

SYSTEMATIC REVIEW

Computed tomography imaging superimposition protocols to assess outcomes in orthognathic surgery: a systematic review with comprehensive recommendations

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Objectives: A systematic review was performed to analyze the current evidence on three-dimensional (3D) computed tomography (CT) superimposition protocols used to assess dentomaxillofacial changes after orthognathic and orthofacial surgery. Accuracy, reproducibility, and efficiency were evaluated.

Methods: The search was divided into Main Search (PubMed, EMBASE, Cochrane Library, LILACS, and SciELO), Grey Literature search (Google Scholar and Open Grey), and Manual search. Thirteen studies were included. Of these, 10 reported data on accuracy, 10 on reproducibility and five on efficiency. Seven proposed or evaluated methods of voxel-based superimposition, three focused on the surface-based technique, one compared surface- and voxel-based superimposition protocols, one used the maximum mutual information algorithm, and one described a landmark-based superimposition method. Cone-beam computed tomography (CBCT) was the most common imaging technique, being used in 10 studies.

Results: The accuracy of most methods was high, showing mean differences smaller than voxels' dimensions, ranging between 0.05 and 1.76 mm for translational accuracy, and 0.10–1.09° for rotational accuracy. The overall reproducibility was considered good as demonstrated by the small mean error (range: 0.01–0.26 mm) and high correlation coefficients (range: 0.53–1.00). Timing to complete virtual superimposition techniques ranged between a few seconds up to 40 min.

Conclusions: Voxel-based superimposition protocols presented the highest accuracy and reproducibility. Moreover, superimposition protocols that used automated processes and involved only one software were the most efficient.

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Introduction

Orthognathic and orthofacial surgery are meanwhile routine procedures performed to treat dentomaxillofacial deformities, leading to both good clinical functional and aesthetic results.¹ To maintain, however, high standard accuracy of the transfer of the 3D virtual treatment plan and appropriate handling of both function and facial aesthetics, quality assessment in orthognathic surgery is of major importance and crucial towards diagnosis, virtual treatment planning and outcome evaluation in order to improve the common surgical techniques and decrease patient morbidity.¹⁻³

Treatment outcomes of orthognathic procedures were traditionally assessed in two dimensions (2D), using pre- and postoperative lateral cephalometric radiographs.⁴ In conventional cephalometry, different anatomic reference systems have been proposed for both craniofacial growth and treatment evaluation.^{2,5} The most widely spread were based on the Frankfort Horizontal (FH) and the anterior cranial base (ACB) using the S-N line.⁶⁻⁸ Conventionally, surgical outcomes were assessed by using 2D cephalometry as advocated by Proffit *et al*⁹ in his reference system with the horizontal plane six degrees tilted from the S-N line. His evaluation was based on the superimposition of pre- and postoperative cephalometric 2D reference systems on the ACB.^{2,9}

In the last decades, however, computed tomography (CT), especially by cone-beam CT (CBCT), has become the gold standard for pre- and postoperative assessments, and CT superimposition is state-of-the-art when it comes to orthognathic surgical planning and evaluation.^{2,10-13} Swennen *et al* introduced three-dimensional (3D) cephalometry with the 3D anatomic cartesian reference system, making the bridge between 2D and 3D assessments by modifying Proffit's 2D superimposition method.^{2,14,15} Nowadays, the superimposition of 3D images, also called image rigid registration or image fusion,¹⁶ is considered a vital step on which different protocols associated with 3D software usually rely, as it involves the spatial alignment of similar structures for accurately quantifying skeletal changes.^{13,17,18}

Towards 3D outcome assessment based on the superimposition of multi detector CT (MDCT) and CBCT images, there is no clear gold standard yet.¹⁹ In 2018, a systematic review (SR) that synthesized the scientific literature concerning the reliability of 3D superimposition methods on the ACB²⁰ was unable to draw solid conclusions. Furthermore, several protocols for superimposing CT datasets have been suggested and validated using different anatomic structures as alternative Volumes of Interests (VOI) to the ACB. Therefore, the purpose of this SR is to identify, compare, and summarize the current evidence on the 3D CT image superimposition methods used to assess changes after orthognathic and orthofacial surgery, considering their accuracy, reproducibility, and efficiency. The secondary

aim of this study is to recommend different protocols to clinicians and researchers.

Methods and materials

The SR was performed following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) criteria.²¹ A pilot search for relevant Medical Subject Headings (MeSH), Emtree terms, Health Sciences Descriptors (DeCS), and keywords was performed to build the search strategies. The review protocol was not registered in advance. On March 15, 2021, a comprehensive search was carried out on PubMed, EMBASE, Cochrane Library, LILACS, and SciELO databases, as well as in Google Scholar and OpenGrey.eu. The searches were repeated before finishing the manuscript to detect any new studies that could also be included (search deadline: May 31, 2021). There were no restrictions in the search strategy regarding language or year of publication. Keywords and Boolean operators ("OR" and "AND") were used to join terms (thesaurus or words) related to "superimposition protocols for computed tomography volumes" and "orthognathic surgery".

Search strategies

In Main Search, the PubMed and Cochrane Library searches were conducted using MeSH terms. For the EMBASE search, Emtree terms and relevant keywords were used. Health sciences descriptors (DeCS) in the English language were used to search the LILACS and SciELO databases. A grey literature search was performed on Google Scholar and OpenGrey.eu using MeSH terms and relevant keywords (Supplementary Material 1 - *Search Strategies*). A manual search in the reference lists of the studies selected for full-text reading was carried out for further articles that were not retrieved by the search strategies.

Study selection

The systematic search was performed by one of the authors (F.O.A). Duplicates were removed and the retrieved articles were then selected independently by two authors (F.O.A. and O.L.H.J.), based on the titles and abstracts (screening). Studies were assessed according to inclusion and exclusion criteria. The following inclusion criteria were used: (1) clinical studies on 3D superimposition protocols for CT/CBCT images used in orthognathic surgery to assess postoperative changes, based on different craniofacial structures; (2) validation or comparative investigations assessing superimposition methods. The exclusion criteria were: (1) studies assessing superimposition methods between CTs and other imaging datasets (digital dental models, 3D photography, stereophotogrammetry, 3D facial

laser/optical scans; 3D photorealistic skin surface acquisitions); (2) studies in which the superimposition method was developed for purposes or areas of expertise other than orthognathic surgery (*e.g.* cleft lip and palate patients, growing patients, patients with temporomandibular disorders (TMD), as well as for dental implants, endodontics, periodontology, forensic dentistry, etc.); (3) studies on image-guided surgery, surgical navigation, facial volumetric changes, postoperative soft tissue changes, and airway volume evaluation; (4) meetings' posters and abstracts, book chapters, review articles, personal opinions, and case reports. Studies that fulfilled the aforementioned characteristics were selected for full-text reading. If the authors disagreed on the selection of a paper, the entire manuscript was read in detail.

Study eligibility

The eligibility of the studies was checked independently by the same two authors (F.O.A. and O.L.H.J.). To ensure consistency in the analysis of the articles, a standardized form was created. The full text of the selected articles were read, and further exclusion was done according to the following eligibility criteria: (1) the paper had to be focused on CT/CBCT superimposition methods that can be used for orthognathic/orthofacial surgery outcome evaluation; (2) the study had to be original; (3) the article had to report data on accuracy, reproducibility and/or efficiency of the superimposition method, or be a validation/comparative study assessing accuracy (precision), reproducibility (reliability), or efficiency for the suggested protocol. In case of disagreement between the two independent researchers, the study was discussed with a third, more experienced author (G.R.J.S. or R.G-M.). Studies that did not meet the eligibility criteria were excluded from the analysis and the reason for exclusion was reported. If questions arose regarding the methodology or results of a paper, the authors were contacted by e-mail to obtain the necessary information. All studies were included or excluded by consensus.

Data extraction

Demographic and methodological data were extracted from the studies that met the eligibility requirements independently by the same two authors (F.O.A. and O.L.H.J.). Qualitative and quantitative data were collected. In case of disagreement between the two authors, the study was discussed with a third author (G.R.J.S. or R.G-M.). Any disagreement in either phase was resolved by consensus. If any doubts persisted, the author of the study in question was contacted by e-mail.

Using a standardized form, the following data were registered: author, year, country, title, language, type of study, aim of the study, type of CT scan used, sample, superimposition method, VOI for superimposition (VOIS), region of interest (ROI) for outcome evaluation and/or for method validation. Regarding methodological data, image acquisition methods (apparatus, field

of view (FOV), voxel size, scan time, occlusion, and head position), data superimposition software, type of assessment (accuracy, reproducibility, efficiency), validation instrument or method, and statistical analysis were collected.

Methodological quality of the studies

The risk of bias of the included studies was assessed using the Methodological Index for Non-Randomized Studies (MINORS) scoring system.²² This system evaluates eight items for non-comparative studies and 12 items for comparative studies. The scores range is between 0 and 2 ("0" if not reported, "1" when inadequately reported, and "2" if properly reported). Since the maximum score per item is 2, the ideal global score is 16 for the non-comparative studies and 24 for the comparative studies. Therefore, the closer the score is to 16 or 24, for non-comparative and comparative studies, respectively, the lower is the risk of bias of the study. The scoring was performed independently by two authors (F.O.A. and O.L.H.J.), and if any disagreement occurred concerning the quality assessment, it was discussed with a third reviewer (G.R.J.S. or R.G-M.) and resolved by means of discussion and consensus.

Results

A flowchart of the SR, describing the steps from the initial search and screening to the final article inclusion, is presented in [Figure 1](#). The Main Search was carried out on March 15, 2021. The same search strategies were repeated on May 31, 2021, and although an increase in the number of hints could be observed, no additional study was included. A total of 1210 papers were retrieved (PubMed, $n = 677$; EMBASE, $n = 415$; Cochrane Library, $n = 108$; LILACS, $n = 25$; SciELO, $n = 380$). Grey Literature search, which was carried out on the same date, yielded 2,419 articles more (Google Scholar, $n = 2330$; Open Grey, $n = 89$).

Study selection

After duplicates were excluded and the screening of titles and abstracts was completed, 33 records remained for eligibility assessment (Main Search = 27; Grey Literature = 6).

Study eligibility

Eight studies met the eligibility criteria for inclusion in the SR. The other 25 studies (Main Search = 22; Grey Literature = 3) were excluded for the following reasons: 14 did not assess the accuracy (precision), reproducibility (reliability), or efficiency of the superimposition method (they only used it for evaluation or to complete further steps),²³⁻³⁶ four focused on the superimposition of digital dental models or impressions on CT,^{11,37-39} and three were conference posters or abstracts⁴⁰⁻⁴²; one evaluated superimposition of 3D photographs/

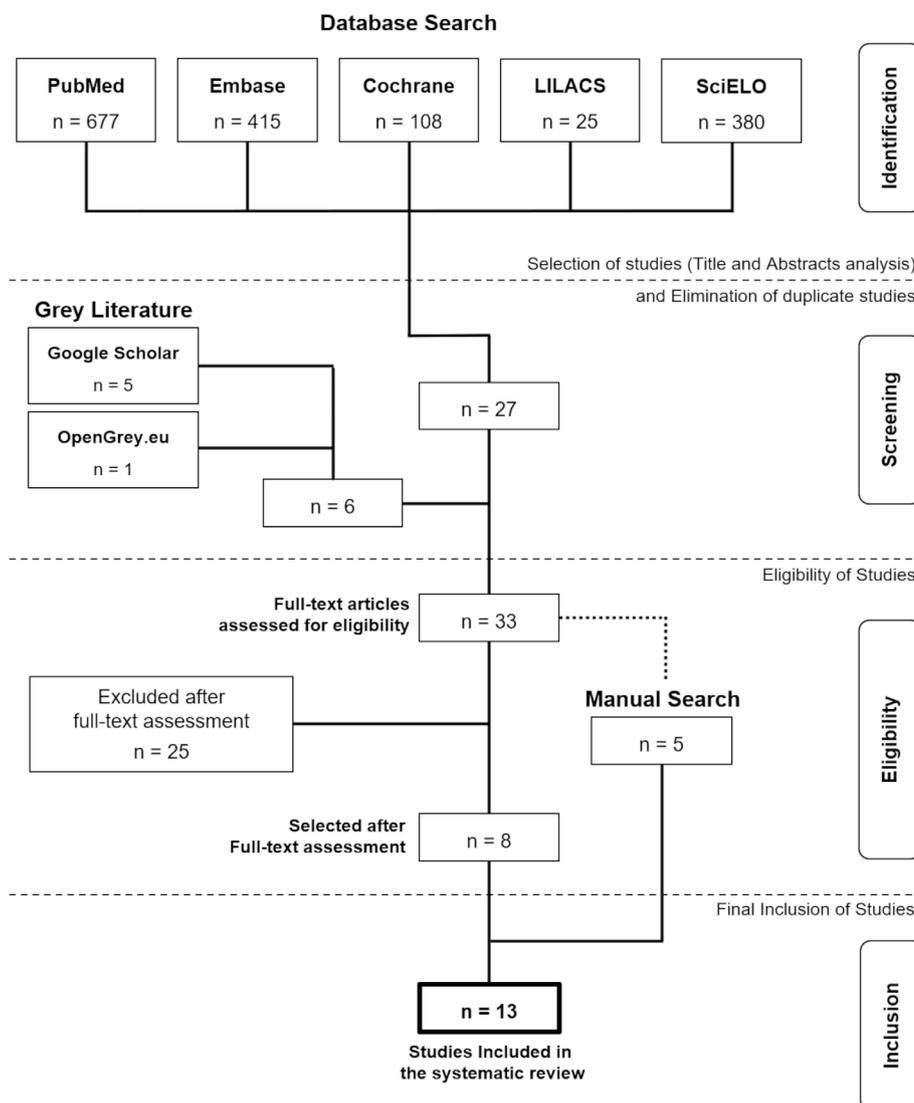


Figure 1 Flowchart of the systematic review, describing the steps from the initial search and screening to the final inclusion of the studies.

stereophotogrammetry on CT,⁴³ one focused on patients with TMD,⁴⁴ one focused on growing patients,³ and one cropped the images of the maxilla and mandible before superimposition to simulate a smaller FOV, making the method ineligible for orthognathic assessment.¹⁷ Since all the retrieved studies were original, no one was excluded for this specific criterion. There were no disagreements between the two reviewers at this stage ($k = 1$).

The manual search yielded five more articles. Finally, 13 studies fulfilled all the criteria and were included in this systematic review for data extraction and qualitative synthesis (Main Search = 5^{18,45–48}; Grey Literature = 37,13,49; Manual Search = 5^{8,50–53}).

Data extraction

From the included studies, 10 reported data on accuracy, 10 on reproducibility, and five on efficiency. Seven studies proposed or evaluated methods of voxel-based

superimposition (VBS), three focused on the surface-based superimposition (SBS) technique, one compared surface- and voxel-based protocols, one used the maximum mutual information (MMI) algorithm, and one assessed landmark-based superimposition (LBS). CBCT was the most common imaging technique, being used in 10 studies, while the remaining used conventional CT images. One study used both CBCT and CT for different validation steps.⁴⁶

Among the studies that analyzed VBS, the mean differences ranged between 0.09 mm and 0.67 mm for translational accuracy, and between 0.10° and 1.09° for rotational accuracy. The correlation coefficients for intra- and interobserver reliability were between 0.53 and 1.00, and the mean differences ranged from 0.02 to 0.26 mm. The time spent varied from 10 s up to 40 min. Regarding SBS studies, the mean distances in the accuracy assessments ranged between 0.12 mm and 1.76 mm,

with a maximum reproducibility error of 0.2 mm, and a mean time of 25 min. The study that assessed LBS reported only its reproducibility, with method errors from 0.01 to 0.13 mm.

Due to the heterogeneity identified between the included studies, a quantitative synthesis (meta-analysis) of the extracted data was not performed. Therefore, the authors present a narrative synthesis with the main outcomes and, in the discussion, the main differences among studies and between their superimposition methods are further addressed. Tables 1 and 2 present demographic and methodological data of the included articles, as well as their quality assessment results. MINORS final scores ranged between 12 and 15 out of 16 for the non-comparative studies, and both comparative studies scored 21 out of 24. The studies presented a low-to-moderate risk of bias. The complete itemized quality assessment scores according to the MINORS is presented in Supplementary Material 2 (*Quality Assessment*).

Discussion

Traditionally, the evaluation of craniofacial growth and the effects of treatment was performed through the superimposition of serial 2D cephalometric radiographs.⁵⁴ Nowadays, once the superimposition of CT images became a valuable ally for 3D assessments, several protocols have been developed to evaluate outcomes and stability after orthognathic and orthofacial procedures.^{20,49,55,56} With the improvement of imaging acquisition technologies and 3D virtual planning and evaluation software, the superimposition protocols have also progressed in terms of user independence, process simplification, and assessment possibilities. Decreasing the number of required softwares, together with more user-friendly interfaces, is currently leading to the development of accurate 3D superimposition software's that will be applicable in the near future in the daily clinical routine and will become an indispensable quality control tool for both clinicians and researchers.

Different validation instruments have been used to evaluate protocols' accuracy. Among SBS studies, Xia *et al*⁵¹ calculated the mean difference between coordinates of pre- and postoperative sets of stable landmarks (MD: $<0.12\text{ mm} \pm <0.19\text{ mm}$; upper and lower limits of agreement: -0.37 mm ; 0.42 mm ; the precision of lowest and highest limits: -0.24 mm ; 0.28 mm). Gkantidis *et al*⁸ used mean distances (MD) between superimposed datasets at three form-stable anatomical areas in the ACB and foramen magnum (FM). ACB +FM was the most accurate (MD: $<0.17\text{ mm}$) followed by BZ and ACB alone with a similar level of accuracy (MD: $<0.5\text{ mm}$); 3P and 1Z were the least accurate ($0.79 < \text{MD} < 1.76\text{ mm}$, $p < 0.005$). The method used by Jabar *et al*⁵³ was not considered accurate since it underestimated by one-third to one-half the actual surgical movement performed, and according to Almkhtar *et al*⁴⁶, VBS and SBS of

hard tissues showed the same values in the absolute MD between the models, $0.05 \pm 0.21\text{ mm}$ and $0.47 \pm 0.26\text{ mm}$, respectively, with no significant difference between both methods ($p > 0.05$). Regarding VBS studies, Nada *et al*⁷ tested accuracy using color-coded distance maps between two models in four different regions. They compared the means of corresponding measurements following VBS on the ACB and LZA (MD range: $0.20\text{--}0.37 \pm 0.08\text{--}0.16\text{ mm}$ for the ACB; and $0.20\text{--}0.45 \pm 0.09\text{--}0.27$ for LZA). The accuracy of one zygomatic arch alone was later questioned by Gkantidis *et al*,⁸ whose study considered this VOI inappropriate, less accurate, and with higher errors. Instead, using BZ was recommended since both are normally seen in small FOV images. Lee *et al*⁵² assessed errors in image fusion using distances between 16 titanium markers on the skull (external surface of the midface, temporal surface, and cranial fossa). They compared the superimposition errors in different head positions and mandibular occlusions with a standard image. The mean error of the superimposition was $0.396 \pm 0.142\text{ mm}$, not being affected by the positional change. Weissheimer *et al*¹³ quantified superimposition errors by color-coded surface distances in the ACB using closest-point color maps on 3D surface models (qualitative visualization: $<0.5\text{ mm}$ for most regions). Bazina *et al*⁴⁷ compared superimpositions from two methods using the absolute closest point color map to quantify the differences between the Dolphin 3D superimposition and the method presented by Cevidanes *et al*⁴⁵. The smallest difference was found in the left zygomatic arch region with a mean of $0.099 \pm 0.072\text{ mm}$, and the largest in the right gonial angle with $0.210 \pm 0.136\text{ mm}$. Haas *et al*⁴⁹ calculated the rotational accuracy using the absolute mean difference (in degrees) and the translational accuracy with the weighted mean difference between landmarks (in mm), between base and second volume head orientations after superimposition. They found a mean rotational difference of $0.12 \pm 0.06^\circ$ (range: $0.03\text{--}0.33^\circ$) along the P axis, $0.10 \pm 0.06^\circ$ (range: $0.01\text{--}0.23^\circ$) along the R axis, and $0.198 \pm 0.16^\circ$ (range: $0.00\text{--}0.58^\circ$) along the Y axis. The translational mean differences were $0.24 \pm 0.11\text{ mm}$ (range: $0.06\text{--}0.48\text{ mm}$) in the transverse, $0.23 \pm 0.10\text{ mm}$ (range: $0.05\text{--}0.51\text{ mm}$) in the vertical, and $0.20 \pm 0.10\text{ mm}$ (range: $0.04\text{--}0.46\text{ mm}$) in the sagittal axis. Shujaat *et al*¹⁸ assessed the translational and rotational accuracy at time three intervals. The maximum mean difference in one group was observed in the Z axis translational movement ($0.67 \pm 0.8\text{ mm}$) and pitch ($1.09^\circ \pm 1.37^\circ$), as in the other group, which also presented a maximum mean difference in Z axis translational movement ($0.64 \pm 0.51\text{ mm}$) and pitch ($0.42^\circ \pm 1.30^\circ$). The combined translational and rotational movements showed an MD $<0.5\text{ mm}$ and $<0.5^\circ$. In general terms, the accuracy of the methods was high, since most of the differences were smaller than voxel's dimensions and CTs slice thickness, being considered clinically irrelevant by most of the authors. The VBS provides the best results in terms of precision, being the method of choice

Table 1 Overview of the included studies, with main information and characteristics

<i>Author, year (country)</i>	<i>Title</i>	<i>Imaging technique (sample)</i>	<i>Superimposition method (VOI for superimposition)</i>	<i>ROI for outcome evaluation or for Validation</i>
McCance et al ³⁰ (GBR)	A three-dimensional analysis of soft and hard tissue changes following bimaxillary orthognathic surgery in skeletal III patients	CT (16 adult Class III patients; preoperative with 1.5-mm-thick slices; and 1 year after orthognathic surgery, with 6mm slice spacing to reduce radiation – from the supraorbital ridges to just below the mandible)	Landmark-based (Right and Left Orbital Margins, Nasion, Right and Left zygomatic Arches Base)	Mandible body, Maxilla, Chin, Teeth (incisors, canines and molars)
Cevidaneş et al ⁴⁵ (USA)	Superimposition of 3D cone-beam CT models of orthognathic surgery patients	CBCT (10 patients undergoing maxillary advancement; acquired before and 1 week after surgery)	Voxel-based (Anterior Cranial Base)	Rami (Condyle and Posterior border) Rami Position: Rotation and Displacement (non-morphologic)
Xia et al ⁵¹ (USA)	Accuracy of the computer-aided surgical simulation (CASS) system in the Treatment of Patients With Complex Craniomaxillofacial Deformity: A Pilot Study	CT (5 patients with complex CMF deformities; acquired before and within the first six postoperative weeks)	Surface-based (Bones that had not been moved during surgery)	Maxilla, Mandible and Chin
Nada et al ⁷ (NLD)	Accuracy and reproducibility of voxel-based superimposition of cone beam computed tomography models on the anterior cranial base and the zygomatic arches	CBCT (16 patients with severe maxillary transverse deficiencies + Class II, Class III or open bite; acquired prior to treatment and before the second orthognathic surgery, average 18 ± 4.6 months of interval)	Voxel-based (Anterior Cranial Base and Left Zygomatic Arch)	Anterior Cranial Base, Forehead, Right and Left Zygomatic Arches (for Validation) Accuracy test between VOIS)
Lee et al ⁵² (KOR)	The 3D CT superimposition method using image fusion based on the maximum mutual information algorithm for the assessment of oral and maxillofacial surgery treatment results	CBCT/CT (25 scans of a dry skull in different spatial conditions/41 patients' pre- and postoperative scans for robustness assessment)	Maximum Mutual Information Algorithm (Global Anatomic Structures of Head and Neck Area)	External surface of the Midface, Temporal surface, and Cranial Fossa of the human skull (for Validation, Accuracy and Reproducibility tests)
Almukhtar et al ⁴⁶ (GBR)	Comparison of the accuracy of voxel-based registration and surface-based registration for 3D assessment of surgical change following orthognathic surgery	CBCT (31 orthognathic patients; acquired within 1 month before surgery and at a minimum of 6 months after surgery)	Surface-based and Voxel-based (Anterior Cranial Base)	Anterior Cranial Base (for Validation) Accuracy test between Methods)
Weissheimer et al ¹³ (BRA)	Fast three-dimensional superimposition of cone-beam computed tomography for orthopedics and orthognathic surgery evaluation	CBCT (18 patients ⁴ , four adult patients whose scans were acquired before and 1 year after orthognathic surgery)	Voxel-based (Anterior Cranial Base)	Anterior Cranial Base (for Validation) Accuracy test between pre- and postoperative Scans)
Gkantidis et al ⁸ (CHE)	Evaluation of 3-dimensional superimposition techniques on various skeletal structures of the head using surface models	CT (8 pairs of pre- and post-treatment scans acquired from non-growing patients that underwent mini-implant-assisted rapid maxillary expansion)	Surface-based (Anterior Cranial Base, Foramen Magnum, and Zygomatic Arches)	Maxilla (piriform apertures and central incisors' mesial-incisal corners)/Anterior Surface of Sella Turcica, and posterior right and left sides of the Foramen Magnum (Accuracy test)

(Continued)

Table 1 (Continued)

<i>Author, year (country)</i>	<i>Title</i>	<i>Imaging technique (sample)</i>	<i>Superimposition method (VOI for super-ROI for outcome evaluation or for Validation)</i>
Jabar <i>et al</i> ⁵³ (HKG)	The validity of using surface meshes for evaluation of three-dimensional maxillary and mandibular surgical changes	CBCT (33 scans acquired in a plastic skull in which the jaws were manipulated to simulate movements to different positions: unidirectional maxilla advancement or down graft, mandible advancement, and simultaneous maxillary advancement and down graft)	Surface-based (Skull Base) Maxilla and Mandible
Bazina <i>et al</i> ⁴⁷ (USA)	Precision and reliability of Dolphin 3-dimensional voxel-based superimposition	CBCT (31 orthognathic patients; acquired within 1 month before surgery and within 12 months after surgery)	Voxel-based (Cranial Base) <i>Cranial base and seven different areas (for Validation and comparison between methods)</i>
Haas <i>et al</i> ⁴⁹ (BRA)	Cranial base superimposition of cone-beam computed tomography images: A voxel-based protocol validation	CBCT (25 full-face scans of patients with dental implants)	Voxel-based (Anterior Cranial Base) <i>Implant apexes (for Validation/Accuracy and Reproducibility tests)</i>
Verhelst <i>et al</i> ⁴⁸ (BEL)	Validation of a 3D CBCT-based protocol for the follow-up of mandibular condyle remodeling	CBCT (10 patients that underwent BSSO orthognathic surgery; 1 week and 6 months follow-up postoperative scans ⁶)	Condyle (Morphology and Volume)
Shujaat <i>et al</i> ¹⁸ (BEL)	Accuracy and reliability of voxel-based dentoalveolar registration (VDAR) in orthognathic surgical patients: a pilot study with two years' follow-up	CBCT (25 class II/III patients that underwent bimaxillary surgery; postoperative scans acquired at four time-points: 6 weeks, 6 months, 1 year and 2 years)	Dentoalveolar Segment (Translational and Rotational Movements)

BSSO, Bilateral sagittal split osteotomy; CBCT, Cone-beam computed tomography; CHE, Switzerland; CMF, Cranio-maxillo-facial; CT, Multi-detector computed tomography; 2D, Bidimensional; 3D, Three-dimensional; ROI, Region of interest; VOI, Volume of interest.

^a14 subjects were growing patients (not the focus of this study).

^bSample regarding to superimposition process/evaluation only.

Table 2 Methodological data of the studies included in the review and MINORS scores

Author, year Superimposition (Imaging Technique)	Image acquisition methods	Software(s) used for Superimposition	Validation Method	MINORS score ^a
McCance et al ³⁰ LBS (CT)	FOV: Not mentioned/Voxel Size: Not mentioned Machine: NewTom 9000/Scan Time: 70 secs Occlusion: Not mentioned/HP: Not mentioned	Not mentioned	Reproducibility	12 of 16
Cevidane et al ⁴⁵ VBS (CBCT)	FOV: 23 × 23 cm/Voxel Size: 0.58 × 0.58 × 0.6 mm Machine: NewTom 9000 Scan Time: 70 secs Occlusion: Not mentioned/HP: Not mentioned	ITK SNAP: semiautomatic segmentation MIRIT: computed fully automatic registration CASS Planning System	Reproducibility Accuracy	13 of 16 12 of 16
Xia et al ⁵¹ SBS (CT)	FOV: Not mentioned/Voxel Size: Not mentioned Machine: Not mentioned/Scan Time: Not informed Occlusion: Not mentioned/HP: Not mentioned	Maxilim	Accuracy Reproducibility Efficiency	13 of 16
Nada et al ⁷ VBS (CBCT)	FOV: 22 × 16 cm/Voxel Size: 0.4 × 0.4 × 0.4 mm Machine: iCAT 3D/Scan Time: Not informed Occlusion: Not mentioned/HP: Not mentioned	OnDemand3D	Accuracy Reproducibility	13 of 16
Lee et al ⁵² MMI (CBCT/CT)	Skull - FOV: 23 × 17 cm/Voxel Size: 0.2 × 0.2 × 0.2 mm Machine: KaVo CT 3D/Scan Time: Not mentioned Occlusion: C, MO, LE, PT HP: S, UP, LW, LF, LR, RR, LT, RT Patients - FOV: 23 × 17 cm/Voxel Size: Not mentioned Machine: SOMATOM/Scan Time: Not mentioned Occlusion: Not mentioned/HP: Not mentioned			
Almukhtar et al ⁴⁶ SBS and VBS (CBCT)	FOV: Not mentioned/Voxel Size: Not mentioned Machine: iCAT Classic/ScanMaxilim: Voxel-based superimposition VR.Mesh: Surface-based superimposition		Accuracy	21 of 24
Weissheimer et al ¹³ VBS (CBCT)	FOV: Large/Voxel Size: 0.25 × 0.25 × 0.25 mm Machine: iCAT/Scan Time: 40 s OnDemand3D Occlusion: Not mentioned/HP: Not mentioned		Accuracy Efficiency	12 of 16
Gkantidis et al ⁸ SBS (CT)	FOV: 21 × 21 × 12 cm/Voxel Size: 0.8 × 0.8 × 0.8 mm Machine: Philips Brilliance/Scan Time: 2.5 s Occlusion: Not mentioned/HP: Not mentioned	OSIRIX: conversion of DICOM to STL Geomagic Quality 2012: final superimposition	Accuracy Reproducibility Efficiency	21 of 24
Jabar et al ⁵³ SBS (CBCT)	FOV: 22 × 22 cm/Voxel Size: 0.4 × 0.4 × 0.4 mm Machine: iCAT/Scan Time: Not informed Occlusion: d.n.a./HP: Frankfurt parallel to stage	MeVisLab: convert DICOM to surface mesh (STL) VR.Mesh: superimposition	Reproducibility	12 of 16
Bazina et al ⁴⁷ VBS (CBCT)	FOV: 12 in/Voxel Size: 0.38 × 0.38 × 0.38 mm Machine: CB MercuRay/Scan Time: 9.5 s Occlusion: Not mentioned/HP: Not mentioned	Dolphin Imaging 3D	Accuracy Reproducibility Efficiency	12 of 16
Haas et al ⁴⁹ VBS (CBCT)	FOV: 22 × 17 cm/Voxel Size: 0.4 × 0.4 × 0.4 mm Machine: iCAT/Scan Time: 2 × 20 s Occlusion: MIC or CR (thin wax bite) HP: NHP, seated and looking forward	Dolphin Imaging 3D	Rotational Accuracy Translational Accuracy Reproducibility Efficiency	13 of 16
Verhelst et al ⁴⁸ VBS (CBCT)	FOV: 24 × 19 cm/Voxel Size: 0.3 × 0.3 × 0.3 mm Machine: Newtom VGi evo/Scan Time: Not informed Occlusion: CR (thin wax bite)/HP: NHP (seated)	Amira	Reproducibility	13 of 16
Shujaat et al ¹⁸ VBS (CBCT)	FOV: 23 × 26/24 × 14 cm Voxel Sizes: 0.3 × 0.3 × 0.3/0.6 × 0.6 × 0.6 mm Machines: Planmeca ProMax/Newtom VGi evo Scan Time: Not informed Occlusion: Not mentioned/HP: Not mentioned	Amira	Rotational Accuracy Translational Accuracy Reproducibility	15 of 16

(Continued)

Table 2 (Continued)

Author, year Superimposition (Imaging Technique)	Image acquisition methods	Software(s) used for Superimposition	Validation Method	MINORS score ^a
CBCT, Cone-beam computed tomography; CR, Centric relation; CT, Multi-detector computed tomography; DICOM, Digital imaging and communications in medicine; FOV, Field of view; HP, Head position; LE, Lateral excursion; LMS, Landmark-based superimposition; LR, Left rotation; LT, Left tilting; LW, Lower; MIC, Maximum intercuspitation; MMI, Maximum mutual information; MO, Mouth open; NHP, Natural head posture; PT, Protrusion; RR, Right rotation; RT, Right tilting; S, Standard; SBS, Surface-based superimposition; STL, Standard triangle language or standard tessellation language; UP, Upper; VBS, Voxel-based superimposition; d.n.a, Does not apply.				
^a The complete quality assessment according to the Methodological Index for Non-Randomized Studies (MINORS) is presented in the Supplementary Material 2.				

due to its higher accuracy and user independency, as it aligns the VOI by maximizing the overlap of the grey-scale values of the individual voxels,^{34,57} thus eliminating the necessity to identify cephalometric landmarks and the possibility of human error.¹⁹ In this sense, the LBS and SBS methods have limitations inherent to their operator-dependent process, as they rely on the identification and manual selection of landmarks, which is directly related to the accuracy of anatomic structures identification.^{54,58-61}

Regarding reproducibility analysis, in the LBS study by McCance *et al*⁵⁰, the lowest and highest method errors between the landmarks in each coordinate were respectively: X (0.01 ± 0.01 mm; 0.11 ± 0.15 mm), Y (0.02 ± 0.14 mm; 0.09 ± 0.24 mm), and Z (0.01 ± 0.11 mm; 0.13 ± 0.07 mm). Of the SBS studies, Gkantidis *et al*⁸ assessed the distances between two 3D models at four specific landmarks in the piriform apertures and central incisors. No difference among the three operators or between the 1 month intervals was identified in the precision of each superimposition technique ($p > 0.05$). In the study of Jabar *et al*⁵³, superimpositions were remeasured for 10 random surgical movements after 4 weeks (error study); systematic and random errors were assessed and the maximum error between readings was 0.2 mm. Among the VBS studies, Cevidanes *et al*⁴⁵ evaluated the interobserver reliability by measuring a subset of ten CBCT scans (before and after surgery for five patients, by three observers) and illustrating differences with 3D color-coded maps. The interobserver variability was considered negligible (not more than 0.26 mm), and the reproducibility among all three observers was also confirmed by the color-coded distance maps. Nada *et al*⁷ evaluated the intra observer reliability (between superimpositions on the ACB, for the mean distances at four regions) and the interobserver reliability (mean differences between superimpositions performed by two observers for each of the four regions). Intra observer reliability was regular to good (CC ranged between 0.53 and 0.94 for the mean distances at the four regions) and the interobserver variability was very small, with mean differences of 0.02 ± 0.1 mm for ACB, 0.05 ± 0.05 mm for the forehead (FH), -0.04 ± 0.18 mm for the right zygomatic arch (RZA), and 0.02 ± 0.14 mm for the left zygomatic arch (LZA). Lee *et al*⁵² measured the intra- and interobserver errors; the errors between examiners were not significant ($p = 0.380$) and the mean errors of each examiner were 0.171 ± 0.126 mm and 0.206 ± 0.181 mm, estimated to be around 0.2 mm ($p = 0.313$ and $p = 0.892$). Bazina *et al*⁴⁷ used intraclass correlation coefficients (ICC) to evaluate the reliability, and the same investigator repeated the superimpositions of 10 subjects after 2 weeks. The ICC was 0.964 (0.941–0.978), showing excellent reproducibility. Haas *et al*⁴⁹ assessed reproducibility in 10 scan pairs, showing an excellent reproducibility, with an ICC of 1 for all rotational and translational parameters on intra observer analysis and an ICC range of 0.921 to 1 for interobserver reliability.

Verhelst *et al*⁴⁸ assessed intra- and interobserver agreement regarding the translation and rotational values of the transformation matrices. Excellent ICC's (0.94–0.99) were obtained for the VBS technique using both modified rami (MR1 and MR2). Absolute mean differences between and within operators remained below 1 mm for translation and 1.2° for rotation. Interobserver and intra observer reliability was also assessed by Shujaat *et al*,¹⁸ and all translational and rotational measurements showed excellent reliability between the two time points. The lowest ICC was seen for inter observer reliability of roll (0.9741) in group A and pitch (0.9603) in group B. No significant difference was observed between observers for both groups. As suggested by Gaber *et al*,¹⁹ inter- and intra observer agreement should always be used to validate the results in studies like these. Most of the studies used ICC to assess intra- and/or interobserver reliability, comparing different observers (up to 3^{8,45} and time-points with weekly or monthly intervals. The automated nature gives VBS protocols the advantage of being less susceptible to intra- and interobserver variations during the superimposition process, minimizing errors and increasing its reproducibility. Meanwhile, LBS and SBS methods are more vulnerable to human mistakes, and despite being calibrated, examiners present lower reliability if compared to fully automated processes.

Few studies reported the time for the superimposition process. Moreover, while some considered the entire process with evaluation, others considered only the superimposition itself. Gkantidis *et al*⁸ took 25 min to complete SBS and its analysis. Nada *et al*⁷ estimated a time between 30 and 40 min per set of scans, including the construction of 3D models, VBS, distance calculation, and construction of color-coded distance maps. Lee *et al*⁵² said it only took them “a few seconds”, and Weissheimer *et al*,¹³ who used the same principle,^{52,62} reported a time of 10 to 15 s to complete their fast 3D VBS method. According to Bazina *et al*,⁴⁷ their VBS method took less than 5 min, similar to the study of Haas *et al*⁴⁹ where the mean time spent on their three steps – landmark superimposition, voxel-based superimposition, and head orientation – was estimated at 198 sec (3.3 min). Although Cevidanes *et al*⁴⁵ did not report information about the time to complete their superimposition method, two of the included studies assessed or commented about its efficiency. According to Weissheimer *et al*,¹³ it should take 45 to 60 min, while Bazina *et al*⁴⁷ informed it took them 3 h. Although the scientific literature lacks information about methods' efficiency, also being heterogeneous regarding the criteria to evaluate the exact required time, those methods that use fully automated techniques and only one software are clearly the least time-consuming.^{13,47,49} The more efficient a superimposition protocol is, the more useful it can be in clinicians' daily practice, with higher applicability and without consuming too much working time. Therefore, faster superimposition protocols will provide

a valuable tool in the daily clinical routine to allow reliable comparison between the surgical outcome and the 3D virtually planned objective as well as long-term follow-up.

All regions that are not subject to volumetric changes after orthognathic and orthofacial surgery can potentially be used as VOIS.⁶³ Nevertheless, for any analysis protocol, its proper selection is considered a crucial step that needs to be chosen in accordance with the objective of the analysis.⁶⁴ Although the ACB is considered by many authors the most accurate rigid registration structure for 3D superimposition,^{7,49} the mandibular movements relative to the maxilla cannot be assessed by superimposing this VOI.^{5,65} For this purpose, the superimposition of two scans can be performed on maxillary structures as the dental segment and part of the alveolar bone.¹⁸ In the same way, regional superimposition on the coronoid process and mandibular ramus is an interesting alternative to evaluate the volume and morphology of the condyle.^{48,63,64} For the evaluation of chin movement after genioplasty in relation to its original position in the mandible, a regional superimposition can be performed on its distal segment, with the advantage that it can still be used if the patient undergoes a mandibular osteotomy as well.^{66,67} The proximity to the ROI must be taken into account when choosing the VOIS, once it is known that the more distant the ROI is relative to the superimposed structures, the greater its inaccuracy and the theoretical error of measurement.²⁰ Ionizing radiation is also an important issue when discussing superimposition protocols once the same patient is exposed at least twice to it. A smaller FOV (13 cm) is associated with significant dose reduction,^{7,68–70} which can be up to 50% in comparison to the extended one (22 cm),^{7,68} being one of the main reasons why authors have advocated for the use of zygomatic arches as VOIS since they can be identified easily in reduced height scans.⁷

As widely known and well established in the literature, the most common superimposition protocols are the LBS,^{50,58,59,71} the SBS,^{8,46,51,53} and the VBS.^{6,7,11,13,45,46,49,72,73} There is consensus, however, in that LBS and SBS have some limitations inherent to their user dependence.^{54,58–61} This fact, together with the lack of precision of virtual model surface segmentation,⁸ is considered the major drawbacks and the main causes of inaccuracy, being directly related to observers' experience and calibration.^{2,19} These methods, therefore, are considered operator-dependent, non-automated and time consuming.^{8,49,73} The high cost of most of the commercially available software is still an important issue for many maxillofacial surgeons and orthodontists towards the dissemination and implementation of CT superimposition protocols in their daily clinical routine. Likewise, the learning curve, the necessary dedication, and the time required to become able to use it, which are inherent to the introduction of these methods into the daily workflow, are also drawbacks to be considered. From a biological point of view, the obvious necessity

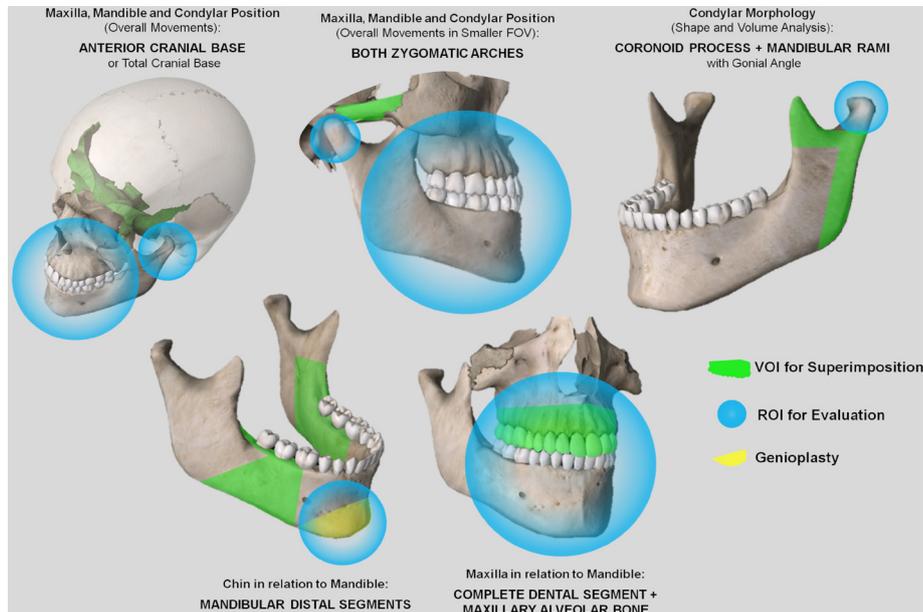


Figure 2 Recommended Volumes of Interest for Superimposition (VOIS) according to the Region of Interest (ROI) for Evaluation.

for repeated CBCT scans with additional radiation exposure can be considered as another potential shortcoming that should not be neglected. On the other hand, the benefit of having a highly accurate quality control of surgical outcomes by CT superimposition, in combination with the lower radiation exposure of CBCT, outweigh potential disadvantages on this regard.

Precise 3D CBCT superimposition enables the assessment of surgical techniques' accuracy, the comparison between the virtually planned goals and the achieved results,⁷⁴ as well as the evaluation of surgical relapse

and stability over time among different surgical and fixation techniques. Furthermore, it is possible to assess the exact amount of hard versus soft tissue changes after surgery, enhancing the predictability of different orthognathic and orthofacial procedures in order to improve 3D virtual planning workflows and software. The SR protocol was not registered in PROSPERO since it did not aim to include studies, which outcomes were directly related to human health or animal research,²¹ but focused on technical aspects of imaging process and its evaluation.

Table 3 Suggested radiographic and superimposition methods and characteristics

Radiographic Methods	Recommended
Imaging Technique	CBCT
Scan Time	Short (to reduce radiation dose)
FOV	Smaller as possible (13 cm height, if suitable, to reduce radiation dose)
Voxel Dimensions	<0.4 x 0.4 x 0.4 mm
Standardized Occlusion	Centric Relation (small thin wax bite)
Standardized Head Posture	Natural Head Position (Mirror position)
Superimposition Method	Recommended
Type of superimposition	Voxel-based
N° of Software	One software for all steps
Process	Fully automated (user-independent)
ROI (type of evaluation)	Recommended VOIS
Maxillary Position (overall spatial movement)	ACB or TCB, if FOV ≥22 cm BZ, if FOV = 13 mm
Mandibular Position (overall spatial movement)	
Condylar Position (overall spatial movement)	
Condylar Morphology (Volume and shape analysis)	Coronoid Process +Mandibular Rami with Gonial angle
Maxillary Position related to Mandible (relative movement)	Complete dental segment with part of the Maxillary alveolar bone
Chin Position related to Mandible (relative movement)	Distal segments of the Mandible

ACB, Anterior cranial base; BZ, Both zygomatic arches; CBCT, Cone-beam computed tomography; FOV, Field of view; ROI, Region of interest; TCB, Total cranial base; VOI, Volume of interest.

Conclusions

The use of a VBS method is recommended, ideally performed using only one user-friendly software, a fully automated (user-independent) process, and choosing a stable VOIS close to the ROI for evaluation. CBCT should be the imaging technique of choice, with preferably a smaller FOV to reduce the radiation dose - if available, convenient, and adequate for the evaluation purposes. Moreover, a standardized occlusion and head posture between the pre, postoperative, and follow-up scans must be adopted. Table 3 summarizes the authors' suggestions about superimposition and radiographic

methods, and Figure 2 illustrates the different VOIS where clinicians and researchers can accurately superimpose CT images for postoperative assessments, according to the region and outcome of interest.

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