3D cephalometric analysis obtained from computed tomography. Review of the literature

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Summary

Introduction. **The aim of this systematic review is to estimate accuracy and reproducibility of craniometric measurements and reliability of landmarks identified with computed tomography (CT) techniques in 3D cephalometric analysis.**
Methods. **Computerized and manual searches were conducted up to 2011 for studies that addressed these objectives. The selection criteria were: (1) the use of human specimen; (2) the comparison between 2D and 3D cephalometric analysis; (3) the assessment of accuracy, reproducibility of measurements and reliability of landmark identification with CT images compared with two-dimensional conventional radiographs. The Cochrane Handbook for Systematic Reviews of Interventions was used as the guideline for this article.**
Results. **Twenty-seven articles met the inclusion criteria. Most of them demonstrated high measurements accuracy and reproducibility, and landmarks reliability, but their cephalometric analysis methodology varied widely.**
Conclusion. **These differencies among the studies in making measurements don't permit a direct comparison between them. The future developments in the knowledge of these techniques should provide a standardized method to conduct the 3D CT cephalometric analysis.**

Key words: three-dimensional cephalometry, computed tomography, accuracy, reliability, reproducibility.

Introduction

Conventional cephalometric analysis presents the same limits of the radiograph on which it is performed: the two-dimensional character and geometric distortion of the anatomical structures being imaged. The 2-D cephalometric radiography allows bidimensional evaluation of craniofacial morphology and growth, but ignore the mediolateral axis. Frontal cephalometric radiographs are useful for facial asymmetry assessment but neglect the postero-anterior dimension.
These problems may be overcome using computed tomography (CT) imaging techniques that produce three-dimensional images of cranial bone, jaws and the surrounding tissues, allowing to focus the anatomic structures more accurately than 2D conventional radiography. Different techniques has been developed in order to obtain three-dimensional landmarks and to generate 3-D cephalograms, after combining and integrating the data of both 2-D cephalograms (lateral and postero-anterior).
The advantages of three-dimensional medical computed tomography (CT) imaging are already well established in different dental specialities: management of trauma to the maxillofacial skeleton, surgical facial reconstruction, orthognathic surgery, dental implants, complicated extractions and endodontic treatments (1-3). Nevertheless, its use has been limited in orthodontics due to high-radiation dose, cost, lack of availability, poor resolution and difficulty in interpretation. These issues may be addressed by recent cone beam innovations in CT technology, and could substantially alter the way that patients who have potentially complex orthodontic problems are managed.
Afterwards, the advantages brought by Cone Beam Computed Tomography (CBCT) technology, as lower radiation dose, clearer images, more precision and reliability during the visulizing of landmarks compared with conventional CT, bring to ask if 3D cephalometry obtained with CBCT technology can fully replace the traditional cephalometry. Moreover, because many of the patients had conventional cephalometric records in the past as part of their documentation, it is important to know whether cephalometric radiographs obtained from CBCT scans are comparable to conventional cephalometric records when evaluating a longitudinal series that contains both types of radiographs. If the two types of radiographs are not comparable, then the cephalometric data obtained from CBCT scans cannot be used to evaluate growth and treatment outcomes longitudinally[4].
The aims of this review are to assess the quality of three-dimensional cephalometic analysis obtained from computed tomography and to determine if there is general consensus in the literature concerning the reliability, accuracy and reproducibility of cephalometric landmarks and measurements obtained from CT 3D images.

Methods

Criteria for considering studies for this review
The follow criteria were used to select the studies for this

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review: general measures to find studies on three-dimensional cephalometric analysis, specific selection criteria to improve the quality of the study and exclusion criteria.

General selection criteria included: (1) studies that identified landmarks in the maxillofacial area on CT images; (2) studies that explained how to conduct 3D cephalometric analysis; (3) only human radiographic studies.

Specific selection criteria included studies that (1) evaluated accuracy and reliability of cephalometric measurements conducted on three-dimensional CT images; (2) evaluated the reproducibility of cephalometric landmarks on 3D CT images; (3) determined whether cephalometric measurements performed on CT cephalograms are comparable with measurements on conventional cephalograms; (4) used both human dry skulls and orthodontic patients.

Exclusion criteria: (1) measurements of internal cranial structures and temporomandibular joint (TMJ) were excluded because the focus was on skeletal landmarks that are of interest to clinical orthodontist; (2) areas outside the maxillofacial boundaries; (3) facial trauma or tumor in the maxillofacial area were also excluded because they would distort the normal anatomy of the region.

No sex and age restriction was applied.

Methods of this review

The following electronic data bases were searched through September 2011: Google Scholar beta, PubMed and Science Direct. The following keywords were used: three-dimensional cephalometry; computed tomography; accuracy cephalometric measurements; reliability three-dimensional cephalometry; reproducibility.

To determine whether the keywords had covered all articles on 3D cephalometry, the following journals were manually screened: *The American Journal of Orthodontics and Dentofacial Orthopedics, The Angle Orthodontist, The European Journal of Orthodontics.*

In addition, references from each identified article were manually screened for articles that were missed by electronic search engines. Finally, all manual and electronic searches were solicited for review articles.

All abstract that dealt CT three-dimensional cephalometric analysis were read, and the full texts of all relevant articles were collected and reviewed. Ambiguous articles were also read to avoid inappropriate exclusion. All procedures were performed indipendently by two authors (GR, CC), and differencies were resolved by rereading and discussion until consensus was reached.

Results

A total of 480 abstracts without overlap were found by the search methods. Only 43 abstracts met the inclusion criteria or were retrieved because the abstract did not provide enough information to justify exclusion. Fourteen articles were excluded according to the selection and exclusion criteria. Two more were excluded after reading and discussing, because one tested the accuracy of an algorithm that corrects measurements made on conventional lateral head film to corresponding dimensions observed in a CBCT scan, and the other one scanned an acrylic head phantom to determine the reproducibility of maxillofacial anatomic landmarks. Therefore 27 studies remained.

Nine articles were selected from the American Journal of Orthodontic and Dentofacial Orthopedics; 7 were from the Angle Orthodontist; 2 from the International Journal of Oral Maxillofacial Surgery, and 3 from the Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontology; the last articles were selected from the Journal of Craniomaxillofacial Surgery, Dentomaxillofacial Radiology, Journal of Orofacial Orthopedics, Journal of Oral and Maxillofacial Surgery, European Journal of Orthodontics, Biomedical Imaging and Interventional Journal.

Fourteen studies used orthodontic subjects and thirteen human dry skulls.

A summary of the results from the 27 articles is presented in Table 1.

Measurement accuracy and landmark reliability

Lagravère and Major[5] examined the intra-examiner reliability of a new proposed skeletal landmark, ELSA, located equidistant to centers of foramina spinosum. Ten adolescent patients were scanned using a NewTom QR-DVT 9000 CBCT scanner (Aperio Services, Verona, Italy). Images were analyzed with AMIRA software (Mercury Computer System, Berlin, Germany). Axial, sagittal, coronal, and 3D reconstructions were used in locating the landmark. The intra-examiner reliability has a kappa value of 0.998. The authors concluded that this novel landmark is an adequate landmark for use as a reference in 3D cephalometric analysis with 3D volumetric images. Moshiri et al.[6] compared the accuracy of linear measurements made on conventional lateral cephalograms (LCs) captured on photostimulate phosphor cephalograms (PSP) with 3 methods for simulating lateral cephalograms with CBCT. The linear distances between anatomical landmarks on dentate dry human skulls were measured by observers using digital calipers for S-N, Ba-N, M-N, ANS-N, ANS-PNS, Pog-Go, Go-M, Po-Or, and Go-Co. The skulls were imaged with CBCT with a single 360° rotation, producing 306 basis images and achieving 0.4 mm isotrophic voxel resolution on volumetric reconstruction for making ray-sum reconstructed cephalograms. Two other cephalogram approaches were used with the CBCT system: a single transmission image generated as a scout image designed to check patient positioning before CBCT, and a single-frame lateral basis image. Conventional digital lateral cephalograms (LCs) were acquired with the photostimulable phosphor system. Images were imported into a cephalometric analysis program (Dolphin Imaging Cephalometric and Tracing Software, Chatsworth, Calif) to compute the included linear measurements. Analyses were repeated 3 times and statistically compared with measured anatomic truth with ANOVA ($P \leq .05$). The intraclass correlation coefficient was determined as an index of intra- and inter-examiner reliability. The intraclass correlation coefficient (ICC) for the LCs was significantly less than for the measured anatomic truth and for all CBCT-derived images. CBCT images either produced with individual frames or reconstructed from the volumetric data set were accurate for all measurements except Pog-Go and Go-M. CBCT scout images had the second highest accuracy for all measurements except Pog-Go, Go-M, and Go-Co. Conventional LCs had the least accuracy, and were accurate only for Po-Or and ANS-N. In conclusion CBCT-derived 2-dimensional LCs proved to be more accurate than LCs for most linear measurements calculated in the sagittal plane. No advantage was found over single-frame basis images in using ray-sum generated cephalograms from the CBCT vol-

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Table 1 - Search results.

Authors	***Sample size***	***Landmarks and measurements***	***Focus of study***	***Results***
Lagravère and Major 2005	10 patients	1 landmark: ELSA	To examine the intra-examiner reliability of ELSA.	ELSA is an adequate landmark for use as a reference in 3D cephalometric analysis.
Swennen et al. 2006	1 subjects		To evaluate the accuracy and reliability of 3D quantitative data.	MS-CT and CBCT 3D cephalometry was highly accurate and reliable.
Park et al. 2006	30 subjects	Landmark: P, Na, Or, ANS, A, B, Pog, Me, PNS, Po, CP, Go, Mx, ZP, Bc, R, Pr Measurements: SNA, SNB, ANB, Mn plane angle.	To determine the reproducibility of landmark identification on a new type of 3D CT cephalometric analysis.	All landmark were reproducible and there was no significant intra-examiner error between 2 sessions of landamrk identification.
Moshiri et al. 2007	23 dry skulls with an indelible marker	Landmarks: S, N, Or, ANS, PNS, Pog, M, Go, Ba, Po, Co. Measurements: S-N, Ba-N, PNS-ANS, Na-A, Na-M, Na-B, N-ANS, Pog-Go, Go-M, Po-Or, Go-Co.	To compare the cephalometric measurements accuracy of CBCT images with conventional lateral cephalograms (LCs).	In the sagittal plane simulated 2D lateral cephalometric projection from CBCT proved to be more accurate than conventional LCs.
Olszewski et al. 2007	26 dry skulls	Landmarks: m, mid m, pcp, mid pcp, sos, od, fm, mid fm, fr, pti, mid pti, at, np, mid np, na, sopraorbitale, optic.	To adapt Delaire's 2D cephalometric analysis into the third dimension.	Inter- and intra-examiner reproducibility were superior ($p <$ 0.0001) following the 3D CT method.
Cattaneo et al. 2008	34 subjects	17 angles: Pr-N-Ss, CL-ML, Ils-NL, Ili-ML, Ss-N-Pg, Ss-N-Sm, NL-Ols, Oli-ML, NL-ML, S-N-Ss, S-N-Pg, NSL-NL, NSL-ML, N-S-Ar, N-S-Ba, Beta angle, Jaw angle.	To compare CBCT cephalometric measurements with measurements on conventional cephalograms.	The RayCast technique proved to be more reproducible than the MIP.
Periago et al. 2008	23 dry skulls	20 linear distances: Midsagittal Planes: S-Na, Na-Ba, ANS-PNS, Na-A, Na-B, Na-Me, Na-ANS, Ba-ANS. Bilateral Planes: Pog-Go, Pog-Co, Go-Me, Go-Co, Go-Gn, Po-Or.	To compare the reliability and accuracy of linear measurements made on 3D reconstructions to direct measurements made on ex vivo human skulls.	Most of linear measurements can be considered to be sufficiently clinically accurate (- 1.13% ± 1.47%) for craniofacial analyses.
Lopes et al. 2008	28 dry skulls	9 landmarks: A, G, Me, N, Co, ANS, Go, Pog, B. Measurements: N.A.Pog, G.ANS.Pog, N.ANS.Me, N.Me.Go, Co.Go.Me, N.A.B.	To demonstrate the accuracy of angular measurements by using 3-D volume-rendering imaging using 64-row multislice CT.	Angular measurements obtained from 64-row MSCT 3D reconstrutions are precise and accurate.
Kumar et al. 2008	31 subjects	12 measurements: ANS-Me, N-ANS, N-Me, Co-Gn, Co-ANS, AN, BN, PgN. 5 angular measurements: SNA, SNB, FMA, USN LMP.	To compare measurements from synthesized CBCT lateral cephalograms with those from conventional cephalometric radiographs.	The cephalometric modalities were not statistically different for any of the 12 linear measurements.
Brown et al. 2009	19 dry skulls	15 landmarks: N, ANS, A, PNS, B, Me, Mo, NC, Ag, Go, Za, Co, Z, Mf, J. Measurements: Na-Me, Co-Go, Co-Go, Z-Ag, Na-ANS, ANS-PNS, Na-A, Na-Bf, Go-Go, Mf-Mf, Mo-Mo, Za-Za, NC-NC, Z-Zk, J-J.	To compare the in vitro reliability and accuracy of linear measurements made on CBCT lateral cephalograms and human skulls.	Linear measurements on 3D shaded surface renderings from CBCT datasets using commercial cephalometric analysis software have variable accuracy.
Berco et al. 2009	1 dry skull	17 landmarks: N, A, B, Pg, Me, Or, Po, Condyle, Go, Ag, S, Ba. Linear measurements: N-A, N-B, N-Pog , N-Me, A-B, A-Pog, A-Me, B-Pog, B-Me, Po R-Go, Co R-Go, AG-AG, Or R-Or L, Go R-Go L, Po R-Po L, Co R-Co L, Ba-S, Or R-Po R, Or L-Po L, N-Or, Or R-A, Or R-Pog, Or L-A, Or L-Pog, Co R-Go L, Co L-Go R.	To test the accuracy and reliability of 3D CBCT craniofacial measurements.	No significant intra- or inter-examiner differences were observed. CBCT allows for clinically accurate and reliable 3-dimensional linear measurements of the craniofacial complex.
Bholsithi et al. 2009	40 subjects	Linear measurements: A-B, ANS-Me, N-ANS, S-ANS, S-N, A-Or, A – Cond, A-Cc, Cc-Go, Gn – Cond, Me-Cc, Me-Go, Me-Or, Pog – Cond, CcR – CcL, GoR – GoL, OrL-OrR, N-ANS/ANS-Me. Angular measurements: SNA, SNB, ANB, NSBa, ANS-PNS to SN, A to FHL, A to FHR, Me to Go to Cc, Gn-Go to Cond, Me-Go to SN, Gn - Go to POP, Me-Go to FH, ANS-PNS to FH, SN to POP, SN to FH, SN to Go – Gn, FH to POPL, CcR to A to CcL, CcR to Me to CcL, GoR to Me to GoL, OrR to A to OrL, OrR to Me to OrL, GoR-GoL to AO, OrR-OrL to AO.	To comapre 3D cephalometric analysis with corresponding 2D lateral and frontal analysis with repeated measurements.	Most linear measurements and some angular measurements were not different, while other types of measurements were significantly different.
van Vlijmen et al. 2009	40 dry skull	15 landmarks: S, N, A, B, ANS, PNS, Ar, Pog, Me, Go, Gn, ML, BOP. 14 measurements: SNA, SNB, ANB, NSL/NL, NSL/ML, NL/ML, Interincisal angle, NSL/BOP, Ar to A, Ar to Pog.	To compare the reliability and the reproducibility of linear measurements made on conventional and CBCT lateral cephalograms.	Intra-examiner reliability for both cephalometric radiographs was good for all measurements. Reproducibility of measurements in the CBCT cephalograms was high.
Moreira et al. (2009)	15 dry skulls	Linear measurements: A-Pg, Co-A, Co-Pg, ANS-PNS, ANS-Me, ANS-N, ANS-A, N-A, N-B, N-Me, N-Pg, Po-Or, Zm-Zm, B-Me, Ba-N. Angular measurements: N.A.Pg, G.ANS.Pg, N.ANS.Me, N.Me.Go, Co.Go.Me, N.A.B.	To demonstrate the precision and accuracy of maxillofacial measurements obtained by CBCT.	No statistically significant difference between inter- and intra-examiner analysis.
Ludlow et al. 2009	20 subjects	Landmarks and measurements: A, ANS, B, Co, Gn, Go, Me, N, Or, Pog, Po, S.	To compare the precision of landmark identification on CBCT images and conventional lateral cephalograms.	Identification of cephalometric landmarks was significantly more precise with CBCT than with conventional lateral cephalograms

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Table 1 - Search results. *(continued)*

de Oliveira et al. 2009	12 subjects	Landmarks: S, N, A, B, Pog, Gn, Me, ANS, Go, Co, Or, RP, Tb, ZS.	To evaluate reliability in 3D landmark identification using CBCT.	The intra- and inter-examiner reliability was excellent.
Hassan et al. 2009	8 dry skulls	10 linear distances: OrL-OrR, OrL-ANS, OrR-ANS, ANS-PNS, CoL-CoR, CorL-CorR, CoL-CorL, CoR-CorR, CoL-CorR, CoR-CorL.	To assess the accuracy of measurements on 3D CBCT datasets and to compare them with those made on 2D tomographic slices and on 2D lateral and PA cephalometric projections.	3D CBCT measurements are accurate and closer to the physical measurements than the 2D slices and 2D projection images.
Lagravère et al. 2009	24 subjects	FS, ELSA, AEM, DFM, N, A, B, Prt, MIS, Zm, Pf, Or, Ekm, ANS, PNS.	To evaluate the reliability of 3D CBCT-generated landmarks previously used in traditional 2D cephalometry.	Intra- and inter-examiner reliability for all landmarks were acceptable.
Cevidanes et al. 2009	12 subjects	SNA, SNB, ANB, A to N, B to N, Pg to N, A-N, B-N, Pog-N, Co-ANS, Co-Gn, Co-Gn – Co-ANS, Pog-NB, FMIA, N-Me, N-ANS, ANS-Me, Co-Gn, FMA, SN-GoGn, Occ plane to SN, Occ Plane to FH, FH-SN.	To determine the reliability of 2D cephalometric measurements using two virtual head orientations from CBCT models.	Good reliability both within each head orientation and between orientations.
Olszewski et al. 2010	13 subjects	Landmarks: Da, fm, Fr, M, np, pcp, Ps, pti, Pyr, at, od, sso, N, ZyFrn, Go, Inferior orbital rim, Infraorbitale, Me, Po, Zygion, A, ANS, B, Ba, cg, S, Me, Pog.	To measure the reproducibility of landmark identified with 3D-ACRO and 3D-Swennen analyses.	3D-ACRO analysis was significantly more reproducible than 3D-Swennen analysis.
Nalçaci et al. 2010	10 subjects	18 landmarks: S, A, B, D, Gn, Me, ANS, PNS, Pog, Or, Po, Go, N, Ba. 14 measurements:SNA, SNB, ANB, SND, NA-Pog, AB-NPog, Ns-Ba, IMPA, FMIA, SN ANS-PNS.	To compare the reliability of 3D angular measurements with traditional 2D cephalometry.	The 3D angular cephalometric analysis is a fairly reliable method, like the traditional 2D cephalometric analysis.
van Vlijmen 2010	40 dry skulls	Landamrks: S, N, A, B, ANS, PNS, Pog, Gn, Go, NSL, NSP, ML, MP, NL, NP, BOP, BOP (3D). Measurements: SNA, SNB, ANB, NSL/NL, NSP/NP (3D), NSL/ML, NSP/MP (3D), NL/ML, NP/MP (3D), NSL/BOP, NSP/BOP (3D).	To compare the reliability and reproducibility of landmark identification on CBCT images and conventional lateral cephalograms.	Intra-examiner reliability was good for all measurements. The reproducibility of the measurements on the conventional cephalometric radiographs was higher compared with the reproducibility of measurements on the 3D models.
Lagravère et al. 2010	10 subjects	18 landmarks: N, Or, A, B, Pg, Gn, Me, Go, Po, S, Ba, ANS, PNS, Co.	To compare the reliability of landmark identification on CBCT images and conventional lateral cephalograms.	Intra- and inter-examiner reliabilities of landmarks were high for all CBCT landmarks and most 2D lateral cephalometric landmarks.
Olmez et al. 2011	13 dry skulls	18 landmarks: N, G, A, B, Pog, ANS, Go, Me, Or, Po, Cor, ZyFrn, ZyMax. Measurements: ANS-Me, N-ANS, N-Me, Cor-A, Cor-Pog, Cor-Go, Po-A, Po-B, Po-Or, Po-ZyFrn, Gla-Go, Gla-Or, Gla-ZyFrn, Gla-ZyMax, ZyFr-ZyFr, ZyMx-ZyMax, GoL-GoR, OrL-OrR.	To compare the accuracy of landmark identification on CBCT images and conventional lateral cephalograms.	CT scans have more accurate high-resolution images for measurement of hard tissue structures than do conventional 2D cephalometric measurements.
Medelnik et al. 2011	1 fresh-frozen cadaver head	Landmarks: ANS, PNS, Pr, Gn, Pog, Genion, Mental, Mf, Kr. Measurements: Mfl-Mfr, Spa-Pr, Id-Gn, Krl-Krr, Spa-Spp. Angle: Krl-Krr- Ge.	To evaluate the reproducibility of anatomical landmarks and the accuracy of different cone-beam CTs (CBCTs/DVTs) and a multislice spiral CT (MSCT) scanner.	The reproducibility of landmark identification in all volume images was good.
Frazão Gribel et al. 2011	25 dry skulls with 10 fiducial markers	Landmarks: G, A, Gn, Me, PNS, ANS, Go, Co. Measurements: Gl-Me, Gl-ANS, ANS-Me, ANS-PNS, Co-A, Co-Gn, Go-Me, Go-Co.	To assess the accuracy and reliability of measurements made on CBCT scans and lateral cephalograms.	CBCT craniometric measurements were extremely accurate. No statistically significant difference between the CBCT measurements and the direct craniometric measurements.
Damstra et al. 2011	25 subjects	Landmarks: S, N, ANS, A, B, Pog, Gn, Me, Ba, Go, Co, Or, Po. Measurements: SNA, SNB, ANB, SN-FHPL, SN-PPL, SN-MdPL, PPL-MdPL, y-axis, BaSN, ANS-Me, Co-A, Co-Gn, AFH, PFH.	To determine the reliability 3D cephalometric analysis.	The intra- and inter-examiner reliability of the 3D measurements was also very good.

ELSA (midpoint on line connecting both foramen spinosum Landmark), S (Sella), N (Nasion), Or (Orbitale), ANS (Anterior Nasal Spine), PNS (Posterior Nasal Spine), Pog or Pg (Pogonion), M (Menton), Go (Gonion), Ba (Basion), Po (Porion), Co (Condylion), A (deepest point of the maxillary alveolar bone concavity), B (the deepest point of the mandibular alveolar concavity), m (junction of maxillary, nasal and frontal suture), pcp (posterior clinoid process), ara (articulare anterior), od (odontoid), fm (frontomaxillar), pts (pterygoid superior), pti (pterygoid inferior), at (atlas), np (nasopalatine foramen), G (glabella), Ag (Antegonion), Gn (Gnathion), Ar (articularis), Ba (basion), Pr (prosthion), Sm (supramentale, B-point), Ss (subspinale, A-point), CL (chin Line), ML (mandibular line), NL (nasal line), NSL (nasion-sella line), Da (Dacryon), Fr (Foramen rotondum), Ps (Planum sphenoidale), Pyr (Pyriform rim), Oli (occlusal line, inferior), Ols (occlusal line, superior), FH (Frankfort horizontal), Mf (Mental foramen), Kr (Coronion), Pr (Prosthion), Ge (Genion), ZyFrn (zygomaticofrontal), ZyMax (zygomaticomaxillary), Mo (medio-orbitale), Za (zygomatic arch), J (jugale; maxillare), NC (lateral piriform aperture), Z (zygomaticofrontal medial suture point).

umetric data set. Olszewski et al.[7] tested the accuracy of the measurements done on 3D CT surface renderings (ACRO 3D) in relation to those directly taken on 26 dry skull with the help of a 3D measuring instrument. There were no significant differences in the accuracy of measurements between the ACRO 3D software and the 3D measuring instrument. Periago et al.[8] performed 20 orthodontic linear measurements between anatomical landmarks on 23 human skulls, using a digital caliper. The skulls were imaged with CBCT using the i-CAT system, and the CBCT data

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were exported from the XoranCat software in DICOM multi-file and imported into Dolphin 3D (version 2.3) on the same computer. While many linear measurements between cephalometric landmarks on 3D volumetric surface renderings obtained using Dolphin 3D software generated from CBCT datasets may be statistically different from anatomic dimensions, most can be considered to be sufficiently clinically accurate for craniofacial analyses. Lopes et al.[9] studied the accuracy of 6 angular measurements based upon 9 conventional craniometric anatomical landmarks on 28 dried skulls, that were scanned with a 64-row multislice CT. These angular measurements were identified independently in 3D CT images by 2 radiologists, twice each. Subsequently, physical measurement were made by a third examiner. The results demonstrated no statistically significant difference between inter- and intra-examiner analysis. The mean difference between the physical and 3D-based angular measurements was -1.18% and -0,89%, respectively, for both examiners, demonstrating high accuracy. Maxillofacial analysis of angular measurements using 3D CT volume rendering by 64-row multislice CT is established and can be used for orthodontic and dentofacial orthopedic applications. Cevidanes et al.[10] have used presurgery CBCT scans of 12 patients (6 class II and 6 class III) randomly selected from a pool of 159 patients to determine the reliability of obtained two-dimensional cephalometric measurements using two virtual head orientations from cone-beam computed tomography (CBCT) models: visual natural head position (simulated NHP) and 3D intracranial reference planes (3D IRP). The CBCT scans were obtained by NewTom 3G (QR-NIM s.r.l., Verona, Italy) and the volume data were exported in DICOM format into Dolphin Imaging software (version 10.5, Dolphin Imaging & Management Systems, Chatsworth, Calif). Three observer created and digitized four CBCT-generated lateral cephalograms per patient, two using simulated NHP and two using 3D IRP at intervals of at least 3 days. ICC (intraclass correlation coefficients) indicated good reliability both within each head orientation and between orientations. Of the 50 measurements, the reliability coefficients were $\geq$ 0.9 for 45 measurements obtained with 3D IRP orientation and 36 measurements with simulated NHP. The difference in mean values of the two orientations exceeded 2 mm or 2° for 14 (28%) of the measurements. Lagravère et al.[11] evaluated intra- and inter-examiner reliability of 3D CBCT-generated landmarks in patients who needed maxillary expansion. CBCT scans were taken using the NewTom 3G (Aperio Services, Verona, Italy) at 110 kV, 6.19 mAs, and 8 mm aluminum filtration. CBCT images were converted to DICOM format and rendered into a volumetric images with AMIRA software (AMIRA, Mercury Computer Systems Inc, Berlin, Germany). Sagittal, axial, and coronal volumetric slices, as well 3D reconstruction of the image, were used to determine landmark positions. In this system, the XY-plane moves from top to bottom, the XZ-plane moves from front to back, and the YZ-plane moves from left to right. The predetermined coordinate system and origin (0, 0, 0) established by AMIRA for each image were used and were the same for every examiner. Then examiners located landmarks on the images. Intra-examiner reliability for x, y, and z coordinates for all landmarks was greater than 0.97 with 95% confidence interval (CI, 0.96, 0.99). Inter-examiner reliability for x, y, and z coordinates for all landmarks was greater than 0.92 (CI, 0.87, 0.96), with the exception of the x-components of the auditory external meatus left 0.84 (CI, 0.61, 0.94), auditory external meatus right 0.90 (CI, 0.73, 0.96), orbit left 0.83 (CI, 0.52, 0.93), and orbit right 0.80 (CI, 0.49, 0.92) landmarks. Foramen Spinosum (FS), Center Coordinate Point (ELSA), Auditory External Meatus (AEM), and Dorsum Foramen Magnum (DFM) demonstrated adequate reliability and could be used for determining a standardized reference system. The same Author[12] afterwards confirmed his previous results: the intra-observer reliability was good for all measurements. The correlation coefficient between the first and second measurements ranged between 0.69 and 0.98, with an average of 0.91. The standard error for the conventional cephalometric radiographs was significantly smaller for nine measurements out of 12, as compared with the standard error of the measurements on the 3D models. Berco et al.[13] determined the accuracy and reliability of 3D cranio-facial measurements obtained from CBCT scans of a dry human skull, obtained with 2 skull orientations. Seventeen landmarks were identified on the skull, and twenty-nine interlandmark linear measurements were made directly on the skull and compared with the same measurements made on the CBCT scans. All measurements were made by 2 operators on 4 separate occasions. The method errors were 0.19, 0.21, and 0.19 mm in the x-, y- and z-axes, respectively. Repeated measures analysis of variance (ANOVA) showed no significant intra- or inter-examiner differences. The mean measurement error was –0.01 mm (SD, 0.129 mm). Five measurement errors were found to be statistically significantly different. The Authors concluded that CBCT allows for clinically accurate and reliable 3D linear measurements of the craniofacial complex and that skull orientation during CBCT scanning does not affect the accuracy or the reliability of these measurements. Hassan et al.[14] assessed the accuracy of linear measurements on 3D surface-rendered images of 8 dry human skulls generated from CBCT datasets and compared them with those made on 2D tomographic slices and on 2D lateral and PA cephalometric projections. Moreover, the Authors evaluated the influence of head position of the patient in the scanner on measurement accuracy as Berco done[13]. Ten linear distances were defined for cephalometric measurements. The physical and radiographic measurements were repeated twice by three independent observers and were compared using repeated measures analysis of variance ($P = 0.05$). The radiographic measurements were also compared between the ideal and the rotated scan positions. The radiographic measurements of the 3D images were closer to the physical measurements than the 2D slices and 2D projection images. No statistically significant difference was found between the ideal and the rotated scan measurements for the 3D images and the 2D tomographic slices. A statistically significant difference ($P < 0.001$) was observed between the ideal and rotated scan positions for the 2D projection images. The findings indicate that measurements based on 3D CBCT surface images are accurate and that small variations in the patient's head position do not influence measurement accuracy. Van Vlijmen et al.[4] compared the conventional cephalometric measurements with those obtained with the CBCT cephalometric radiographs taken from 40 dry human skulls. Intra-examiner reliability for both the conventional cephalomentric radiographs and CBCT-constructed cephalometric radiographs was good for all measurements. The correlation coefficient between the first and the second measurements ranged between 0.91 and 0.99, with an av-

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erage of 0.97. The standard error for CBCT-constructed cephalometric radiographs was significantly smaller for 8 measurements, compared with the standard error of the conventional cephalometric radiographs. Brown et al.[15] compared the in vitro reliability and accuracy of linear measurements between cephalometric landmarks on CBCT 3D volumetric images with varying basis projection images to direct measurements on human skulls. The Authors directly measured 16 linear dimensions between 24 anatomic sites marked on 19 human skulls, which were imaged with CBCT (i-CAT). No difference in mean absolute error between the scan settings was found for almost all measurements. The average skull absolute error between marked reference points was less than the distances between unmarked reference sites. CBCT resulted in lower measurements for nine dimensions (mean difference range: 3.1 mm ± 0.12 mm to 0.56 mm ± 0.07 mm) and a greater measurement for one dimension (mean difference 3.3 mm ± 0.12 mm). No differences were detected between CBCT scan sequences. Moreira et al.[16] demonstrated the accuracy of 15 maxillofacial linear and 6 angular measurements obtained by CBCT (i-CAT - Imaging Sciences International, Hatfield, PA) images marked on 15 intact human skulls. No statistically significant differences were found of the comparison between the physical and CBCT-based linear and angular measurements for both examiners ($P = .968$ and .915, $P = .844$ and .700, respectively). de Oliveira et al.[17] evaluated intra- and inter-examiner reliability in 3D landmark identification using CBCT images. Twelve presurgery CBCTs were randomly selected from 159 orthognathic surgery patients. Three observers independently repeated 3 times the identification of 30 landmarks in the sagittal, coronal, and axial slices. The ICC was >0.9 for 86% of intraobserver assessments and 66% of interobserver assessments. Only 1% of intraobserver and 3% of interobserver coefficients were <0.45. The systematic difference among observers was greater in X and Z than in Y dimensions, but the maximum mean difference was quite small. Overall the intra- and inter-observer reliability was excellent. Nalçaci et al.[18] assessd the reliability of 3D angular cephalometric approaches and the reproducibility of landmark identification by comparing this method with authenticated traditional 2D cephalometry. Eighteen cephalometric landmarks and 14 cephalometric angular measurements were used. Two different orthodontists performed both 2D and 3D cephalometric analyses. To assess intraobserver reproducibility two sets of recordings made by each observer in each modality were used. The intraobserver reproducibility for the first and the second observer ranged from 0.35° to 0.57° and from 0.42° to 0.65°, respectively. Furthermore, no significant differences were observed between the measurements of the two observers ($P > 0.05$). A comparison of 2D and 3D cephalometric measurements showed significant differences in U1-NA and U1-SN parameters ($P < 0.05$). However, the parameters SNA, SNB, ANB, SND, NA-Pog, AB-NPog, Ns-Ba, IMPA, FMIA, SN Ans-Pns, L1-APog and L1- NB did not show any significant differences ($P > 0.05$). The Authors also concluded that the 3D angular cephalometric analysis is a fairly reliable method, like the traditional 2D cephalometric analysis. Olmez et al.[19] used different sections of 13 dry skulls to determine the accuracy and the differences between manual and cephalometric measurements, using computer-assisted three-dimensional (3D) analysis and conventional two-dimensional (2D) techniques. The skulls were scanned with a Philips MX 8000 IDT Multi-slice CT System (V 2.5; Philips Medical Systems, The Netherlands) with a high-resolution bone algorithm, 512 X 512 matrix, 120 kV, and 100 mA. Axial scans were obtained with a 1-mm slice thickness and parallel to the Frankfurt horizontal plane. The 3D model of the axial images was reconstructed using Mimics v12.01 (Materialise) software, and 3D cephalometric analyses were performed. Standard lateral and frontal cephalograms of the dry skulls, on which clay markers were replaced with metallic balls and pins, were taken by Odontorama PC (85kV, 10 mA; Trophy Radiologie, Croissy-Beauborg, France). All metric measurements were made between the outermost points of balls and pins during manual and 3D virtual model measurements. All measurements on 2D radiograms were made between the center points of pins and balls. In all cephalometric analyses, 18 landmarks and 29 measurements (17 lateral and 12 frontal) were used. Measurements were evaluated in three groups, as follows: group I (computer-assisted 3D cephalometric measurements), group II (physical cephalometric measurements) and group III (conventional 2D cephalometric measurements). All measurements were statistically insignificant between the computer-assisted 3D and manual measurements. On the other hand, the differences between the conventional 2D and the manual measurements were statistically significant. The greatest amount of magnification was found at the Nasion-Menton distance (14.6%), which was located at the farthest distance from the central x-ray beam in the lateral cephalogram ($P < .01$). For the same reason, the greatest enlargement (16.2%) was observed in the distance between the zygomaticomaxillary sutures on the conventional frontal cephalogram ($P < .01$). The computer-aided 3D cephalometric measurements were found to be more accurate than the conventional cephalometric measurements. Medelnik et al.[20] evaluated the accuracy of different cone-beam CTs (CBCTs/DVTs) and a multislice spiral CT (MSCT) scanner. A human fresh-frozen cadaver head was scanned with four CBCTs (Accuitomo 3D, 3D eXam, Pax Reve 3D, Pax Zenith 3D) and one MSCT (SOMATOM Sensation 64) scanner. The three- dimensional (3D) reconstruction of the volume data sets and location of the anthropometric landmarks (n=11), together with linear (n=5) and angular (n=1) measurements were carried out by three examiners using the program VoXim® 6.1. The measurements were taken twice at a 14-day interval. Descriptive analyses were made and the standard deviations were used to compare differences in the accuracy of landmark identification. The descriptive statistics showed distinct differences in the reference points in the three axes of the coordinate system. Because of anatomical and morphological factors, the pogonion and gnathion reference points displayed higher standard deviations when set on the transverse plane (SDCBCT Pog: 0.66–1.57 mm; SDMSCT Pog: 0.14–1.09 mm; SDCBCT Gn: 1.05–1.77 mm; SDMSCT Gn: 0.20–0.85 mm), thus showing less accuracy. However, standard deviations on the sagittal and vertical planes were smaller. Genion, anterior nasal spine and infradentale had very low standard deviations on all three planes. The distance Mfl-Mfr and angle Krl-Krr-Ge revealed significantly smaller standard deviations in the MSCT (SDCBCT Krl-Krr-Ge: 0.51–0.75 mm; SDMSCT Krl-Krr-Ge: 0.22 mm). Frazão Gribel et al.[21] assessed the accuracy and reliability of craniometric measurements made on CBCT scans and lateral cephalograms of twenty-five

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human skulls. CT scans were made using the iCAT Next Generation (Imaging Sciences International, Hatfield, Pa) CBCT unit. A standardized protocol of the iCAT for the extended (17 X 23 cm) field of view (FOV) with 0.3 mm slice thickness, 26.9 seconds acquisition time was used. The raw images were exported using the iCAT native software (iCAT Vision) into DICOM 3 multifiles. The DICOM images were loaded into SimPlant Ortho 2.0 (Materialise Dental, Lueven, Belgium) software. A custom analysis was created using the dedicated "3D Cephalometric" software module. The custom 3D analysis (COMPASS 3D) was saved to be used with all CT scans. The same skulls subsequently were used to obtain lateral cephalograms. The x-ray unit was calibrated optimally at 60 kV, 66 mA, and 0.16 seconds. Linear and angular measurements were performed on both 3D and 2D cephalograms. At the end linear distances were directly measured using a digital caliper on the skulls. The Authors concluded that no statistically significant difference was noted between CBCT measurements and direct craniometric measurements (mean difference, 0.1 mm). All cephalometric measurements were significantly different statistically from direct craniometric measurements (mean difference, 5 mm). Significant variations among measurements were noted. Some measurements were larger on the lateral cephalogram and some were smaller, but a pattern could be observed: midsagittal measurements were enlarged uniformly, and Co-Gn was changed only slightly; Co-A was always smaller. However CBCT craniometric measurements computed by a dedicated "3D Cephalometric module" are extremely accurate. Damstra et al.[22] determined the reliability and the measurement error (by means of the smallest detectable error) of 17 commonly used cephalometric measurements made on 3-dimensional (3D) cone-beam computed tomography images. Twenty-five CBCT scans were randomly selected, and 3D images were rendered, segmented, and traced with the SimPlant Ortho Pro software (version 2.1, Materialise Dental, Leuven, Belgium). This was repeated twice by 2 observers during 2 sessions at least 1 week apart. Measurement error was determined by means of the smallest detectable difference. Differences were analyzed with Wilcoxon signed rank tests. Intraobserver and interobserver reliability values were calculated by means of intraclass correlation coefficients (ICC) based on absolute agreement. The Authors concluded that there were great variations of measurement errors between the angular (range, 0.88°-6.29°) and linear (range, 1.33-3.56 mm) variables. The greatest measuring error was associated with the dental measurements U1-FHPL, L1-MdPL. and L1-FHPL (range, 3.80°-6.29°). ANB angle was the only variable with a measuring error of 1° or less for both observers. The intraobserver agreement of all measurements was very good (ICC, 0.86-0.99). Except for SN-FHPL (ICC, 0.76), interobserver agreement was very good (ICC, >0.88).

Reproducibility of measurements

Park et al.[23] assessed the reproducibility of the landmarks and a subject was chosen at random; 19 landmarks were identified 5 times in 1 session by an operator 2 weeks after the first session. A paired *t*-test between the 2 sessions was carried out by using SAS version 8.2. The Author concluded that all landmarks were reproducible, with a no significant intra-examiner error between the 2 sessions (P >.0.1). Olszewski et al.[7] evaluated the reproducibility of the 3D CT cephalometric method using 26 dry skulls ×2 observers × 2 identifications ×9 measured distances × 2 methods = 1872 measurements. The intra-observer intraclass coefficient of correlation for the 2D X-rays methods lay between 0.6040 and 0.9053. The inter-observer intraclass coefficient of correlation for the 2D X-ray method lay between 0.1330 and 0.8409. The inter-observer intraclass coefficient of correlation for the 3D CT method lay between 0.9362 and 0.9965. The Authors concluded that inter- and intra-observer reproducibility proved to be significantly superior (p < 0.0001) following the 3D CT method, compared with the Delaire's two-dimensional cephalometric analysis. The same Author in 2010[24] measured the reproducibility of osseous landmark identification from two recently described three-dimensional (3D) cephalometric analyses: 3D-ACRO and 3D-Swennen analyses. A total of 1144 measurements were performed to estimate intra-observer reproducibility for both of the 3D cephalometric analyses. A total of 2288 measurements were performed to estimate inter-observer reproducibility for both of the 3D cephalometric analyses. This study shows that the 3D-ACRO analysis is significantly more reproducible than the 3D-Swennen analysis (p1⁄40.0027). Cattaneo et al.[25] in order to evaluate the landmarks reproducibility analyzed a conventional lateral cephalogram and 2 sets of CBCT-synthesized cephalograms, maximun intensity projection (MIP) and RayCast from 34 patients. The absolute differences in degree between 3 observers were calculated for every angle, and independently for each of the 3 imaging tecniques. The Student-Newman-Keuls post-hoc test showed: significant statistical differences between the 3 observers for 3 angular measurements on the conventional cephalograms (Ili-ML, P = 0.026; NL-Ols, P = 0.045; Oli-ML, P = 0.038). No angular measurements were statistically different for the MIP technique; 1 angular measurement had a statistically difference for the RayCast technique (N-S-Ba, P = 0.042). However, in all cases, the differences were much smaller than the accepted 1 standard deviation (SD) for the respective angle according to the Björk analysis. The calculated measurements did not differ between the 3 image technique. The Ray-Cast technique proved to be more reproducible than the MIP. Van Vlijmen et al.[4] assessed the reproducibility of the landmarks identifing 15 landmarks on both types of cephalometric radiographs on all images 5 times with a 1-week interval. The Authors found that the reproducibility of measurements in the CBCT-constructed cephalometric radiographs was higher, compared with the reproducibility of measurements in conventional cephalometric radiographs. There was a statistically significant difference (P<.05) between this two methods of radiographs for the following measurements: SNB, Ar-A, Ar-Pog, NSL/NL, NL/ML, ILs/NL, Lii/ML, interincisal angle, and Ii to A-Pog. For most of these measurements the actual mean average difference ranged from – 1.54° to 1.45°, similar to, or smaller than, the standard error for the repeated measurements. Only the difference between CBCT measurements and conventional measurements for the absolute distance Ar-A and Ar-Pog was greater than their standard error, but still less than 1 mm. In 2010 the same Author[26] identified 17 landmarks on the cephalometric radiographs and on the 3D models. All images and 3D models were traced five times with a time-interval of 1 week and the mean value of repeated measurements was used for further statistical analysis. Distances and angles were calculated. Reproducibility of the measurements on the conventional cephalometric radiographs was higher, compared with the reproducibility of the measurements on the 3D models. A statistically significant difference between the conventional cephalometric radiographs and the 3D models was found for the following measurements: ANB, SNB, NL/ML, NSL/BOP, NSL/ML, NSL/NL, Is to A-Pog. The average difference ranged from –3.118° to 0.828°. For most measurements this difference was considerably smaller than the standard deviation of the variable measured. For SN/ML the difference (3.118) was 89% of standard deviation, for the SN/NL difference (1.748) this was 66%. For all other measurements it was less than 40%. In the study conducted by Lagravère et al.[11] the principal investigator located the landmarks in the XY, XZ and YZ planes five times on different days, and four other investigators located the landmarks once for each image. Spherical markers of 0.5 mm diameter were placed, indicating the position of the landmark. Intra- and inter-examiner reliability values were determined using ICCs. Intra- and inter-examiner reliability for x, y, and z coordinates for all landmarks were acceptable, all being greater than 0.80. Most of the mean measurement differences obtained from trials within the principal investigator in all three axes were less than 1.5 mm. Inter-examiner mean measurement differences generally were larger than the intra-examiner differences. Ludlow et al.[27] compared the precision of landmark identification on CBCT images and conventional lateral cephalograms. The Authors radiographed twenty presurgical orthodontic patients with conventional lateral cephalograms (Ceph) and CBCT techniques, and then five observers plotted 24 landmarks using computer displays of multi-planer reconstruction (MPR) CBCT and Ceph views during separate sessions. The Authors concluded that the MPR displays of CBCT volume images provide generally more precise identification of traditional cephalometric landmarks. More precise location of condylion, gonion, and orbitale overcomes the problem of superimposition of these bilateral landmarks seen in Ceph.

Medelnik et al.[20], as reported before in this review, beyond the accuracy landmarks evaluation, assessed the reproducibility of anatomical landmarks of different cone-beam CTs (CBCTs/DVTs) and a multislice spiral CT (MSCT) scanner, on a human fresh-frozen cadaver head, from the standard deviations on the three planes. The Authors cocnluded that MSCT yielded smaller (sometimes significantly) standard deviations than CBCT in maxillary distance (Spa-Spp), mandibular height (Id-Gn), bimental width (Mfl-Mfr), and coronoid-genio angle (Krl-Krr-Ge), and that the reproducibility of landmark identification in all the volume images was good.

Discussion

The multislice CT and Cone beam computed tomography overcomes most of the limitations of intra-oral radiography. The increased diagnostic data should result in more accurate diagnosis and monitoring and therefore improved decision making for the management of orthodontic problems. When indicated, three-dimensional CBCT scans may supplement conventional two-dimensional radiographic techniques and can be used in conjunction with routine craniofacial bidimensional evaluation. Olszewski et al.[7] affirmed that although diagnoses based on both two- and three-dimensional analyses were adequate, the three-dimensional analysis gave more informations such as the possibility of comparing the right and the left side of the skull, and the anatomic structures were not superimposed which improved the visibility of the reference landmarks. The Authors found more advantages of the CT technique: the real possibility to perform three-dimensional measurements on the lines and the angles and to visualized simultaneously soft tissues including the fat, muscle and the air way. Cattaneo et al.[25], after comparing cephalometric measurements performed on conventional cephalograms with those on CBCT-synthesized images, found that CBCT-synthesized cephalograms could successfully replace conventional headfilms.

Several studies have confirmed the three-dimensional geometric accuracy of CBCT technique[8,9,19]. Most Authors stated that CBCT gave accurate two- and three-dimensional measurements regardless of skull orientation, and that CBCT was reliable for taking linear measurements of the maxillo-facial skeleton[4,6,10,12,14,17,21,22,25-28]. Most of them have used human dry skulls in order to increase measurements accuracy and landmarks reliability. This reduced the chance of errors in landmark identification because it made an accurate identification of bony landmarks more likely since there was no overprojection of soft tissues. Identification of landmarks were very important in comparative studies. Although the landmarks could be determined on computer software, clay and metallic markers were placed on dry skulls to use the exact same points in all measurements. Clay markers were preferred to the metallic markers to prevent artifacts during the CT imaging.

Berco et al.[13] and Bholsothi et al.[29] concluded that linear measurements on 3D shaded surface renderings from CBCT datasets using commercial cephalometric analysis software had variable accuracy: most midline-to-midline linear measurements and some midline-to-midline angular measurements were not different, while other types of measurements were significantly different. Moreira et al.[16] did not find statistically significant differences between the physical and CBCT-based linear and angular measurements.

Van Vlijmen et al.[26] showed that for most measurements there was no clinically relevant difference between angular and linear measurements performed on conventional cephalometric radiographs, compared with cephalometric measurements on 3D models of skulls. They demonstrated also that the measurement error for 3D measurements was larger than that for conventional 2D measurements. This could be explained by the fact that adding the third dimension an additional source of inaccuracy is introduced.

Some other Authors[4,7,11,20,23,24,26,28] found that the reproducibility of their own measurements in the CBCT-constructed cephalometric radiographs was higher, compared with the reproducibility of measurements in conventional cephalometric radiographs.

Conclusion

This review of the literature allows to reach the following conclusions:

- in literature there is a limited number of studies regarding the accuracy of measurements and reliability of landmarks identification with computed tomography (CT) technique in the maxillofacial area;
- the few studies present in the literature described dif-

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ferent landmarks identification and measurements, which impede a direct comparison between them;
- a standardized and widely approved 3D cephalometric analysis is still not described;
- the high accuracy and reproducibility of measurements and reliability of cephalometric landmarks on CT images permit to perform a successfully and safely cephalometric analysis;
- to obtain consistent and reproducible data from three-dimensional landmark identification on CT images it would be mandatory to follow a protocol for operator training and calibration.

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