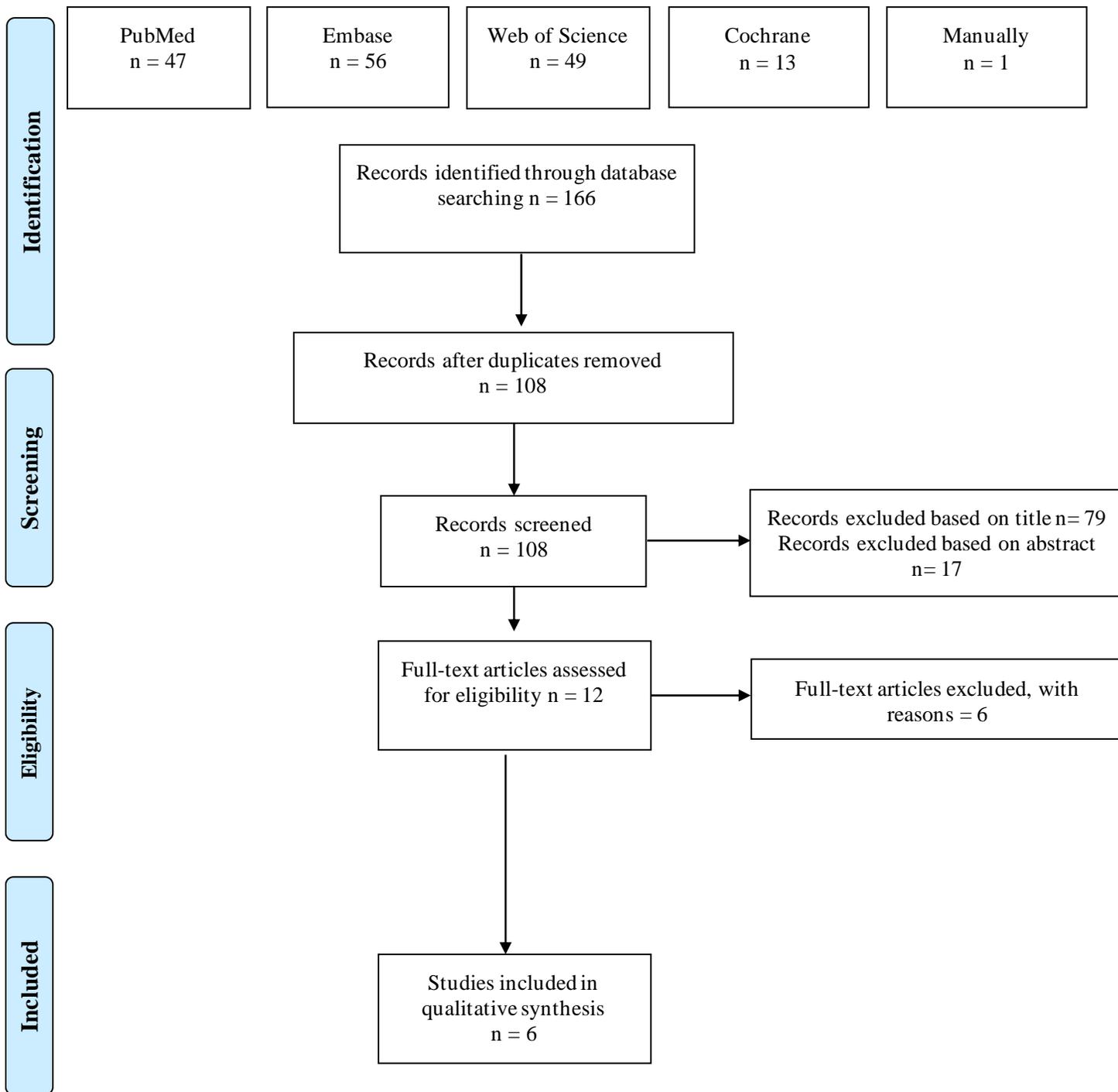
The number of records identified through electronic databases (PubMed, Embase, Cochrane, Web of Science) and manually searched reference lists was 166. Duplicates were removed by Endnote X9 software, resulting in 108 articles. Based on the title and abstract screening, 96 articles were excluded. Twelve articles were selected for full-text reading from which 6 were excluded with reasons (Table 2).

Table 2. Excluded studies with reason.

Author	Reason
Hansen et al, 2007, Germany(35)	Syndromic Patients
Lee et al, 2012, South Korea(36)	
Kahnberg et al, 2005, , Swedn(10)	
Lee et al, 2018, Korea(38)	
Cureton et al, 1999, USA(39)	Case report
Lisboa et al, 2017, Brazil(37)	

Finally, 6 studies were considered eligible to be included for qualitative synthesis. A quantitative synthesis was not possible due to the heterogeneity in relation to assessment methodologies and reported outcomes among the included studies. Figure 1 shows the PRISMA flow diagram describing the selection process (18). The excluded case reports were evaluated root resorption was listed in (Table 7).

Figure 1. Flow diagram of selection process (PRISMA 2009 format).



3.2 Study characteristics

The characteristics of the six included studies are presented in Table 3. The total sample size was 287 patients (mean age: 28.5 years and 2493 teeth). Gender distribution was reported by only three studies. The corresponding authors (19-21) were contacted for additional information about missing data with no response.

Table 3. Characteristics of included articles.

Author	Study design	Gender	Mean Age	Participants	X-ray
Ellingsen et al. 1993(20)	Retrospective	X	38	93	PAN-PA
Schultes et al. 1998(19)	Retrospective	X	34	30	PAN-PA
Mordenfeld et al. 1999(22)	Retrospective	M=8 F=12	28	20	PA
Verlinden et al. 2011(21)	Retrospective	X	28	63	PA
Jensen et al. 2015(13)	Retrospective	M=24 F=37	23	61	Occlusal
Kayalar et al. 2016(23)	RCT	M=9 F=11	19.37	20	CBCT

X: Not indicated, M: Male, F: Female, CBCT: cone-beam computed-tomography, PAN: panoramic radiograph, PA: periapical radiograph, RCT: randomized clinical trials.

3.3 Results of the qualitative analysis

Table 4 describes the pre-treatment malocclusion classification, intervention, duration of patient follow-up, imaging modality, and comparison of RS between only orthodontic therapy, combined orthodontic and orthognathic treatment and only orthognathic surgery. The included studies lacked an orthodontic treatment-based control group to assess the impact of orthognathic surgery on RR. Therefore, a control group was selected based on the findings of a previous systematic review, which showed a RS of 1 to 4 mm (4.5-62%) following orthodontic therapy only at a follow-up period of 12 months (41). In five articles (13,19-22), all patients underwent a combined orthodontic and orthognathic surgical treatment and one study included patients who underwent orthognathic surgery alone without any orthodontic intervention (23). The surgical interventions included, LFI (19,22), LFI + BSSO and SARME (13,21,23). Five articles assessed RS based on two-dimensional radiographic modalities (periapical, occlusal and panoramic radiography) (13, 19-22), whereas only 1 study utilized cone-beam computed-tomography (CBCT) (23). The assessment methodology involved Sharpe classification (13, 21) Newman classification (19), subjective evaluation (20, 22) and linear measurements (23). The amount of RS was variable ranging between 1 % and 36% depending on the surgical procedure, where SARME showed the highest RS (28.6-36%), followed by LFI (6.7%) and BSSO (1%).

Table 4. Comparison of root resorption between only orthodontic, orthodontics + orthognathic and only orthognathic treatment.

Authors, Publication Year, Country of Origin	Pre-op skeletal class	Intervention	Sample size (n=)	Examined teeth Number	Follow-up period	Assessment		Results	Comment	
						Methods	Image modality	Outcome (% of teeth affected by RR)		
De Brito et al, 2016, Brazil ⁽⁴¹⁾	X	Orthodontic	892	262 A 16852 F	12M	Linear measurement	2D	1-4 mm 4.5-62%		
Ellingsen et al, 1993, USA ⁽²⁰⁾	X	Orthodontic + Orthognathic (Le Fort I+BSSO)	143	2185 F	6-120M	Subjective	2D	1 %		
Schultes et al, 1998, Austria ⁽¹⁹⁾	CLASS II	Orthodontic + Orthognathic (Le Fort I)				Newman ⁽³⁴⁾			6.7%	
Mordenfeld et al, 1999, Sweden ⁽²²⁾	CLASS III					Subjective				
Verlinden et al. 2011, Netherlands ⁽²¹⁾	CLASS III	Orthodontic + Orthognathic (SARME)		126 A	6-66M	Sharpe ⁽³⁵⁾	28.6-36%	Exp.R:0.3 3 mm/day		
Jensen et al, 2015, Denmark ⁽¹³⁾				124					122 A	Exp.R:0.5 mm twice/day
Kayalar et al, 2016, Turkey ⁽²³⁾	CLASS III	Orthognathic (SARME)	20	TB:40 P	0-6M	Linear measurement	3D	TB:0.3-1 mm	Exp.R:0.2 5 mm twice/day	
				TBB:20 P				TBB: 0.3- 0.6 mm		

X: not indicated, SARME: Surgical Assisted Rapid Maxillary Expansion, TB: tooth born, TBB: tooth and bone born, Exp.R: expansion rate, M: Month, W: Week, F: Full arch, A: anterior teeth, P: posterior teeth, Gray background: systematic review selected as control group, Green background are included studies in this systematic review, Yellow background is included study in this systematic review.

3.4 Risk of bias within studies

Based on the ROBINS-I tool, a moderate risk of bias was found for two studies (13,22), one with critical risk (19) and two with serious risk (20,21) (Table 5). Only one study (23) was evaluated by the RoB-2 tool, which showed a moderate risk of bias (Table 6).

Table 5. Assessment of risk of bias for non-randomized studies (ROBINS-I tool).

	Author	Bias Due to Confounding	Bias in Selection of Participants	Bias in Classification of Interventions	Bias due to deviations from Intended Interventions	Bias due to Missing Data	Bias in Measurement of Outcomes	Bias in Selection of Reported Results	Overall bias
1	Ellingsen et al, 1993, USA ⁽²⁰⁾	Moderate	Moderate	Moderate	Moderate	Serious	Moderate	Moderate	Serious
2	Schultes et al, 1998, Austria ⁽¹⁹⁾	Moderate	Serious	Critical	Moderate	Serious	Moderate	Serious	Critical
3	Mordenfeld et al, 1999, Sweden ⁽²²⁾	Moderate	Moderate	Low	Low	Low	Moderate	Moderate	Moderate
4	Verlinden et al. 2011, Netherlands ⁽²¹⁾	Moderate	Serious	Low	Low	Serious	Low	Low	Serious
5	Jensen et al, 2015, Denmark ⁽¹³⁾	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate

Table 6. Revised Risk of Bias (RoB-2) tool for randomized controlled trials.

		Bias arising from the randomization process	Bias due to deviations from intended interventions	Bias due to missing outcome data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall RoB judgement
1	Kayalar et al, 2016, Turkey ⁽²³⁾	Low	Low	Low	Low	Low	Low

Table 7. Case reports-evaluation of root resorption after orthognathic and orthodontic treatment.

Authors, Publication Year, Country of Origin	Sample size	Intervention	Pre-op skeletal class	Examined teeth Number	Follow-up period	Assessment		Results	Comment
						Methods	Image modality	Outcome (% of teeth affected by RS)	
Lisboa et al, 2017, Brazil ⁽³⁷⁾	1	Orthodontics + Orthognathic (Le Fort I+BSSO)	CLASS II	24 F	36M	Subjective	2D	No RS had shown	The applied force of the orthodontic appliance was 250-300 g
Cureton et al, 1999, USA ⁽³⁹⁾	4	Orthognathic (SARME)	CLASS I	8 C	18-30M	Subjective	2D	45%	
			CLASS III						

SARME: Surgical Assisted Rapid Maxillary Expansion, M: Month, F: Full arch, C: Central incisors, RS: Root resorption.

4. Discussion

This systematic review aimed to provide evidence related to the RS in patients who underwent orthognathic surgery. Overall, the prevalence of RS ranged between 1 % and 36%. The anterior teeth were found to be more susceptible to RS (13,19,21,22) which might be attributed to the fact that the roots of anterior teeth are much more likely to touch the alveolar bone during the pre-surgical orthodontic decompensation phase and once combined with the cortical osteotomy, there is an increased risk of RS (24,25). Additionally, the anterior teeth are also more susceptible to RS due the blunted or bottle-shaped nature of the root form.

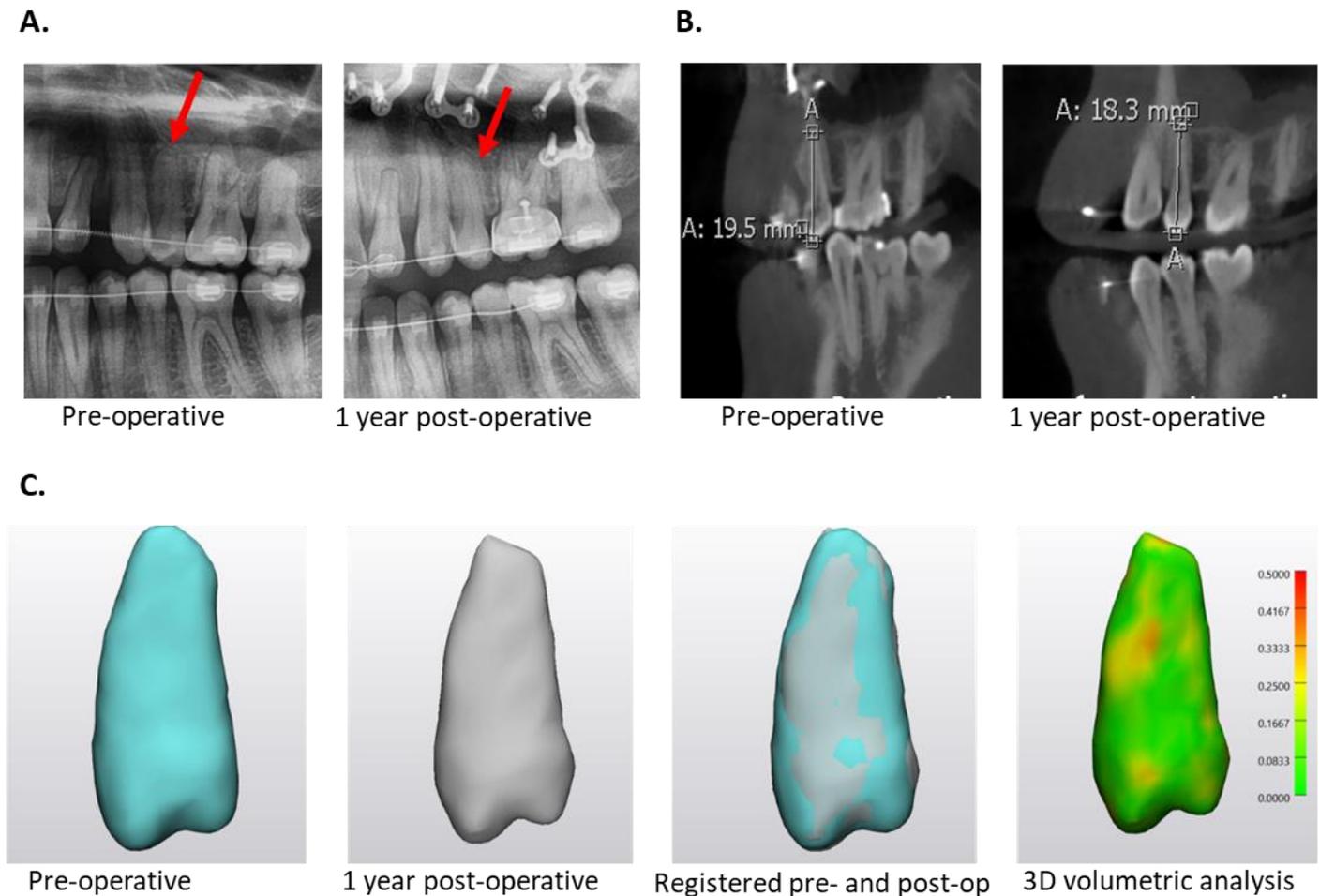
The findings of the review suggested that a combined orthodontic and orthognathic surgical approach showed higher RS compared to orthodontic treatment only. A possible explanation for this increased RS with orthodontic treatment could be the blood flow impairment which might be lessened with an orthodontic treatment (37). Based on the surgical procedure, patients who underwent LFI maxillary osteotomy showed discoloration of teeth with pulp necrosis in maxillary teeth and RS ranged between 3.2 to 6.7%. However, due to the heterogeneous nature of the involved sample which consisted of multiple LFI osteotomy subtypes such as, single and multi-piece osteotomies without any specific inclusion criteria, it was deemed impossible to draw a proper conclusion related to the amount of RS for a specific surgical procedure. Studies with a proper control group and more specified inclusion criteria might enable quantification of RS related to each type of maxillary osteotomy. Only one study included in this review showed RS following BSSO, which was found to be minimal (1 %) without any impact on the RS (20). These findings suggest that the degenerative pulpal changes due to ischemia might occur less frequently with mandibular osteotomies compared to maxillary surgical procedures as the mandibular bony cuts are not in proximity to the apical blood supply of teeth (11,15,19,20).

Patients undergoing SARPE showed a maximal number of teeth with RS (36%), where a higher resorption was observed with patients having an expansion of 0.5mm compared to 0.33 mm per day. These findings imply that the expansion rate might be considered as a risk factor for resorption (26-28). Storey et al. recommend an expansion rate of 0.5–1.0 mm per week to allow the repairing process to be activated and to decrease the probability of RS (28).

The majority of studies involved in this review relied on 2D radiographic imaging such as periapical, panoramic and occlusal radiographs for determining the amount of RS (13,19-22.). The inherent errors associated with 2D imaging, such as, structural superimposition, deformation, under/over estimation of RS and magnification cannot be ignored (29). One study in the review relied on occlusal radiographs for assessing RS following SARPE (13), where the authors reported more events of resorption compared to other studies which applied panoramic and periapical radiography (19-22). This overestimation on occlusal radiographs might have occurred due to the distortion of root length and structural overlap. Additionally, previous evidence also suggests that the panoramic radiographs overestimate the amount of RS by at least 20% (7, 30). Therefore, 2D radiographs might not be considered as a modality of choice for assessing RS. To overcome the inherent limitations associated with 2D imaging, CBCT might act as a more accurate and reliable

alternative for assessing RS, especially following orthognathic surgery where CBCT imaging is a vital part of postsurgical follow-up protocol (23,31). Currently, only one study exists in literature which used CBCT imaging and assessed RS based on linear measurements on 2D slices (23). However, it should be noted that the risk of human error and observer variability is high based on landmark-based linear measurements independent of the choice of imaging modality (32). A more promising approach might be the use of segmentation tools to allow a more realistic visualization and accurate true 3D representation of apical root remodeling and eventual RS over time (40). Hence, it is recommended that future studies should focus on investigating RS using 3D CBCT-based volumetric evaluation methods. To provide a more clinically oriented quantification of RS, segmented roots should be superimposed based on their crowns, while morphological changes should be assessed using color-coded distance mapping (33,34) Figure 2 illustrates an example of a Le Fort I surgery case showing traditional (Figures 2a-b) and proposed method (Figure 2c) for the assessment of RS at follow-up.

Figure 2. The different methods used to evaluate root resorption explained on a patient undergoing Le Fort 1 surgery comparing pre- to one year post-treatment. a. Using panoramic radiograph. b. Using linear measurement from CBCT images. c. Using volumetric analysis on 3D segmented model.



The main strength of this systematic review was the inclusion of studies evaluating RS following orthognathic surgery procedures which has not been previously investigated. However, the review had certain limitations. Firstly, a limited number of studies existed assessing RS following orthognathic surgery and the majority of included studies were characterized by a moderate to high risk of bias with the quality of evidence being mainly limited due to retrospective design. Secondly,

all the studies were single-arm without the inclusion of a control group and most of them did not account for confounding variables such as root displacement and total treatment time. Thirdly, substantial heterogeneity existed in relation to study design, surgical procedure and assessment methodologies with variable outcome measurements which might have led to bias within our findings. Finally, no study was found investigating RS using 3D CBCT-based volumetric information.

5. Conclusions

The number of teeth with RS was found to be highest with SARPE and LF I, whereas BSSO had the least impact. However, the findings reported in the review should be interpreted with caution due to the limited number of studies and absence of a control non-surgical group. Currently, evidence remains poorly documented in relation to objective quantification of RS following orthognathic surgical procedures, its impact on a patient's dental condition at follow-up and role of patient- and surgery-related risk factors. Thereby, prospective studies should be conducted in the future using the proposed CBCT-based volumetric analysis as such to strive for a better understanding of the influence of different surgical procedures on RS an eventual adaptation of these procedures.

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ARTICLE 2: A novel deep learning system for multi-class tooth segmentation and classification on cone-beam computed-tomography. A validation study.

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Abstract

Objectives: Automatic tooth segmentation and classification from cone-beam computed-tomography (CBCT) have become an integral component of the digital dental workflows. Therefore, the aim of this study was to develop and validate a deep learning approach for an automatic tooth segmentation and classification from CBCT images.

Methods: A dataset of 186 CBCT scans was acquired from two CBCT machines with different acquisition settings. An artificial intelligence (AI) framework was built to segment and classify teeth. Teeth were segmented in a three-step approach with each step consisting of a 3D U-Net and step 2 included classification. The dataset was divided into training set (140 scans) to train the model based on ground-truth segmented teeth, validation set (35 scans) to test the model performance and test set (11 scans) to evaluate the model performance compared to ground-truth. Different evaluation metrics were used such as precision, recall rate and time.

Results: The AI framework correctly segmented teeth with optimal precision (0.98 ± 0.02) and recall (0.83 ± 0.05). The difference between the AI model and ground-truth was 0.56 ± 0.38 mm based on 95% Hausdorff distance confirming the high performance of AI compared to ground-truth. Furthermore, segmentation of all the teeth within a scan was more than 1800 times faster for AI compared to that of an expert. Teeth classification also performed optimally with a recall rate of 98.5% and precision of 97.9%. **Conclusions:** The proposed 3D U-Net based AI framework is an accurate and time-efficient deep learning system for automatic tooth segmentation and classification without expert refinement.

Keywords: Cone-beam computed-tomography; Deep learning; Artificial intelligence; Neural network models; Three-dimensional imaging; Teeth

1. Introduction

Tooth segmentation is of vital importance in a daily clinical practice. The identification of teeth with their exact shapes and boundaries on two-dimensional (2D) and three-dimensional (3D) images can guide dental practitioners by allowing an improved precision for early disease detection and diagnosis, treatment planning and outcome prediction (1). Furthermore, an accurate tooth segmentation for the creation of a 3D tooth model from cone-beam computed-tomography (CBCT) images is a prerequisite for digital dental workflows (2,3).

An accurate digital model of individual tooth geometry could be beneficial for a number of clinical applications, such as, prosthetic evaluation, orthodontic analysis, orthodontic treatment planning, computer-aided digital implant planning, follow-up of root resorption after orthodontic treatment, canine eruption assessment and tooth auto-transplantation (4-7). Additionally, correct tooth detection and segmentation on CBCT images is also crucial for diagnosing pathologies, allowing morphological and positional visualization of teeth to aid the clinical decision-making process (1). However, an accurate segmentation of individual teeth is an extremely challenging and a time-consuming process.

The conventional image processing techniques for performing tooth segmentation on CBCT images are semi-automated in nature as these require manual intervention and are prone to human error (8). Similarly, template-based fitting approaches lack robustness for segmenting multi-rooted teeth, and level-set methods need numerous mathematical operations. Furthermore, the vague edges between tooth root and alveolar socket and image intensity inhomogeneity could lead to false segmentation (9). The aforementioned classical segmentation approaches require laborious manual corrections for achieving an accurate segmentation and are considered as highly time-consuming, operator-dependent and inaccurate especially in the presence of artefacts related to high-density materials (10).

Recently, convolutional neural networks (CNNs) have been widely employed in the field of dentistry for overcoming the limitations associated with the conventional segmentation approaches. Deep neural networks trained end-to-end have the ability to outperform classical pipeline-based systems. These networks have been applied in various fields of image processing, such as, feature extraction, image classification, and semantic segmentation (11). In context to dentistry, deep learning has allowed detection and segmentation of teeth based on 2D radiography, prediction of third molar eruption, detection and diagnosis of dental caries, and cyst and tumor classification (1,(12-16)). However, lack of evidence exists related to the application of deep learning for the segmentation and/or classification of teeth from CBCT

images (2,3,10,11,(17-21)).

A successful tooth segmentation from a clinician's perspective should exhibit the following; accurate segmentation of complete 3D individual teeth, correct classification of each tooth, and fast segmentation and classification (22) Failure of any of these measures would result in an unsuccessful segmentation task. Additionally, previous evidence also suggests the necessity of further research with more robust, accurate and fast systems, capable of achieving a high segmentation and classification performance for all the teeth groups with images acquired from different devices and protocols (21).

Therefore, the aim of the following study was to develop and validate a clinically operational CNN-based system allowing an accurate and time-efficient segmentation and classification of 3D teeth from CBCT images.

2. 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 of Leuven (reference number: S57587). Informed consent was not required for this retrospective study as patient-specific information was kept anonymous.

2.1 Dataset

The artificial intelligence (AI) networks were developed based on CBCT scans. All images were recruited from the Hospital's database which were utilized for the diagnostics and/or treatment planning of patient with dentomaxillofacial deformities and diseases. No additional scans were taken specifically for this study. The inclusion criteria involved, high quality images, sufficient field of view (FOV) for visualizing all upper and lower jaw teeth (with or without restorative filling) with the exception of missing wisdom teeth. Scans with metal artefacts from implants or brackets, motion artefacts and partial edentulism were excluded.

Two CBCT devices were utilized in this study: 3D Accuitomo 170 (J Morita, Kyoto, Japan) and NewTom VGi evo (Cefla, Imola, Italy). The acquisition settings were; 90 kV, voxel size: $0.25 \times 0.25 \times 0.25 \text{ mm}^3$, FOV: $100.75 \times 100.75 \times 100 \text{ mm}^3$ or $170.25 \times 170.25 \times 120 \text{ mm}^3$ for 3D Accuitomo 170 and 110 kV, voxel size: $0.2 \times 0.2 \times 0.2 \text{ mm}^3$, FOV: $122.8 \times 122.8 \times 80.2 \text{ mm}^3$ or $103.2 \times 103.2 \times 100.8 \text{ mm}^3$ or $244.8 \times 244.8 \times 188.7 \text{ mm}^3$ for Newtom VGi evo.

The total dataset consisted of 186 CBCT scans and was split into the following subsets:

- Training set (scans=140, teeth=400), to train the AI model where individual teeth were segmented from each scan. The selection of teeth was random, however, covering the 32 teeth classes.
- Validation set (scans=35, teeth=100), to test the model performance based on the training set. The selection of teeth was random, however, covering the 32 teeth classes.
- Test set (scans=11, teeth=332) to evaluate the model performance by comparing with ground-truth segmented teeth where all teeth per scan were segmented.

The training and test ground-truth datasets were prepared by segmenting the CBCT Digital Imaging and Communications in Medicine (DICOM) images using a previously validated AI tool (3) which allowed segmentation of individual teeth instead of the complete arch. The CBCT DICOM images were taken as an input and the user manually cropped the image around each tooth individually for segmentation. Thereafter, 3D contours were suggested automatically as described in a previous study (23). The tool also allowed the user to manually adjust contours for optimally segmenting the teeth. The segmentation process for training and testing was performed by a single expert and later verified by another expert.

2.2 AI framework

The two main tasks required from the AI framework as an output involved; segmentation of each individual tooth and classification to a particular tooth class.

Segmentation of individual teeth was achieved using a three-step approach as the size of the image (full CBCT DICOM scan) was usually too large to be used in a deep neural network. In the first step, the original image was down-sampled to a fixed size ($96 \times 128 \times 128$). All teeth were segmented as a single class on the down-sampled image for producing a binary image to overcome the variety of FOVs such as complete skull, all lower teeth or only a part of the teeth, since the model was trained with different FOVs.

In the second step, the dental region in the full resolution image was cropped based on the binary image then down-sampled to a fixed resolution of $0.7 \times 0.7 \times 0.7$ mm. The cropping and down-sampling allowed the use of deep neural networks and facilitated multi-class segmentation. The model in this step performed a multi-class segmentation of the image into 33 classes, with each tooth being a separate class (i.e. 32 classes) and a background class representing all structures not belonging to a tooth class.

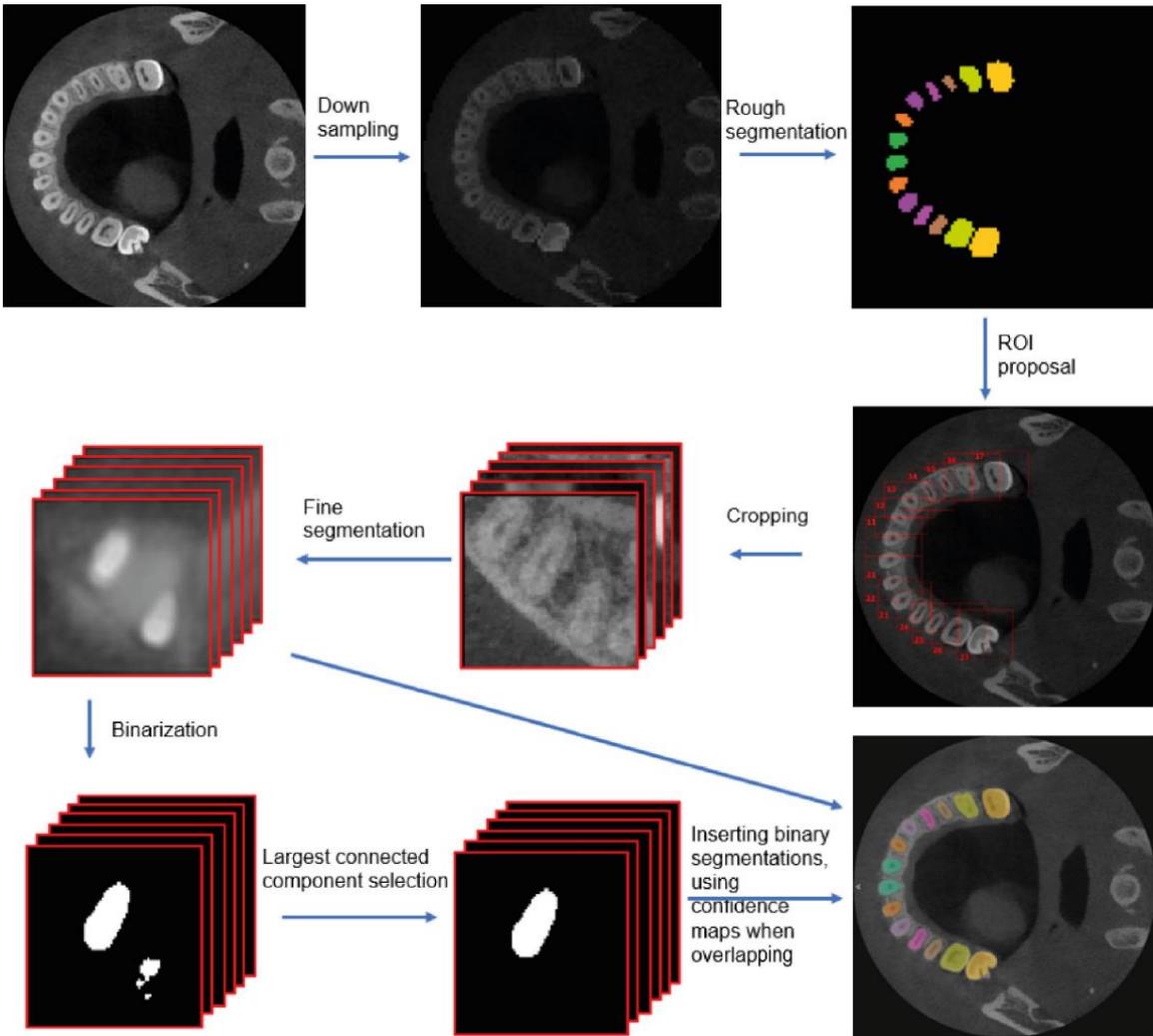
The third step consisted of segmenting each of the 32 teeth classes individually. A crop was taken around each tooth which was bounded with a cuboid called the bounding box of the tooth. This small crop (i.e. bounding box) for each tooth was segmented in full resolution by a third

network. Thereafter, the segmented teeth were inserted into a global label map with their class label corresponding to that of the bounding box. As the bounding boxes of the 32 teeth were axis-aligned, a significant overlap was usually observed between them. The overlap sometimes led to the false segmentation of the voxels as tooth by more than one bounding box. To resolve this issue, the confidence of the model, i.e., Sigmoid activation of the model output was applied to decide which label each voxel finally obtained.

All the three steps consisted of a 3D U-Net network structure composed of 4 encoding and 3 decoding blocks, where each block was made up of 2 convolutions followed by ReLU activation and group normalization with 8 feature maps (24). The number of features after the first encoder was 64 which was doubled in each of the following encoders. All convolutions had a kernel size of $3 \times 3 \times 3$, stride 1 and dilation 1. Max pooling was applied after each encoder with kernel size $2 \times 2 \times 2$ and stride 2, reducing the resolution with a factor 2 in all dimensions.

The training of the first and third models was performed with a binary cross entropy loss, and the second model with cross entropy. All models were optimized using the adam optimizer with initial learning rate of 10^{-4} , which was reduced in several steps until 10^{-7} during the training for fast convergence. Random rotation, scaling, elastic deformation, and cropping were applied as data augmentation strategies. Fig. 1 explains step 2 and 3 of the AI framework for segmenting and classifying the teeth. The AI model is available via an online user-interactive cloud-based platform, Virtual Patient Creator (Relu BV, Leuven, Belgium) (25) that is accessible upon registration and allows users to import DICOM datasets, visualize, manually correct if required and export the segmented teeth in STL file format.

Figure 1. Steps 2 and 3 of the AI framework for segmenting and classifying the teeth.



2.3 Evaluation metrics

The evaluation metrics consisted of two sets, one for tooth segmentation and another for classification:

1. Evaluation metrics for tooth segmentation

A confusion matrix (voxel-wise comparison) was used to compare the prediction of the AI model to the ground truth based on four variables: true positive (TP), true negative (TN), false positive (FP), false negative (FN), where TP are the correctly segmented voxels of a tooth. TN are the correctly not segmented voxels of a tooth. FP are the incorrectly segmented voxels and FN are missed from segmentation voxels. The following metrics were used for segmentation evaluation:

- Recall is the rate of correctly identified voxels in the predicted model compared to ground truth

$$\text{Recall} = \frac{TP}{TP+FN}$$

- Precision is the percentage of the accurately identified segmented region from the completely segmented region

$$\text{Precision} = \frac{TP}{TP+FP}$$

- Accuracy is the rate of correctly identified voxels to all the voxels

$$\text{Accuracy} = \frac{TP+TN}{TP+FP+TN+FN}$$

- Intersection over union (IoU) is the amount of overlapping voxels between the predicted model and the ground truth

$$\text{IoU} = \frac{TP}{TP+FP+FN}$$

- Dice similarity coefficient (DSC): is the score of similarity between the segmented region and the ground truth

$$\text{DSC} = \frac{2*TP}{2*TP+FP+FN} = \frac{2*IoU}{1+IoU}$$

- 95% Hausdorff Distance (HD) is the 95 percentile of the maximal distance between the predicted model and ground truth

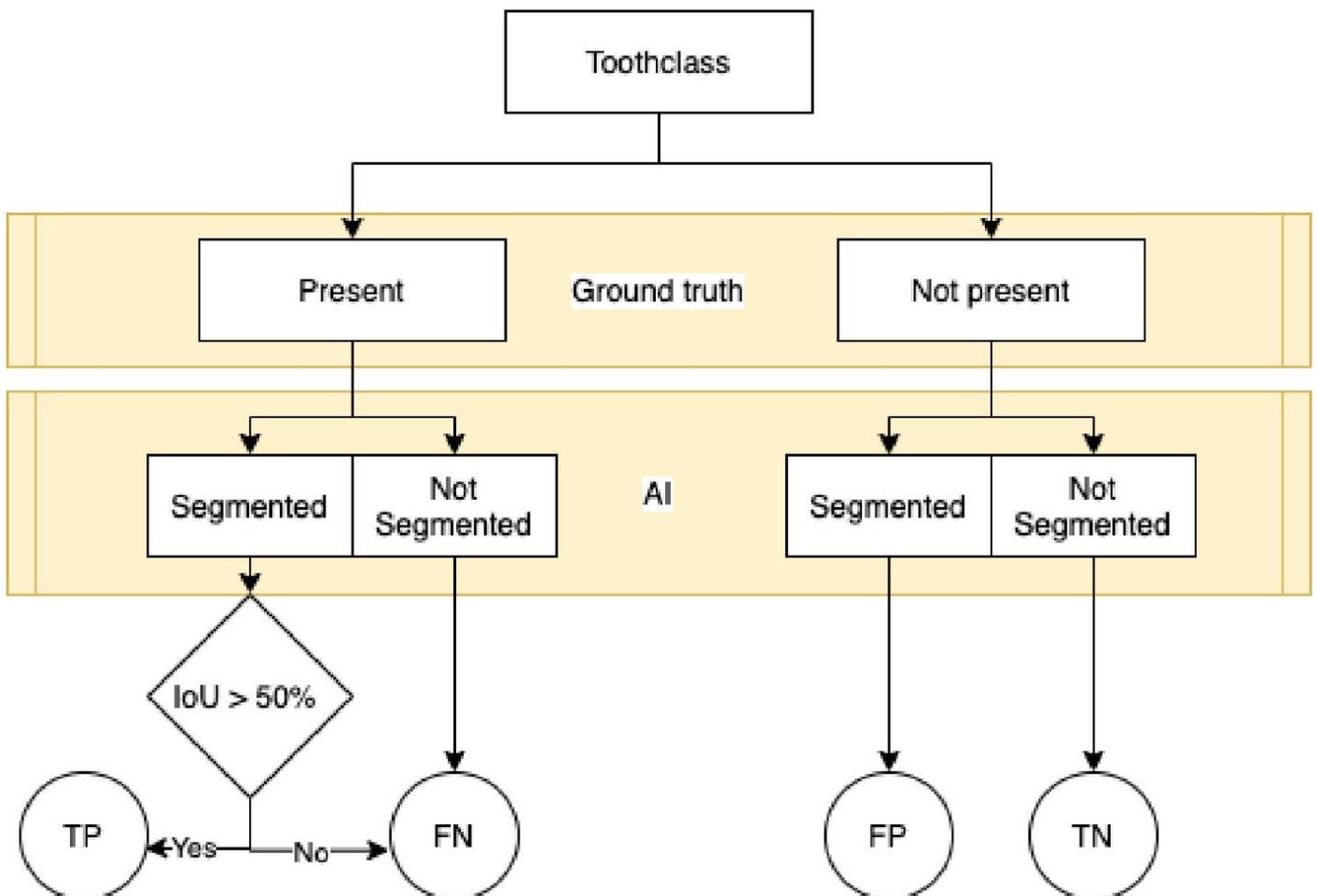
$$p_{95} \left(\min_{g \in G} \|p - g\|^2 \cup \min_{p \in P} \|p - g\|^2 \right)$$

- Time is the number of seconds to segment all teeth from a CBCT image whether using the expert or AI method. For the expert method the timing was calculated from the point when the DICOM data was opened in the segmentation software till a STL file was produced. For the AI method, timing was automatically recorded by the algorithm by calculating the number of seconds needed to produce a multi-class segmentation map excluding the DICOM data upload.

2. Evaluation metrics for classification

Fig. 2 illustrates the tooth classification pipeline, where TP, TN, FP and FN variables are defined differently from that of segmentation, TP is correctly identified tooth class compared to ground truth with $IoU > 50\%$, TN is a correctly identified tooth as not present, FP is a non-existing identified tooth, FN is a non-identified existing tooth ($IoU < 50\%$). The equations for accuracy, precision and recall rate remained the same as mentioned above.

Figure 2. Diagram explaining the tooth classification pipeline.



2.4 Evaluation of subgroups

Data were analyzed using MedCalc Statistical Software version 16.2.0 (MedCalc Software bvba, Ostend, Belgium). Mean and standard deviation (SD) values of the validation metrics were reported to evaluate the performance of the network for complete dataset segmentation, separate teeth sub-groups segmentation (incisors, canines, premolars and molars) and teeth classification. The comparison between segmented teeth subgroups was performed using Kruskal Wallis test with Bonferroni correction as the data had a non-parametric distribution. A p-value of <0.05 was considered as statistically significant.

3. Results

The timing of segmentation and classification of all the teeth based on the test dataset of a single scan ($n = 11$ scans with 332 teeth) with the AI model was 13.7 ± 1.2 s compared to that of an expert ($25,353.6 \pm 4284$ s or 7 ± 1.2 h). Thereby, indicating that the AI performed more than 1800 times faster than an expert.

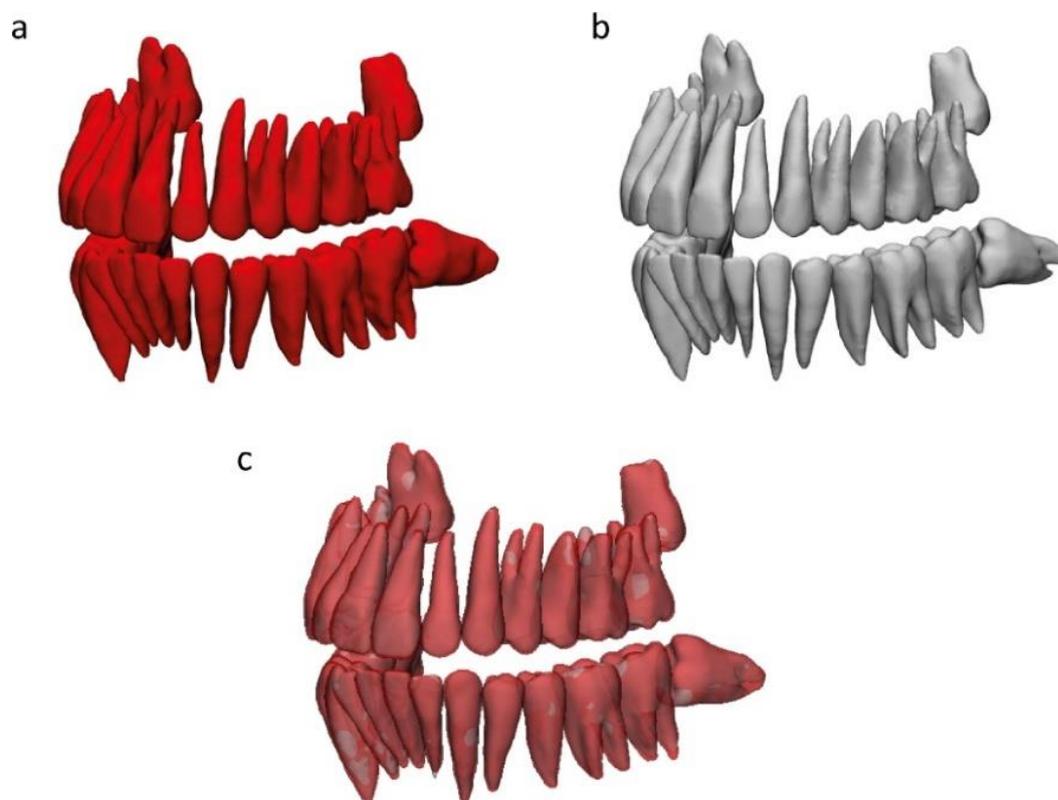
Table 1 describes the accuracy metrics which were calculated for the segmentation evaluation by comparing the AI model to the ground truth. Fig. 3 shows an example of segmentation from the AI model versus ground truth.

Table 1. Accuracy results of segmentation by comparing AI model segmentations to the ground truth segmentations (Mean \pm SD).

Accuracy metrics	Mean \pm SD
IoU	0.82 \pm 0.05
Precision	0.98 \pm 0.02
Recall	0.83 \pm 0.05
DSC	0.90 \pm 0.03
95% HD (mm)	0.56 \pm 0.38
Time	13.7 sec

IoU: intersection over union, DSC: Dice, HD: Hausdorff distance.

Figure 3. An example from the validation dataset with a. Ground truth segmentation in red, b. AI model segmentation in gray, c. AI segmentation superimposed on Ground truth.



The classification of teeth to the correct class (32 classes and 1 background class) performed well with an accuracy of 96.6%, recall rate of 98.5% and precision of 97.9%.

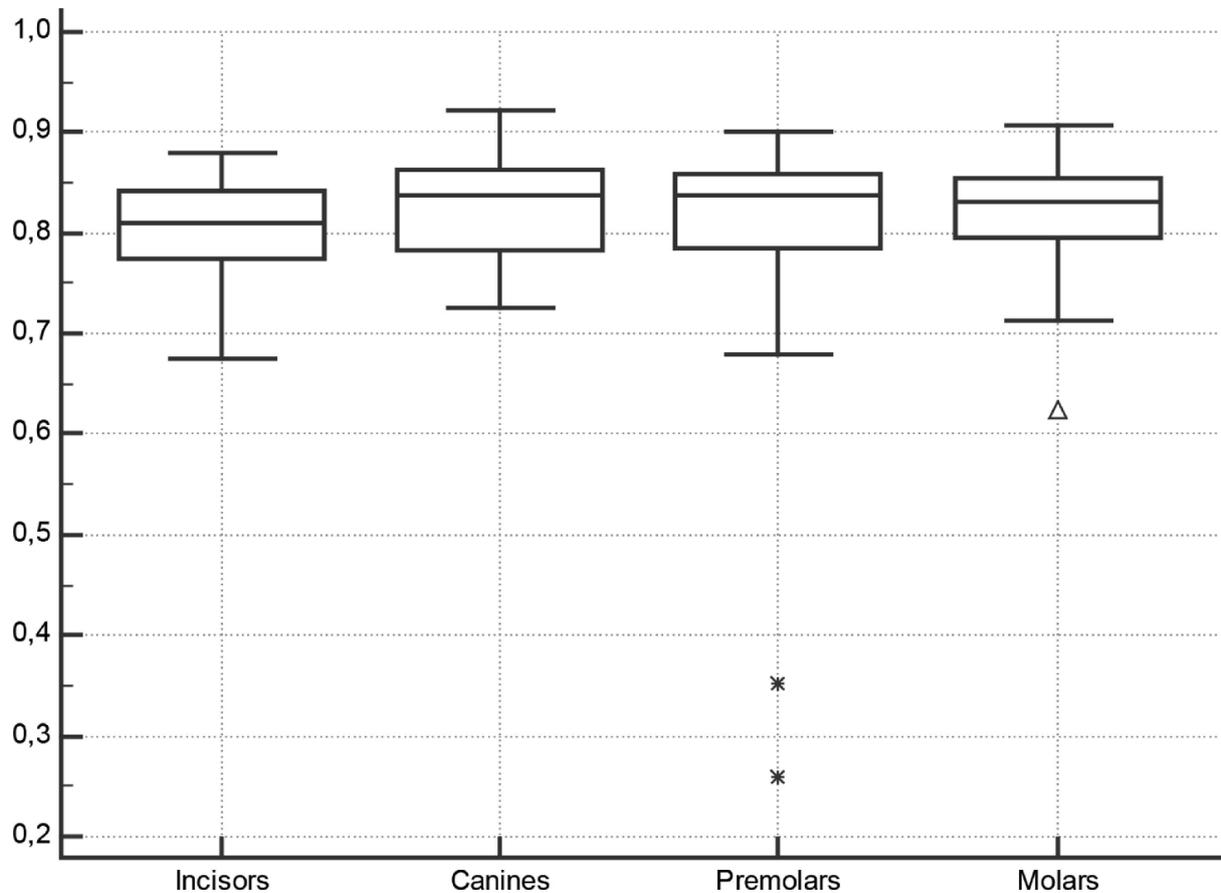
Table 2 and Fig. 4 show the IoU values for segmentation of different teeth sub-groups. The IoU values were within a similar range, however, the canine subgroup scored the highest followed by molar and premolar. The incisor sub-group had the lowest IoU with a statistically significant difference compared to all other sub-groups ($p < 0.05$). No other significant differences were observed.

Table 2. IoU of segmentation of the different teeth subgroups (incisors, canines, premolars and molars).

Teeth subgroups	Number of teeth	Mean IoU \pm SD
Average		0.80 ± 0.05
Incisors	87	0.83 ± 0.05
Canine	43	0.81 ± 0.09
Premolars	86	0.82 ± 0.04
Molars	116	
p-value		
Incisors vs Canine	0.003*	
Incisors vs Premolars	0.019*	
Canines vs Premolars	0.003*	
Canines vs Molars	0.352	
Premolars vs Molars	0.869	

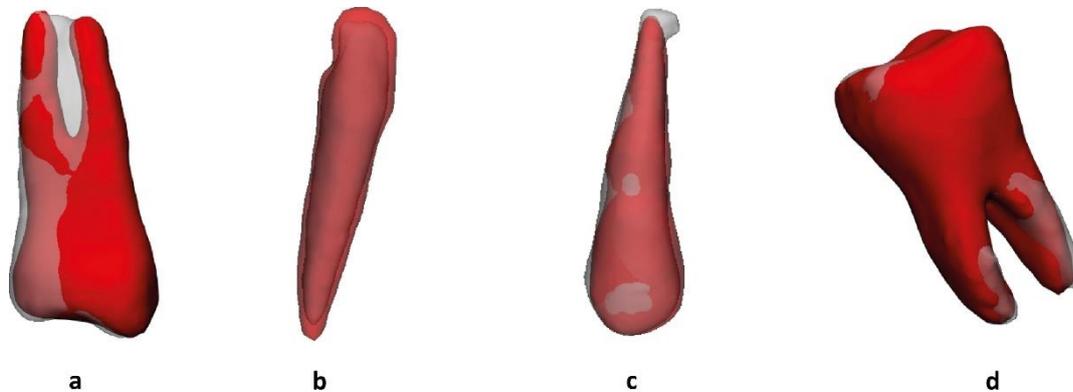
IoU: intersection over union, , * indicates significant difference

Figure. 4. Box plot comparing IoU resulting from segmentation for the different subgroups: incisors, canines, premolars and molars.



The AI system was incorporated with several tools that allowed refinement of the automatic segmentation. However, this study only investigated the fully AI-based task without any manual correction. Fig.5 demonstrates some cases requiring minor corrections.

Figure 5. Examples of cases requiring minor corrections based on the comparison of the AI segmentation (gray) versus Ground truth (red). a. Overestimation, b. Underestimation, c. and d. Deformed root.



4. Discussion

The 3D visualization and segmentation of human teeth has become an indispensable component for computer aided diagnostics and treatment planning in many fields of digital dentistry. The following study validated a new system for automatic tooth segmentation and classification based on CBCT images acquired by two different acquisition devices with a variety of FOVs and protocol settings. The use of three different CNNs yielded a high accuracy. Furthermore, the AI-driven system performed 1800 times faster compared to an expert-based segmentation. Additionally, the proposed method overcame some of the limitations associated with the existing deep learning-based algorithms. Recently, few studies have developed and validated CNN based tools for tooth segmentation (2, 3, 10, 11, (17), (18), (19), (20)). However, comparison with the previous studies was limited due to the non-standardization in metrics, sample heterogeneity and lack of clinical applicability of some of the previously developed algorithms.

Fenster & Chiu (2005) stated that designing or choosing an appropriate effectiveness measure for an object segmentation is challenging (22). For the purpose of providing information relevant to the task, the authors suggested categorizing the requirements of medical image segmentation evaluation into accuracy (the degree to which the segmentation results agree with the ground-truth segmentation), precision (correct classification), and efficiency which is mostly related to time duration. In present study, all accuracy metrics demonstrated high values for segmentation and classification of teeth. Cui et al. (2019) relied on a 2D-stage approach with two 3D networks which required a specialized software and an advanced hardware to run

efficiently (17). Another study also focused on segmentation using a multi-task 3D fully CNNs for predicting the tooth region and surface (19). However, both studies failed to report the time taken for segmentation meanwhile requiring heavy processing.

Until now, three studies have been published related to the application of CNNs for individual 3D CBCT-based tooth segmentation (3,10,20), where only one study proposed a multiclass CBCT image segmentation system for automatically creating 3D surface models of the teeth in a preliminary dataset of 30 CBCT images of patients who underwent orthodontic treatment. Duan et al. (2021) developed a two-phase deep learning solution for tooth and pulp cavity segmentation (20). However, only 20 CBCT images were recruited as the dataset and were acquired from a single device with similar acquisition parameters. Lahoud et al. (2021) assessed the performance of an innovative CNN-based algorithm for performing tooth segmentation but segmentation of molar sub-group was precluded (3). To the best of our knowledge, as the present study was the first to test all the performance metrics proposed by Fenster et al. (2005), which included: accuracy, precision and efficiency (22). Hence, serving as a groundwork for the present study where a newly developed multiclass system was employed for automatically generating 3D models of all the teeth.

The efficiency of image segmentation algorithm provides information related to its practical use, which is often measured as the segmentation time and should include all aspects of user interaction and whether the approach could be suitable for all images (22). Unfortunately, majority of the previous studies did not evaluate this metric. Some of the algorithms allowed only single tooth segmentation at a time-point following complete image upload, which could be considered a time-consuming and less robust method. In contrast, a multi-class tooth segmentation approach was utilized in the present study which allowed segmentation of the complete arch at the same time-point. Furthermore, the algorithm was deployed onto a cloud-based platform in order to serve a wider audience for digital dental applications independent of the hardware specifications of the personal computers.

The CBCT scans were acquired from young patients without dental implants or orthodontic devices to avoid the influence of metal artefacts. Nonetheless, slight artefacts due to dental fillings were present. In a daily clinical practice, the findings of the current study should be interpreted with caution, as the presence of such artefacts might degrade the quality of segmentation. So far, the system has proven to be highly accurate and consistent, considering training with data from two CBCT devices with different FOV and acquisition settings. Further training remains mandatory, which can be achieved by allowing the system to master more CBCT artefacts generated by high-density materials such as, dental implants and/or orthodontic

brackets. Additionally, inclusion of more CBCT devices with different scanning parameters might allow to increase the generalizability of the system.

5. Conclusions

This study developed and validated a new cloud-based deep learning system for automatic tooth segmentation and classification without expert refinement. The proposed system is accurate and time-efficient, enabling potential future applications in the digital workflows of dental diagnostics and treatment planning while reducing clinical workload.

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ARTICLE 3: Deep convolutional neural network-based automated segmentation and classification of teeth with orthodontic brackets on cone-beam computed-tomographic images: a validation study.

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Abstract

Objectives: Tooth segmentation and classification from cone-beam computed-tomography (CBCT) is a prerequisite for diagnosis and treatment planning in the majority of digital dental workflows. However, an accurate and efficient segmentation of teeth in the presence of metal artefacts still remains a challenge. Therefore, the following study aimed to validate an automated deep convolutional neural network (CNN)-based tool for the segmentation and classification of teeth with orthodontic brackets on CBCT images. **Methods:** A total of 215 CBCT scans (6880 teeth) were retrospectively collected, consisting of pre- and post-operative images of the patients who underwent combined orthodontic and orthognathic surgical treatment. All the scans were acquired with NewTom CBCT device. A complete dentition with orthodontic brackets and high-quality images were included. The dataset was randomly divided into three subsets with random allocation of all 32 tooth classes: training set (140 CBCT scans-400 teeth), validation set (35 CBCT scans-100 teeth) and test set (pre-operative:25, post-operative:15= 40 CBCT scans-1280 teeth). A multi-class CNN-based tool was developed and its performance was assessed for automated segmentation and classification of teeth with brackets by comparison with a ground-truth. **Results:** The CNN model took 13.7 ± 1.2 seconds for the segmentation and classification of all the teeth on a single CBCT image. Overall, the segmentation performance was excellent with a high intersection over union (IoU) of 0.99. Anterior teeth showed a significantly lower IoU ($p < 0.05$) compared to premolar and molar teeth. The DSC score of anterior (0.95 ± 0.20) and premolar teeth (0.91 ± 0.29) in the pre-operative group was slightly lower compared to the post-operative group. The classification of teeth to the correct 32 classes had a high recall rate (99.9%) and precision (99%). **Conclusions:** The proposed CNN model outperformed other state-of-the-art algorithms in terms of accuracy and efficiency. It could act as a viable alternative for automatic segmentation and classification of teeth with brackets.

Keywords: Cone-beam computed-tomography, Deep Learning, Artificial Intelligence, Neural network models, Three-dimensional imaging, Teeth

1. Introduction

Tooth segmentation on cone-beam computed-tomography (CBCT) images is a fundamental task in the majority of computer-aided dental workflows. It provides a high resolution three-dimensional (3D) volumetric data of a tooth and is most commonly employed for guiding diagnosis, treatment planning phase and/or follow-up evaluation of orthodontic therapy, orthognathic surgery, dental implantology, guided-endodontics, restorative dentistry and tooth auto-transplantation (1). Currently manual segmentation acts as the gold standard for segmenting teeth, which is a time-consuming and tedious task as the operator has to manually delineate the boundaries of a tooth and check for any deformity in all the slices of the CBCT image. To overcome these limitations, alternative solutions have been utilized mainly in the form of threshold-based semi-automatic commercial or open-source software programs (2). Although these tools offer a faster approach compared to its manual counterpart, development and optimization of such software has been primarily based on medical CT images, which are superior in segmentation accuracy as compared to CBCT (3). Furthermore, segmentation on CBCT images is below the standard due to the presence of beam-hardening artefacts, heterogeneous intensity distribution, lacking Hounsfield units, low-contrast resolution and unclear boundaries between inter-tooth proximity, root and alveolar bone (4,5). The error introduced by an inaccurate segmentation could negatively influence the later steps of the digital workflows and the final expected outcome.

Recently, the application of artificial intelligence (AI) in the form of deep convolutional neural networks (CNN) have been extensively used for developing automated tools to achieve an accurate and efficient tooth segmentation and classification (6,7). These AI approaches have the ability to learn non-linear spatial characteristics in a scan and have overcome the limitations associated with both manual and semiautomatic approaches (8-11).

Various studies have assessed different CNN models and found their performance to be higher compared to other conventional and state-of-the-art approaches for classifying and segmenting pristine teeth and those with high-density restorative materials (12-21). However, the main challenge that still persists with both conventional and automated CNN-based segmentation tools is their inability to segment teeth with metal artefacts originating from orthodontic brackets. The integration of automated tools allowing accurate segmentation and isolation of teeth from brackets could further optimize the efficacy of current digital dental workflows and decrease a clinicians workload with the possibility of improving patient care.

To our knowledge, no study has previously investigated the application of CNN models for the segmentation of teeth with brackets on CBCT images. Therefore, this study aimed to validate an automated multi-class deep CNN-based tool for an accurate and efficient segmentation and classification of teeth with brackets on CBCT images.

2. Materials and methods

This study was conducted following the Helsinki World Medical Association Declaration on Medical Research. Ethical approval was obtained from the Ethical Review Board of the University Hospitals of Leuven (reference number: S57587). Informed consent was not required as patient-specific information was anonymized.

2.1 Dataset

A total of 215 CBCT scans (1780 teeth: anterior = 646, premolars = 486, molars = 648) were retrospectively collected from LORTHOG database of the University Hospital, which consisted of pre- and post-operative images of the patients who underwent combined orthodontic and orthognathic surgical treatment for the correction of dentoskeletal deformities.

All scans were acquired with NewTom VGi evo (Cefla, Imola, Italy) CBCT device with the following acquisition parameters: 110 kV, voxel size: $0.2 \times 0.2 \times 0.2 \text{ mm}^3$, FOV: $122.8 \times 122.8 \times 80.2 \text{ mm}^3 / 103.2 \times 103.2 \times 100.8 \text{ mm}^3 / 244.8 \times 244.8 \times 188.7 \text{ mm}^3$. The inclusion criteria were presence of both maxillary and mandibular complete dentition (anterior, premolars and molars) with orthodontic brackets and high-quality images. Patients with partial edentulous jaws, dental implants and motion artefacts were excluded.

The complete dataset was randomly divided into three subsets with random allocation of all 32 tooth classes as follows:

- Training set (140 CBCT scans- 400 teeth), to train the CNN model
- Validation set (35 CBCT scans- 100 teeth), to assess the model performance based on trained set and hyperparameter optimization.
- Test set (40 CBCT scans- 1280 teeth), to assess the performance of CNN-based automated segmentation compared to the ground-truth. This set was further divided into two sub-groups, pre-operative (25 CBCT scans) and post-operative groups (15 CBCT scans), both of which consisted of all tooth groups. The difference between pre- and post-operative images was the inclusion of

artefacts generated from osteotomy lines, fixation plates and screws in the post-operative images as such to assess the robustness of the algorithm.

Both training- and test-sets were prepared by two experts, where one expert segmented and labeled all teeth, followed by verification by another expert to ensure quality control.

The segmentation procedure has been adopted from similar work (6), where the training set was developed by a previously validated method (23). The operator manually trimmed the CBCT image around each tooth, followed by automated 3D contouring and segmentation of the individual teeth in axial, sagittal and coronal views while carefully excluding the brackets. Manual refinement of the contours was performed when needed, however, the contouring protocol described by EzEldeen et al. (23) overcame the inaccurate estimation of the tooth contour around bracket-tooth contact region. Furthermore, a second expert validated and corrected the segmentation.

The test set ground-truth was prepared with a hybrid approach using an online cloud-based AI system, known as “Virtual Patient Creator” (Relu BV, Leuven, Belgium) (24).

Firstly, the CBCT images were imported in Digital Imaging and Communication in Medicine (DICOM) format and the platform automatically generated initial segmentation of individual maxillary and mandibular teeth. Thereafter, the discrepancies in the segmentation of AI were refined by an expert and called corrected AI (C-AI) segmentation.

2.2 CNN framework

The CNN framework for the automated segmentation and classification of pristine teeth without brackets or any type of artefacts has been previously described and validated (6). The same pipeline was applied which is configured based on multiple U-Net models (25). All of which function at different spatial resolutions and each model focuses on a different sub-problem for creating a high-resolution multi-class tooth segmentation and classification to 32 tooth classes. These models were implemented in Pytorch and optimized using Adam optimization (26) to decrease the learning rate. The loss function in the training procedure was a binary cross entropy loss for the first and third model and cross entropy loss for the second model (6). To prevent over fitting the training was stopped early. During the training phase, random spatial augmentations were performed which included rotation, scaling and elastic deformation.

2.3 Evaluation metrics

The evaluation metrics for comparing automated and C-AI ground-truth segmentation consisted of intersection over union (IoU), dice similarity coefficient (DSC), precision, recall, accuracy, 95% Hausdorff Distance (HD) and segmentation time. For automated segmentation, the time was recorded starting from the DICOM upload till the generation of multiclass segmentation and classification of all the teeth on a CBCT image. Additionally, the time for C-AI segmentation was assessed by summing up the automated segmentation time and correction time required after the expert carefully examined and identified the slices that required corrections per tooth group (anterior, premolar, molar). However, the time required for import, export and inspection of the data prior to corrections was not included. The classification of teeth was evaluated based on accuracy, precision and recall rate. The specifications of the computing device used for assessing the segmentation time have been listed in Table 4.

Data were analyzed using MedCalc statistical software (version 16.2.0, Ostend, Belgium). Mean and standard deviation values were calculated for assessing the network's performance for complete dataset segmentation, individual segmentation of tooth sub-groups (anterior, premolar, molar), and classification. The performance of tooth segmentation in pre- and post-operative sub-groups for each tooth group was calculated using the Kruskal-Wallis test with Bonferroni correction. A p-value of <0.05 was considered statistically significant.

3. Results

The mean segmentation and classification time of all the teeth on a single CBCT image with the CNN model was 13.7 ± 1.2 , which was three times faster than the C-AI approach (43.56 ± 20.31 seconds).

Table 1 demonstrates the overall performance metrics for segmentation which were calculated by comparing CNN model with the C-AI ground truth. The CNN model showed a high IoU, DSC, precision and recall score of 0.99, indicating towards a near to perfect segmentation. In addition, the overlap between the automated segmentation and ground-truth was excellent, which was confirmed by the 95% HD value of 0.12 ± 0.15 mm. Figure 1 illustrates an example of a case with an almost perfect overlap between automated segmentation and ground-truth.

Table 1. Overall accuracy metrics results by comparing automated with ground-truth segmentation

Accuracy metrics	Mean \pm SD
Intersection over union (IoU)	0.99 \pm 0.02
Dice similarity coefficient (DSC)	0.99 \pm 0.06
Precision	0.99 \pm 0.02
Recall	0.99 \pm 0.01
Accuracy	0.99 \pm 0.01
95% Hausdorff distance (HD) (mm)	0.12 \pm 0.15
Time	43.56 \pm 20.31

Figure 1. Ground-truth and automated teeth segmentation on a cone-beam computed-tomographic image showing almost perfect overlap (A) Axial view of cone-beam computed-tomographic image with delineation of ground-truth teeth boundaries, (B) Ground-truth segmentation, (C) Superimposed automated and ground-truth segmentation, (D) Automated segmentation.

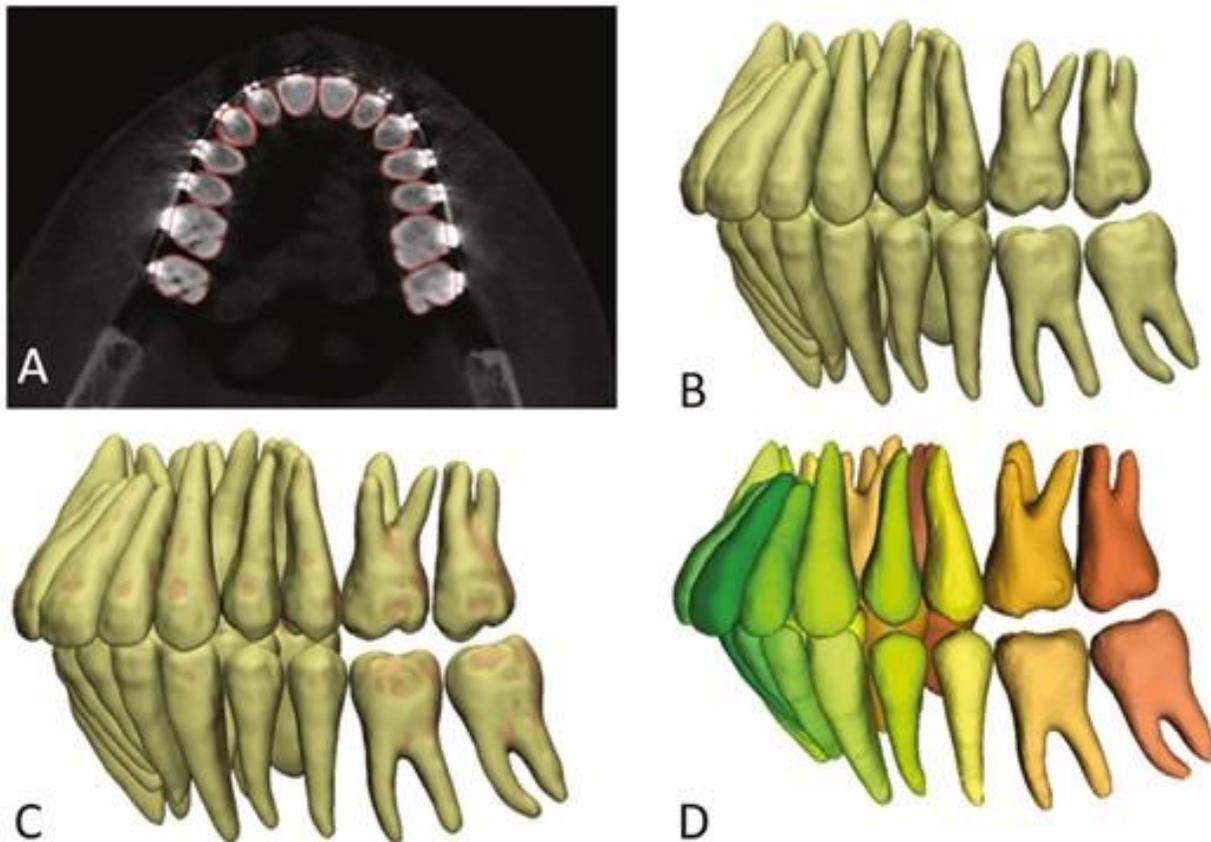


Table 2 describes the segmentation metrics of pre- and post-operative sub-groups based on different tooth types. All the performance metrics in both sub-groups showed a high score ranging between 0.97 and 0.99. Figure 2 illustrates some cases requiring minor correction. In addition, Figure 3 displays the difference and the impact of AI training on teeth with brackets segmentation. According to Table 3, anterior teeth showed a significantly lower IoU ($p < 0.05$) compared to premolar and molar teeth in both pre- and post-operative groups. The classification of teeth to the correct 32 classes showed an almost perfect performance with a high accuracy (100%), recall rate (99.9%) and precision (99%).

Figure 2. Examples of cases requiring manual correction, where red color refers to automated segmentation and yellow color refers to the ground-truth segmentation.

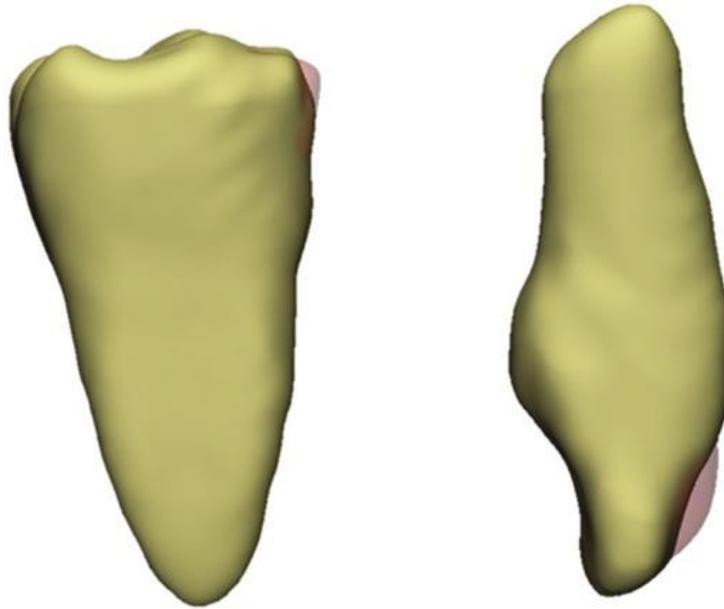


Figure 3. Example of a case where (A) refers to before training and (B) refers to after the training on teeth with brackets segmentation.

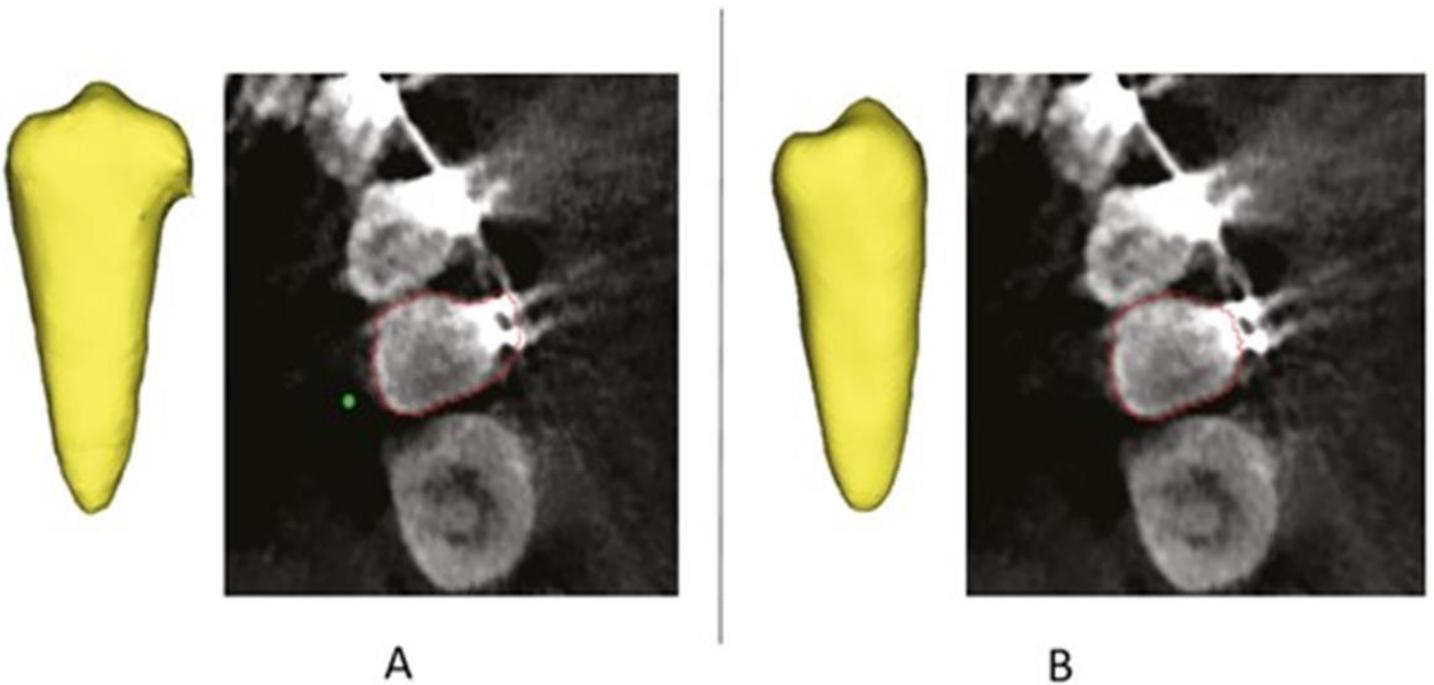


Table 2. Accuracy metrics for comparison of automated with ground-truth segmentation based on different tooth types.

Metrics	Teeth group	Pre-operative	Post-operative
		Mean \pm standard deviation	Mean \pm standard deviation
Intersection over union (IoU)	Anterior teeth	0.97 \pm 0.12	0.98 \pm 0.02
	Premolars	0.99 \pm 0.5	0.99 \pm 0.02
	Molars	0.99 \pm 0.6	0.99 \pm 0.1
Dice similarity coefficient (DSC)	Anterior teeth	0.99 \pm 0.02	0.99 \pm 0.02
	Premolars	0.99 \pm 0.10	0.98 \pm 0.14
	Molars	0.99 \pm 0.44	0.99 \pm 0.01
Precision	Anterior teeth	0.99 \pm 0.2	0.98 \pm 0.03
	Premolars	1.00 \pm 0.01	0.99 \pm 0.02
	Molars	1.00 \pm 0.02	1.00 \pm 0.01
Recall	Anterior teeth	0.99 \pm 0.02	1.00 \pm 0.01
	Premolars	1.00 \pm 0.01	1.00 \pm 0.01
	Molars	1.00 \pm 0.01	1.00 \pm 0.02
Accuracy	Anterior teeth	1.00 \pm 0.01	1.00 \pm 0.01
	Premolars	1.00 \pm 0.01	1.00 \pm 0.01
	Molars	1.00 \pm 0.01	1.00 \pm 0.01
95% Hausdorff distance (HD) (mm)	Anterior teeth	0.16 \pm 0.16	0.18 \pm 0.15
	Premolars	0.2 \pm 0.14	0.12 \pm 0.14
	Molars	0.5 \pm 0.1	0.3 \pm 0.02
Time (seconds)	Anterior teeth	41.8 \pm 19.36	44.82 \pm 18.91
	Premolars	47.9 \pm 21.77	41.67 \pm 14.74
	Molars	46.37 \pm 27.58	39.81 \pm 14.18

Table 3. Intersection over union (IoU) of different tooth types groups.

	Pre-operative		Post-operative	
Teeth group	Number of teeth	Mean IoU \pm SD	Number of teeth	Mean IoU \pm SD
Anterior teeth	288	0.97 \pm 0.12	176	0.98 \pm 0.02
Premolars	182	0.99 \pm 0.5	104	0.99 \pm 0.02
Molars	211	0.99 \pm 0.6	131	0.99 \pm 0.1
p-value				
Pre-op vs Post-op	0.456			
Anterior teeth vs Premolars	0.008*		0.002*	
Anterior teeth vs Molars	0.009*		0.006*	
Premolars vs Molars	0.046		0.268	

SD: standard deviation, * Indicates statistical significance ($p < 0.05$).

Table 4. Specifications of computing device.

<ul style="list-style-type: none"> ○ Model name: AMD Ryzen 7 3700X ○ Number of CPU cores: 8 ○ Number of threads: 16 ○ Base clock: 3.6GHz ○ L1/L2/L3 cache: 512KB/4MB/32MB ○ Total memory: 32GB 	<ul style="list-style-type: none"> ○ Model name: NVIDIA GeForce RTX 3060 ○ CUDA cores: 3584 ○ Total memory: 12GB
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CPU: Central processing unit, GPU: Graphics processing unit, CUDA: Compute unified device architecture

4. Discussion

The present study was conducted to validate an innovative CNN-based tool for multiclass segmentation of teeth with brackets and classification on CBCT images. Our findings showed that the tool was time-efficient and highly accurate in the presence of brackets.

Previous studies have shown that manual segmentation is a time-consuming process, as it might take approximately 3.5-7 hours for segmenting all the teeth in a single scan depending on the observer's experience (6,7). Similarly, semi-automatic approaches also suffer from the limitations of time-consumption, where a single or double-rooted individual tooth could take up to 6.6 minutes to correctly segment (7). Another study reported a time of 29.8 seconds with a CNN model for segmentation of teeth with dental fillings (27). In contrast, the presented CNN-based model took 13.7 ± 1.2 seconds for simultaneous segmentation and classification of all the teeth in a scan independent of the number of roots. Thereby, implying that it could act as a more efficient alternative in dental workflows where either manual or semi-automatic segmentation approaches still remain a clinical standard. Furthermore, the ability of the model to segment teeth with brackets magnifies its clinical potential for dental applications such as orthodontic analysis, surgical guide and/or wafer designing in orthognathic surgery, dental implantology and tooth auto-transplantation, and follow-up assessment of tooth eruption and root resorption. As segmentation of teeth with brackets is time-consuming with manual approaches and thresholding-based semi-automatic techniques fail to optimally separate the brackets from teeth due to the presence of a same range of thresholding value to that of teeth, thereby, requiring a laborious post-processing phase for manual correction. Hence, the integration of this automated tool in the digital dental workflow could lower the possibility of error associated with the non-automated steps of the workflows which could further improve the standard of patient care.

Based on the accurate preparation of the training dataset, the CNN model was able to segment teeth with brackets with higher performance (DSC: 0.99 ± 0.06) compared to other previously reported state-of-the-art algorithms which focused on tooth segmentation without brackets (6,28). Lee et al. (2019) applied a multiphase strategy to train a U-Net-based architecture with a DSC score ranging between 0.91 to 0.92 (20). Cui et al. (2019) presented a 2-stage network consisting of a tooth edge map extraction network and a region proposal network with a DSC of 0.93 (19). Shaheen et al. (2021) assessed the performance of a CNN-based model for tooth segmentation with a DSC score of 0.90 (6). In addition, Wang et al. (2021) used a mixed-scale dense CNN model and found a DSC

of 0.95 (28). The lower performance of the previous studies could be associated with a smaller training set which was not the case in the present study. It is generally a common knowledge that a large labeled training dataset is essential to avoid overfitting of a model, enhance its learning and optimization, and to effectively capture the inherent data distributions.

However, further studies are required to confirm the cause of this minimal error to avoid the chances of a higher accumulative error at the later steps of image processing in the digital workflows.

The findings also showed that the surface deviation between the automated segmentation and C-AI ground-truth was 0.12 ± 0.15 mm. In comparison, Wang et al. reported a slightly higher value of 0.20 ± 0.06 mm for segmenting teeth without brackets(28). Similarly, Shaheen et al. also observed a surface deviation of 0.56 ± 0.38 mm for segmenting teeth without the inclusion of artefacts from implants or brackets (6).

It should be noted that in the majority of digital dental workflows (implantology, orthodontics, orthognathic surgery) three main individual steps exist, which include segmentation of CBCT dataset, segmentation of intraoral scanned dataset and registration (fusion) of both datasets. The first and the most vital step is the segmentation of teeth from CBCT datasets which is then used for registration or fusion with the intraoral scanned datasets (mainly using surface-based fusion or iterative closest point algorithm) (29). If the segmentation of CBCT data is sub-optimal then it would impact the accuracy of fusion step. Therefore, in the present study we proposed an accurate, reliable and time-efficient automated segmentation approach of the CBCT data which could replace the conventional semi-automatic methods. Moreover, having the possibility of lowering the accumulative error of the digital workflows. The next step for future research would be to propose and investigate the accuracy of automated intraoral scanned data segmentation and fusion/registration between CBCT and intraoral scanned data which at the moment is outside the scope of current study.

Furthermore, from a technical point of view, automated fusion is only possible after achieving individual automated segmentation of the CBCT (present aim) and intraoral scanned data (30-32).The strength of the following study was the inclusion of teeth with brackets, which enhances its clinical applicability. However the training of the CNN model was limited to CBCT dataset acquired from a single device with different acquisition settings. Hence, its generalizability and performance with other devices is still questionable.

Future studies are planned to improve its performance and robustness by training with data from multiple devices and cases with dental implants, high-density restorative materials and partial edentulism. Furthermore, accuracy of automated versus C-AI segmentation needs to be qualitatively and quantitatively investigated to appropriately define the regions where maximal corrections are required, for facilitating improvements in the performance of the network.

5. Conclusions

The proposed multi-class CNN model showed excellent performance with high accuracy and efficiency for segmentation and classification of teeth with brackets. It could act as a viable alternative to existing segmentation approaches. Its integration into various digital workflows might increase efficacy of patient-specific treatment planning, while ensuring predictable outcomes.

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ARTICLE 4: Automated three-dimensional quantification of root changes following combined orthodontic-orthognathic surgical treatment. A validation study.

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Abstract

Objectives: Three-dimensional (3D) quantitative assessment of root changes following combined orthodontic-orthognathic surgical treatment is vital for ensuring an optimal long-term tooth prognosis. In this era, lack of evidence exists applying automated 3D approaches for assessing root resorption and remodeling. Therefore, this study aimed to validate a protocol for 3D quantification of root changes on cone-beam computed-tomography (CBCT) images following combined orthodontic-orthognathic surgical treatment. **Methods:** Twenty patients who underwent combined orthodontic-orthognathic surgical treatment were recruited. Each patient had CBCT scans acquired with NewTom Vgi evo (NewTom) at three time-points i.e., 4-weeks prior to surgery (T0), 1-week (T1) and 1-year after surgery (T2). Patients were divided into two groups, group A (surgical Le Fort I osteotomy group: 10 patients) and group B (orthodontic group without maxillary surgical intervention: 10 patients). Root resorption was assessed by measuring length changes and remodeling by volumetric changes of maxillary premolar to premolar teeth (central and lateral incisors, canines, 1st and 2nd premolars= 10 teeth) at T0-T1 and T0-T2 time intervals in both groups. The protocol consisted of convolutional neural network based segmentation followed by surface-based superimposition and automated 3D analysis. **Results:** The intra-observer intra-class correlation coefficient (ICC) was found to be excellent (1.0) with an average error of 0 mm and 0 mm³ for assessing root length and volume, respectively. The entire protocol took 56.8±7 seconds for quantifying root changes. Both group of patients showed negligible changes in length and volumetric ratio at T0-T1 time-interval. Furthermore, group A had lower changes ratio with decreased root volume and length compared to group B at T0-T2 time-interval. **Conclusions:** The proposed protocol was found to be time-efficient, accurate and reliable for 3D quantification of root resorption and remodeling on CBCT images. It could act as a viable automated option for assessing root changes.

Keywords: cone-beam computed tomography, root resorption, orthognathic surgery, neural network models, orthodontic brackets.

1. Introduction

Orthognathic surgical procedures have been widely employed for the correction of dentoskeletal deformities (1). The most common surgical approach includes Le Fort I osteotomy (LF I) performed either alone or in combination with bilateral sagittal split osteotomy (BSSO) (2,3). One of the potential risks associated with LF I is root resorption, which results in postoperative pathological loss of dental root substance due to postsurgical inflammation, vascular damage and development of ischemic necrotic tissue zones within the periodontal ligaments. In addition, other potential causes include proximity of osteotomy cuts and placement of osteosynthesis screws close to the root surface (4). The degree of resorption might range from mild to severe. It is of vital importance to objectively quantify root resorption following orthognathic surgical procedures at follow-up to ensure that an optimal long-term tooth prognosis is achievable (5). As compromised crown-root ratios and shortening in root dimensions might result in tooth mobility or complicate future prosthetic treatment (6,7).

The most broadly applied radiological methods for quantifying root changes include two-dimensional (2D) panoramic, periapical and cephalometric radiography. These 2D techniques have some inherent flaws, such as image magnification, distortion, superimposition of anatomical structures and incorrect patient positioning. All these pitfalls could negatively impact the precision of quantifying root resorption (8-11). To overcome these limitations, the advent of three-dimensional (3D) cone-beam computed-tomography (CBCT) imaging has made it possible to evaluate root resorption with greater precision compared to its conventional 2D counterparts. Nevertheless, the proposed CBCT approaches for quantifying resorption rely on observer dependent landmark-based linear measurement on 2D slices, which are prone to human error and variability. As root changes is a 3D phenomenon involving both length and volumetric changes, mere localization of generic landmarks on 2D slices cannot also be translated to a 3D root anatomy (12,13).

Nowadays, 3D surfaces of teeth derived from CBCT images are being fabricated for root changes evaluation based on length and volumetric measurements, especially in the field of orthodontics (14). However, no studies have reported the application of 3D modeling for linear and volumetric root evaluation in orthognathic surgery. Furthermore, these 3D surfaces are modeled through the process of segmentation, which mostly relies on conventional manual or semi-automatic thresholding-based algorithms integrated into commercial or open-source 3D software programs.

Manual intervention is mandatory to improve the root surface anatomy and carefully adjust areas impacted by artefacts from orthodontic brackets. Hence, making the process both time-consuming and observer dependent (15-17). Recently artificial intelligence based convolutional neural networks (CNN) have been employed to automate and improve the accuracy and efficiency of tooth segmentation on CBCT images (18). However, no study exists quantifying root changes using CNN-based segmentation models.

Based on a recent systematic review, the majority of studies assessing root resorption following orthognathic surgery relied on landmark-based linear measurements using either 2D radiography or orthogonal planes of CBCT images (19). To our knowledge, no methodology has been reported in either orthognathic surgery or any other field of dentistry allowing an automated objective 3D quantification of root changes. Hence, the following study was conducted to overcome the drawbacks associated with both currently advocated 2D and 3D methodologies by integrating CNN-based and custom-made automated algorithms, which could help us better understand the resorption/remodeling phenomenon and further improve the level of evidence.

The aim of the present study was to present and validate a novel automated approach for objectively quantifying linear and volumetric root changes on CBCT images following combined orthodontic-orthognathic surgical treatment.

2. Materials and methods

The study was retrospective in design and conducted in compliance with the World Medical Association Declaration of Helsinki on medical research. Ethical approval was obtained from the Ethical Review Board and patient-specific information was anonymized.

2.1 Patient record selection

Patients who underwent combined orthodontic and orthognathic surgical treatment for the correction of dentoskeletal deformities were recruited from the Hospital's LORTHOG radiological database. Sample size was in accordance with prior validation studies (20,21) and also calculated using a priori power analysis in Gpower 3.1 at a power of 80% and 5% significance level. The patients were further allocated into two group. Group A (surgical group) included patients who underwent orthodontic treatment and mono-maxillary Le Fort I advancement surgery. Patients in group B (orthodontics only group) had orthodontic brackets and underwent isolated BSSO advancement according to Hunsuck/Epker approach without any maxillary surgical intervention

(22). Rigid internal fixation was performed with titanium miniplates and monocortical screws for the fixation and stabilization of bony segments. All surgical procedures were performed by the same team of surgeons.

Inclusion criteria consisted of patients with a minimum age of 18 years, complete dentition and good quality pre- and post-operative CBCT images without motion artefacts. Exclusion criteria were history of maxillofacial trauma, multi-piece LF I and craniofacial syndromes. In addition, patients who had dentoalveolar surgery or other dental restorative procedure during a 1-year follow-up period were also excluded.

2.2 CBCT data acquisition

Pre- and post-operative CBCT scans were acquired at three time-points i.e., 4-week prior to surgery (T0) and 1-week (T1) and 1 year after surgery (T2). All scans were made using a standardized radiological protocol with NewTom Vgi evo (Cefla, Imola, Italy) and the scanning parameters were as follows: 240x190 mm² field of view, 0.3 mm voxel size, 110kV, and 15.3 mAs. Root resorption was assessed from maxillary premolar to premolar region (central incisors, lateral incisors, canines, 1st premolar and 2nd premolar= 10 teeth) at T0-T1 and T0-T2 time-intervals in groups A and B. All the scans were saved in Digital Imaging and Communication in Medicine (DICOM) format.

2.3 Root resorption assessment protocol

The steps of the root changes assessment protocol consisted of segmentation, registration and 3D analysis, details of which are covered in the following sub-sections:

1. Segmentation

The DICOM images at each time-point were individually uploaded onto a CNN-based online cloud tool, ‘Virtual Patient Creator’ (Relu BV, Leuven, Belgium). The tool automatically segmented all the teeth in a scan and has been previously validated for segmenting dentition both with and without orthodontic brackets. Its pipeline was configured using multiple U-Net models and was trained to create a high-resolution multi-class tooth segmentation with high performance metrics. The segmentation outcome was generation of a virtual 3D model of each tooth in Standard Tessellation Language (STL) file format (Figure 1A).

2. Registration and 3D analysis

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The segmented dentition was imported to 3-matic software (version 16.0, Materialise N.V., Leuven, Belgium) A custom-written script was coded in open-source Python programming language (version 3.8; Python Software Foundation, Wilmington, DE, USA, Available at <https://www.python.org>). The script was incorporated into the 3-matic software for the quantification of root changes based on root length and volumetric. The script selected an area of interest including maxillary dentition from left 2nd premolar to right 2nd premolar (Figure 1B). It was programmed to generate a cutting plane for separating the crowns from their roots. The region of cutting plane for each tooth type was defined based on a normal average crown length reported in literature (Table 1) (23-25). Following crown and root separation, iterative closest point (ICP) surface-based registration algorithm already available in the software was applied to register the corresponding crowns of each tooth at the three time-points, where T0 acted as a reference and both T1 and T2 were registered onto it. Registration works on the principle of least point-to-point distance between overlapped surfaces where the final outcome showed no visible spatial changes. The roots at T0-T1 and T0-T2 time-intervals were then isolated from the registered coronal sections. Thereafter, the root length and volumetric ratios (LR, VR) were generated from the reference plane to the root apex. The ratios were automatically calculated by dividing T1 and T2 by T0 values of both length and volumetric measurements. Figure 2 illustrates a flowchart of all the steps involved in the root changes assessment protocol. The complete procedure was repeated twice by a single observer at an interval of 1 week for assessing intra-observer reliability.

Figure 1. Automated segmentation. A. complete dentition, B. area of interest of maxillary premolar-to-premolar region.

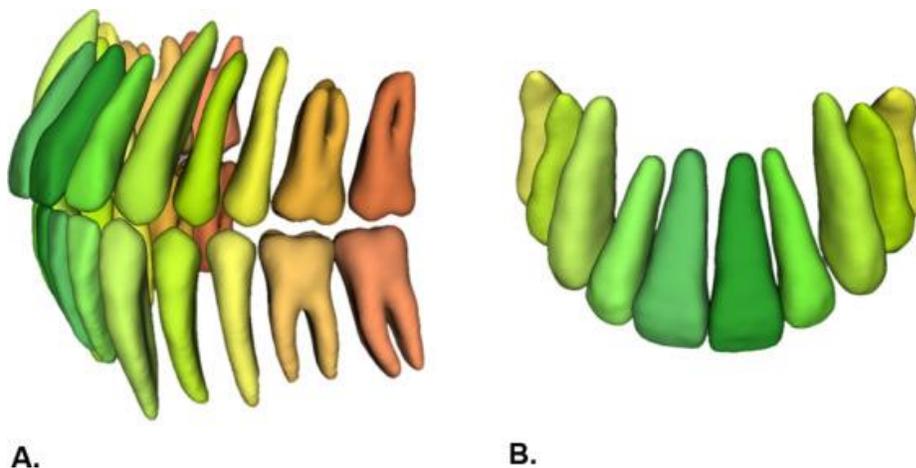
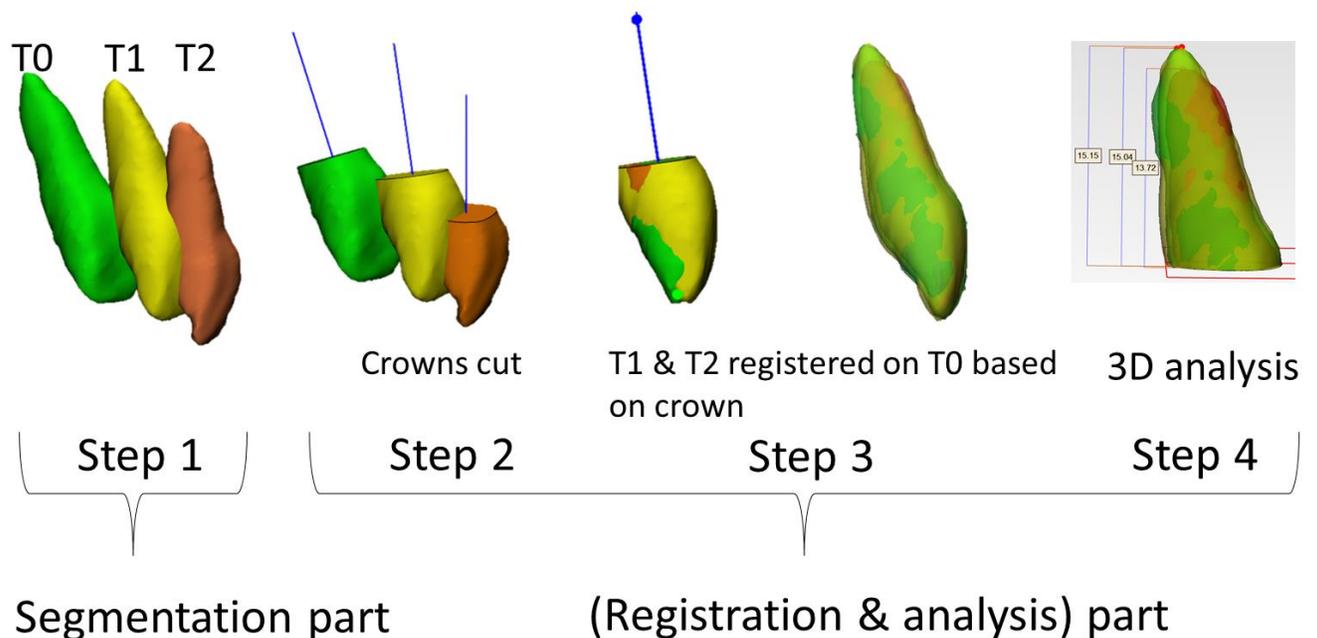


Table 1. Normal crown length (mm) selection for defining the automated crown and separation cutting plane.

	Bassey et al.(23)	Shahid et al.(24)	Volchansky et al.(25)	Reported maximum length	Final selected length
CI	11.4 mm	10.1 mm	11 mm	11.4 mm	12 mm
LI	10 mm	8.7 mm	9.7 mm	10 mm	10 mm
C	9.9 mm	9.8 mm	10.9 mm	10.9 mm	11mm
1stP	8.4 mm	7.9 mm	9.1 mm	9.1 mm	10 mm
2ndP	7.3 mm	6.7 mm	7.9 mm	7.9 mm	8 mm

CI: central incisor, LI: lateral incisor, C: canine, 1stP: first premolar, 2nd P: second premolar.

Figure 2. Illustrates a flowchart of all the steps involved in the root changes assessment protocol. The complete procedure was repeated twice by a single observer at an interval of 1 week for assessing intra-observer reliability.



Statistical Analysis

Statistical data analyses were performed with MedCalc statistical software (version 12.0, Ostend, Belgium). Intra-Class Correlation Coefficient (ICC) of repeated measures was applied at a 95% confidence interval for assessing intra-observer reliability where 0.50 = poor reliability; 0.50–0.75 = moderate reliability; 0.75–0.90 = good reliability; >0.90 = excellent reliability (26).

Descriptive statistics were applied for assessing the mean time duration and volumetric and length differences based on the ratio of linear and volumetric measurements at T0-T1 and T0-T2 time-intervals. Root length ratio was represented as: 1= no root resorption, <1= presence of root resorption based on length and root volume ratio was represented as 1= no root remodeling, <1= presence of root remodeling based on volume.

3. Results

The statistical sample size calculation revealed a minimum sample of 18 patients to obtain a statistical power of 80%, which was also in accordance with prior studies. Twenty patients were recruited (males: 12, females: 8; age range: 18-40 yrs; mean age 21 yrs) and further divided into two groups. Group A included 10 patients (males: 6, females: 4; age range: 18-33 yrs; mean age: 24 yrs) and group B also had 10 patients (males: 5, females: 5; age range: 18-25 yrs; mean age 23 yrs). The total CBCT dataset consisted of 60 scans (T0= 20, T1=20, T2= 20), with each patient having 1 scan per time-point and 10 teeth were evaluated for length and volume changes per patient (maxillary left 2nd premolar to right 2nd premolar = 10 teeth) at T0-T1 and T0-T2 time-intervals in both groups (10 teeth per CBCT x 10 patients = 100 teeth per group).

The intra-observer ICC of the complete methodology was excellent (1.0) in both groups with a mean error of 0 mm and 0 mm³ for root length and volume, respectively. The average time required by the automated protocol for quantifying root changes was 56.8 ± 7 seconds, where segmentation of teeth at three CBCT time-points took 41.1 ± 5 seconds, while 15.7 ± 1 seconds were required for registration and 3D analysis of T0-T1 and T0-T2 measurements.

Table 2 describes LR and VR values at T0-T1 and T0-T2 in both groups. Overall, the mean LR and VR values at T0-T1 time-interval in both treatment groups were close to 1, with an almost negligible root changes. The values at T0-T2 showed that the root changes ratio in group A was lower (LR= 0.94 ± 0.05 , VR= 0.86 ± 0.1) compared to group B (LR= 0.96 ± 0.05 , VR= 0.90 ± 0.06). These ratios indicated that the root length and volume reduced by 6% and 14% in group A and 4%

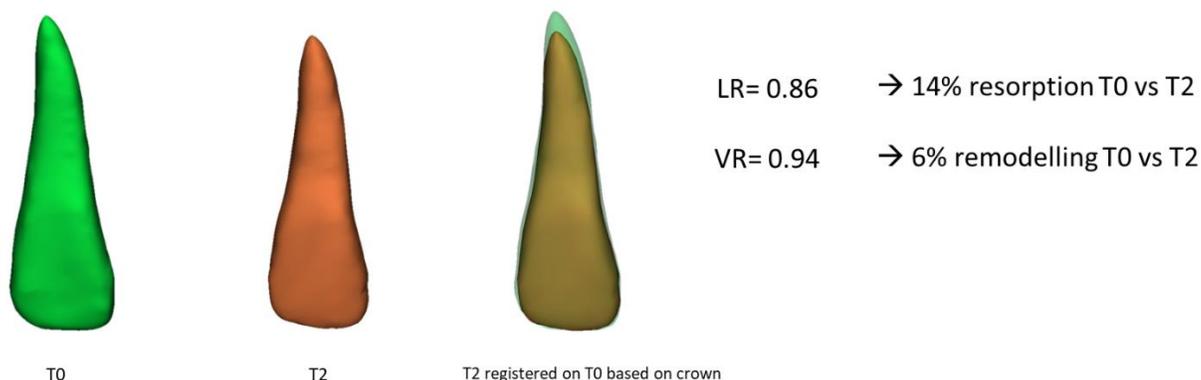
and 10% in group B at T0-T2 time-interval, respectively. Figure 3 shows an example illustrating the changes in LR & VR between T0-T2 time points for a single tooth.

Table 2. Mean \pm standard deviation of root length and volumetric ratios indicating root changes at different time-intervals.

Teeth	T0-T1 ratio				T0-T2 ratio			
	Group 1		Group 2		Group 1		Group 2	
	Length	Volume	Length	Volume	Length	Volume	Length	Volume
R-CI	0.99 \pm 0.04	1.00 \pm 0.14	0.99 \pm 0.03	0.99 \pm 0.06	0.93 \pm 0.08	0.89 \pm 0.16	0.97 \pm 0.04	0.92 \pm 0.13
L-CI	0.99 \pm 0.05	0.99 \pm 0.12	0.99 \pm 0.03	0.99 \pm 0.05	0.92 \pm 0.05	0.81 \pm 0.10	0.97 \pm 0.03	0.94 \pm 0.11
R-LI	0.99 \pm 0.04	1.00 \pm 0.01	0.99 \pm 0.02	0.99 \pm 0.03	0.92 \pm 0.08	0.82 \pm 0.14	0.93 \pm 0.07	0.84 \pm 0.10
L-LI	0.99 \pm 0.04	0.99 \pm 0.06	0.98 \pm 0.02	0.99 \pm 0.05	0.94 \pm 0.04	0.83 \pm 0.12	0.95 \pm 0.03	0.89 \pm 0.07
R-C	0.99 \pm 0.06	1.00 \pm 0.11	0.99 \pm 0.01	1.00 \pm 0.02	0.94 \pm 0.06	0.87 \pm 0.10	0.97 \pm 0.03	0.91 \pm 0.09
L-C	0.99 \pm 0.03	1.00 \pm 0.08	0.99 \pm 0.04	0.99 \pm 0.07	0.94 \pm 0.05	0.86 \pm 0.10	0.97 \pm 0.05	0.89 \pm 0.09
R-1stP	1.00 \pm 0.07	1.00 \pm 0.09	0.99 \pm 0.05	0.99 \pm 0.06	0.94 \pm 0.03	0.86 \pm 0.13	0.97 \pm 0.06	0.88 \pm 0.12
L-1stP	1.00 \pm 0.04	1.00 \pm 0.11	1.00 \pm 0.06	1.00 \pm 0.02	0.96 \pm 0.04	0.92 \pm 0.10	0.97 \pm 0.07	0.90 \pm 0.12
R-2ndP	1.00 \pm 0.03	1.00 \pm 0.02	0.99 \pm 0.02	1.00 \pm 0.01	0.96 \pm 0.04	0.90 \pm 0.07	0.97 \pm 0.04	0.89 \pm 0.10
L-2ndP	0.99 \pm 0.04	0.99 \pm 0.09	1.00 \pm 0.03	1.00 \pm 0.02	0.97 \pm 0.02	0.89 \pm 0.06	0.99 \pm 0.05	0.92 \pm 0.08
All teeth	0.99 \pm 0.01	1.00 \pm 0.05	0.99 \pm 0.02	1.00 \pm 0.01	0.94 \pm 0.05	0.86 \pm 0.1	0.96 \pm 0.05	0.90 \pm 0.06

T0: Preoperative, T1: one-week postoperative, T2: one-year postoperative, R-CI: right central incisor, L-CI: left central incisor, R-LI: right lateral incisor, L-LI: left lateral incisor, R-C: right canine, L-C: left canine, R-1stP: right first premolar, L-1stP: left first premolar, R-2ndP: right second premolar, L-2ndP: Left second premolar.

Figure 3 Example of root changes of central incisor comparing T0 (4 weeks pre-op) and T2 (1 year post-op).



4. Discussion

The 3D reconstruction and modeling of craniomaxillofacial anatomical structures has become a necessary component for treatment planning and follow-up evaluation in the current era of digital dentistry (27-31). To the best of our knowledge, no study has been conducted to evaluate root changes based on length and volumetric differences using an automated methodology. The following study was the first to introduce and validate an innovative automated 3D technique for quantifying root resorption and remodeling following combined orthodontic-orthognathic surgical treatment, which could facilitate clinicians with more clinically oriented feedback and improve the current standard of clinical decision support system.

The present study applied a validated CNN-based automated segmentation approach which has previously shown to have a high performance for segmenting dentition with orthodontic brackets (18). The approach does not require any manual intervention for separating brackets from teeth and is able to delineate root margins with high performance, thereby confirming its clinical applicability. The performance metrics such as, precision, recall and intersection over union scored 0.99 which indicated towards a near to perfect segmentation. The automated segmentation not only overcame the limitations associated with conventional 3D semi-automated approaches but also was

able to achieve a higher performance compared to other state-of-the-art automated algorithms proposed in literature (15,32).

In relation to the reproducibility of the technique, the ICC showed an excellent intra-observer reliability of 1.0 with a zero error for both root volume and length evaluation. A comparison with similar studies was deemed impossible as no automated approach existed in literature for quantifying linear and volumetric changes. At the same instance, volumetric root changes measurements with both manual and semi-automated methodologies have also been found to offer excellent inter- and intra-observer reliability in patients following orthodontic treatment. However, certain limitations have been associated with these methodologies, such as, the need for manual confirmation of the interpolation between slices, refinement of surface anatomy due to beam hardening artefacts from orthodontic brackets, issue of observer variability based on clinician's experience and excessive time-consumption (16). In contrast, the presented methodology overcame all the aforementioned limitations by offering an automated and time-efficient quantification of 3D root changes. Furthermore, the approach was deterministic in nature, which meant that similar results would be achievable with an exact consistency if a same scan was evaluated twice by a single or multiple observers.

As for the root length assessment, landmark-based approaches have been applied universally and no automated approach exists as well. Previous studies suggested that both 2D and 3D landmark-based evaluation methods had moderate to high inter- and intra-observer reliability for assessing root length(33-35). Their reliability and accuracy varied depending on reference landmarks selection, type of tooth being evaluated or observer experience. On the contrary, our approach was built with an automated reference plane selection which was similar for teeth at all time-points, as T0 plane was replicated at the same level of T1 and T2, allowing automated measurement from the middle of reference plane to the root apex.

Unlike prior subjective methodologies, surface-based superimposition allowed a more realistic visualization and quantification of the length and volumetric changes. The accuracy of superimposition is mainly dependent on the segmentation step (36). If segmentation is unable to delineate the root surface with precision then the resulting superimposition would be flawed, and chances of accumulative error would be higher. The zero error of our methodology suggested that there was no risk of error as the segmentation step was accurate and reliable. A previous study also found the tooth crown to be a highly reliable region for superimposition (37).

However, further studies are required to assess whether crown changes over time due to attrition or any other anomaly causing surface tear would influence the accuracy of superimposition.

Based on the percentage of root resorption, both treatment groups showed almost negligible change in root volume and length at T0-T1 time-interval. This is to be expected as the preoperative scan was taken following approximately 4 weeks before surgery and orthodontic treatment is put on hold till after the surgery, whereas immediate scan was acquired 1 week after surgery. Hence, the chances of root changes at a short-term interval are minimal as there is a less risk of tooth movement and early changes in blood flow due to osteotomy are not sufficient to cause either root resorption or remodeling (38). Nevertheless, the surgical group A showed more root resorption at an interval of 1 year compared to the orthodontic group B. This could be attributed to either long-term effect of vascular changes following osteotomy cuts alone or in combination with pressure induced on roots from postoperative orthodontic compensation. It should be kept in mind that these findings should be interpreted with caution, as the present study was only focused towards validating an automated imaging approach. It could act as a viable option ensuring consistent and standardized reporting of root changes data. Further clinical studies are to be performed using the proposed methodology with a large sample size, long-term follow-up period, and/or inclusion of doppler flowmetry assisted blood flow assessment for better understanding the impact of combined orthodontic-orthognathic surgical treatment on root resorption and remodeling.

The study had certain limitations. Firstly, the selection of an automated plane for separating crown and root surfaces based on average crown length might not be applicable to all patients, as the length varies at an individual patient level. However, this way of isolating roots provided a quick and standardized cutting plane for teeth at all time-points. Nevertheless, future studies are recommended to incorporate automated detection and selection of cemento-enamel junction as the reference region for introducing patient-specificity to the approach. Secondly, the complete root volume was reported thus objective specification of region of resorption was missing requiring future work by dividing the root volume into coronal, middle and apical thirds. Thirdly, the region of interest was limited to only maxillary premolar to premolar region. Further studies are warranted to assess linear and volumetric root changes of complete dentition.

5. Conclusions

The proposed protocol provides a time-efficient, accurate and reliable approach for objectively quantifying root changes following combined orthodontic-orthognathic surgical treatment. It could be applied as a feasible alternative to conventional methods of root evaluation methods in both orthodontic and orthognathic surgery patients. This could in turn guide the clinicians in understanding the 3D root surface changes and further improve the standard of care and the decision-making process.

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Part 2: Clinical

ARTICLE 5: Three-dimensional assessment of root changes after Le Fort I osteotomy.

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Abstract

Objectives: This study aimed to correctly assess volumetric, linear and morphological changes of root remodeling and resorption of upper teeth following Le Fort I osteotomy and to investigate the possibility of relationships between root changes and the different patient- and/or treatment-related factors. **Methods:** A total of 60 patients (585 teeth) were retrospectively collected from patients who underwent combined treatment of orthodontic and orthognathic surgery. Study group was 30 patients undergoing one-piece Le Fort I osteotomy. Control group was 30 patients undergoing bilateral sagittal split osteotomy (BSSO). Four cone-beam computed-tomography (CBCT) scans were acquired: preoperative, 6 months, 1 year and 2 years postoperative. **Results:** A validated and fully automatic protocol for three-dimensional (3D) evaluation of root changes was applied. Significant differences were found between study and control groups for morphological changes at the apical and middle parts ranging between 10-28% at 1 and 2 years postoperative. Canines, 1st and 2nd premolars were mostly affected by root remodeling in the study group compared to the control group. The Spearman correlation coefficient showed a positive relation with root remodeling, where larger advancement contributes in increased root remodeling.

Conclusions: This study may assist surgeons and orthodontists to accurately evaluate root changes due to treatment.

Keywords: Root resorption, Le Fort I osteotomy, Orthognathic surgery, Cone-beam computed-tomography, Three-dimensional imaging, Tooth root.

1. Introduction

Orthognathic procedures are frequently performed in many centers across the world to treat facial deformity and malocclusions. Maxillary osteotomy was initially reported in the early 20th century, with Le Fort I osteotomy introduced by Rene Le Fort in 1901 as an osteotomy cut extending from the nasal septum above the teeth root apices into the pterygomaxillary junction. It is a common procedure for correcting malocclusion and maxilla-mandibular abnormalities such as midfacial hypoplasia and vertical excess of the maxillary bone (1–3).

Orthognathic surgery is mostly combined with orthodontic treatment to correct a wide range of abnormalities, including cleft lip and/or palate, hemifacial microsomia, jaw discrepancies, and other craniofacial abnormalities (4,5). In order to achieve the proper occlusion, the necessary skeletal movements must be accompanied by a customized orthodontic treatment. Possible complications of such treatment include infection, paresthesia, periodontal abnormalities, degenerative pulpal alterations or root resorption (6,7) with the degree of vascular damage often linked to the severity of the complications (8).

One of the frequently reported problems of combined orthognathic-orthodontic treatment is undoubtedly root resorption (RS) of the teeth involved. RS is a physiological or pathological process caused by clastic activity that results in the breakdown and loss of hard tissue of the tooth root (9–11). It was even reported that up to 73% of patients suffered from RS after orthodontic treatment (13–15). At the same time, research also seems to point towards orthognathic surgery as being a risk factor for RS (12–14). Maxillary incisors, canines, and premolars appear most prone to resorption following Le Fort I osteotomy (15–18). Buckley et al. (1999), asserted that Le Fort I osteotomy inhibits maxillary blood flow, resulting in obvious impairment in viability and discoloration of the anterior teeth (19).

To assess RS, both two dimensional (2D) and 3D imaging methods can be applied. The vast majority of RS assessment methodologies after orthognathic surgeries rely on either subjective methods or 2D linear measurements on 2D images or 2D sectional images of cone-beam computed-tomography (CBCT) as reported in a recent systematic review by Al Qahtani et.al (12). Since RS is a type of volume loss that happens irregularly and in 3D at root surfaces, these methods are not correctly evaluating RS. Therefore, Al Qahtani et al. (16) recommended 3D assessment methods to be developed that take into account the full volume and length of individual teeth.

The main aim of this study was to correctly assess volumetric, linear, and morphological changes of upper teeth following Le Fort I osteotomy using a fully automated and validated 3D protocol over a period of two years and to compare these findings to root changes in a control group. A subobjective was to investigate possible patient- and/or treatment-related factors contributing to root changes within each group (study and control groups).

2. Materials and methods

2.1 Ethical approval

This retrospective study was conducted according to the World Medical Association's Declaration of Helsinki on medical research, and it was authorized by the local Ethical Review Board (S57587) of the University Hospitals of Leuven.

2.2 Patient record selection

In this study, patients between 18 and 39 years were included to avoid the presence of physiological remodeling as reported in the literature due to incomplete formed teeth (under 18 years) or peak of physiological root remodeling (over 39 years) (25). Patients undergoing a one-piece Le Fort I osteotomy combined with orthodontic treatment were included as "study group". At the same time, patients who underwent isolated bilateral sagittal split osteotomy (BSSO) surgery without any maxillary surgical intervention also combined with orthodontic treatment served as "control group." Exclusion criteria included a history of maxillofacial trauma, previous maxillary surgery, cleft lip and/or palate, and syndromic disorders. The number of patients included was decided via a priori sample size analysis Gpower 3.1 at a power of 80% and 5% significance level to be at least 26 patients in each group. After searching the LORTHOG database and applying inclusion and exclusion criteria, 30 patients were included in the study group (15 males and 15 females, with mean age of 26.3 years) and 30 other patients were included in the control group (15 males and 15 females, with mean age of 26.6 years). According to the standard clinical protocol for orthognathic surgery, each of the sixty patients had 4 CBCT scans: preoperative (Pre), six months postoperative (6M), one-year postoperative (1Y), and two-years postoperative (2Y).

2.3 CBCT data acquisition

CBCT scans were collected using the Newtom Vgi-evo (Cefla, Imola, Italy) with conventional scanning parameters of 96-110 KV, 230x260-240x190 field of view (FOV), and 0.2-0.3mm slice

thickness (20). All 4 CBCT scans were pseudonymized and saved in the Digital Imaging and Communications in Medicine (DICOM) format.

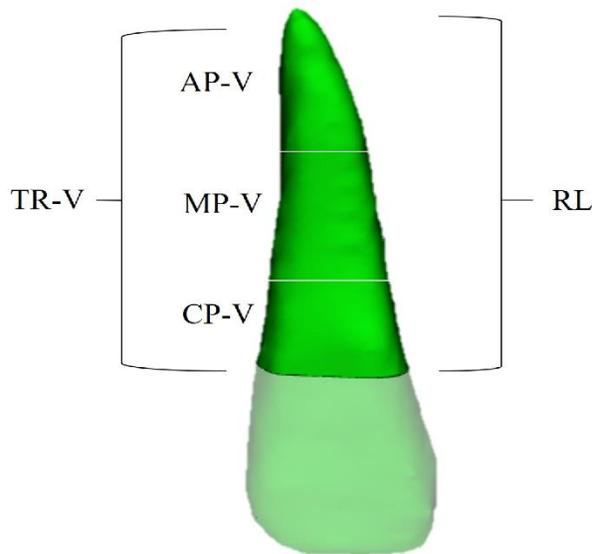
2.4 Root changes assessment protocol

The previously validated root changes 3D assessment protocol included segmentation, registration, and 3D analysis described as follows (21):

For every patient, each CBCT scan was separately uploaded to the “Virtual Patient Creator” online cloud platform (Relu BV, Leuven, Belgium), which is based on convolutional neural networks (CNN) and previously validated for segmenting teeth from CBCT images (22,23). Each segmented 3D tooth was then exported in Standard Tessellation Language (STL) file format.

The segmented teeth were uploaded into a validated fully automatic tool developed in 3-matic software (version 16.0, Materialise N.V., Leuven, Belgium). The tool selected the teeth of interest from the upper jaw: central incisors, lateral incisors, canines, 1st and 2nd premolars and performed surface based registration (SBR) (24). The SBR was based on the crown of each tooth from each postoperative tooth on the corresponding preoperative tooth crown. Further 3D analysis on the root part was applied and resulted into the following measurements: 1. Root length (RL), 2. Total root volume (TR-V), 3. Morphological changes: apical part volume (AP-V), middle part volume (MP-V) and coronal part volume (CP-V) as illustrated in Figure 1.

Figure 1. Illustration of 3D analysis of total root volume, root length and morphological volume changes of the tooth root.



Each measurement in postoperative time point was divided on the corresponding preoperative measurement time point (baseline) to get the ratio of changes in volume (remodeling) and ratio of changes in length (resorption) (31).

2.5 Statistical analysis

Data was analyzed by a biostatistician using S-Plus 8.0 for Linux software. At 6M, 1Y, and 2Y time points, a linear mixed model was used to compare root volume, root length, and morphological ratio changes between and within groups. The teeth were further subdivided to subcategories: central incisors, lateral incisors, canines, 1st premolars and 2nd premolars. Analyses were performed once for all teeth and once for the different subcategories. The Spearman rank correlation test was used to examine the relationships between gender, age, maxillary advancement, and root changes for all teeth and for the different subcategories of teeth within each group. P-value<0.05 was considered statistically significant.

3. Results

A normal quantile plot of the residual values and a residual dot plot showed that the residuals were normally distributed with a uniform variability.

A total of 585 teeth were evaluated from the sixty patients included in this study. Table 1 shows the clinical characteristics of the participants.

Table 1. Clinical characteristics of included participants.

Variable	Study	Control
	Mean \pm SD	Mean \pm SD
Continuous variable		
Age (years)	26.3 \pm 4.8	26.6 \pm 4.5
Orthodontic treatment duration (months)	29.7 \pm 8.8	18.8 \pm 6
Maxillary advancement (mm)	3.6 \pm 1.4	none
Categorical variables		
Sample size		
Gender		
Male	15	15
Female	15	15
Teeth	294	291
Teeth subcategories		
Central incisors	60	60
Lateral incisors	60	60
Canines	60	60
1 st premolars	57	56
2 nd premolars	57	55

3.1 Root changes of study vs control groups

Table 2 presents percentage of root changes between study and control groups in terms of volume, length, and morphological measurements for all teeth. No significant difference was found between the study group and the control group when all teeth were taken into account at any of the

follow-up time points for linear and total root volume measurements. However, overall morphological measurements at the apical and middle parts showed significant remodeling at 1 and 2 years follow-up as compared to baseline. Figures 2 and 3 showed an example of root changes assessment for a central incisor of both control (Figure 2) and study group (Figure 3).

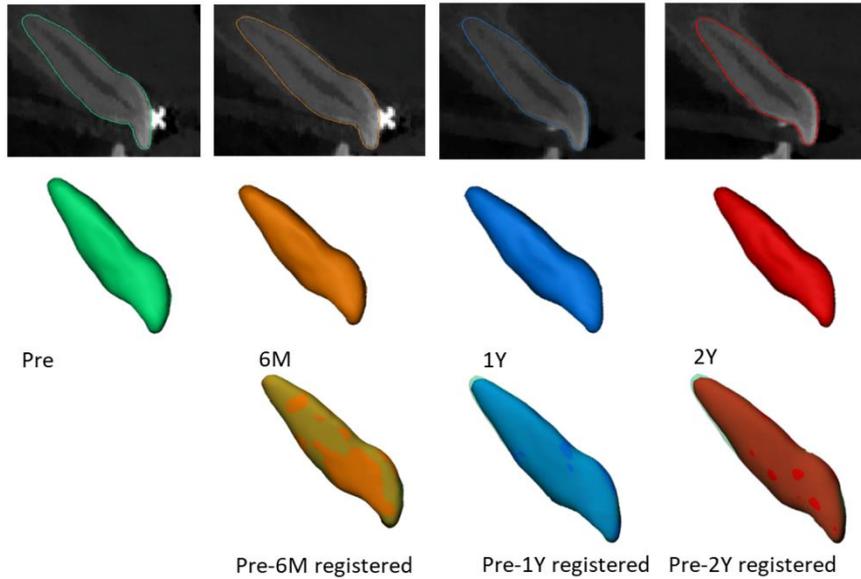
Central and lateral incisors showed no significant difference in root remodeling between study and control groups. On the other hand, significant differences were detected between study and control groups for canines, first and second premolars.

Table 2. Root changes in terms of volume, length and morphological measurements for all teeth

		Study		Control		P-value
		Ratio	% of changes	Ratio	% of changes	
		Mean \pm SD	Mean \pm SD	Mean \pm SD	Mean \pm SD	
Pre-6M	TR-V	0.99 \pm 0.09	1 \pm 0.09	0.99 \pm 0.10	1 \pm 0.10	0.36
	RL	0.99 \pm 0.04	1 \pm 0.04	0.99 \pm 0.06	1 \pm 0.06	0.55
	CP-V	0.99 \pm 0.06	1 \pm 0.06	0.99 \pm 0.07	1 \pm 0.07	0.49
	MP-V	0.99 \pm 0.09	1 \pm 0.09	0.99 \pm 0.09	1 \pm 0.09	0.37
	AP-V	0.97 \pm 0.22	3 \pm 0.22	0.98 \pm 0.24	2 \pm 0.24	0.48
Pre-1Y	TR-V	0.85 \pm 0.08	15 \pm 0.08	0.89 \pm 0.11	11 \pm 0.11	0.06
	RL	0.95 \pm 0.03	5 \pm 0.03	0.95 \pm 0.06	5 \pm 0.06	0.42
	CP-V	0.89 \pm 0.06	11 \pm 0.06	0.92 \pm 0.07	8 \pm 0.07	0.05
	MP-V	0.87 \pm 0.08	13 \pm 0.08	0.91 \pm 0.11	9 \pm 0.11	0.04*
	AP-V	0.73 \pm 0.16	27 \pm 0.16	0.80 \pm 0.24	20 \pm 0.24	0.03*
Pre-2Y	TR-V	0.85 \pm 0.07	15 \pm 0.07	0.87 \pm 0.11	13 \pm 0.11	0.08
	RL	0.94 \pm 0.04	6 \pm 0.04	0.94 \pm 0.07	6 \pm 0.07	0.69
	CP-V	0.88 \pm 0.05	12 \pm 0.05	0.90 \pm 0.07	10 \pm 0.07	0.07
	MP-V	0.88 \pm 0.07	12 \pm 0.07	0.90 \pm 0.10	10 \pm 0.1	0.03*
	AP-V	0.72 \pm 0.16	28 \pm 0.16	0.77 \pm 0.25	23 \pm 0.25	0.03*

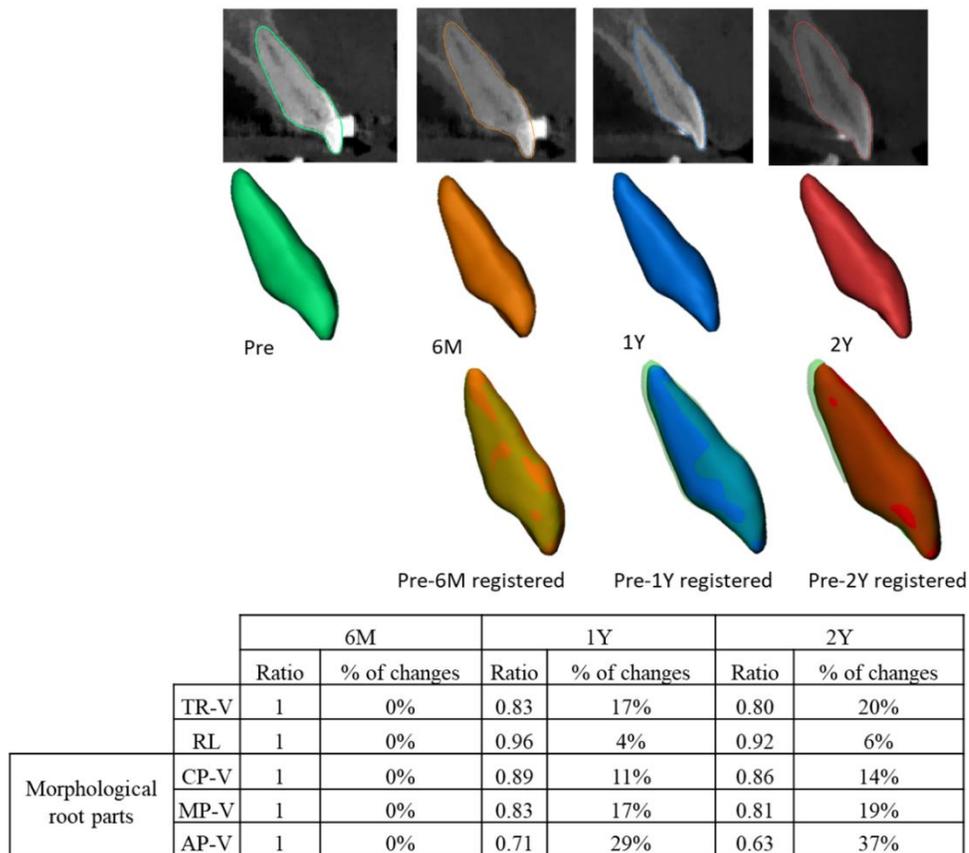
TR-V: Total root volume, RL: Root length, CP-V: Coronal part volume, MP-V: Middle part volume, AP-V: Apical root volume, * indicates significant difference between control and study group.

Figure 2. Example of a CBCT depicting a central incisor with follow-up images after orthodontic treatment, illustrating changes of volume, length and morphology of the tooth root.



		6M		1Y		2Y	
		Ratio	% of changes	Ratio	% of changes	Ratio	% of changes
Morphological root parts	TR-V	1	0%	0.90	10%	0.89	11%
	RL	1	0%	0.96	4%	0.96	4%
	CP-V	1	0%	0.92	8%	0.92	8%
	MP-V	1	0%	0.94	6%	0.92	8%
	AP-V	1	0%	0.89	11%	0.80	20%

Figure 3. Example of a CBCT depicting a central incisor with follow-up images after combined orthognathic-orthodontic treatment, illustrating changes of volume, length and morphology of the tooth root.



3.2 Root changes related factors

Overall, the Spearman correlation test revealed no significant correlation between the amount of root changes and the different factors such as gender and length of orthodontic treatment when analyzing volumetric and linear measurements. Yet, there was a significant negative relation with root volume within the control group with younger patients experiencing more root remodeling in apical and middle root part than older patients. As for the maxillary advancement (only for study group), the Spearman correlation coefficient showed a positive relation with root volume changes, where larger advancement contributes in higher root remodeling in apical and middle root part.

4. Discussion

The purpose of the study was to evaluate the impact of Le Fort I surgery on root changes when compared to a control group. Earlier studies attempting to evaluate root changes during only orthodontic treatment or combined with orthognathic surgery relied on 2D and 3D radiographs using unreliable subjective or linear methods (25–28). The majority of these studies focused on root resorption as the evaluation methods were linear while not reporting volumetric changes that represent root remodeling. Only two studies evaluated root remodeling for only one-year post-treatment on orthodontic population (29,30) with one study considering morphological changes (35).

This study is considered the first 3D study evaluating the impact of Le Fort I surgery (study group) and orthodontic treatment (control group) on root changes considering volumetric, length and morphological changes up to two years post-treatment.

By examining all teeth, linear measurements were considered negligible and identical (1%) for both groups at 6 months postoperative and slightly increased (6%) at 2 years postoperative indicating that the surgery didn't have an impact on root resorption. However, the surgery considerably changed the overall volume ratio at 1 and 2 years postoperative, primarily in the apical third of the root showing up to %15 of root remodeling indicating the possibility that root remodeling might even continue beyond 2 years postoperative.

Additional assessment of subcategories revealed significant higher remodeling for study group compared to control group for canines, 1st and 2nd premolars which can be explained by the canine root length and influence of blood supply alteration following Le Fort I osteotomy (31). These findings cannot be confirmed by other studies, however, are considered to be consistent with earlier studies in terms of higher incidence of remodeling compared to other tooth subcategories (30,31). In a series of literature reviews aiming to identify the different factors contributing to root resorption and/or remodeling, it was found that there is a conflict whether gender can be considered as a factor which was confirmed from our findings that no relationship can be established between gender and root remodeling (13). As for the age factor, previous research found the factor of age to be directly associated with the increased frequency of root resorption following orthodontic treatment while others did not find greater prevalence of resorption in adults. In this study and for only the control group the age was negatively correlated to root remodeling, meaning that younger patients had more root remodeling than older patients.

There are conflicting studies linking the duration of orthodontic treatment to root resorption. When treatment duration is plotted against the change in root for each tooth, some studies found no changes with less than 18 months of orthodontic treatment duration (9), while others discovered a significant correlation between treatment time over 25 months and the degree of resorption (32–38).

The study's potential limitations should be highlighted. The teeth of interest were upper central incisors, lateral incisors, canines, first and second premolars. However, future research should consider all maxillary teeth in even larger prospective trials. Also, it might be interesting to study root changes progress beyond 2 years for various orthognathic surgeries and even up to 5 years follow-up.

5. Conclusions

In conclusion, this was the first study evaluating root changes in terms of volumetric, linear and morphological changes after Le Fort I surgery using a fully automated 3D protocol for a follow-up period of two years post-operative and compared the results to those of a control group representing orthodontic population. Results showed identical and almost negligible root resorption measurements for both control and study groups (1-6%). However, the surgery group experienced significant higher root remodeling at the apical and middle parts at 1 and 2 years follow-up when evaluating all teeth. Canines, 1st and 2nd premolars were mostly affected by root remodeling in the study group compared to the control group. The amount of maxillary advancement is positively related to increased root remodeling. This study may assist surgeons and orthodontists to accurately evaluate root changes due to treatment.

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ARTICLE 6: Three-dimensional assessment of root changes after multi-pieces Le Fort I osteotomy.

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Abstract

Objectives: The purpose of this study was to accurately assess linear, volumetric and morphological changes of maxillary teeth roots following multi-pieces Le Fort I osteotomy. A secondary objective was to assess whether patient- and /or treatment-related factors might influence root remodeling. **Methods:** A total of 60 patients (590 teeth) who underwent combined orthodontic and orthognathic surgery were studied retrospectively. The multi-pieces group included 30 patients who had either 2-pieces or 3-pieces Le Fort I osteotomy. The other 30 patients underwent one-piece Le Fort I osteotomy. Preoperative, 1 year, and 2 years postoperative cone-beam computed-tomography (CBCT) scans were obtained. **Results:** A validated and fully automated method for evaluating root changes in three dimensions (3D) was applied. No statistical significant differences were found between multi-pieces and one-piece Le Fort I for all measurements. The Spearman correlation coefficient revealed a positive relationship between maxillary advancement and root remodeling, with more advancement leading to more root remodeling. **Conclusions:** This research may allow surgeons to properly assess root remodeling after combined treatment of orthodontics and the different Le Fort I osteotomies.

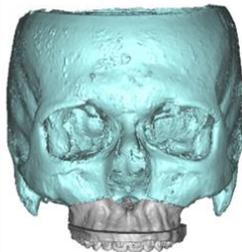
Keywords: Root resorption, Le Fort I osteotomy, Orthognathic surgery, Cone-beam computed-tomography, Three-dimensional imaging, Tooth root.

1. Introduction

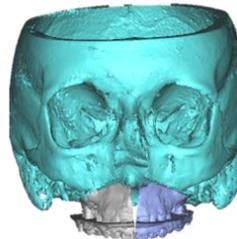
Orthognathic surgery is a cornerstone for surgically treating dentofacial deformities. The most common maxillary orthognathic procedure is Le Fort I osteotomy. However, multi-pieces Le Fort I (MP-LFI) can be an alternative to one piece Le Fort I (OP-LFI) for patients with severe dental crowding or narrow palate or multi-level occlusal plane resulting in an anterior open bite, etc (1,2). OP-LFI osteotomy is a procedure where a single surgical cut is made from the nasal septum to the pterygomaxillary junction above the apices of maxillary teeth roots for correcting the vertical, sagittal and horizontal position of the upper jaw. MP-LFI is similar to OP-LFI with extra surgical cuts created interdentally commonly between central incisors in case of 2 pieces (2P-LFI) or between lateral incisors and canines for 3 pieces (3P-LFI) for correcting the transverse, sagittal and vertical discrepancies (3–5). Figure 1 presents an illustration of the different Le Fort I osteotomies.

Figure 1. Illustration of different Le Fort I osteotomies: A. One-piece Le Fort I, B. Two-pieces Le Fort I, C. Three-pieces Le Fort I.

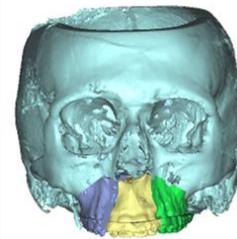
A. One-piece Le Fort I



B. Two-pieces Le Fort I



C. Three-pieces Le Fort I



Research tends to hint towards Le Fort I surgery being a risk factor for root resorption among other postoperative complications such as infection, paresthesia, periodontal abnormalities, degenerative pulpal changes and the extent of vascular damage is generally correlated with the severity of the complications (7,8). Multi-pieces Le Fort I osteotomy involves extra cuts of the maxilla into several segments compared to OP-LFI that can result in significant changes to the position and orientation of the dental roots. Repositioning of these segments can cause alterations in the biomechanical stress distribution within the surrounding bone, leading to changes in the forces exerted on the teeth and their supporting structures. Additionally, surgical manipulation of the maxilla can also affect blood supply, leading to a reduced blood flow to the dental roots, increasing

the risk of root damage (3,6). Following MP-LFI osteotomy, maxillary anterior teeth are the most likely to encounter changes (9–12). Therefore, careful consideration of the potential dental complications associated with this technique are required (7,8).

To evaluate root resorption, both two-dimensional (2D) and three-dimensional (3D) imaging methods have been used. According to a recent systematic review by Al Qahtani et al. (2022), the overwhelming majority of root changes evaluation techniques following orthognathic surgery are limited to subjective methods or linear measurements (13). These methods do not provide an adequate assessment since root resorption and/or remodeling are a form of volume loss in 3D in an irregular manner. Therefore, Al Qahtani et al. developed and validated an automated 3D assessment protocol based on cone-beam computed-tomography (CBCT) imaging to fully evaluate root changes over time (14).

The primary objective of this study was to accurately assess volumetric, linear, and morphological changes of upper teeth following multi-pieces Le Fort I osteotomy using a fully automated and validated 3D protocol over a two-year period and to compare these changes to those observed for a one-piece Le Fort I group. Furthermore, within the multi-pieces Le Fort I group, root remodeling was compared between two and three-pieces subgroups. Moreover, patient- and treatment-related factors that may have contributed to root remodeling in each group (MP-LFI and OP-LFI groups) were investigated.

2. Materials and methods

2.1 Ethical approval

This retrospective study was approved by the local Ethical Review Board (S57587) of the University Hospitals of Leuven and carried out in accordance with the World Medical Association's Declaration of Helsinki on medical research.

2.2 Patient record selection

Inclusion criteria were patients who received orthognathic treatment in the University Hospitals Leuven and between 18 and 39 years old considering maturation of teeth and jaw bones, with bone and tooth structures being less malleable than in younger patients (15). A priori sample size analysis (G*power 3.1) was used to determine the number of patients per group. At 80% power and 5% level of significance, at least 26 patients should be included in each group. Patients who underwent multi-pieces Le Fort I osteotomy combined with orthodontic treatment were included in the study

as “MP-LFI group”. Patients undergoing one-piece Le Fort I osteotomy combined with orthodontic treatment were included in the study as “OP-LFI group”. The study enrolled the CBCT images from 60 patients with 30 patients in MP-LFI group comprising 15 males: (7 3P-LFI and 8 2P-LFI), 15 females: (7 3P-LFI and 8 2P-LFI)with mean age: 25.6 ± 5.5 years and 30 patients in OP-LFI group (15 males and 15 females with mean age: 26.3 ± 4.8 years). Exclusion criteria were history of maxillofacial trauma, history of other maxillary surgery, cleft lip and/or palate, or syndromic diseases. Each of the sixty patients, in accordance with the standard clinical protocol for orthognathic surgery, had three CBCT scans as follows: preoperatively (Pre), one year postoperatively (1Y), and two years postoperatively (2Y).

2.3 CBCT data acquisition

CBCT scans were acquired using the Newtom Vgi-evo (Cefla, Imola, Italy) with typical scanning settings of 96-110 KV, 230x260-240x190 FOV, and 0.2-0.3mm slice thickness. Following the acquisition of the three CBCT scans, all data were anonymized and saved in Digital Imaging and Communications in Medicine (DICOM) format.

2.4 Root changes assessment protocol

Segmentation, registration, and 3D analysis, all of which were part of a previously validated 3D assessment protocol, are outlined below(14):

Each CBCT scan for each patient was uploaded independently to the online cloud platform “Virtual Patient Creator” (Relu BV, Leuven, Belgium), which is based on convolutional neural networks (CNN) and was previously validated for segmenting teeth from CBCT images (16,17). Standard Tessellation Language (STL) file format was used to save each individual segmented 3D tooth.

The segmented teeth were loaded to a fully automated tool created in 3-matic software (version 16.0, Materialise N.V., Leuven, Belgium). The tool selected the teeth of interest, including the central incisors, lateral incisors, canines, first premolars, second premolars and applied surface-based registration on the crown (16) of each postoperative tooth on the crown of the preoperative tooth. Additional 3D assessment of the root part was performed, yielding the following measurements: 1. Root length (RL), 2. Total root volume (TR-V), 3. Morphological changes: apical part volume (AP-V), middle part volume (MP-V), and coronal part volume (CP-V).

Each postoperative measurement time point was divided by the preoperative measurement time point (baseline) to get the volume ratio (remodeling) and length ratio (resorption).

2.5 Statistical analysis

Analysis was performed by a biostatistician using S-Plus 8.0 software for Linux. A linear mixed model was utilized at time periods of 1 and 2 years to retrieve all 5 measurements within and among groups. Further categorization of the teeth resulted in the following subcategories: central incisors, lateral incisors, canines, first premolars, and second premolars. Analyses were carried out twice: once for all teeth, and once for teeth subcategories. The Spearman rank correlation test was utilized in order to investigate the correlations between gender, age, duration of orthodontic treatment, maxillary advancement, and root remodeling for all teeth and subcategories. A p-value of less than 0.05 indicated statistical significance.

3. Results

A total of 590 teeth were evaluated from the sixty patients included in this study. Table 1 shows the clinical characteristics of the participants.

Table 1. Clinical characteristics of included participants.

Variable	One-piece	Multi-pieces
	Mean±SD	Mean±SD
Continuous variable		
Age (years)	26.3±4.8	25.6±5.5
Orthodontic treatment duration (months)	29.7±8.8	29.8±8.5
Maxillary advancement (mm)	3.6±1.4	3.35±1.1
Categorical variables		
Number of piece		
Two-pieces		14
Three-pieces		16
Gender		
Male	15	15
Female	15	15
Teeth	294	296
Teeth subcategories		
Central incisors	60	60
Lateral incisors	60	60
Canines	60	60
1 st premolars	57	58
2 nd premolars	57	58

3.1 MP-LFI vs OP-LFI

Table 2 shows the percentage of volume, length, and morphological changes for all teeth between OP-LFI and MP-LFI groups. No significant difference was identified between both groups when all teeth or subcategories were considered at any of the follow-up time points for all measurements. Table 3 shows no significant difference between 2P-LFI and 3P-LFI subgroups when all teeth and

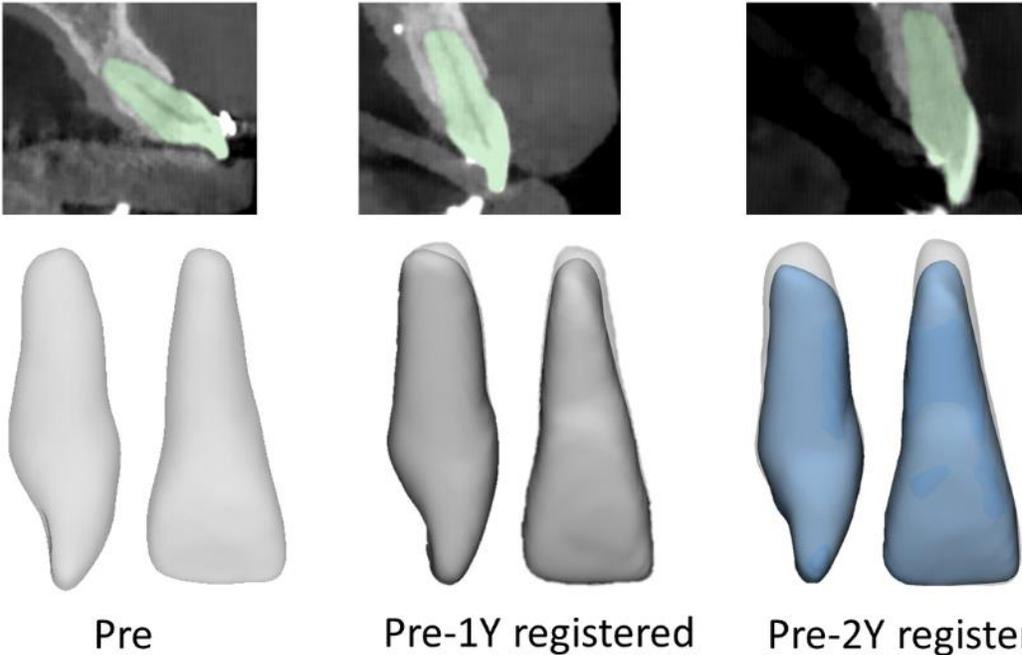
subcategories were evaluated at any of the follow-up time points for all measurements. Figures 2 and 3 showed an example of a central incisor once for multi-pieces Le Fort I (Figure 2) and another for one-piece Le Fort I patient (Figure 3).

Table 2. Root changes in terms of volume, length and morphological measurements for all teeth

		One-piece		Multi-Pieces		P-value
		Ratio	% of changes	Ratio	% of changes	
		Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Pre-1Y	TR-V	0.85 ± 0.08	15±0.08	0.86±0.1	14±0.1	0.8
	RL	0.95 ± 0.03	5±0.03	0.93±0.06	7±0.06	0.2
	CP-V	0.89 ± 0.06	11±0.06	0.90±0.07	10±0.07	0.7
	MP-V	0.87 ± 0.08	13±0.08	0.86±0.1	14±0.1	0.6
	AP-V	0.73 ± 0.16	27±0.16	0.73±0.2	30±0.2	0.8
Pre-2Y	TR-V	0.85 ± 0.07	15±0.07	0.83±0.1	17±0.1	0.3
	RL	0.94 ± 0.04	6±0.04	0.91±0.07	9±0.07	0.4
	CP-V	0.88 ± 0.05	12±0.05	0.87±0.07	13±0.07	0.8
	MP-V	0.88 ± 0.07	12±0.07	0.87±0.1	13±0.1	0.8
	AP-V	0.72 ± 0.16	28±0.16	0.71±0.2	29±0.2	0.2

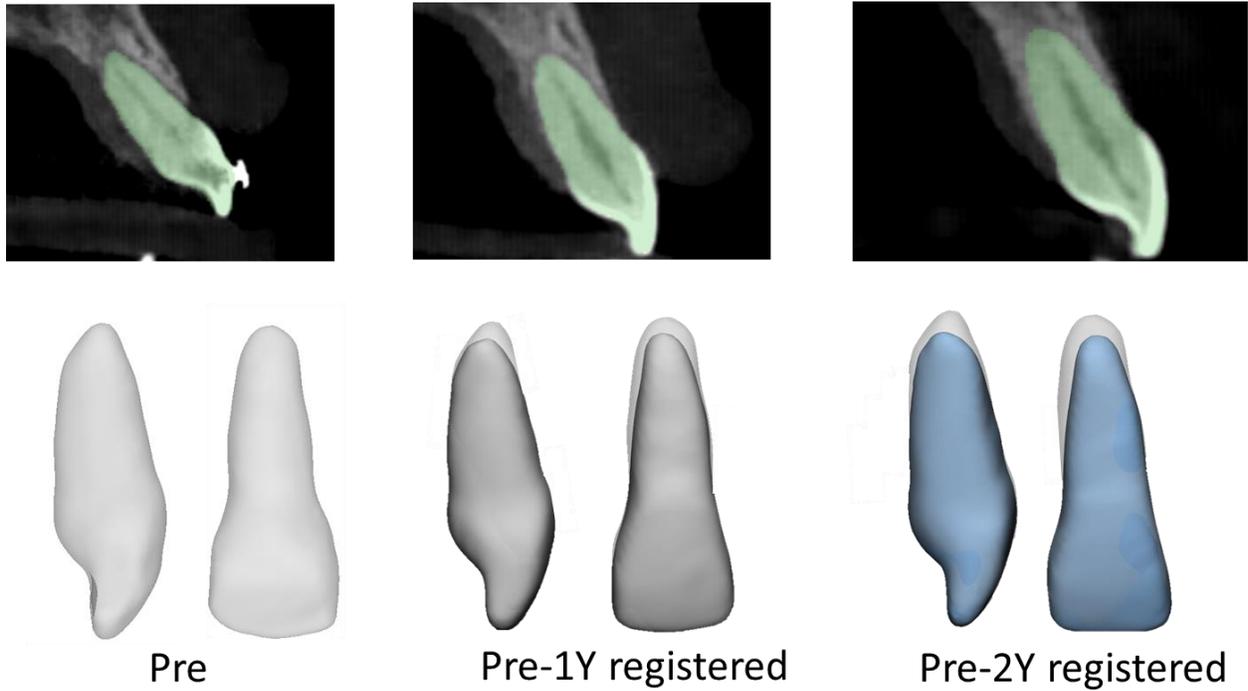
Pre: Preoperative, 1Y: One year postoperative, 2Y: Two years postoperative, TR-V: Total root volume, RL: Root length, CP-V: Coronal part volume, MP-V: Middle part volume, AP-V: Apical root volume, * indicates significant difference between multi-pieces and one-piece group.

Figure 2. Example of a central incisor of a three-pieces Le Fort I patient for the different timepoints. Pre: preoperative (white transparent), 1Y: 1 year postoperative (gray) and 2Y: 2 years postoperative (blue). Each timepoint is illustrated on CBCT and 3D registered segmentations



		1Y		2Y	
		Ratio	% of changes	Ratio	% of changes
Morphological root parts	TR-V	0.65	35%	0.60	40%
	RL	0.81	19%	0.75	25%
	CP-V	0.76	24%	0.74	26%
	MP-V	0.73	27%	0.72	28%
	AP-V	0.51	49%	0.42	58%

Figure 3. Example of a central incisor of a one piece Le Fort I patient for the different timepoints. Pre: preoperative (white transparent), 1Y: 1 year postoperative (gray) and 2Y: 2 years postoperative (blue). Each timepoint is illustrated on CBCT and 3D registered



		1Y		2Y	
		Ratio	% of changes	Ratio	% of changes
Morphological root parts	TR-V	0.75	25%	0.72	28%
	RL	0.87	13%	0.85	15%
	CP-V	0.86	14%	0.85	15%
	MP-V	0.82	18%	0.79	21%
	AP-V	0.50	50%	0.45	55%

Table 3. Root changes in terms of volume, length and morphological measurements for all teeth

		Two-pieces		Three-pieces		P-value
		Ratio	% of changes	Ratio	% of changes	
		Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Pre-1Y	TR-V	0.88±0.1	12±0.01	0.86±0.09	14±0.09	0.8
	RL	0.94±0.06	6±0.05	0.93±0.06	7±0.06	0.2
	CP-V	0.92±0.08	8±0.08	0.92±0.06	8±0.07	0.9
	MP-V	0.91±0.1	9±0.01	0.90±0.07	10±0.07	0.9
	AP-V	0.79±0.2	21±0.03	0.75±0.01	25±0.01	0.5
Pre-2Y	TR-V	0.85±0.1	15±0.01	0.83±0.01	17±0.01	0.6
	RL	0.91±0.06	9±0.06	0.90±0.08	10±0.07	0.6
	CP-V	0.89±0.07	11±0.07	0.90±0.07	10±0.07	0.8
	MP-V	0.88±0.08	12±0.07	0.89±0.09	11±0.01	0.6
	AP-V	0.74±0.2	26±0.16	0.71±0.2	29±0.2	0.3

Pre: Preoperative, 1Y: One year postoperative, 2Y: Two years postoperative, TR-V: Total root volume, RL: Root length, CP-V: Coronal part volume, MP-V: Middle part volume, AP-V: Apical root volume, * indicates significant difference between multi-pieces and one-piece group.

3.2 Root remodeling related factors

Except for maxillary advancement, no significant relation was found between gender, age, number of osteotomy pieces (only for MP-LFI group), and root remodeling. The Spearman correlation coefficient revealed a positive relationship between root volume and maxillary advancement, with more advancement contributing to increased root remodeling.

4. Discussion

Postoperative complications following multi-pieces Le Fort I osteotomy such as infection, tooth discoloration, bone loss, and bleeding have been reported (18–21). So far, root remodeling after multi-pieces Le Fort I has not yet been quantified in literature. Therefore, this study aimed to evaluate the impact of a combined orthodontic/orthognathic surgery treatment of multi-pieces Le Fort I group compared to one-piece Le Fort I group on root resorption and remodeling.

Two-dimensional radiographs are commonly used for subjective or linear root assessment after orthognathic surgery (15,22–24). Recently, the assessment of volumetric root changes following orthodontic treatment was evaluated (25,26) with only one study considering morphological changes (27). This is the first study to assess the effect of MP-LFI surgery on root changes in terms of volumetric, linear, and morphological changes up to two years after treatment using a 3D evaluation protocol.

Two years after surgery, there were no significant differences in root resorption between the various types of Le Fort I osteotomies. However, both types of combined treatments (multi- and one-piece Le Fort I) notably changed the overall root volume 2 years postoperatively. This was particularly the case for the apical third of the root, demonstrating a range between (15 – 17%) of root remodeling.

A prior study found that maxillary advancement of more than 9 mm increases the risk of blood flow complications (18). The average amount of maxillary advancement in our study was 4 mm, which can explain the minor differences between groups. However, a positive relationship between root volume changes and maxillary advancement was found, with larger advancement contributing to higher root remodeling.

Although gender might be considered a factor related to root remodeling in certain situations such as hormonal changes during puberty that can affect the development and growth of roots in both male and female individuals (7), our findings established no relation between gender and root remodeling.

Age can be a contributing factor to root remodeling especially in older patients due to occlusal stress, hormonal changes and the fully developed jaw bones and teeth, as the roots are more anchored in the bone and less malleable. Additionally, older patients may have more significant

bone loss and weaker bone density, which can affect the stability of the teeth and roots (28,29). In the current study, we discovered no correlation between age and root remodeling in either group. Studies that attempted to relate the length of orthodontic treatment to root remodeling produced inconsistent outcomes but some research concluded that orthodontic treatment less than 25 months will minimize the impact on root remodeling (27,30–35). In the present study the average time of orthodontic treatment in both groups was 30 months with no significant relationship between the length of orthodontic treatment and root remodeling.

This requires relying on advanced imaging techniques to visualize the surgical site and ensure precise placement of the bone segments. Additionally, minimizing trauma to the surrounding tissues during the surgery and carefully monitoring the healing process can also be important in minimizing any potential negative effects on the roots.

It is important to highlight any potential study limitations. The teeth of interest were upper central incisors, lateral incisors, canines, first and second premolars. Therefore, larger prospective trials should be conducted in future studies employing all maxillary teeth. Also, it could be noteworthy to investigate root remodeling up to 5 years follow-up.

5. Conclusions

This was the first research to evaluate volumetric, linear, and morphological changes of teeth roots two years following a combined orthodontic treatment with MP-LFI versus OP-LFI surgeries. Evaluation of all teeth and subcategories revealed no statistically significant differences between the MP-LFI and OP-LFI groups for all measurements at any postoperative time point concluding that these types of osteotomies do not have an extra effect on root remodeling. Furthermore, the quantity of maxillary advancement correlates positively with increased root remodeling. This research may help surgeons to correctly assess root remodeling, enabling postoperative reporting and facilitating patient communication.

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ARTICLE 7: Recommendations to minimize tooth root remodeling in patients undergoing maxillary osteotomies and orthodontics only

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Abstract

Objectives: The purpose of this study was to report root remodeling/resorption percentages of maxillary teeth following the different maxillary osteotomies; i.e. one-piece, two-pieces, three-pieces Le Fort I, surgically assisted rapid palatal expansion (SARPE). The possibility of relationships between root remodeling and various patient- and/or treatment-related factors were further investigated. **Methods:** A total of 110 patients (1075 teeth) who underwent combined orthodontic and orthognathic surgery were studied retrospectively. The sample size was divided into: 30 patients in one-piece Le Fort I group, 30 patients in multi-pieces Le Fort I group, 20 patients in SARPE group and 30 patients in an orthodontic only group. Preoperative and 1 year postoperative cone-beam computed-tomography (CBCT) scans were obtained. **Results:** A validated and automated method for evaluating root remodeling and resorption in three dimensions (3D) was applied. SARPE group showed the highest percentage of root remodeling. Spearman correlation coefficient revealed a significant positive relationship between maxillary advancement and root remodeling, with more advancement contributing to more root remodeling. On the other hand, the orthodontic group showed a significant negative correlation with age indicating increased root remodeling in younger patients. Based on the reported results of linear, volumetric and morphological changes of the root after 1 year, clinical recommendations were provided in the form of decision tree flowchart and tables. **Conclusions:** These recommendations can serve as a valuable resource for surgeons in estimating and managing root remodeling and resorption associated with different maxillary surgical techniques.

Keywords: Practice guideline, Root resorption, Le Fort I osteotomy, Orthognathic surgery, Cone-beam computed tomography, Three-dimensional imaging, Tooth root.

1. Introduction

Orthognathic surgery, also known as corrective jaw surgery, is a type of surgical treatment that aims to correct and improve the position and function of the jaws and teeth. This surgery is typically indicated for patients with severe skeletal discrepancies or congenital deformities that cannot be corrected with orthodontic treatment alone (1–4).

One-jaw surgery, also known as single-jaw surgery, is correcting the position and alignment of only one jaw that involves mainly Le Fort I in the upper jaw or bilateral sagittal split osteotomy (BSSO) in the lower jaw. One-jaw surgery is typically recommended for patients with minor jaw discrepancies while bimaxillary surgery, also known as two-jaw surgery involves correcting the position and alignment of both the upper and lower jaws (2,3).

There are several types of maxillary orthognathic osteotomies that can be performed depending on the patient's individual needs and the severity of their dental and skeletal deficiencies. Most commonly known type of maxillary osteotomy is Le Fort I, which involves cutting and repositioning upper jaw in vertical, horizontal or sagittal directions as one-piece Le Fort I. This technique is indicated for patients with vertical maxillary excess, sleep apnea, midface hypoplasia and/or facial asymmetry (5). Two-pieces Le Fort I osteotomies are additional osteotomies performed in two separate pieces to correct transversal hypoplasia up until 5-7mm. Three-pieces Le Fort I osteotomies add the possibility to close an anterior open bite (6-9). Finally, surgically assisted palatal expansion (SARPE) is another type of maxillary orthognathic osteotomy with gradual expansion of narrow upper jaws or crossbites using a tooth-borne or bone-borne device (10–13). Whereas multiple-pieces osteotomies need interposition of bone graft, this is not necessary in transverse distraction of the upper jaw with SARPE.

Complications associated with maxillary orthognathic surgery can include nerve damage, infection, bleeding, mouth opening limitation, changes in facial aesthetics and root resorption (14–18). Additionally, changes in blood flow to the teeth can also be a potential complication during the procedures of maxillary orthognathic surgeries due to the disruption of the blood vessels supplying the teeth leading to a decrease in the delivery of oxygen and nutrients to the teeth causing root remodeling, resorption and even tooth loss (19,20,21).

Several methods can be used to evaluate root changes after maxillary orthognathic surgeries such as panoramic radiographs or cone-beam computed tomography (CBCT) scans (22). These images are utilized to measure the distance between the root apex and certain anatomical landmarks, such

as cortical bone or cemento-enamel junction, to determine if root resorption has occurred (12,18). More appropriately is to use CBCT images to apply 3D analysis allowing more extensive, elaborate and accurate measurements than only linear such as volumetric and morphological changes of the root (23–26). Three-dimensionally based methods would help surgeons and orthodontist to accurately assess the extent of root resorption/remodeling after maxillary orthognathic surgeries. The aim of this study is to provide an overview of the potential root resorption/remodeling that can occur following different types of maxillary orthognathic osteotomies and to offer recommendations to surgeons in order to minimize root resorption and provide estimates of root remodeling occurring after various osteotomies.

2. Materials and methods

2.1 Ethical approval

This retrospective study was approved by the local Ethical Review Board (S57587) of the University Hospitals of Leuven and carried out in accordance with the World Medical Association's Declaration of Helsinki on medical research.

2.2 Patient record selection

Inclusion criteria were patients who underwent orthognathic surgery and orthodontic treatment in the University Hospitals of Leuven between ages of 18 and 39 years. Patients who had a previous history of orthognathic surgery, orthodontic treatment, trauma to the maxillofacial region, and syndromic diseases or cleft lip/palate were excluded. In this study, we included 110 patients who met the inclusion criteria. Of these patients, 30 underwent one-piece Le Fort I osteotomy (15 males and 15 females), fifteen underwent two-pieces Le Fort I osteotomy (7 males and 8 females), fifteen underwent three-pieces Le Fort I osteotomy (7 males and 8 females), and twenty underwent SARPE by using tooth-borne device (5 males and 15 females). We also included 30 patients who underwent BSSO and only orthodontic treatment in the upper jaw (15 males and 15 females) that is called orthodontic group. Each of the 110 patients, in accordance with the standard clinical protocol for orthognathic surgery, had two CBCT scans as follows: preoperatively (Pre) and one year postoperatively (1Y).

2.3 CBCT data acquisition

CBCT scans were acquired using the Newtom VGi-evo (Cefla, Imola, Italy) with typical scanning settings of 96-110 KV, 230x260-240x190 FOV, and 0.2-0.3mm slice thickness (27). Following the acquisition of the Pre and 1Y CBCT scans, all data were anonymized and saved in Digital Imaging and Communications in Medicine (DICOM) format.

2.4 Root changes assessment protocol

A previously validated 3D assessment protocol was applied including 3 main steps: segmentation, registration and 3D analysis (28). Segmentation refers to the process of separating the teeth from the CBCT images, which was performed using a convolutional neural network-based online cloud platform (Relu BV, Leuven, Belgium) called "Virtual Patient Creator" that was previously validated for this purpose (29,30). The segmented teeth were then saved in a standard Tessellation Language (STL) file format and imported into a fully automated tool within 3-matic software (version 16.0, Materialise N.V., Leuven, Belgium), that selected specific teeth from the upper jaw: central incisors, lateral incisors, canines, first premolars, and second premolars. The tool applied surface-based registration on the crown of one year postoperative tooth to the crown of the preoperative tooth. Additionally, the root part of the teeth was assessed in 3D, including measurements of root length (RL), total root volume (TRV), and volumes for 3 parts of the root: apical (AP-V), middle (MP-V), and coronal (CP-V). To quantify changes over time, 1 year postoperative measurement was divided by the preoperative measurement to obtain volume ratios for remodeling and length ratios for resorption.

2.5 Patient and surgery factors

In the current study, we investigated the relationships between variables that might be related to root remodeling after maxillary orthognathic osteotomies. Patient related variables are age and gender while treatment related variables included maxillary advancement and planned palatal expansion described by the amount in mm calculated from the number of days the patient used the expander multiplied by the expansion rate of 0.5 mm per day for SARPE patients.

2.6 Statistical analysis

The biostatistician utilized S-Plus 8.0 software for Linux to analyze the data. Mean and standard deviation of percentage of root remodeling (RE) and resorption (RS) in terms of volume, length, and morphological changes (apical part (AP), middle part (MP) and coronal part (CP)) for all teeth and teeth subcategories were reported for the five groups: one-piece Le Fort I, two-pieces Le Fort

I, three-pieces Le Fort I, SARPE and orthodontic only. The Spearman rank correlation test was used to investigate correlations between gender, age, maxillary advancement (Le Fort I groups), planned palatal expansion (SARPE group), and root remodeling. A p-value of less than 0.05 was used as the threshold for statistical significance.

3. Results

A total of 1075 teeth were evaluated from the images 110 patients included in this study. Table 1 shows the clinical characteristics of the participants.

Table 1. Clinical characteristics of included participants.

Variable	One-piece	Two-pieces	Three-pieces	SARPE	Orthodontics only
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD
Continuous variable					
Age (years)	26.3±4.8	26.2±3.5	26.7±4.5	25.6±5.5	26.6±4.5
Maxillary advancement (mm)	3.6±1.4	3.35±1.1	3.4±1.3	none	none
Categorical variables					
	Sample size	Sample size	Sample size	Sample size	Sample size
Gender					
Male	15	8	7	9	15
Female	15	8	7	11	15
Teeth	294	156	140	194	291
Teeth subcategories					
Central incisors	60	32	28	40	60
Lateral incisors	60	32	28	40	60
Canines	60	32	28	40	60
1 st premolars	57	30	28	37	56
2 nd premolars	57	30	28	37	55

3.1 Root changes related to surgery type

Table 2 presents percentage of root resorption and remodeling of the five treatment types for all patients and all teeth. The least percentage of root resorption among groups was the orthodontics only followed by SARPE, one-piece Le Fort I, two-pieces Le Fort I and three-pieces Le Fort I

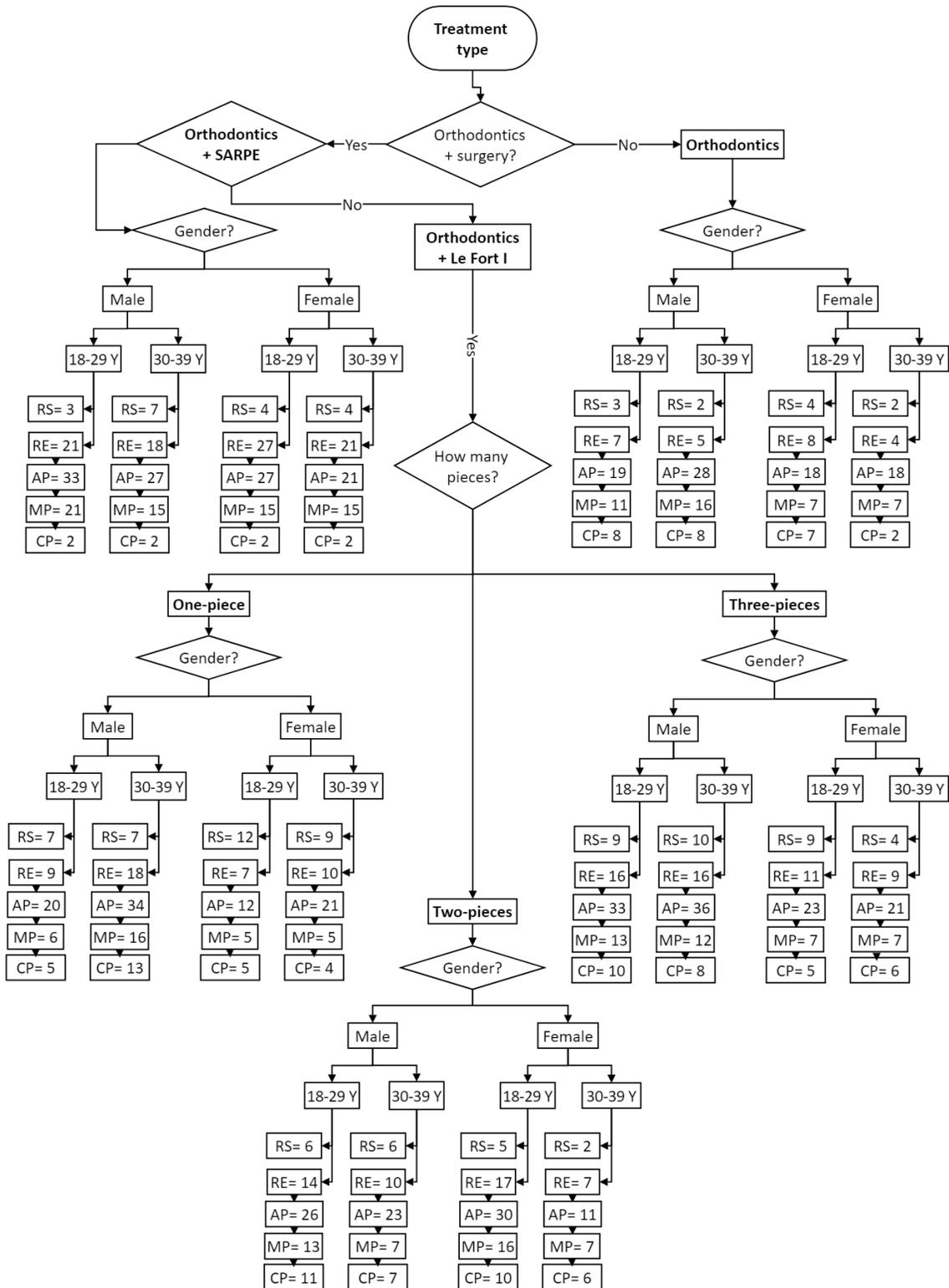
respectively. In addition, results indicated that SARPE group had the highest percentage of root remodeling, followed by three-pieces Le Fort I , two-pieces Le Fort I, one-piece Le Fort I, and finally the orthodontics only group. Root remodeling was the largest in the apical part with a range between $20\% \pm 0.24\%$ and $29\% \pm 0.16\%$.

Table 2. Root resorption (RS), remodeling (RE) and morphological changes (AP: apical part, MP: middle part, CP: coronal part) percentages for all teeth following different maxillary osteotomies.

Treatment type	RS %	RE %	AP %	MP %	CP %
	Mean \pm SD				
Orthodontics only	4 \pm 0.02	9 \pm 0.11	20 \pm 0.24	10 \pm 0.05	9 \pm 0.06
Orthodontics + SARPE	5 \pm 0.03	19 \pm 0.08	29 \pm 0.19	13 \pm 0.07	9 \pm 0.02
Orthodontics + One-piece Le Fort I	5 \pm 0.08	11 \pm 0.06	25 \pm 0.01	8 \pm 0.05	5 \pm 0.04
Orthodontics + Two-pieces Le Fort I	6 \pm 0.05	12 \pm 0.01	26 \pm 0.09	10 \pm 0.1	6 \pm 0.07
Orthodontics + Three-pieces Le Fort I	7 \pm 0.06	14 \pm 0.09	27 \pm 0.04	13 \pm 0.03	5 \pm 0.01

For better visualization, the flowchart in Figure 1 summarizes the percentage of root changes (all five measurements) observed in each group. The flowchart starts by treatment type then divided based on gender then further subdivided into 2 age subgroups: 18-29 years and 30-39 years. For example, a female patient aged between 18 and 29 years who underwent SARPE treatment developed the following: RS: 4%, RE: 27%, AP: 27%, MP: 15% and CP: 2%.

Figure 1. Flowchart reporting the percentage of root remodeling (RE), resorption (RS) and morphological changes (AP: apical part, MP: middle part, CP: coronal part)



For more detailed results of teeth subcategories, we refer to Table 3 that reported the percentage of RE and RS in terms of volume, length, and morphological changes (AP, MP, CP) for all five treatment groups per gender, age subgroup and tooth subcategory. Figure 2 illustrates via example the root resorption and remodeling measurements for a typical central incisor of a male aged between 18-29 years undergoing the five treatment types investigated in this study as reported in Table 3. Figures 3 showed examples of root changes of central incisors of patients, once undergoing orthodontic treatment and the other undergoing orthodontics combined with three-pieces Le Fort I treatment.

Table 2. Detailed root remodeling (RE), resorption (RS) and morphological changes (AP: apical part, MP: middle part, CP: coronal part) percentage for subcategories teeth.

Treatment type	Gender	Age (years)	Subcategories	RS %	RE %	AP %	MP %	CP %
Orthodontics only	M	18-29	Centrals	5	11	17	9	2
			Laterals	6	12	19	11	8
			Canines	4	8	15	7	5
			1st Premolars	6	16	28	16	11
			2nd Premolars	3	12	17	10	11
	M	30-39	Centrals	9	19	37	16	13
			Laterals	6	18	30	16	18
			Canines	8	16	3	18	16
			1st Premolars	7	20	1	19	20
			2nd Premolars	6	17	1	16	17
	F	18-29	Centrals	7	11	22	8	7
			Laterals	8	12	26	9	8
			Canines	4	6	13	5	4
			1st Premolars	4	8	16	6	7
			2nd Premolars	4	9	13	7	8
	F	30-39	Centrals	4	10	22	7	6
			Laterals	8	13	24	9	9
			Canines	5	11	24	9	7
			1st Premolars	2	8	13	5	8

			2nd Premolars	2	5	6	4	5
Orthodontics + SARPE	M	18-29	Centrals	6	21	24	21	1
			Laterals	3	25	36	23	2
			Canines	4	21	34	20	1
			1st Premolars	1	16	34	19	2
			2nd Premolars	4	22	37	21	2
	M	30-39	Centrals	5	12	14	12	3
			Laterals	4	16	18	14	2
			Canines	5	14	17	14	1
			1st Premolars	9	28	51	22	1
			2nd Premolars	10	21	35	15	3
	F	18-29	Centrals	3	16	24	19	1
			Laterals	4	21	27	19	2
			Canines	4	14	23	14	2
			1st Premolars	4	10	15	7	1
			2nd Premolars	5	18	32	18	3
F	30-39	Centrals	2	10	11	10	2	
		Laterals	2	14	15	13	3	
		Canines	4	15	22	14	4	
		1st Premolars	8	22	34	19	1	
		2nd Premolars	4	16	24	17	2	
Orthodontics + One-piece Le Fort I	M	18-29	Centrals	4	11	19	8	3
			Laterals	6	14	26	10	10
			Canines	5	13	23	10	10
			1st Premolars	6	17	33	13	13
			2nd Premolars	6	17	32	14	13
	M	30-39	Centrals	6	9	20	7	6
			Laterals	6	10	18	9	7
			Canines	6	8	16	6	7
			1st Premolars	7	12	32	8	8
			2nd Premolars	7	7	27	6	7
	F	18-29	Centrals	4	14	22	13	11
Laterals			5	17	26	14	14	

			Canines	6	17	31	16	13		
			1st Premolars	7	20	38	19	16		
			2nd Premolars	5	17	31	16	14		
			F	30-39	Centrals	3	11	18	11	9
					Laterals	3	5	8	4	5
					Canines	3	8	16	6	5
1st Premolars	2	6			15	6	5			
2nd Premolars	0	5			7	3	0			
Orthodontics + Two-pieces Le Fort I	M	18-29	Centrals	9	14	33	11	2		
			Laterals	12	15	30	9	9		
			Canines	5	9	19	8	6		
			1st Premolars	7	5	6	4	3		
			2nd Premolars	6	3	10	0	0		
	M	30-39	Centrals	11	17	33	14	10		
			Laterals	17	19	31	16	14		
			Canines	11	15	31	14	11		
			1st Premolars	16	19	39	16	14		
			2nd Premolars	13	20	35	17	15		
	F	18-29	Centrals	5	8	14	5	6		
			Laterals	7	9	18	7	6		
			Canines	3	8	14	7	6		
			1st Premolars	2	6	13	5	4		
			2nd Premolars	1	2	1	1	1		
	F	30-39	Centrals	26	26	61	13	10		
			Laterals	12	18	34	11	11		
			Canines	3	5	5	0	0		
			1st Premolars	0	3	2	1	5		
			2nd Premolars	2	4	5	2	5		
Orthodontics + Three-pieces Le Fort I	M	18-29	Centrals	10	17	35	13	5		
			Laterals	11	17	34	12	9		
			Canines	7	12	25	10	8		
			1st Premolars	11	20	45	20	13		
			2nd Premolars	6	12	24	10	10		

	M	30-39	Centrals	7	10	29	6	4
			Laterals	5	17	32	12	12
			Canines	11	18	27	15	12
			1st Premolars	14	15	43	10	11
			2nd Premolars	9	17	32	15	15
	F	18-29	Centrals	12	18	34	13	11
			Laterals	11	14	26	8	8
			Canines	10	8	17	5	6
			1st Premolars	5	7	22	4	5
			2nd Premolars	4	8	15	6	7
	F	30-39	Centrals	4	3	10	1	0
			Laterals	4	8	19	6	5
			Canines	6	11	26	8	9
			1st Premolars	1	16	30	17	10
			2nd Premolars	4	8	18	6	6

Figure 2. Illustration of root changes in 3D for a typical central incisor of male patients aged between 18-29 years undergoing the five treatment types: A. Orthodontics only, B. SARPE + orthodontics, C. One-piece Le Fort I + orthodontics, D. Two-pieces Le Fort I + orthodontics, E. Three-pieces Le Fort I + orthodontics reporting root resorption (RS) and root remodeling (RE). Preoperative tooth is in transparent red and 1 year postoperative tooth in gray.

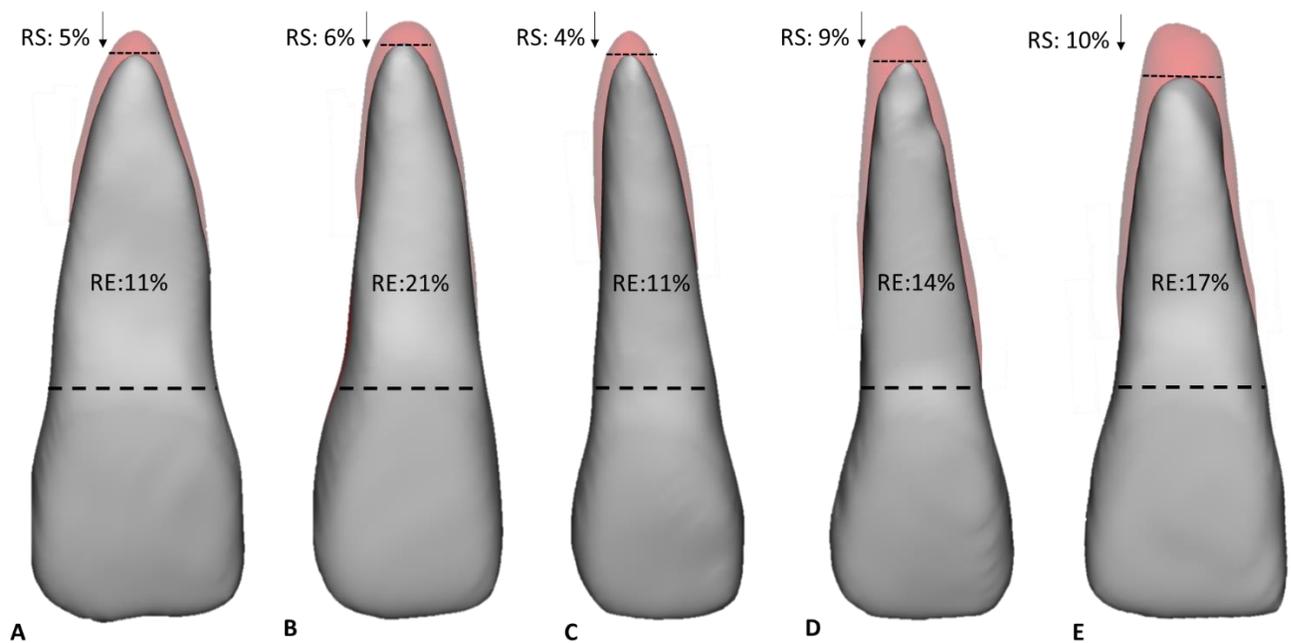
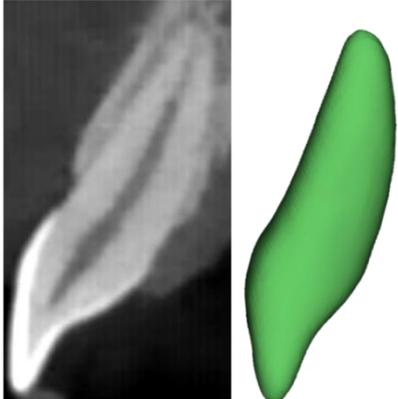
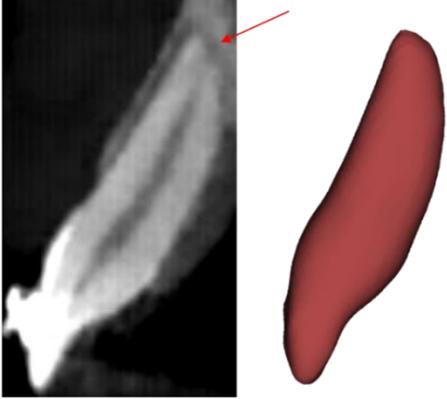
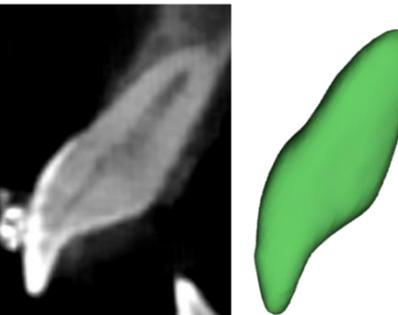
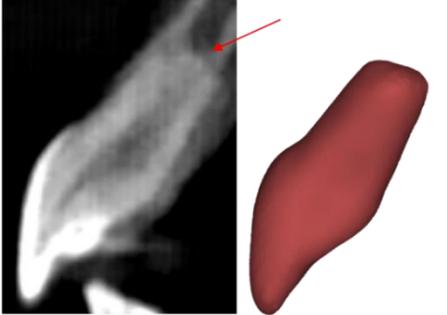


Figure 3. Examples of CBCT images and 3D reconstructions depicting central incisors at preoperative (green) and one-year postoperative (red) time points for a patient from orthodontics only group and another patient from combined orthodontic + three-pieces Le Fort I group, illustrating root changes as indicated by red arrow.

Treatment type	Preoperative	One-year postoperative
Orthodontic		
Orthodontic + Three-pieces Le Fort I		

3.2 Root remodeling related factors

Regarding patient related factors, the Spearman correlation coefficient showed that younger patients in orthodontics only group had a higher chance of developing root remodeling during orthodontic treatment. Among the variables related to surgery, patients with more maxillary advancement were more likely to have root remodeling. The other variables evaluated in this study did not reveal statistically significant correlations. In addition, no teeth were lost among the various treatment groups one year postoperatively.

4. Discussion

The assessment of root remodeling/resorption after maxillary orthognathic surgeries holds significant importance as it has not been thoroughly investigated in existing literature (9,15,31,32). By comprehensively evaluating root changes, this study aimed to provide valuable information about the potential effects of orthognathic surgery on the root, which can help optimize treatment outcomes and minimize potential risks in the future.

Previous studies used subjective and linear methods to assess root resorption following either orthodontic treatment or orthognathic surgery (33–38) however, these methods have limitations in terms of precision and accuracy (39–42).

Recently, volumetric analysis have emerged as a more reliable and accurate tool for assessing root remodeling after isolated orthodontic treatment (23). These methods can also aid in quantifying the magnitude and distribution of root remodeling in different dimensions, facilitating a more precise and objective assessment (25,26). In the present study, a previously validated 3D fully automated protocol for assessing root changes was applied for patients who underwent orthognathic surgery (28).

Root resorption is a common complication that may occur during isolated orthodontic treatment or combined with orthognathic surgery. In this study, the overall percentage of the amount of root resorption among different treatment types ranged between 4% and 7% and can be considered minimal. On the other hand, results have shown that SARPE group is associated with the highest percentage of root remodeling described by root volume measurements. A possible explanation can be that SARPE is often performed in patients with transverse maxillary deficiency or a constricted maxillary arch, where roots of teeth are already positioned close to cortical bone, potentially leading to root remodeling because of increased mechanical forces. In addition, tooth-borne appliances may have more impact on root remodeling since they transmit more force directly to teeth, which can lead to increased pressure on the periodontium and root surfaces (11,12). This pressure can cause cellular and molecular changes in the periodontium and alveolar bone, leading to remodeling of surrounding tissues and possible root resorption (22). In our study, all patients undergoing SARPE were treated with a tooth-borne rapid palatal expansion appliance with an expansion rate of 0.25 mm twice a day. However, it is important to note that even with a slower rate of expansion, there is still a risk of root remodeling in patients undergoing SARPE.

Three-pieces Le Fort I surgery also resulted in root remodeling followed by two-pieces and one-piece Le Fort I surgery respectively, due to the involvement of more segments, potentially larger surgical movements and blood flow impairment (6,16,43). On the other hand, the orthodontics only group had the least amount of root remodeling. The extent and pattern of root changes can vary depending on the type and magnitude of surgical movements, treatment sequence, and patient-specific factors. Therefore, careful consideration of the specific treatment combination and its order is crucial in treatment planning and postoperative management to minimize the risk of root resorption or remodeling and optimize patient outcomes.

In this study, a negative correlation has been observed between root remodeling and younger patients in the orthodontic group. There are several possible reasons for this negative correlation. First, younger patients generally have less mature root structures, as root development continues until late adolescence or early adulthood. Immature roots may be more susceptible to remodeling or resorption in response to the mechanical forces applied during orthodontic treatment or orthognathic surgery. Additionally, younger patients may have more active cellular processes in the periodontal ligament and bone as result of a combination of factors, including growth, tooth eruption, tissue adaptation, functional forces, hormonal effects, and efficient healing mechanisms, which could potentially influence root remodeling (44).

In contrast, a significant positive correlation has been observed between root remodeling and the amount of maxillary advancement. The relationship between increased maxillary advancement during orthognathic surgery and increased root remodeling can be attributed to the repositioning of the maxilla during surgery contributing to changes in blood flow and positioning. This can lead to altered forces on the roots, including increased tensile and compressive forces on the labial and palatal surfaces of the upper teeth, as well as shear forces due to changes in tooth movements (7). According to the findings of this study, the amount of root resorption was considered minimal within the range of 4% to 7% for isolated orthodontic treatment or combined with maxillary surgery, respectively. In case of diagnosed root resorption, caution should be taken when planning SARPE or large maxillary advancement for Le Fort I osteotomies as they were associated with increased root remodeling. On the other hand, in patients with orthodontic relapse resulting in an anterior open bite and narrow maxilla, a three pieces Le Fort I osteotomy is preferred over a SARPE procedure followed by a single piece Le Fort I osteotomy. Furthermore, estimation of root

resorption/remodeling for each treatment type, gender, age group and tooth subcategories were presented in tables (2 and 3) to assist surgeons with decision making of treatment planning.

The study has limitations that should be considered in interpreting the findings. Firstly, the follow-up duration of only one year may not capture the complete remodeling or resorption processes that can occur over a longer timeframe. Secondly, the study relied on the planned amount of palatal expansion (SARPE group) as the only available documented measurement of expansion in the patient files, which may not accurately reflect the actual amount of expansion achieved during the surgical procedure. Further studies should be conducted on prospectively controlled trials with a larger sample size. The findings of more studies may allow generating a larger amount of data to build a predictive model for assessing root resorption risk. In addition, the relationship between genetics and susceptibility to root resorption is a subject of scientific interest. Genetic factors influence the regulation of processes related to tooth development, mineralization, and immune responses, impacting an individual's likelihood of experiencing root resorption. Further research is essential to comprehend the intricate interplay between genetics and external factors, leading to improved personalized dental care approaches (38).

This might allow surgeons and orthodontist to more effectively predict outcomes and tailor treatments to individual patients, ultimately leading to improved surgical outcome with less complications.

5. Conclusions

The present study is the first ever to address root remodeling and resorption 1 year after a combined orthodontic/orthognathic treatment procedure, meanwhile looking to volumetric, linear, and morphological changes and compare these to root remodeling occurring after isolated orthodontic treatment. The current recommendations give more insight to surgeons in estimating possible root remodeling and resorption associated with different maxillary surgery techniques serving a valuable resource for patient specific treatment planning.

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General discussion, conclusions and future perspectives

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1. General discussion

Root resorption is a common dental condition that occurs due to various factors. Trauma, orthodontic treatment, inflammation, impacted teeth, and genetics are common triggers (1,2). It can lead to pain, sensitivity, and in severe cases, tooth loss. Quantification of root resorption and remodeling is an essential tool for dental professionals to assess the progression of the condition, assess the effectiveness of treatment, and determine the prognosis of affected teeth (3–6). Furthermore, accurate quantification provides valuable information that can guide treatment planning and help dentists make informed decisions regarding the most appropriate treatment options for their patients (7–9). Overall, the importance of root resorption quantification cannot be overstated, as it plays a crucial role in maintaining oral health and preventing irreversible damage to the dentition. The main objectives of this doctoral thesis were to develop a 3D automated assessment protocol in order to accurately investigate the impact of different maxillary orthognathic osteotomies on root resorption and to provide clear guidelines for orthodontists and surgeons on the extent and severity of root resorption and remodeling associated with different orthognathic procedures.

In **article 1**, the objective of the systematic review was to investigate whether orthognathic surgery has an impact on root resorption. We systematically searched for articles published up to April 2022 and selected six studies that reported on root resorption following orthognathic surgery. The findings suggest that certain orthognathic procedures, such as surgically assisted rapid maxillary expansion and Le Fort I osteotomy, may have an impact on root resorption, but further studies are needed to better understand the relationship between orthognathic surgery and root resorption (10–15). In the review article, it was recommended to use 3D CBCT imaging to assess root resorption more accurately, as previous studies relied on 2D radiographs which are limited.

In **article 2**, we created and validated a computer-based system that can accurately and quickly segment and classify 3D teeth from CBCT images using deep learning techniques. The system was developed to overcome the limitations of traditional segmentation approaches and to provide a more efficient and effective method for dental diagnosis and treatment planning (16,17). The CBCT scans used in the study were obtained from patients with no heavy metal artifact, however, slight artefacts due to dental fillings were present, which may affect the quality of segmentation. The system developed in the study has shown high accuracy and consistency, but further training was needed to handle artefacts generated by high-density materials such as dental implants and

orthodontic brackets. The system achieved high accuracy and was 1800 times faster than expert-based segmentation. The proposed method overcame some limitations of existing deep learning-based algorithms, although comparison with previous studies was limited due to differences in metrics and sample heterogeneity.

In article 3, the same tool in **article 2** was further trained with CBCT images including teeth with orthodontic brackets and heavy metal artefacts. The study evaluated the performance of the AI model for segmenting and classifying teeth with brackets artefacts in CBCT images with a high accuracy score of IoU (0.99) and an excellent overlap 95% HD ($0.12 \pm 0.15\text{mm}$) with the ground-truth segmentation. These findings suggest that the AI model can provide a near-perfect segmentation of teeth in CBCT images, which can be useful for dental diagnosis and treatment planning. The ability of the tool to segment teeth with brackets also expands its potential use in orthodontic analysis, surgical guide design, dental implantology, and follow-up assessments.

In article 4, an innovative 3D automated protocol was introduced and validated for accurately assessing changes in the root length, volume and morphological parts using CBCT images after combined orthodontic and orthognathic surgery over time. The protocol involves segmenting teeth from DICOM images using the AI tool presented in **articles 2 and 3**, generating a 3D model of each tooth, and using a custom-written Python script to separate the crowns from the roots and register corresponding crowns at different time points. The root length and volumetric ratios are then calculated to assess changes in root remodeling and resorption. The protocol showed excellent intra-observer reliability and overcame limitations of previous subjective and linear root changes assessment approaches, such as the need for manual confirmation and excessive time consumption (10–14). The use of a 3D automated assessment protocol allowed for more precise and accurate measurements compared to traditional 2D imaging techniques.

In article 5, the validated protocol in **article 4** was applied on orthognathic patients undergoing Le Fort I osteotomy over a period of two years to assess volumetric, linear, and morphological changes of upper teeth. The study also compared these findings to root changes in a control group and investigated possible patient and treatment-related factors contributing to root changes within each group. We evaluated 585 teeth from 60 patients and analyzed the relationships between gender, age, maxillary advancement, and root remodeling. The results showed that there were no significant differences between the study and control groups except for root remodeling where volumetric apical remodeling was higher for Le Fort I group in comparison to control group.

In **article 6**, the validated protocol in **article 4** was used to evaluate changes in the upper teeth of patients who underwent multi-pieces Le Fort I osteotomy over a two-year period and compared these changes to those patients who underwent a one-piece Le Fort I osteotomy. Also, root changes between two-pieces and three-pieces subgroups within the multi-pieces group were compared. The study evaluated 590 teeth from 60 patients and analyzed the correlations between gender, age, maxillary advancement, and root remodeling for all teeth and subcategories. The results showed no significant differences between one-piece and multi-pieces groups. These findings suggest that both types of surgeries may be equally effectiveness in terms of root changes. **Article 5**, revealed a significant negative relationship between age and root remodeling in the control group, while **articles 5 and 6** demonstrated a significant positive relationship between the amount of maxillary advancement and root remodeling in the Le Fort I groups.

In **article 7**, we evaluated root changes after maxillary orthognathic surgery as this was not extensively studied before. The study aimed to provide valuable recommendations on the potential effects of maxillary osteotomies on the root (18–21). The study included 110 patients who underwent orthognathic surgery at the University Hospitals Leuven between the ages of 18 and 39 years. This study enabled a better understanding of the relationship between different surgical techniques and the extent of root changes, and helped to identify factors that contribute to the development of root remodeling. The results of this study have important implications for clinical practice, as it provides a more accurate assessment of the risks associated with different orthognathic osteotomies and help to guide treatment outcomes.

2. Conclusions

The following conclusions can be drawn from the thesis:

- Root resorption is a dental condition that can lead to tooth loss and requires accurate quantification for effective monitoring and treatment planning.
- **Article 1:** suggests that certain orthognathic procedures, specifically maxillary osteotomies, contribute to root resorption. The use of the fully automated 3D protocols which we developed can help to assess the impact of these procedures more accurately.
- **Articles 2 & 3:** demonstrate the ability of artificial intelligence to accurately, quickly segment and classify teeth in 3D from CBCT images, also segmentation of teeth with brackets expands

its potential use in orthodontic treatment, surgical guide design, dental implantology, and follow-up assessments.

- **Article 4:** an innovative automated 3D protocol was introduced and validated for quantifying changes in root length, volume, and morphological parts using CBCT images after combined orthodontic and orthognathic surgery.
- **Article 5:** conducted the first evaluation of root changes following one-piece Le Fort I surgery using the fully automated 3D protocol. The surgery group demonstrated significantly higher root remodeling in the apical and middle parts at the 1- and 2-year follow-up, encompassing all teeth. Moreover, the amount of maxillary advancement exhibited a positive correlation with increased root remodeling.
- **Article 6:** the objective of this study was to examine the volumetric, linear, and morphological changes of teeth roots two years after combined orthodontic treatment with multi-pieces Le Fort I versus one-piece Le Fort I surgeries. The study compared measurements between the two groups and found no statistically significant differences for all measurements at any postoperative time point. This suggests that the type of osteotomy (MP-LFI or OP-LFI) does not have an additional effect on root remodeling. However, the study did find a significant positive correlation between the amount of maxillary advancement and increased root remodeling.
- **Article 7:** provided recommendations to orthodontists and surgeons regarding root remodeling and resorption over a period of one year after different surgical maxillary osteotomies. The findings indicate that root resorption during orthodontic treatment, whether conducted alone or combined with maxillary surgery, remained minimal, with rates ranging from 4% to 7%. However, caution is advised when planning procedures like surgically assisted rapid palatal expansion or extensive maxillary advancement through Le Fort I osteotomies, as they were found to be associated with increased root remodeling. In cases where patients experience orthodontic relapse leading to an anterior open bite and narrow maxilla, the study suggests that a three-piece Le Fort I osteotomy is preferable over a combination of SARPE followed by a single-piece Le Fort I osteotomy. This suggests that the three-piece Le Fort I osteotomy may be more effective in addressing these specific orthodontic concerns. These findings have important implications for clinical practice and can help to optimize treatment outcomes and minimize risks.

3. Future perspectives

- Further development of automated 3D protocol: the thesis highlights the importance of fully automated 3D protocol in accurately assessing root resorption and changes in root length, volume, and morphology.
- Future research can focus on expanding this protocol in different clinical scenarios. This would contribute to better treatment planning for patients with root resorption.
- Integration of artificial intelligence in dentistry: the use of artificial intelligence in segmenting and classifying teeth from CBCT images has shown promising results. Future studies can explore the integration of AI algorithms in orthodontic treatment planning, surgical guide design, dental implantology, and follow-up assessments. This would streamline and improve the efficiency of these processes, benefiting both clinicians and patients.
- Long-term follow-up studies: while the thesis provides insights into root changes over a period of one to two years, considering the ALARA concept a long-term follow-up studies can provide a more comprehensive understanding the potential long-term consequences of root remodeling. Investigating the effects of root changes beyond the two years follow-up period would enhance the knowledge base and help refine treatment protocols.
- Refinement of treatment strategies: the thesis offers recommendations for optimizing treatment outcomes and minimizing risks associated with root remodeling. Future research can focus on developing and refining treatment strategies to further reduce the incidence and severity of root resorption during orthodontic and orthognathic treatment. This would improve patient care and contribute to better long-term oral health outcomes.
- Studies about possible other factors playing a role in root resorption like molecular, biological and functional difference among patients.

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Summary

The use of three-dimensional imaging in quantifying root changes is of significant importance in various dental applications. Therefore, in **article 1**, we therefore learn the traditional 2D radiographs, such as periapical and panoramic images, which have limitations in accurately assessing root resorption. 2D imaging can suffer from structural superimposition, magnification errors, and distortion, leading to under- or overestimation of root changes. On the other hand, CBCT imaging provides a more accurate and reliable alternative for assessing changes following orthognathic surgery or other dental procedures. In **articles 2&3**, using teeth segmentation, allows for a true 3D representation of the teeth structures, enabling precise measurement and visualization of root changes over time. Additionally, in **article 4**, a fully automatic three-dimensional root changes assessment protocol is developed that can overcome the limitations associated with subjective and linear assessment either on 2D or 3D radiographs, offering improved assessment of resorption and remodeling and facilitating better treatment planning and follow-up protocols. In two separate studies, **article 5** and **article 6**, the impact of Le Fort I surgery on root changes was investigated. **Article 5**, aimed to evaluate root changes compared to a control group, while **article 6**, compared the postoperative root changes between multi-pieces and one-piece Le Fort I osteotomies. **Article 5**, found that Le Fort I surgery did not significantly impact root resorption, as indicated by negligible and identical linear measurements for both groups 6 months postoperative. However, significant changes in overall root volume were observed at 1 and 2 years postoperative, particularly in the apical third of the root, suggesting up to 15% root remodeling. Canines, first and second premolars showed higher levels of remodeling in the study group compared to the control group. Gender was not found to be a significant factor in root remodeling, but younger patients in the control group exhibited more significant root remodeling. **Article 6**, investigated the root resorption and remodeling after multi-pieces Le Fort I surgery compared to one-piece Le Fort I surgery. Both types of surgery did not show significant differences in root resorption after two years. However, both groups experienced notable changes in overall root volume, particularly in the apical third, indicating a range of 15-17% root remodeling. Larger maxillary advancement was associated with higher root remodeling. Gender was not found to be a significant factors in root remodeling. However, both studies recommend the development of comprehensive recommendations for the assessment of root resorption and remodeling in the context of maxillary orthognathic surgery and orthodontic treatment.

Article 7, we provided valuable recommendations for understanding the potential effects of maxillary orthognathic surgery on the teeth root, considering gender and age for all maxillary teeth and subcategories to optimizing treatment outcomes, and minimizing risks. The overall percentage of root resorption among different treatment types is small, ranging between 4% and 7%. However, the study finds that SARPE group is associated with the highest percentage of root remodeling. The findings of this doctoral thesis showed that 3D assessment of root changes may allow a more careful treatment planning to further improve the surgical outcome and enhance the decision-making process.

Samenvatting

Het gebruik van driedimensionale beeldvorming bij het kwantificeren van wortelveranderingen is van groot belang in verschillende tandheelkundige toepassingen. Daarom hebben traditionele 2D-röntgenfoto's, zoals periapicale en panoramische beelden, in artikel 1 beperkingen bij het nauwkeurig beoordelen van wortelresorptie. Routinematig gebruikte 2D-beeldvorming wordt geplaagd door structurele superpositie, vergrotingsfouten en vervorming, wat leidt tot onder- of overschatting van wortelveranderingen. CBCT-beeldvorming biedt daarentegen een nauwkeuriger en betrouwbaarder alternatief voor het beoordelen van veranderingen na orthognatische chirurgie of andere tandheelkundige procedures. In artikels 2&3 maakt tandsegmentatie echter een reële 3D-weergave van de tandstructuren mogelijk, waardoor nauwkeurige meting en visualisatie van wortelveranderingen in de loop van de tijd mogelijk is. Bovendien kan in artikel 4 een volautomatisch driedimensionaal beoordelingsprotocol voor wortelveranderingen de beperkingen overwinnen die gepaard gaan met subjectieve en lineaire beoordeling op 2D- of 3D-röntgenfoto's, waardoor een verbeterde beoordeling van resorptie en remodelering wordt geboden en een betere behandelingsplanning en Opvolging protocollen worden vergemakkelijkt. In twee afzonderlijke studies, artikel 5 en artikel 6, werd de impact van Le Fort I-chirurgie op wortelveranderingen onderzocht. Artikel 5, gericht op het evalueren van wortelveranderingen in vergelijking met een controlegroep, terwijl artikel 6, de postoperatieve wortelveranderingen vergeleek tussen meerdelige en eendelige Le Fort I-osteotomieën. Artikel 5, vond dat Le Fort I-chirurgie geen significante invloed had op de wortelresorptie, zoals aangegeven door verwaarloosbare en identieke lineaire metingen voor beide groepen 6 maanden na de operatie. Significante veranderingen in het totale wortelvolumen werden echter waargenomen op 1 en 2 jaar na de operatie, met name in het apicale derde deel van de wortel, wat wijst op tot 15% wortelremodelering. Hoektanden, eerste en tweede premolaren vertoonden hogere niveaus van remodelering in de studiegroep in vergelijking met de controlegroep. Geslacht bleek geen significante factor te zijn bij wortelremodelering, maar jongere patiënten in de controlegroep vertoonden meer wortelremodelering. Artikel 6, onderzocht de wortelresorptie en remodelering na meerdelige Le Fort I-chirurgie in vergelijking met een enkelvoudige Le Fort I-operatie. Na 2 jaar bleek er geen significant verschil tussen beide types chirurgie in de veroorzaakte wortelresorptie. Beide groepen beleefden echter opmerkelijke veranderingen in het totale wortelvolumen, met name in het apicale derde, wat wijst op een bereik van 15-17% wortelremodelering. Een grotere naar voren geschoven

maxillaire beweging werd geassocieerd met een hogere wortelremodelering . Geslacht en leeftijd bleken geen significante factoren te zijn bij wortelremodelering. Beide studies bevelen echter de ontwikkeling aan van uitgebreide richtlijnen voor de beoordeling van wortelresorptie en remodelering in de context van maxillaire orthognatische chirurgie en orthodontische behandeling. Artikel 7 bood waardevolle richtlijnen voor het begrijpen van de potentiële effecten van orthognatische chirurgie op de wortel, rekening houdend met geslacht en leeftijd voor alle tanden en subcategorieën om de behandelingsresultaten te optimaliseren en risico's te minimaliseren. Het totale percentage wortelresorptie bij verschillende behandelingsstypen is minimaal, variërend tussen 4% en 7%. Uit de studie blijkt echter dat de SARPE-groep geassocieerd is met het hoogste percentage wortelremodelering.

De bevindingen van dit proefschrift toonden aan dat 3D-beoordeling van wortelveranderingen een zorgvuldigere behandelingsplanning mogelijk maakt, waardoor de chirurgische uitkomst en het besluitvormingsproces verder kunnen verbeterd worden.

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Article 1:

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Personal contribution

The author, Khalid Ayidh Alqahtani, conceived the project, collected data, performed the experiments, and wrote the research publications with the scientific support of his promotor Prof. dr. Reinhilde Jacobs and co-promotor Dr. Eman Shaheen. Khalid Ayidh Alqahtani is the first author in Articles 1, 3, 4, 5, 6, 7 and third author in Article 3. Khalid Ayidh Alqahtani is the corresponding author in Articles 1, 3, 4, 5, 6 and 7.

Conflicts of interest

The authors declare no conflicts of interest concerning the publications of this work.

Curriculum vita



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- 11th Arab Society of Pediatric Dentistry and the 1st Saudi Society of Pediatric Dentistry Conference "Pediatric Dentistry is a Challenge in the Arab World" on 30 November-01 December 2016.

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PUBLICATIONS

- **Alqahtani KA**, Shaheen E, Morgan N, Shujaat S, Politis C, Jacobs R. Impact of orthognathic surgery on root resorption: A systematic review. *J Stomatol Oral Maxillofac Surg.* 2022;123(5):e260-e267. doi:10.1016/j.jormas.2022.04.010
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VOLUNTARY EXPERIENCE

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- Appreciation Certificate from General organization of military industries for Campaign (oral care needed).

