Cone Beam CT in Orthodontics

Olivier van Vlijmen

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Olivier Johannes Cornelis van Vlijmen
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Promotoren:

Prof. dr. A.M. Kuijpers-Jagtman
Prof. dr. S.J. Bergé

Manuscriptcommissie:

Prof. dr. P.J. Slootweg (voorzitter)
Prof. dr. Y. Ren (Universitair Medisch Centrum Groningen)
Dr. L.L.M.H. Habets (Academisch Centrum Tandheelkunde Amsterdam)

Paranimfen:

Drs. K. Seubring
Drs. F.A. Rangel

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Olivier Johannes Cornelis van Vlijmen
Born on the 4th of April 1980
in Nijmegen, Netherlands

Supervisors:
Prof. dr. A.M. Kuijpers-Jagtman
Prof. dr. S.J. Bergé

Doctoral Thesis Committee:
Prof. dr. P.J. Slootweg (chairman)
Prof. dr. Y. Ren (Groningen University)
Dr. L.L.M.H. Habets (Academic Centre for Dentistry Amsterdam)

Paranymphs:
Drs. K. Seubring
Drs. F.A. Rangel

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Hierdie is vir jou.
Laat hy val waar hy wil,
Maar net nie op de grond nie, want dan is dit mors!

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Chapter 1

General introduction

1.1 Introduction

For an accurate diagnosis and treatment planning of orthodontic patients, a comprehensive view of a patient's face and all structures forming the face, is needed. Thereto orthodontic records are made, visualizing the craniofacial complex. With these records a clinician is able to study soft tissues, bony structures, the airway and the dentition of a patient to make a diagnosis, determine the best treatment plan, evaluate craniofacial growth and development and assess treatment outcome.

In the beginning of the 20th century, orthodontic records consisted of clinical facial photographs, plaster casts of the patient's dentition and occasionally plaster casts of the patient's face. A revolutionary idea to orient the plaster casts of the dentition and the face in their proper anatomical relation, within the so called "Cubus Cranioforus" was originally described in 1915 by the Dutch clinician Van Loon[1]. According to Van Loon, a proper orthodontic diagnosis could only be made if the relation between dentition and the rest of the face was determined in a three-dimensional (3D) system (Figure 1.1). Van Loon developed several methods to orient the dentition to a patient's face[2], of which some are displayed in Figures 1.2 and 1.3. However, the procedures to produce these orientations, though very inventive, were time consuming and therefore not very useful in daily clinical orthodontic practice.

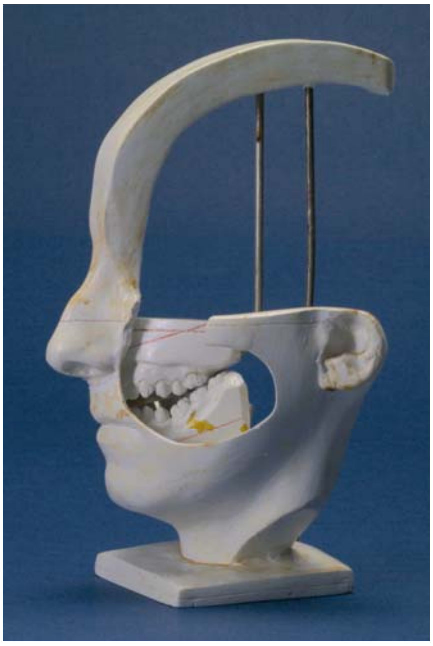

Figure 1.1 *Dental cast mounted behind the plaster face mask.*
From the dentistry collection, University Museum Utrecht, The Netherlands.

Figure 1.2 *Porionkubus. A system to perform three dimensional measurements on a face or skull with fixed reference points. From the dentistry collection, University Museum Utrecht, The Netherlands.*

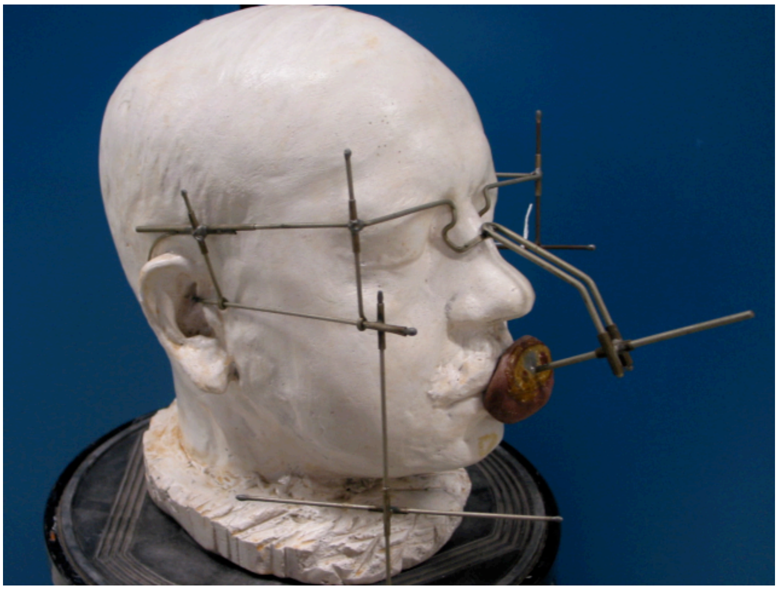

Figure1.3 *Prosoposcope, which consists of a spectacle frame with extensions, one resting on each ear, one on the labial surface of the upper incisors.*
From the dentistry collection, University Museum Utrecht, The Netherlands.

In the early 1930s, conventional frontal and lateral cephalometric radiographs were added[3,4] to the orthodontic record collection, which provided insight into the underlying bony structures and superseded the need for impressions for facial plaster casts. The original idea of measuring faces came from the field of physical anthropology. Back in 1884 on a conference in Frankfurt am Main (Germany) anthropologists decided to orient facial plaster casts and skulls in a horizontal plane formed by the upper border of the left and right pori acoustici externi and the lower border of the left orbit. This plane is called the Frankfurt Horizontal, which became an important plane in both anthropology and cephalometry. Before the cephalometric era, precise measurements could only be done in a craniostat on a dry skull. With the cephalometric technique based on standardized radiographs of the head, it became possible to accurately measure bony structures in a living individual, without soft tissue interference in localisation of the bony landmarks[3]. Later on, areas in the cranial base were determined that represented so called ‘stable’ structures, which enabled superimposition of consecutive radiographs for longitudinal growth and treatment outcome analysis. The collection of serial cephalograms became an important feature in research into normal growth and development of the craniofacial structures. Important longitudinal data were acquired for reference databases e.g. Burlington Growth Study[5], The Case Western Bolton Brush Study[5], The Michigan Growth Study[5] and the Nijmegen growth study[6]. These growth studies were designed to provide information concerning craniofacial growth and development of children in various age groups over a longer period of time. Lateral cephalograms were taken at several points in time with fixed intervals, producing a series of cephalograms available for longitudinal study of facial growth for each subject. The data derived from these series of cephalograms produced an excellent overview of average facial growth and development both of the hard and soft tissues, though only in two dimensions (2D) since conventional cephalometric radiographs and therewith conventional cephalometric analyses reduce the head of the patient, which is a three -dimensional (3D) structure, into two dimensions.

In contrast to the lateral cephalometric radiograph, the frontal cephalometric radiograph has not been used routinely in orthodontic treatment planning[7]. This may be because of the limitations and difficulties of a frontal analysis, such as errors in reproducing head posture, identifying landmarks of superimposed structures and the relatively low added value of frontal radiographs[8]. While lateral cephalometric radiographs provide information on morphology, frontal cephalometric radiographs are of particular importance to assess skeletal asymmetries, crossbites and mandibular displacements. In 1983 Grayson developed a method of analysing craniofacial asymmetry with the use of multi plane frontal cephalometry[9]. In this method, landmarks are identified in different frontal planes at selected levels of the craniofacial complex. This way a first attempt was made to visualize the third dimension. Later, in 2001 Hermann et al. described a method adding an axial cephalometric radiograph to the lateral and frontal radiographs, demonstrating the possibility of obtaining a detailed description of the craniofacial complex in three projections[10]. This was a first step towards working in all three dimensions, which has further developed significantly over the past decade.

1.2 The third dimension

Facial photographs and dental casts, supplemented by a panoramic and a cephalometric radiograph remained the standard set of orthodontic records to document a patient's facial soft tissues, dentition and the facial skeleton until the beginning of this millennium. Except for plaster models all other orthodontic records provided a two-dimensional representation of a three-dimensional object. In fact plaster models were the only 3D patient records for over a century.

In the last two decades, a revolution has become apparent in the diagnosis and treatment planning for orthodontic and orthognathic patients. New 3D image modalities have emerged and can be used for orthodontic purposes[11]. Two-dimensional records, like facial photographs or traditional frontal and lateral cephalometric radiographs used since the early 1930s[3,4], are now replaced by 3D facial photographs and 3D cone beam computer tomography (CBCT) scans[12,13,14]. With 3D imaging also 3D cephalometric analysis[15] and 3D superimpositions[16-18] to compare data sets taken at different points in time, became available. For two dimensional records, software programs that show e.g. the prediction of profile changes caused by orthodontic treatment, are available. It is very likely that in the near future it will also be possible to predict in a three-dimensional way, what a patient's face will look like after treatment.

Many techniques for taking 3D records of a patient's head and face are available today[11,14,19-21] including digital dental models, stereo-photogrammetry, surface laser scanning, magnetic resonance imaging (MRI), CBCT and multi slice computed tomography (MSCT). Ongoing attempts to develop an accurate 3D representation of the human face, including static and dynamic 3D imaging techniques, should ultimately result in a virtual (computer simulated) head of the patient for diagnosis, treatment planning, treatment prediction and evaluation of treatment outcome. These 3D image modalities, are likely to change the way diagnoses and treatment plans are made. This thesis mainly focuses on the application of CBCT in orthodontics and therewith the consequences of applying this new technology in this field.

1.3 The origin of computer tomography

The idea of Computed Tomography (CT) imaging was first described in 1963[22,23] by Allan Cormack, but only became commonly available 20 years later, in the early 1980's. Allan Cormack served as a part-time medical physicist in the radiology department at Cape Town's Groote Schuur Hospital (South Africa) in the 1950's where he started to work on the concept of scanning slices of the body from various angles and rotations. In the sixties he continued his work at Tufts University in Medford Massachusetts (USA) where he became chairman of the Physics Department in 1968. Reasoning that multiple x-rays projected at different angles but in a single plane would produce a more detailed image, he published a set of equations to describe the process in the Journal of Applied Physics. However, his findings, published in 1963 and 1964, had virtually no response[24].

Sir Godfrey Hounsfield, developed the first prototypes of a CT scanner independently from Cormack. The initial idea came to him on one of his many rambling country walks round 1967, after which he carried on experimenting. Several years later, in the early seventies, Hounsfield's work on pattern recognition and the use of computers to analyse readings made the CT scanner possible, which was first clinically used in 1971 in Atkinson Morley's Hospital in Wimbledon London (UK) by James Ambrose and published about nearly two years later[25,26]. Oransky[27] wrote in his obituary for Sir Godfrey Hounsfield in the Lancet in 2004 that '*it might truly be said that without The Beatles, the CT scanner would never have been invented. By 1967, Hounsfield had been working for music and electronics company Electrical and Musical Industries (EMI) for 16 years on projects ranging from radar, guided weapons, and the UK's first all-transistor computer. That year, EMI, enriched considerably by the sale of their recording artists The Beatles, gave Hounsfield the funding he needed to work on the project'*. Cormack and

Hounsfield were jointly awarded the Nobel Prize in Medicine in 1979 “For the development of computer assisted tomography"[28].

1.4 Cone beam computer tomography

CBCT was first described in 1978[29], but it only became commonly available in the late 1990’s[30,31]. Similar to CT, 20 years later after it first had been described. The first CBCT scanner was clinically used for volumetric imaging of moving organ systems like the heart and lungs and for imaging of circulation in organs of the body[31]. The first dedicated CBCT scanner for the oral and maxillofacial region was described in 1998[30], particularly for planning in the field of implantology. Continuing development of high quality flat panel detectors (FPD) resulting in a lower radiation dose, the commonly available computer power needed to build a 3D image and the relative low cost of a CBCT system compared to a MSCT system, all contributed to the success of the CBCT. Today a compact relatively inexpensive CBCT unit which easily fits in any dental or medical office, is widely commercially available[33].

When obtaining a conventional spiral or helical CT scan, a radiation source produces a fan shaped x-ray beam while rotating around a patient (Figure 1.4). The x-ray beam passes through the patient tissues and is captured by a row of detectors. After one full rotation around the patient, a 2D image of the cross-sectional area can be produced. The patient (or the radiation source and detectors) shift axially at a uniform rate and the process is being repeated to produce a cross-sectional image of the next slice. This is continued until the entire desired volume is captured. From the 2D slices, a 3D image is constructed by the computer. Modern CT scanners can capture multiple slices (up to 128) in one single rotation and are called multislice CT (MSCT).

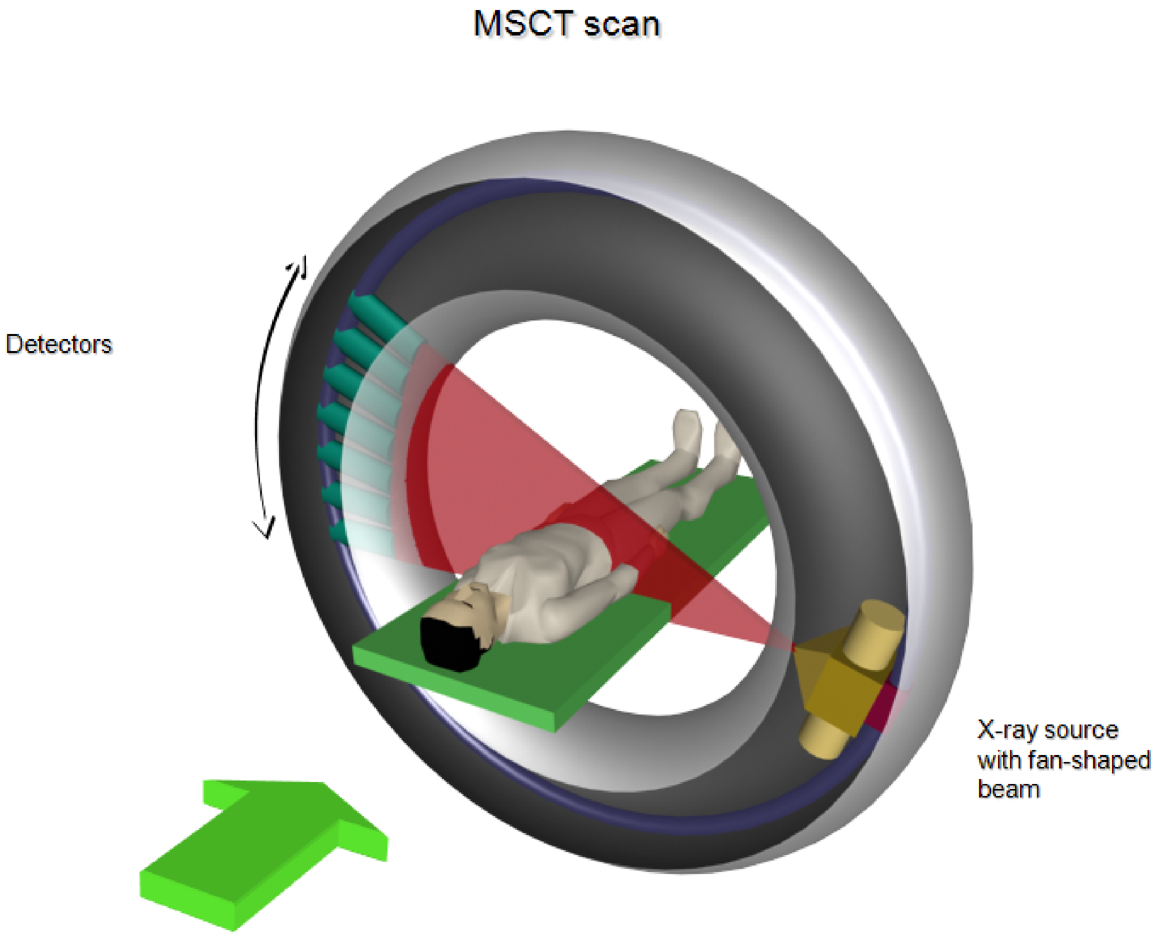

Figure 1.4 Schematic representation of a Multi Slice CT scan.
Image courtesy of Demetrios Halazonetis.

When obtaining a CBCT scan, a radiation source and receptor pair complete a single rotate around the patient (Figure 1.5). Since only one rotation is necessary to capture a volume, the total scan time is relatively short resulting in less radiation exposure and less change of blur caused by patient movement. During a rotation the x-ray source emits a pulsating divergent cone shaped x-ray beam. Time needed for this rotation ranges from 5 to 40 seconds for imaging the maxillofacial region, depending on the CBCT scanner, required resolution, region of interest and protocol setting. The beam size is collimated to match the anatomical region of interest. Instead of utilizing a row of detectors, as MSCT scan methods do, a CBCT system uses a standard charge-coupled device camera, focused on a FPD consisting of scintillator material. The scintillator converts X-ray radiation to visible light, which is picked up by the camera and recorded into an image. When the rotation is completed, up to nearly 600 individual 2D radiographic images are obtained. These 2D images are reconstructed in the computer with dedicated software to produce what is called a digital volume, composed of volumetric pixels called voxels. The smaller the voxel size, the higher the resolution and vice versa. A higher resolution comes with a longer scan time though, plus a longer scan time gives more chance of blur and also exposes the patient to a higher radiation dose. The 3D volume can be visualized and manipulated with the appropriate software[34]. The recent designated CBCT scanners for the maxillofacial region, scan the patient in a sitting position, limiting the size of the CBCT scanner and preventing distortion of soft tissues.

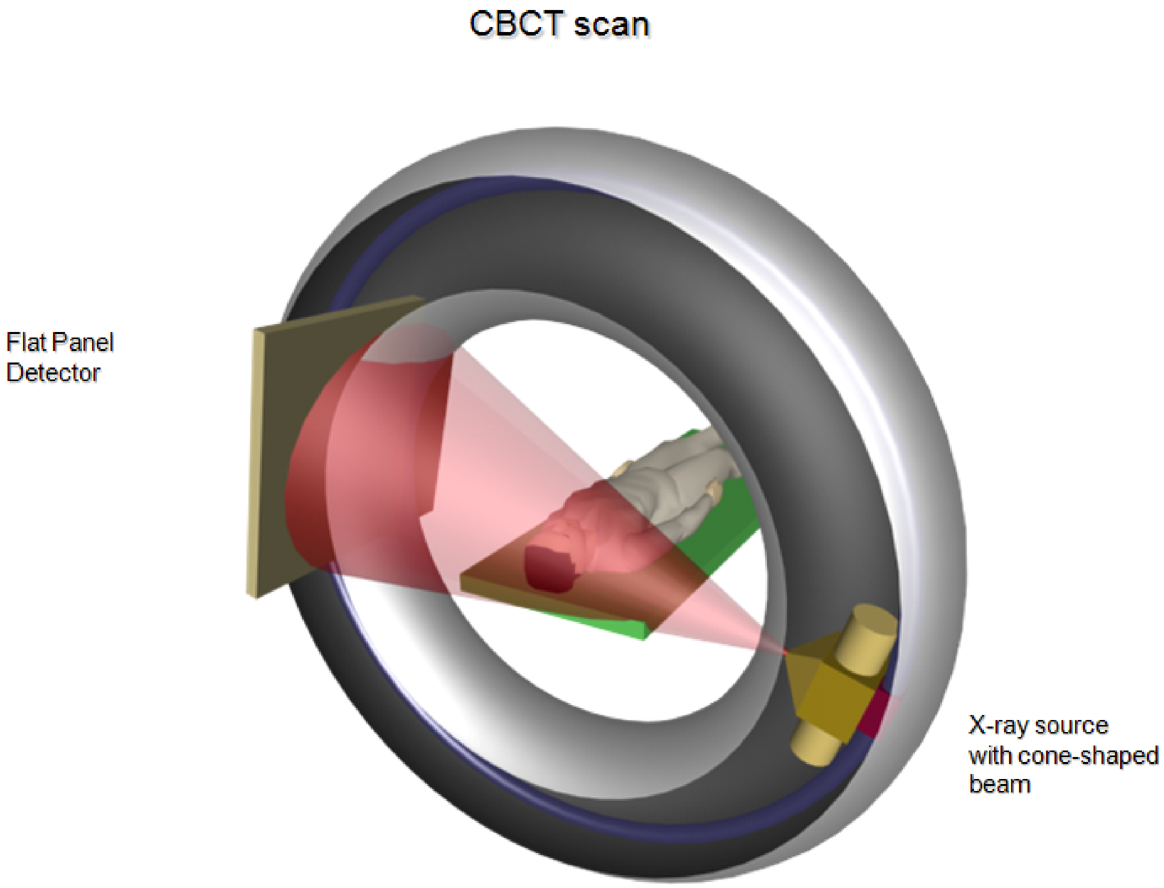

***Figure 1.5** Schematic representation of a Cone Beam CT scan.*
Image courtesy of Demetrios Halazonetis.

1.5 CBCT in orthodontics

According to literature CBCT is used in otorhinolaryngology, maxillo-facial surgery, plastic and reconstructive surgery, endodontics, periodontics, implantology, orthodontics and angiography[11,35-38].There are many claimed benefits within the craniofacial field for the clinical application of CBCT. In the orthodontic field, several benefits of using CBCT images instead of conventional radiographs for orthodontic diagnosis and treatment planning, have been mentioned. Without a doubt CBCT offers a 3D view of the dentition that shows the morphology of teeth and roots, missing or supernumerary teeth, and the 3D spatial orientation of (unerupted) teeth, which are all not visible on 2D radiographs. Also a more comprehensive assessment of the airway is possible. In the past, the upper airway could be analysed on lateral cephalometric radiographs, but merely in 2D. It has been shown that the area of the airway in 2D does not necessarily reflect the volume of the airway in 3D[39]. Therefore one might expect that airway diagnostics in patients with deviating jaw relationships, craniofacial anomalies, or sleep apnoea can benefit from a diagnosis on a 3D CBCT. Other often mentioned useful applications of CBCT in the orthodontic specialty are 3D assessment of alveolar bone height and bone volume in cleft lip and palate patients[40-42]. In cleft patients CBCT can be used to monitor the alveolar bone density and height, displacement of the teeth adjacent to the cleft and morphology of the maxilla. In orthognathic cases, CBCT can be used for 3D treatment planning, -simulation and -evaluation[16,43,44]. Also in determining the best location for and evaluation of temporary anchorage devices (TAD's), CBCT images are claimed to be advantageous[45,46]. Furthermore in cases where there are deviations in tooth number, shape or position, a 3D view is claimed to be beneficial compared to a 2D record for prognostication of treatment duration and treatment complexity and detection of the presence of root resorption of adjacent teeth[11,38,47]. Although there is little known on the value of CBCT for TMJ evaluations, a CBCT provides a 3D visualisation of the TMJ, making 3D assessment of condyle morphology possible which is claimed to be superior to panoramic radiology for evaluation of condylar erosions[48]. As a potential downside of CBCT, a possible lack of knowledge of non-orthodontic findings detectable on CBCT scans resulting in legal and liability consequences, is mentioned. But also an unintentional false positive diagnosis can lead to unwanted side effects[47].

But if all mentioned applications of CBCT indeed lead to altering diagnostics and treatment decisions, ultimately resulting in better treatment results is not (yet) demonstrated[47]. Although unpublished research indicates that a diagnosis is likely to change when using a CBCT, the treatment plan does not[11,49]. As a consequence guidelines to limit the use of CBCT in orthodontic patients were developed. CBCT is only indicated for those cases where conventional radiology cannot supply satisfactory diagnostic information. The 2008 guidelines of the British Orthodontic Society recommend to limit CBCT to CLP patients, orthognathic surgery patients and cases with supernumerary teeth, assessment of unerupted teeth and identification of root resorption[50]. The recently published guidelines of the European SEDENTEXCT project include: CBCT examinations must be justified on an individual basis and CBCT is only indicated when the current imaging method would provide insufficient information or when the current imaging method of choice is MSCT. In these cases the smallest volume size compatible with the situation should be selected. According to the SEDENTEXCT guidelines, the use of CBCT images is unacceptable for routine imaging or screening, caries detection, temporary anchorage device (TAD) placements, as a routine method of imaging periodontal bone support or as a standard method for demonstration of root canal anatomy. Where it is likely the evaluation of soft tissues will be required as part of the patient’s radiological assessment, the appropriate initial imaging should be MSCT or MRI, rather than CBCT[51].

With the use of innovative new 3D technologies, i.e. CBCT and 3D facial photographs, it is now possible not only to document the dentition in 3D with dental casts but to document the whole head of a patient in 3D, resulting in a 3D virtual head on the computer screen. This metamorphosis of orthodontic records, may not only have consequences for orthodontic treatment planning but also affects longitudinal follow-up of patients and especially longitudinal research. Facial growth in patients with severe dysgnathia or with craniofacial malformations needs to be followed over a long period of time which requires good quality cephalograms that are taken in a standardized set-up over the years. Furthermore, orthodontic research is very much focused on long term results which may, among other records, also require cephalograms taken at several points in time. For longitudinal studies, it is crucial to know whether the new 3D records, in particular the 3D CBCT, can be compared with earlier two-dimensional records like 2D frontal en lateral cephalometric radiographs which have been collected in the past.

1.6 Overview of the thesis

In chapter 2 to 6 of this thesis, studies are described to determine whether different 2D and 3D image modalities can be compared and to investigate if images obtained from two different CBCT devices are comparable. In chapter 7, the outcome of a systematic review is reported presenting the current level of available evidence for the use of CBCT for orthodontic purposes and to determine whether a CBCT is justified for these purposes.

The specific aims of the study presented in this thesis are:

- To compare measurements on conventional lateral cephalometric radiographs and on CBCT-constructed lateral cephalometric radiographs taken from dry human skulls (chapter 2).
- To compare 2D measurements on conventional lateral cephalometric radiographs and 3D measurements on 3D models of human skulls, derived from CBCT data (chapter 3).
- To compare measurements on conventional frontal cephalometric radiographs and measurements on CBCT-constructed frontal cephalometric radiographs taken from dry human skulls (chapter 4).
- To compare 2D measurements on conventional frontal cephalometric radiographs and 3D measurements on 3D models of human skulls, derived from CBCT data (chapter 5).
- To compare measurements on 3D models of human skulls derived from two different CBCT scanners to evaluate if the measurements are hardware dependent (chapter 6).
- To systematically review the different applications for the use of CBCT in orthodontics and the corresponding level of evidence on which the decision to use CBCT is based (chapter 7).

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Chapter 2

Comparison of Cephalometric Radiographs Obtained From Cone-Beam Computed Tomography Scans and Conventional Radiographs

O.J.C. van Vlijmen
S.J. Bergé
G.R.J. Swennen
E.M. Bronkhorst
C. Katsaros
A.M. Kuijpers-Jagtman

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Abstract

Purpose: We evaluated whether measurements on conventional cephalometric radiographs are comparable to measurements on cone beam computed tomography (CBCT)-constructed cephalometric radiographs taken from human skulls.

Materials and Methods: The CBCT scans and conventional cephalometric radiographs were made using 40 dry skulls. With I-Cat Vision software (Imaging Sciences International, Inc, Hatfield, PA), a cephalometric radiograph was constructed from the CBCT scan. Standard cephalometric software was used to identify landmarks, and calculate distances and angles. The same operator identified 15 landmarks 5 times on both types of cephalometric radiographs with a 1-week interval.

Results: Intra-observer reliability was good for all measurements. The reproducibility of measurements on cephalometric radiographs obtained from CBCT scans was better, compared with the reproducibility of those on conventional cephalometric radiographs. There was no clinically relevant difference between measurements on conventional and constructed cephalometric radiographs.

Conclusions: Measurements on CBCT-constructed cephalometric radiographs are comparable to conventional cephalometric radiographs, and are therefore suitable for longitudinal research.

2.1 Introduction

Since the early 1930s, conventional cephalometry has been used as the standard procedural tool for analyzing both maxillofacial deformities and orthodontic problems, especially to evaluate growth or treatment changes. Nevertheless, conventional cephalometry is limited, because it provides a 2-dimensional (2D) representation of 3-dimensional (3D) structures. New 3D technology has expanded the diagnostic possibilities, making 3D simulations of surgical and orthodontic procedures possible[1]. At first, multislice computed tomography (MSCT) was used, but because of the high radiation dose of this technique, its use is restricted to selected cases. Several studies showed that 3D computed tomography (CT) analysis seems to be an accurate and reliable approach to cephalometry, which can be regarded as equivalent to conventional cephalometry[2-5]. From a CT scan, a 2D cephalometric radiograph can be constructed and compared to earlier cephalometric radiographs of the same patient[3,6]. These studies all used MSCT scanners[3,6].

A cone-beam CT (CBCT) scan involves reduced radiation, compared with MSCT scans, and can therefore be used in a wider range of patients[7]. A CBCT scan uses a different type of acquisition than traditional MSCT. The x-ray source produces a cone shaped x-ray beam. This makes it possible to capture the image in one sweep, instead of capturing every individual slice separately, as in MSCT. Although we know that a CBCT scan has reduced radiation compared with MSCT scans, CBCT is still not suitable for every orthodontic patient. Cone-beam CT is used increasingly for certain categories of patients. Conventional cephalometric radiographs are no longer made for patients with orofacial clefts, orthognathic issues, or severe maxillofacial deformities. Because these patients undergo long, intensive treatment until late adolescence, their growth and development must be well-documented. Because many of these 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 2 types of radiographs are not comparable, then the cephalometric pictures obtained from CBCT scans cannot be used to evaluate growth and treatment outcomes longitudinally. The potential use of the latter is to provide information that in the past was gained from cephalometric radiographs. The aim of our study was to evaluate whether measurements on conventional cephalometric radiographs are comparable to measurements on CBCT-constructed cephalometric radiographs taken from dry human skulls.

2.2 Materials and Methods

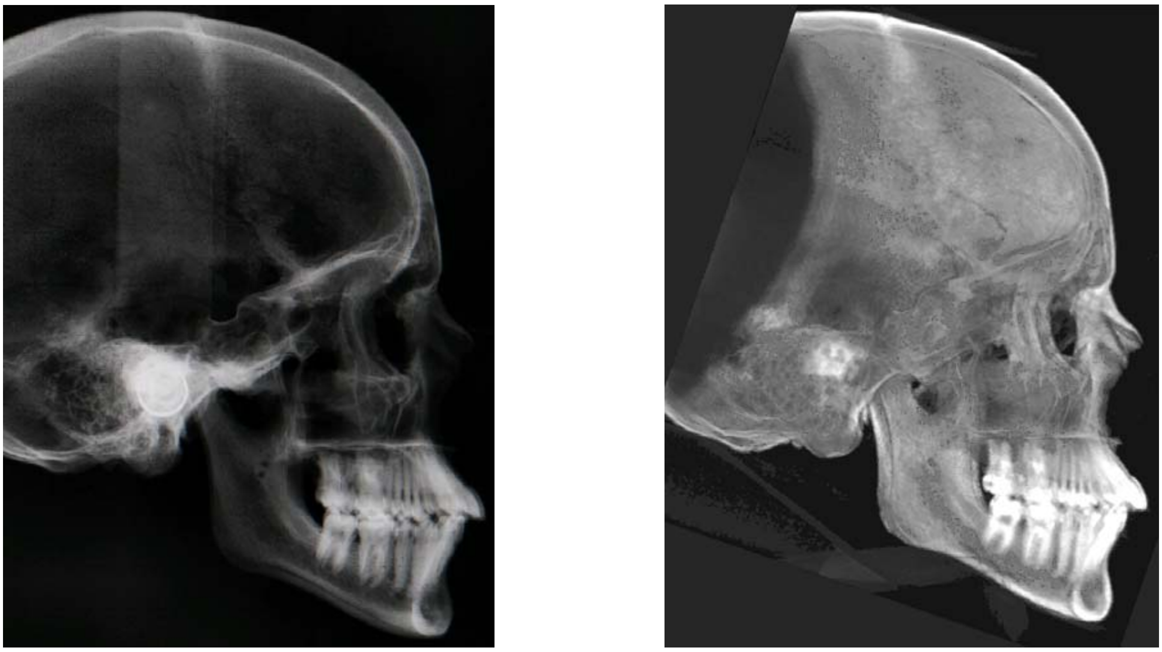
2.2.1 Materials

The sample consisted of 40 dry human skulls obtained from the collection of the Department of Orthodontics and Oral Biology of Radboud University Nijmegen Medical Centre (Nijmegen, The Netherlands). Skulls were selected from a larger sample according to the following criteria: presence of permanent upper and lower incisors, presence of first permanent upper and lower molars, and presence of a reproducible, stable occlusion. The mandible was related to the skull, based on the position of the condyle in the fossa and maximum occlusal interdigitation. The mandibular position was fixed with broad tape from the ipsilateral temporal bone around the horizontal ramus of the mandible to the contralateral temporal bone.

2.2.2 Radiography

Each skull was positioned in the cephalostat (Cranex Tome Ceph; Soredex, Tuusula, Finland) by fixing it between the ear rods. The ear rods were placed in the pori acoustici externi, and the Frankfurt horizontal plane was placed horizontally, parallel to the floor. Cephalometric radiographs were taken according to the following radiographic settings. For larger skulls (n=30), the adult settings were chosen: 70 kV, 10 mA, and 0.6 seconds. For smaller skulls (n=10), pediatric settings were chosen: 70 kV, 10 mA, and 0.5 seconds (Figure 2.1A). Viewbox software (dHAL Software, Kifissia, Greece) was used to identify conventional cephalometric hard-tissue landmarks, and to calculate distances and angles.

The same skulls were placed in the I-Cat CBCT scanner (Imaging Sciences International, Inc, Hatfield, PA), on a foam platform, with the Frankfurt horizontal plane parallel to the floor. The skulls were placed in the centre of the CBCT scanner, using the midline light beam to coincide with the midsagittal plane. A CBCT scan was taken of all skulls in the extended height mode: 129 kVp, 47.74 mA, and 40 seconds, with a resolution of 0.4 voxel. With I-Cat Vision software (Imaging Sciences International, Inc), a cephalometric radiograph was constructed from the 3D CBCT scan by right lateral radiographic projection of the entire volume (Figure 2.1B). This constructed cephalometric radiograph was subsequently digitized with Viewbox software.



A. ***B.***

Figure 2.1 *Cephalometric radiographs of the same skull. (A), Conventional cephalometric radiograph. (B), CBCT-constructed cephalometric radiograph.*

2.2.3 Cephalometry

For the cephalometric analysis, 15 conventional hard-tissue cephalometric landmarks (Table 2.1) were identified, and 14 widely used cephalometric measurements (10 angular and 4 linear measurements) were calculated. The conventional cephalometric radiographs were enlarged by a factor of 1.1244, to compensate for the reduction factor. In Viewbox, the angular and linear measurements listed in Table 2.2 were performed.

Table 2.1 Anatomical landmarks used in this study.

S	Sella	Centre of sella turcica
N	Nasion	Most anterior limit of the frontonasal suture on the frontal bone
A	A - point	Deepest bony point on the contour of the premaxilla below ANS
B	B - point	Deepest bony point of the contour of the mandible above pogonion
ANS	Anterior Nasal Spine	The tip of the anterior nasal spine
PNS	Posterior Nasal Spine	The most posterior point at the sagittal plane on the bony hard palate
AR	Articulare	The point of intersection of the dorsal contours of the processus articularis mandibulae and the pharyngeal part of the clivus
POG	Pogonion	Most anterior point of the symphysis of the mandible
GO	Gonion	Most posterior inferior point of the angle of the mandible
GN	Gnathion	Most anterior inferior point of the bony chin
Is	Incision Superius	The incisal tip of the most anterior upper incisor
UIA	Upper Incisor Apex	The root apex of the most prominent upper incisor
Ii	Incision Inferius	Incisal point the most prominent medial mandibular incisor
LIA	Lower Incisal Apex	Root apex of the most prominent lower incisor
ML	Mandibular line	Line between Gonion and Gnathion
BOP	Bisected Occlusal plane	Line connecting the vertical midpoint, which is estimated visually between Is and Ii and the mesial contact between the first molars

Table 2.2 Cephalometric variables.

SNA	Angle between line SN and line AN
SNB	Angle between line SN and line BN
ANB	Angle between line AN and line BN
NSL / NL	Angle between line SN and line ANSPNS
NSL / ML	Angle between line SN and line GnGo
NL / ML	Angle between line ANS to PNS and the line from Gn to Go
ILs / NL	relative inclination of upper incisors to line from ANS to PNS
ILi / ML	relative inclination of lower incisors to line from Gn to Go
Inter incisal angle	Angle between the lines through long axis of upper and lower incisors
NSL / BOP	Angle between the line from S to N and the occlusal plane
AR to A	Distance in mm between point Ar and point A
AR to POG	Distance in mm between point Ar and point Pog
Is to A-POG	Distance in mm between point UIA and line A - Pog
Ii to A-POG	Distance in mm between point Ii and line A - Pog

2.2.4 Statistical analysis

For both conventional cephalometric radiographs and CBCT-constructed cephalometric radiographs, the same operator (OV) marked the landmarks on all 80 images 5 times, each time after an interval of 1 week. The mean value of these 5 measurements was used for the statistical analysis. Intra-observer reliability was calculated by means of Pearson correlation coefficient for the first and second measurements. For each measurement, the standard error was calculated and compared with the standard error of the same measurement in the other group. Paired *t* tests were performed to compare the means of corresponding measurements on the 2 cephalometric radiographs of the same skull.

2.3 Results

Intra-observer reliability for both the conventional cephalometric radiographs and CBCT-constructed cephalometric radiographs was good for all measurements. The correlation coefficient between the first and second measurements ranged between 0.91 and 0.99, with an average of 0.97 (Table 2.3). The standard error for CBCT constructed cephalometric radiographs was significantly smaller for 8 measurements, compared with the standard error of the conventional cephalometric radiographs. For the conventional cephalometric radiographs, this was the case for 4 measurements. Therefore, reproducibility of measurements in the CBCT constructed cephalometric radiographs was higher, compared with the reproducibility of measurements in conventional cephalometric radiographs.

Table 2.3 Intra-observer reliability expressed as Pearson's Correlation coefficient for first and second measurements and duplicate measurement error for 40 cases with 95 % confidence interval (CI). P-value relates to the test for statistically significant difference between the two methods.

	Conventional			**CBCT-constructed**			
		Duplicate measurement error			Duplicate measurement error		
	Reliability	**Error**	**95% CI**	**Reliability**	**Error**	**95% CI**	***P-value for error***
SNA (°)	0.96	0.57	0.51 – 0.64	0.98	0.58	0.52 – 0.65	0.410
SNB (°)	0.95	0.45	0.40 – 0.50	0.98	0.55	0.49 – 0.62	0.011
ANB (°)	0.93	0.53	0.47 – 0.59	0.99	0.26	0.24 – 0.29	<0.001
AR-A (mm)	0.98	0.62	0.55 – 0.69	0.99	0.34	0.30 – 0.38	<0.001
AR-POG (mm)	0.97	0.84	0.79 – 0.99	0.99	0.55	0.49 – 0.62	<0.001
NSL / NL (°)	0.97	0.51	0.45 – 0.57	0.96	0.76	0.68 – 0.85	<0.001
NSL / ML (°)	0.95	0.66	0.58 – 0.73	0.97	0.79	0.70 – 0.89	<0.001
NL / ML (°)	0.97	0.76	0.67 – 0.84	0.97	0.84	0.74 – 0.93	0.017
ILs / NL (°)	0.94	1.62	1.44 – 1.80	0.98	1.37	1.22 – 1.53	0.126
Is to A-POG (mm)	0.98	0.37	0.33 – 0.41	0.99	0.28	0.25 – 0.31	<0.001
Interincisal angle (°)	0.95	2.96	2.63 – 3.30	0.97	2.32	2.06 – 2.58	<0.001
ILi / ML (°)	0.93	2.62	2.33 – 2.91	0.94	1.93	1.71 – 2.14	<0.001
Ii to A-POG (mm)	0.97	0.58	0.52 – 0.64	0.99	0.33	0.30 – 0.37	<0.001
NSL / BOP (°)	0.96	0.83	0.74 – 0.93	0.91	1.01	0.90 – 1.12	0.013

There was a statistically significant difference between conventional cephalometric radiographs and CBCT-constructed cephalometric radiographs for the following measurements (see Tables 2.1 and 2.2 for expansions of abbreviations): SNB, AR-A, AR-POG, NSL/NL, NL/ML, ILs/NL, LIi/ML, interincisal angle, and Ii to A-POG. Though the average difference for these measurements between the 2 methods was statistically significant ($P<0.05$), for most of them, 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 distances AR-A and AR-POG was greater than their standard error, but still less than 1 mm.

Table 2.4 *The mean difference between corresponding measurements taken on CBCT-constructed cephalometric radiographs and conventional cephalometric radiographs, with 95 percent confidence interval (CI), corresponding P-value and reliability, expressed as Pearson's Correlation coefficient between 2 methods.*

	Difference CBCT – Conv	95% CI	P-value	Reliability
SNA (°)	0.237	-0.04 – 0.51	0.090	0.97
SNB (°)	0.363	0.11 – 0.62	0.007	0.97
ANB (°)	0.126	-0.26 – 0.01	0.062	0.98
AR-A (mm)	0.675	0.39 – 0.96	< 0.001	0.98
AR-POG (mm)	0.901	0.51 – 1.29	< 0.001	0.98
NSL / NL (°)	-0.785	-1.21 – 0.36	0.001	0.88
NSL / ML (°)	-0.267	-0.55 – 0.02	0.065	0.97
NL / ML (°)	0.511	0.23 – 0.80	0.001	0.97
ILs / NL (°)	0.865	-1.44 – 0.29	0.004	0.98
Is to A-POG (mm)	0.027	-0.10 – 0.16	0.679	0.99
Interincisal angle (°)	1.454	0.31 – 2.56	0.014	0.97
Ili / ML (°)	-1.537	-2.58 – 0.49	0.005	0.92
Ii to A-POG (mm)	-0.403	-0.16 – 0.31	< 0.001	0.98
NSL / BOP (°)	-0.038	-0.45 – 0.37	0.853	0.95

2.4 Discussion

In this study, 14 widely used cephalometric measurements in conventional radiographs and CBCT constructed cephalometric radiographs of dry human skulls were compared. We considered it unethical to expose patients twice to the radiation of both a CBCT scan and a conventional cephalometric radiograph; therefore, we used dry skulls. In this way, we obtained 2 images that were utterly comparable. The greatest error in cephalometric studies is in landmark identification[8]. Because the skulls do not have soft tissues, there is no distortion caused by soft tissues. This reduces the likelihood of errors in landmark identification, because it makes an accurate localization of bony landmarks easier. On the other hand, measurements using soft-tissue points are, of course, not possible. For some landmarks, we found statistically significant differences in locating landmarks on conventional cephalometric radiographs compared with CBCT-constructed cephalometric radiographs. However, these differences were similar to, or smaller than, their standard error. For the absolute distances AR-A and AR-POG, the differences were greater than the standard error, but still less than 1 mm, i.e. within clinically acceptable range.

In this study, all measurements were performed by one observer. The question remains whether this observer made a systematic error. Upon reviewing the standard errors in Table 2.3, we concluded that these are acceptable. Systematic errors in the identification of landmarks are the same for both kinds of cephalometric radiographs, and therefore have no influence on reproducibility. Hence it is justified to have 1 observer for this type of study.

In general, orthodontists and maxillofacial surgeons are experienced in the use and interpretation of conventional cephalometric radiographs. However, as evident in Figures 2.1A and B, the cephalometric radiographs created with I-Cat Vision software appear different from the conventional ones. The contrast and transparency of the 2 types of cephalometric radiographs are not the same. Particularly in the area of the jaws containing the teeth, it can be hard to identify the structures and landmarks needed for a proper cephalometric analysis in CBCT-constructed cephalometric radiographs. Therefore, a learning curve is to be expected when switching from conventional 2D cephalometric radiographs to CBCT-constructed cephalometric radiographs.

There are differences between the techniques of image-acquisition in conventional cephalometry and CBCT. In a cephalostat, the distance between the midsagittal plane of the head and the radiation source is fixed, as is the distance from the midsagittal plane to the film. In the CBCT device, the radiation source moves around the patient, very much as in an orthopantogram. These differences may lead to variations in magnifications and distortion. For angular measurements, this is not a problem, e.g. for angle ANB or angle SN/ML. However, absolute distances between landmarks, e.g. AR-A, can show differences between both methods, especially if they are located in different tomographic planes, as previously reported[6]. Chidiac et al[6]. found a close relationship between angular measurements, but a difference in the accuracy of linear measurements. We found statistically significant differences for 8 measurements, but these differences were smaller than or similar to the standard error.

In conventional cephalometry, the position of the patient in the cephalostat is fixed by the ear rods for movements along the long axis of the skull. In the CBCT device, there are no ear rods to fix the position of the patient. Extra care must be taken when placing the patient in the CBCT device. If the patient is not positioned with the midsagittal plane coinciding with the midline light beam of the CBCT device, distortion will occur when 2D images are constructed from the 3D dataset. This can influence cephalometric measurements. In both methods, tilting of the head is still possible, but this does not affect the angular or linear measurement, because all points move in the same direction.

Conventional cephalometrics involves a 2D representation of a 3D structure. This has certain disadvantages. Now that we have the possibility of making a 3D image of the skull, it is also possible to perform a 3D cephalometric analysis. In such an analysis, the actual anatomic structures can be identified, instead of a 2D projection. On the other hand, some other landmarks used in conventional cephalometric analysis cannot be used, eg, articulare, because this is a constructed landmark. Therefore, there is a need to develop and test new 3D-cephalometric analyses, foremost because there are newly defined 3D landmarks. Second, no data are available that can be used as reference values for cephalometric measurements.

There is no clinically relevant difference between angular and linear measurements performed in conventional cephalometric radiographs, compared with measurements in cephalometric radiographs constructed from CBCT scans. All measurements in our study are suitable for longitudinal follow-up in patients who have both 2D and 3D records.

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Chapter 3

A comparison between 2D and 3D cephalometry on CBCT scans of human skulls

O.J.C. van Vlijmen
T.J.J. Maal
C.J. Bergé
E.M. Bronkhorst
C. Katsaros
A.M. Kuijpers-Jagtman

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Abstract

Purpose: The purpose of this study was to evaluate whether measurements on conventional cephalometric radiographs are comparable with 3D measurements on 3D models of human skulls, derived from cone beam CT (CBCT) data.

Materials and Methods: A CBCT scan and a conventional cephalometric radiograph were made of 40 dry skulls. Standard cephalometric software was used to identify landmarks on both the 2D images and the 3D models. The same operator 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.

Results: Intra-observer 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. For a few measurements a clinically relevant difference between measurements on conventional cephalometric radiographs and 3D models was found.

Conclusions: Measurements on conventional cephalometric radiographs can differ significantly from measurements on 3D models of the same skull. The authors recommend that 3D tracings for longitudinal research are not used in cases where there are only 2D records from the past.

3.1 Introduction

Conventional cephalometry has been one of the standard diagnostic tools for analysing maxillofacial deformities and orthodontic problems, and evaluating growth and/or treatment changes. Since cone beam CT (CBCT) technology became available its popularity has increased rapidly. This 3D technology gives a realistic representation of the head of the patient and has expanded the diagnostic possibilities, enabling 3D simulation of surgical and orthodontic procedures[1]. For certain types of patients, such as those with craniofacial anomalies, orofacial clefts or orthognathic cases, conventional cephalograms are no longer the optimal diagnostic tool.

Although the radiation dose of a CBCT scan is lower than that of a multi slice CT (MSCT) scan[2], a CBCT is not suitable for the regular, daily orthodontic patient. To image the full height of a patient's skull, a CBCT device with a large field of view is required. Radiation doses of such a scan are 3-44 times greater than comparable panoramic examination doses, depending on the CBCT device used[2,3]. For the patients mentioned above though, CBCT has many benefits. It has been shown[4,5,6] that conventional cephalometric radiographs, which may be considered the 'gold standard', can be compared with constructed cephalometric radiographs from CBCT scans and thus the latter can be used for longitudinal research. The 3D characteristics are lost, however, because both conventional and constructed cephalograms provide a 2D representation of 3D structures.

New 3D technology is becoming more popular and the number of software programs to analyse 3D data is increasing rapidly, the next step in cephalometry is 3D cephalometry on a 3D radiographic model of the patient's skull. It is important to know whether classic cephalometry, performed since the early 1930s on 2D cephalometric radiographs, is comparable with measurements on 3D constructed models of the patient's skull. In longitudinal studies on growth or treatment outcome, it is important to know if data from 2D cephalometric analyses made in the past can be compared with data from 3D-cephalometric analysis, which will be more common in the future. To the authors' knowledge, there are no studies dealing with the interchange ability of measurements in cephalometric radiographs and 3D measurements on 3D models constructed from CBCT scans. Olszewski et al[7]. reported on cephalometric measurements on 3D models derived from MSCT scans. MSCT has a very high image quality but a tenfold higher radiation dose compared with CBCT. The image quality of the CBCT, specially for soft tissues, is significantly less compared with an MSCT.

The aim of this study was to evaluate whether measurements on conventional cephalometric radiographs are comparable with measurements on 3D constructed models of human skulls derived from CBCT scans.

3.2 Materials and Methods

3.2.1 Materials

The sample consisted of 40 dry skulls obtained from the collection of the Department of Orthodontics and Oral Biology of the Radboud University Nijmegen Medical Centre. The skulls were selected from a larger sample according to the following criteria: presence of permanent upper and lower incisors; presence of first permanent upper and lower molars; and presence of a reproducible, stable occlusion. The mandible was related to the skull, based on the position of the condyle in the fossa and maximum occlusal interdigitation. The mandibular position was fixed with broad tape from the ipsilateral temporal bone around the horizontal ramus of the mandible to the contralateral temporal bone.

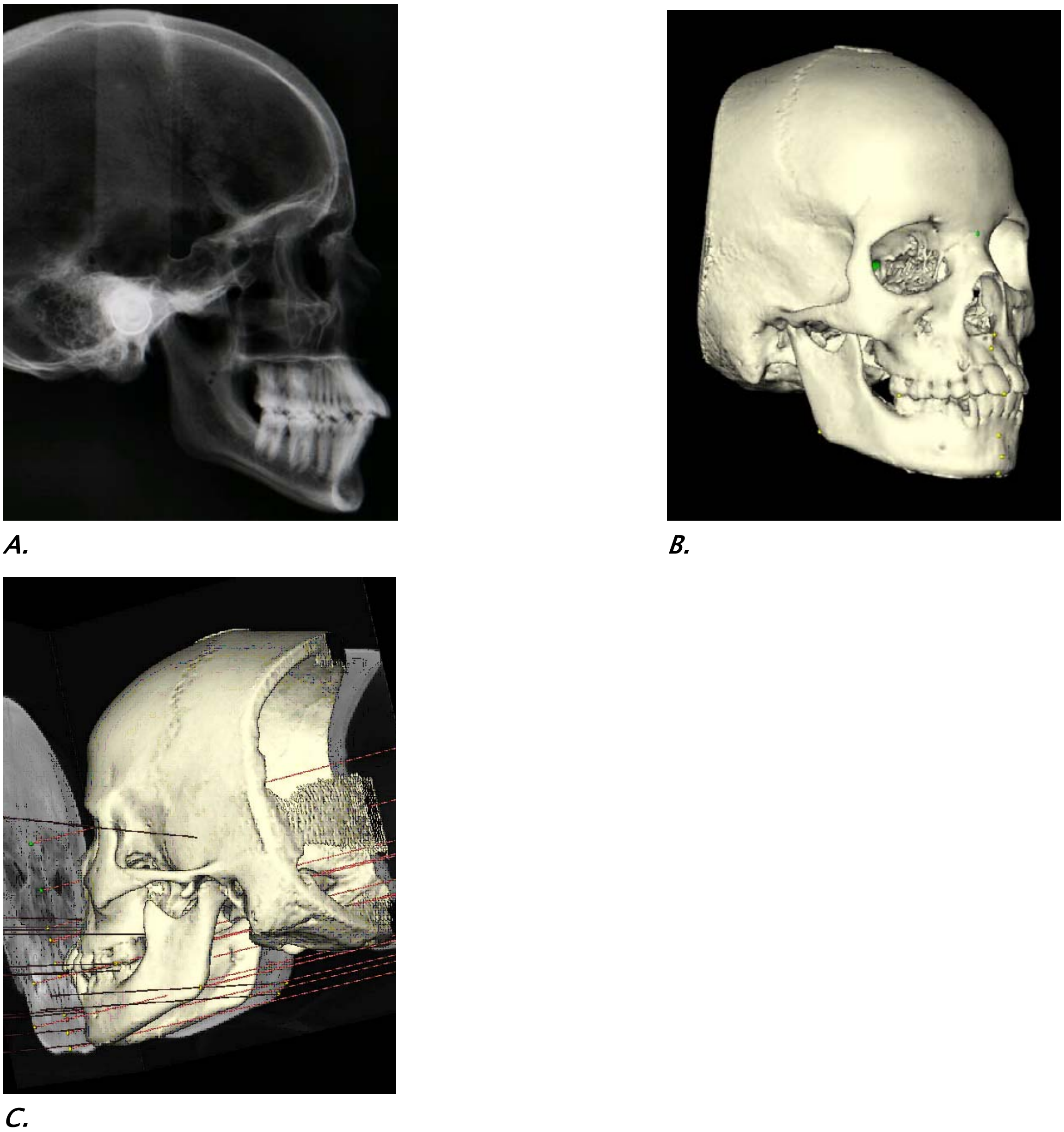
3.2.2 Radiography

Each skull was positioned in the cephalostat (Cranex Tome Ceph, Soredex, Tuusula, Finland) by fixing it between the ear rods. The ear rods were placed in the pori acoustici externi and the Frankfurt Horizontal plane was placed parallel to the floor. Cephalometric radiographs were taken according to the following radiographic settings. For bigger skulls (n=30), the adult settings were chosen: 70 kV, 10 mA, 0.6 s. For smaller skulls (n=10), the child settings were chosen: 70 kV, 10 mA, 0.5 s.

The same skulls were placed in the I-cat® cone beam CT (Imaging Sciences International, Inc. Hatfield, PA, USA), on a foam platform with the Frankfurt horizontal plane parallel to the floor. The skulls were placed in the centre of the CBCT scanner using the midline light beam to coincide with the midsagittal plane. The scan was taken for all skulls in the extended height mode (22 cm): 129 kVp, 47.74 mA, 40 s with a resolution of 0.4 voxel.

3.2.3 Cephalometry

The conventional radiographs (Figure 3.1A) were digitized with Viewbox® (dHAL Software, Kifissia, Greece) to identify landmarks and to calculate distances and angles. 3D skull models were constructed (Figure 3.1B and C) from the CBCT data with Maxilim® (Medicim, Sint-Niklaas, Belgium). The same software was used to cephalometrically analyse the constructed 3D models.



A. ***B.*** ***C.***

Figure 3.1 *Cephalometric radiograph and 3D model of the same skull. (A) Conventional cephalometric radiograph, (B) CBCT-constructed and (C) traced 3D model.*

For the cephalometric analysis 17 hard tissue landmarks (Table 3.1) were identified and 12 (10 angular and 2 linear) widely used cephalometric measurements were used. Table 3.1 presents the landmarks, lines and planes. Table 3.2 presents the measurements that were used in the present study.

Table 3.1 Anatomical landmarks, lines and planes used in this study.

S	Sella	Centre of sella turcica
N	Nasion	Most anterior limit of the frontonasal suture on the frontal bone in the facial midline
A	A - point	Deepest bony point on the contour of the premaxilla below ANS
B	B - point	Deepest bony point of the contour of the mandible above pogonion
ANS	Anterior Nasal Spine	The tip of the anterior nasal spine
PNS	Posterior Nasal Spine	The most posterior point on the bony hard palate
POG	Pogonion	Most anterior point of the symphysis of the mandible
GN	Gnathion	Most anterior inferior point of the bony chin
GO l	Left Gonion	Most posterior inferior point of the left angle of the mandible
GO r	Right Gonion	Most posterior inferior point of the right angle of the mandible
Is	Incision Superius	The incisal tip of the most anterior upper incisor
UIA	Upper Incisor Apex	The root apex of the most prominent upper incisor
Ii	Incision Inferius	Incisal point of the most prominent medial mandibular incisor
LIA	Lower Incisal Apex	Root apex of the most prominent lower incisor
NSL	Nasion Sella line	Line from point S to point N
NSP	Nasion Sella Plane	Plane constructed by projecting NSL on the medial plane
ML	Mandibular line	Line between Gonion and Gnathion
MP	Mandibular Plane (3D)	Plane between left Gonion, right Gonion and Gnathion
NL	Palatal line	Line from ANS to PNS
NP	Palatal plane (3D)	Plane constructed by projecting the line through point ANS and PNS on the medial plane.
BOP	Bisected Occlusal plane	Line connecting the vertical midpoint between Is and Ii and the mesial contact between the first molars.
BOP	Bisected Occlusal plane (3D)	Plane connecting the vertical midpoint between Is and Ii and the mesial contact between the first molars on left side and first molars on the right side.

Table 3.2 Cephalometric variables.

SNA	Angle between point S, point N and point A
SNB	Angle between point S, point N and point B
ANB	Angle between point A, point N and point B
NSL / NL	Angle between line SN and line NL
NSP / NP (3D)	Angle between NSP and NP
NSL / ML	Angle between SN and ML
NSP / MP (3D)	Angle between NSP and MP
NL / ML	Angle between NL and ML
NP / MP (3D)	Angle between NP and MP
ILs / NL or NP	Relative inclination of upper incisors to NL or in 3D to NP
ILi / ML or MP	Relative inclination of lower incisors to ML or in 3D to MP
Inter incisal angle	Angle between the lines through long axis of upper and lower incisors projected on the medial plane
NSL / BOP	Angle between line NSL and the BOP
NSP / BOP (3D)	Angle between plane SN and the BOP
Is to A-POG	Distance in mm between point Is and the line A – POG or in 3D the plane constructed from projecting line A – POG to the medial plane
Ii to A-POG	Distance in mm between point Ii and the line A – POG or in 3D the plane constructed from projecting line A – POG to the medial plane

3.2.4 Statistical analysis

For both the conventional cephalometric radiographs and the CBCT-constructed 3D models, the same operator (OV) marked the landmarks five times, each time with an interval of 1 week. The intra-observer reliability was calculated using the Pearson correlation coefficient for the first and second measurement. The mean value of the five repeated measurements and their variance was used for further statistical analysis. For each measurement, the standard deviation was calculated as the square root of the mean variance. This standard deviation was compared with the standard deviation of the same measurement in the other group. Paired *t* tests were performed to compare the means of corresponding measurements on the cephalometric radiograph and on the 3D model of the same skull.

3.3 Results

Intra-observer reliability for both the conventional cephalometric radiographs and the 3D model is shown in Table 3.3. 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. Reproducibility of the measurements on the conventional cephalometric radiographs was higher, compared with the reproducibility of the measurements on the 3D models.

Table 3.3 *Intra-observer reliability expressed as Pearson's Correlation coefficient for first and second measurements and duplicate measurement error for 40 cases with 95 % confidence interval (CI). P-value relates to the test for statistically significant difference between the two methods.*

	Conventional			**3D Model**			
		Duplicate measurement error			Duplicate measurement error		
	Reliability	**Error**	**95% CI**	**Reliability**	**Error**	**95% CI**	***P-value for error***
ANB (°)	0.92	0.53	0.47 – 0.59	0.98	0.27	0.24 – 0.30	<0.001
SNA (°)	0.96	0.57	0.52 – 0.64	0.87	1.05	0.93 – 1.17	<0.001
SNB (°)	0.95	0.45	0.40 – 0.50	0.84	1.02	0.91 – 1.14	<0.001
NL/ML (°)	0.97	0.76	0.67 – 0.84	0.98	0.81	0.72 – 0.90	0.194
NSL/BOP(°)	0.96	0.83	0.74 – 0.93	0.91	1.55	1.37 – 1.72	<0.001
NSL/ML (°)	0.95	0.66	0.58 – 0.73	0.87	1.12	1.00 – 1.25	<0.001
NSL/NL(°)	0.97	0.51	0.45 – 0.57	0.82	1.09	0.97 – 1.22	<0.001
ILi to ML (°)	0.93	2.62	2.33 – 2.91	0.69	3.82	3.39 – 4.24	<0.001
ILs to NL (°)	0.94	1.62	1.44 – 1.80	0.93	1.95	1.73 – 2.17	0.005
Interincisal angle (°)	0.95	2.96	2.63 – 3.30	0.90	4.42	3.93 – 4.91	<0.001
Is to A-POG (mm)	0.98	0.33	0.29 – 0.37	0.97	0.36	0.32 – 0.41	0.086
Ii to A-POG (mm)	0.97	0.52	0.46 – 0.57	0.73	0.95	0.84 – 1.05	<0.001

Differences between measurements on the 3D models and the conventional radiographs are shown in Table 3.4. 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 -3.11° to 0.82°. For most measurements this difference was considerably smaller than the standard deviation of the variable measured. For SN/ML the difference (3.11°) was 89% of standard deviation, for the SN/NL difference (1.74°) this was 66%. For all other measurements it was less than 40%.

Table 3.4 *The mean difference between corresponding measurements taken on the 3D Model and conventional cephalometric radiographs with 95 % confidence interval (CI), corresponding P-value and reliability expressed as Pearson's Correlation coefficient.*

	Difference 3D - Conv	**95% CI**	**P-value**	**Reliability**
ANB (°)	-0.59	-0.77 – -0.41	<0.001	0.96
SNA (°)	0.19	-0.09 – 0.48	0.177	0.96
SNB (°)	0.82	0.55 – 1.09	<0.001	0.96
NL/ML (°)	-1.32	-1.73 – 0.90	<0.001	0.95
NSL/BOP(°)	0.58	0.02 – 1.14	0.043	0.91
NSL/ML (°)	-3.11	-3.43 – -2.79	<0.001	0.96
NSL/NL(°)	-1.74	-2.21 – -1.27	<0.001	0.87
ILi to ML (°)	-0.23	-1.68 – 1.23	0.755	0.81
ILs to NL (°)	0.45	-1.07 – 1.97	0.551	0.83
Interincisal angle (°)	0.77	-0.56 – 2.11	0.249	0.95
Is to A-POG (mm)	-0.83	-1.03 – -0.64	<0.001	0.97
Ii to A-POG (mm)	0.24	0.00 – 0.47	0.053	0.93

3.4 Discussion

Twelve widely used cephalometric variables calculated on conventional radiographs and CBCT-constructed 3D models of human skulls were compared. Dry skulls were used because it is considered unethical to expose patients twice to radiation (a conventional radiograph and a CBCT). In this way, a 2D cephalometric image and a 3D model were obtained from the same skull, which were comparable. Earlier studies showed that the largest error in cephalometric studies is that of identifying landmarks[8] and that each landmark exhibits a characteristic pattern of error that contributes to measurement inaccuracy[9]. The present study shows that the measurement error for 3D measurements is larger than that for conventional 2D measurements. By adding the third dimension an additional source of inaccuracy is introduced. This could explain the larger standard error in the 3D measurements than in the 2D measurements. Another possible explanation is that there is a learning curve in tracing 3D models, especially when one is used to tracing 2D images.

Dry skulls were used, so no distortion was caused by the presence of soft tissues. This reduces the chance of errors in landmark identification because it makes an accurate identification of bony landmarks more likely since there is no over projection of soft tissues. In this study, it is impossible to test the reliability of soft tissue measurements. A recently published in vivo study found no statistical differences for soft tissue measurements[10].

All measurements were performed by one observer. The standard errors (Table 3.3) were very acceptable. The question remains, whether this observer made a systematic error. Systematic errors in the repeated identification of landmarks do not influence reproducibility, since they are the same each time a landmark is identified. It is therefore justified to have one observer for this type of study.

For most landmarks, the authors found statistically significant differences in locating them on conventional cephalometric radiographs compared with the 3D model. For only four of the measurements, did the difference exceeded its standard error. The absolute difference for Is to A-Pog was more than its standard error, but with -0.83 mm still less than 1 mm, which could be considered to be within a clinically acceptable range. For the three angular variables NSL/ML, NSL/NL and ML/NL the difference exceeded the standard error. An explanation for this could be that in the 3D models the angles between two planes are calculated, compared with angles between two lines in conventional cephalometry (e.g. the mandibular line in conventional cephalometry is formed by the points gonion and gnathion). In the 3D models the mandibular plane is formed by both the left and right gonion and point gnathion. For the palatal plane there is a similar situation. There is a chance that the planes have a different orientation compared with the corresponding line and therefore have a different angle with other planes compared with the use of the lines.

In general, orthodontists and maxillofacial surgeons are experienced in the use and interpretation of conventional cephalometric radiographs. Tracing a 3D model has certain difficulties and landmarks have to be well defined in all three dimensions. Kragskov et al[11]. found that the measurements on 2D images were more reliable than measurements on 3D MSCT, which is in accordance with the present findings. A learning curve is to be expected when switching from conventional 2D cephalometric radiographs to a CBCT-constructed 3D model of the patient's skull. Points that are hard to identify on the 3D model are: sella, upper incisor apex, incision inferius and lower incisal apex. This is because all these points are inside the 3D model, so slices have to be selected to be able to mark their location. A 3D-cephalometric analysis is time consuming. The programs are likely to improve their accuracy and include more intelligent software, improving the user friendliness in the coming years, making good cephalometric analysis easier.

In conventional cephalometry, the position of the patient in the cephalostat is fixed by the ear rods for movements along the long axis of the skull. In the CBCT device there are no ear rods to fix the position of the patient. Extra care must be taken when positioning the patient in the CBCT device. If the patient is not positioned with the midsagittal plane coinciding with the midline light beam of the CBCT device, distortion will occur when 2D images are constructed from the 3D data set. This can influence the cephalometric measurements. For both methods tilting of the head is possible, but this does not affect the angular or linear measurements since all bony points move in the same direction. When working in 3D only, the positioning of the patient in the CBCT device is of no importance, since the patient can be positioned with the software in the desired position.

Conventional cephalometrics remains a 2D representation of a 3D structure. This has disadvantages. Like Adams et al.[12], the authors found differences between the 2D and 3D measurements. Kumar et al.[4] and Moshiri et al.[5] have shown that measurements on a 3D model are comparable with direct measurements on a skull. When interpreting the differences between the 2D measurements on the cephalometric radiographs and the 3D measurements on the 3D models, one might wonder what is more accurate: measurements on a 2D representation of a 3D structure or measurements on a life size model of the 3D structure itself?

In a 3D analysis the actual anatomical structures can be identified instead of their 2D projection, but some other landmarks used in conventional cephalometric analysis cannot be used (e.g. articulare, as this is a constructed landmark which does not exist in 3D). There is a need to develop and test new 3D-cephalometric analyses. There are no data that can be used as reference values for 3D-cephalometric measurements. As long as the radiation dose of CBCT is significantly higher than that of conventional cephalometric radiographs, it is unlikely that 3D reference values will become available from growth studies, as we have for 2D cephalometry. 3D measurements on the same patient can be used before and after treatment to objectify treatment and growth changes.

For most measurements in this study there is no clinically relevant difference between angular and linear measurements performed on conventional cephalometric radiographs, compared with cephalometric measurements on 3D models of skulls. In cases where a line is used as a measurement in conventional 2D cephalometry while a 3D plane is used in the 3D model, there can be clinically relevant differences. 3D tracings are not suitable for longitudinal research in cases where there are only 2D records from the past.

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Chapter 4

A comparison of frontal radiographs obtained from cone beam CT scans and conventional frontal radiographs of human skulls

O.J.C. van Vlijmen
S.J. Bergé
E.M. Bronkhorst
G. R. J. Swennen
C. Katsaros
A. M. Kuijpers-Jagtman

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Abstract

Purpose: This study evaluated whether measurements on conventional frontal radiographs are comparable with measurements on cone beam computed tomography (CBCT)-constructed frontal cephalometric radiographs taken from dry human skulls.

Materials and Methods: CBCT scans and conventional frontal cephalometric radiographs were made of 40 dry skulls. With I-Cat Vision® software, a cephalometric radiograph was constructed from the CBCT scan. Standard cephalometric software was used to identify landmarks and calculate ratios and angles. The same operator identified 10 landmarks on both types of cephalometric radiographs on all Images 5 times with a time-interval of 1 week.

Results: Intra-observer reliability was acceptable for all measurements. The reproducibility of the measurements on the frontal radiographs obtained from the CBCT scans was higher than those on conventional frontal radiographs. There is a statistically significant and clinically relevant difference between measurements on conventional and constructed frontal radiographs.

Conclusions: There is a clinically relevant difference between angular measurements performed on conventional frontal cephalometric radiographs, compared with measurements on frontal cephalometric radiographs constructed from CBCT scans, owing to different positioning of patients in both devices. Positioning of the patient in the CBCT device appears to be an important factor in cases where a 2D projection of the 3D scan is made.

4.1 Introduction

Since the early 1930s, lateral and frontal conventional cephalometry has been used to analyse maxillofacial and orthodontic deformities, especially to evaluate growth and/or treatment changes[1,2]. The frontal cephalogram has not routinely been used in orthodontic treatment planning[3]. This may be because of the limitations and difficulties of such an analysis, such as errors in reproducing head posture, identifying landmarks of superimposed structures and the relatively low added value of frontal radiographs because they only provide additional information about asymmetries and width of the jaws[4]. In surgical cases this information can be important.

A cone beam computed tomography (CBCT) scan has reduced radiation, compared with a Multislice CT (MSCT) scan, and can be used for a wider range of patients[5]. CBCT uses a different type of acquisition than conventional MSCT. The X-ray source produces a cone shaped X-ray beam. This makes it possible to capture the image in one sweep, instead of capturing every slice separately, as is the case in MSCT. A CBCT scan has reduced radiation compared with a MSCT scan, but it is not suitable for routine orthodontic patients[6]. CBCT has benefits for patients with three dimensional (3D) deformities, such as craniofacial anomalies, orofacial clefts or orthognathic cases.

It has been shown[7,8,9,10] that conventional lateral cephalometric radiographs, which may be considered the gold standard, can be compared with constructed cephalometric radiographs from CBCT scans and the latter can be used for longitudinal research in cases where there are conventional radiographic records from the past. To the authors' knowledge there is no study that investigates whether the same holds true for frontal cephalometric radiographs. The aim of this study was to evaluate whether measurements on conventional frontal radiographs are comparable with measurements on CBCT-constructed frontal cephalometric radiographs taken from dry human skulls.

4.2 Material en Methods

4.2.1 Materials

The sample consisted of 40 dry human skulls obtained from the collection of the Department of Orthodontics and Oral Biology of the Radboud University Nijmegen Medical Centre. The skulls where selected from a larger sample according to the following criteria: presence of permanent upper and lower incisors; presence of first permanent upper and lower molars; and presence of a reproducible, stable occlusion. The mandible was related to the skull based on the position of the condyle in the fossa and maximum occlusal interdigitation. The mandibular position was fixed with broad tape from the ipsilateral temporal bone around the horizontal ramus of the mandible to the contralateral temporal bone.

4.2.2 Radiography

Each skull was positioned in the cephalostat (CranexTomeCeph, Soredex, Tuusula, Finland) by fixing it between the ear rods. The ear rods were placed in the outer end of the external acoustic meatuses and the Frankfurt horizontal plane was placed horizontally, parallel to the floor. Cephalometric radiographs were taken according to the following radiographic settings. For larger skulls (n=30), the adult settings were chosen: 70 kV, 10 mA, 0.6 s. For smaller skulls (n=10), the child settings were chosen: 70 kV, 10 mA, 0.5 s (Figure 4.1A). The Viewbox software (dHAL Software, Kifissia, Greece) was used to identify conventional cephalometric hard tissue landmarks and to calculate distances and angles.

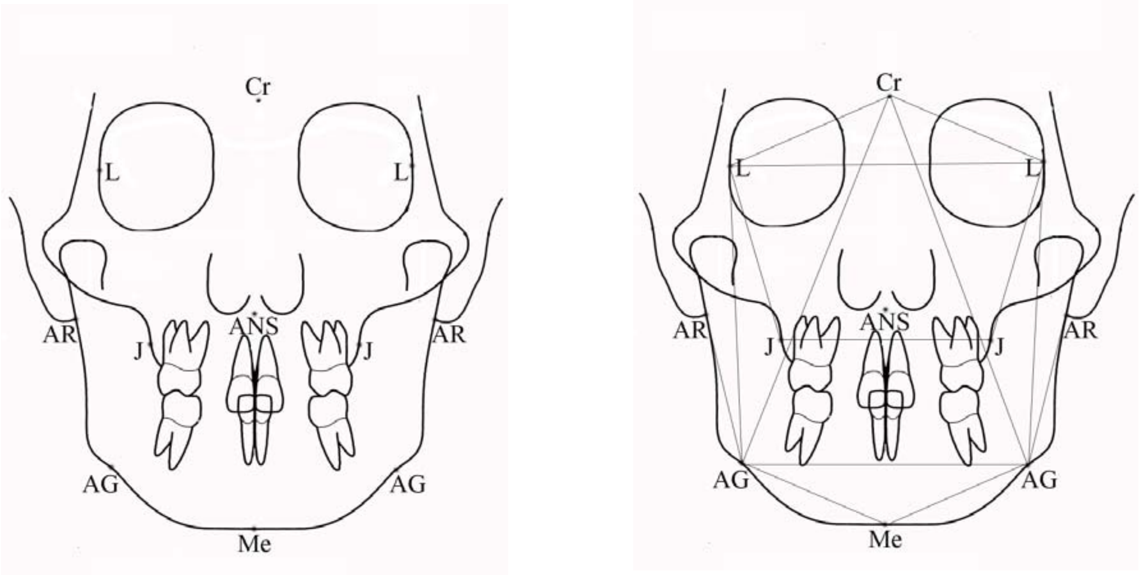
The same skulls were placed in the I-Cat CBCT scanner (Imaging Sciences International, Inc. Hatfield, PA, USA), on a foam platform with the Frankfurt horizontal plane parallel to the floor. The skulls were placed in the centre of the CBCT scanner using the midline light beam to coincide with the midsagittal plane. The CBCT scan was taken for all skulls in the extended height mode: 129 kVp, 47.74 mA, 40 s with a resolution of 0.4 voxel. With I-Cat Vision® software (Imaging Sciences International, Inc. Hatfield, PA, USA), a cephalometric radiograph was constructed from the 3D CBCT scan by frontal radiographic projection of the entire volume. This constructed cephalometric radiograph was then digitised with the Viewbox® software (Figure 4.1B).

A. *B.*

Figure 4.1 *Cephalometric frontal radiographs of the same skull. (A) Conventional radiograph. (B) CBCT-constructed radiograph.*

4.2.3 Cephalometry

For the cephalometric analysis, 10 conventional hard tissue cephalometric landmarks (Figure 4.2, Table 4.1) were identified. Sixteen widely used cephalometric variables (11 angles and 5 linear ratios) were calculated in Viewbox®. (Table 4.2).



A. *B.*

Figure 4.2 *(A) Representation of the landmarks. (B) Angles measured.*

Table 4.1 Anatomical landmarks used in this study.

AGl	Antegonion left	The anteganial notch at the lateral inferior margin of the antegonial protuberances on left side.
AGr	Antegonion right	The anteganial notch at the lateral inferior margin of the antegonial protuberances on right side.
AR	Articulare	The point of intersection of the dorsal contours of the body of the mandible and the pharyngeal part of the clivus. Both on the left and on the right side.
Jl	Jugale left	At the jugal process the intersection of the outline of the maxillary tuberosity and the zygomatic buttress on the left side.
Jr	Jugale right	At the jugal process the intersection of the outline of the maxillary tuberosity and the zygomatic buttress on the right side.
Ll	Lateral orbital margin left	The most lateral point of the orbital cavity on the left side.
Lr	Lateral orbital margin right	The most lateral point of the orbital cavity on the right side.
ANS	Anterior Nasal Spine	The tip of the anterior nasal spine
CR	Crista Galli	Most superior point at its intersection with the sphenoid
ME	Menton	The most inferior point of the symphysis of the mandible, as seen on the lateral jaw projection

Table 4.2 Cephalometric variables.

R ME-AG	Ratio between line ME-AG left and line ME-AG right
R ME-AR	Ratio between line ME-AR left and line ME-AR right
R J-ANS	Ratio between line J left-ANS and line J right-ANS
R CR-L	Ratio between line CR-L left and line CR-L right
R AG-AR	Ratio between line AG left- AR left and line AG right-AR right
ME/AGl/CR	Angle between line ME-left AG and line left AG-CR
ME/AGr/CR	Angle between line ME-right AG and line right AG-CR
AGl/ME/AGr	Angle between line ME-left AG and line ME-right AG
Jl/Jr/Ll	Angle between the line J left- J right and line J left-L left
Jl/Jr/Lr	Angle between the line J left- J right and line J right-L right
AGl/AGr/Ll	Angle between the line AG left- AG right and line AG left-L left
AGl/AGr/Lr	Angle between the line AG left- AG right and line AG right-L right
Gonial angle l	Angle between the line ME-AG left and line AG left- AR
Gonial angle r	Angle between the line ME-AG right and line AG right- AR
AGl-AGr/Ll-Lr	Angle between the line AG left-AG right and line left L-right L
Ll/CR/Lr	Angle between the line left L-CR and line right L-CR

4.2.4 Statistical analysis

For both the conventional frontal cephalometric radiographs and the CBCT-constructed frontal cephalometric radiographs, the same operator (OV) marked the landmarks on all 80 images five times, each time with a time interval of one week. The mean value of these five measurements was used for statistical analysis.

The intra-observer reliability was calculated using the Pearson correlation coefficient for the first and second measurement. For each measurement, the standard error was calculated and compared with the standard error of the same measurement in the other group. Paired *t* tests were performed to compare the means of corresponding measurements on the two cephalometric radiographs of the same skull.

4.3 Results

Intra-observer reliability for both the conventional frontal cephalometric radiographs and the CBCT-constructed frontal cephalometric radiographs was acceptable. The correlation coefficient between the first and second measurements ranged between 0.23 and 0.99 with an average of 0.76 for the conventional frontal radiographs and between 0.57 and 1.00 with an average of 0.85 for the constructed frontal radiographs (Table 4.3).

The duplicate measurement error for the CBCT-constructed frontal cephalometric radiographs was significantly smaller for seven measurements (R J-ANS, AGl/ME/AGr, Jl/Jr/Ll, Jl/Jr/Lr, AGl/AGr/Ll, AGl/AGr/Lr, AGl-AGr/Ll-Lr) compared with the standard error of the conventional frontal cephalometric radiographs. For the conventional cephalometric radiographs this was the case for five measurements (R ME-AR, R CR-L, R AG-AR, gonial angle l, Ll/CR/Lr). For four measurements there were no statistical significant differences between the types of radiographs (R ME-AG, ME/AGl/CR, ME/AGr/CR, gonial angle l). Reproducibility of the measurements on the CBCT constructed cephalometric radiographs was higher, compared with the reproducibility of the measurements on conventional cephalometric radiographs.

Table 4.3 *Intra-observer reliability expressed as Pearson's Correlation coefficient for first and second measurements and duplicate measurement error for 40 cases with 95 % confidence interval (CI). P-value relates to the test for statistically significant difference between the two methods.*

	Conventional			**Constructed**			
		Duplicate measurement error			Duplicate measurement error		***P-value for error***
	Reliability	**Error**	**95% CI**	**Reliability**	**Error**	**95% CI**	
R ME-AG	0.84	0.03	0.03 – 0.04	0.90	0.03	0.03 – 0.04	0.313
R ME-AR	0.82	0.02	0.02 – 0.03	0.78	0.03	0.03 – 0.04	<0.001
R J-ANS	0.49	0.04	0.04 – 0.04	0.79	0.03	0.03 – 0.04	0.030
R CR-L	0.23	0.02	0.02 – 0.02	0.57	0.02	0.02 – 0.03	<0.001
R AG-AR	0.82	0.05	0.05 – 0.06	0.70	0.08	0.07 – 0.08	<0.001
ME/AGl/CR (°)	0.99	0.66	0.59 – 0.73	0.99	0.66	0.59 – 0.73	0.498
ME/AGr/CR (°)	0.99	0.89	0.79 – 0.99	0.99	0.78	0.70 – 0.87	0.067
AGl/ME/AGr (°)	0.99	1.20	1.06 – 1.33	1.00	0.76	0.67 – 0.84	<0.001
Jl/Jr/Ll (°)	0.51	2.28	2.03 – 2.54	0.69	1.70	1.50 – 1.88	<0.001
Jl/Jr/Lr (°)	0.64	2.20	1.95 – 2.44	0.73	1.72	1.53 – 1.92	<0.001
AGl/AGr/Ll (°)	0.96	0.72	0.64 – 0.80	0.96	0.53	0.47 – 0.59	<0.001
AGl/AGr/Lr (°)	0.88	0.72	0.64 – 0.80	0.92	0.52	0.46 – 0.58	<0.001
Gonial Angle l (°)	0.99	0.90	0.80 – 1.00	0.99	0.86	0.76 – 0.95	0.265
Gonial Angle r (°)	0.99	0.72	0.64 – 0.80	0.93	1.52	1.35 – 1.69	<0.001
AGl-AGr/Ll-Lr (°)	0.67	0.95	0.84 – 1.05	0.77	0.77	0.68 – 0.85	0.008
Ll/CR/Lr (°)	0.34	4.18	3.71 – 4.64	0.84	5.12	4.55 – 5.69	0.002

There was a statistically significant difference between the conventional frontal cephalometric radiographs and the CBCT constructed frontal cephalometric radiographs for the following measurements (Table 4.4): R ME-AG, R ME-AR, R JANS, R CR-l, ME/AGl/CR, ME/AGr/CR, AGr/ME/AGl, gonial angle l, gonial angle l, Ll/CR/Lr. Though the average difference for those measurements between the two methods was statistically significant (P<0.001), for most of them the actual mean average difference for repeated measurements ranged from 0.07 to 0.11 for the ratios. For the angles these average differences ranged from 6.44° to 23.15°, which is larger than the standard error for the repeated measurements.

Table 4.4 *The mean difference between corresponding measurements taken on conventional frontal radiographs and constructed frontal radiographs with 95 % confidence interval (CI), corresponding P-value and reliability expressed as Pearson's Correlation coefficient.*

	Difference Conv–CBCT	95% CI	P-value	Reliability
R ME-AG	-0.07	-0.12 – 0.04	<0.001	0.297
R ME-AR	-0.07	-0.09 – 0.04	<0.001	0.152
R J-ANS	-0.11	-0.13 – 0.08	<0.001	0.145
R CR-L	-0.08	-0.09 – 0.07	<0.001	0.285
R AG-AR	<-0.01	-0.04 – 0.04	0.859	0.251
ME/AGl/CR (°)	9.18	7.40 – 10.97	<0.001	0.612
ME/AGr/CR (°)	7.60	5.11 – 10.08	<0.001	0.574
AGl/ME/AGr (°)	-23.15	18.20 – 28.09	<0.001	0.524
Jl/Jr/Ll (°)	0.55	-0.20 – 1.31	0.146	0.605
Jl/Jr/Lr (°)	0.46	-0.46 – 1.38	0.315	0.455
AGl/AGr/Ll (°)	0.21	-0.41 – 0.83	0.496	0.660
AGl/AGr/Lr (°)	0.23	-0.42 – 0.88	0.477	0.433
Gonial Angle l (°)	11.28	8.82 – 13.74	<0.001	0.624
Gonial Angle r (°)	6.44	4.93 – 7.96	<0.001	0.728
AGl-AGr/Ll-Lr (°)	0.17	-0.25 – 0.60	0.415	0.452
Ll/CR/Lr (°)	12.06	8.17 – 15.96	<0.001	-0.110

4.4 Discussion

In this study, 16 widely used cephalometric measurements on conventional frontal radiographs and CBCT-constructed frontal cephalometric radiographs of dry human skulls were compared. Dry skulls were used because it is not ethically acceptable to expose patients to radiation from both a conventional radiograph and a CBCT. Two comparable images were obtained. The largest error in cephalometric studies is the error in landmark identification[11] and each landmark exhibits a characteristic pattern of error that contributes to measurement inaccuracy[12]. Images from dry skulls do not suffer from distortion caused by soft tissues. This reduces the chance of errors in landmark identification because it allows easier and more accurate localisation of bony landmarks. Testing the reliability of soft tissue measurements is not possible.

For some landmarks, statistically significant differences were found in locating landmarks on conventional frontal cephalometric radiographs compared with CBCT-constructed frontal cephalometric radiographs. These differences were beyond any reasonable clinically acceptable range as described by Hajeer[13]. The authors tried to assess what caused these large differences. All angles are larger for the conventional radiographs except for one. The angle AGl/ME/AGr is larger for the constructed radiographs. This means that the skulls in the CBCT were positioned with the chin relatively more upwards than in the cephalostat. This was confirmed by a later experiment, in which a skull with metal markers on the landmarks to be located was placed in the cephalostat and the CBCT device, but in the latter with the chin tilted upwards about 30 degrees. This severe tilt clearly shows how the measured angles are affected.

The cephalostat has ear rods that help to position the patient. This prevents movement along the long axis of the head and gives a reference as how to place the skull in a horizontal manner. The CBCT scanner does not have these ear rods, instead it has a light beam to make placement of the patient in the centre of the scanner more easy and reproducible. Extra care must be taken when placing the patient in the CBCT device. If the patient is not positioned with the midsagittal plane coinciding with the midline light beam of the CBCT device, distortion may occur when 2D images are constructed from the 3D data set. This can influence the cephalometric measurements. As this study shows, it might not be accurate enough using only the human eye to position the Frankfurt horizontal plane parallel to the floor. The authors recommend taking extra care in positioning the patient in the CBCT scanner or using extra light beams in doing so to prevent unwanted tilt of the head.

In this study, all measurements were performed by one observer. The question remains whether this observer made a systematic error. The standard errors in Table 4.3 are very acceptable. Systematic errors in the identification of landmarks are the same for both types of radiographs and therefore do not have any influence on reproducibility. It is justified to have one observer for this type of study.

In general, orthodontists and maxillofacial surgeons are experienced in the use and interpretation of conventional frontal cephalometric radiographs. However, the cephalometric radiographs created with I-Cat Vision® software look different from the conventional ones (Figure 4.1). The contrast and transparency of the two types of cephalometric radiographs are different. The observer who performed the measurements for this study, found point L harder to identify on the conventional radiographs than on the constructed radiographs. ANS and J were harder to identify on the constructed radiographs. It seems as if there is more depth in the conventional radiographs, which makes identification of landmarks easier and which might explain the difficulties in identifying these landmarks on constructed radiographs. A learning curve is to be expected when switching from conventional 2D radiographs to CBCT-constructed radiographs.

Conventional cephalometrics is a 2D representation of a 3D structure. This has disadvantages. Now that it is possible to make 3D models of the skull, it is also possible to perform 3D cephalometric analysis[14,15]. In such an analysis, the actual anatomical structures can be identified instead of a 2D projection. In 2D anterior posterior radiology, positioning of the patient seems to give major difficulties. As long as a 2D projection of 3D scans is used for analysis, positioning the patient remains an important factor. As a CBCT device has no cephalostat, extra care should be taken when positioning the patient in the device. If a 3D model is made and a 3D analysis is carried out, positioning of the patient probably does not have any effect on the measurements of a 3D cephalometric analysis. Future research needs to confirm this hypothesis. There is a need to develop and test new 3D-cephalometric analyses.

There is a clinically relevant difference between angular measurements performed on conventional frontal cephalometric radiographs, compared with measurements on frontal cephalometric radiographs constructed from CBCT scans, owing to different positioning of patients in both devices. Positioning of the patient in the CBCT device seems to be an important factor in cases were a 2D projection of the 3D scan is made.

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Chapter 5

A comparison between two-dimensional and three-dimensional cephalometry on frontal radiographs and on cone beam computed tomography scans of human skulls.

O.J.C. van Vlijmen
T.J.J. Maal
S.J. Bergé
E.M. Bronkhorst
C. Katsaros
A. M. Kuijpers-Jagtman

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Abstract

Purpose: The aim of this study was to evaluate whether measurements performed on conventional frontal radiographs are comparable to measurements performed on three-dimensional (3D) models of human skulls derived from cone beam computed tomography (CBCT) scans and if the latter can be used in longitudinal studies.

Materials and Methods: Cone beam computed tomography scans and conventional frontal cephalometric radiographs were made of 40 dry human skulls. From the CBCT scan a 3D model was constructed. Standard cephalometric software was used to identify landmarks and to calculate ratios and angles. The same operator identified 10 landmarks on both types of cephalometric radiographs, and on all images, five times with a time interval of 1 wk.

Results: Intra-observer reliability was acceptable for all measurements. There was a statistically significant and clinically relevant difference between measurements performed on conventional frontal radiographs and on 3D CBCT-derived models of the same skull.

Conclusions: There was a clinically relevant difference between angular measurements performed on conventional frontal cephalometric radiographs, compared with measurements performed on 3D models constructed from CBCT scans. We therefore recommend that 3D models should not be used for longitudinal research in cases where there are only two-dimensional (2D) records from the past.

5.1 Introduction

Since the early 1930s, both frontal and lateral cephalometry has been utilized for analyzing both maxillofacial and orthodontic deformities, especially to evaluate growth and/or treatment changes[1,2]. The frontal cephalogram, however, has not routinely been used in orthodontic treatment planning[3], possibly because of limitations and difficulties in analysis of the frontal cephalogram, such as identifying landmarks of superimposed structures, errors in reproducing head posture, and relatively low added value of frontal radiographs because they only provide additional information about asymmetries and width of the jaws[4]. For treatment planning of surgical cases, frontal radiographs can be beneficial (e.g. in patients treated with surgically assisted rapid maxillary expansion).

During the last years cone beam computed tomography (CBCT) technology has been increasing in popularity. A CBCT scan exposes the patient to less radiation than a multislice computed tomography (MSCT) scan[5,6] and can therefore be used for a wider range of patients. Cone beam computed tomography uses a different type of acquisition compared with conventional MSCT. The X-ray source produces a cone-shaped X-ray beam. This makes it possible to capture the image in one rotation, instead of capturing every individual slice separately, as is the case in MSCT. Although a CBCT scan has reduced radiation in comparison to a MSCT scan, a CBCT scan is still not suitable for the standard orthodontic patient[7]. However, for patients with craniofacial anomalies and orofacial clefts, or patients requiring orthognatic surgery, CBCT has many benefits.

Recently it has been shown[8-11] that conventional lateral cephalometric radiographs, which may be considered as the ‘gold standard’, can be compared with constructed lateral cephalometric radiographs from CBCT scans and thus the latter can be used for longitudinal research in cases where there are conventional radiographic records from the past. In another study from our group that investigated whether the same holds true for frontal cephalometric radiographs, some differences between the two methods were found. These differences were caused by different positioning of the skulls in both devices. When constructing two-dimensional (2D) images from three-dimensional (3D) data, the positioning of the patient is of utmost importance, but when performing 3D cephalometry[12] the positioning of the patient is of no importance. As 3D scans, and therewith 3D cephalometry, are rapidly gaining popularity, there can be a problem in longitudinal studies because older records will be conventional 2D radiographs. Therefore, the aim of this study was to evaluate whether measurements on conventional frontal radiographs are comparable to measurements on 3D models of human skulls derived from CBCT scans and in addition whether the latter can be used in longitudinal studies.

5.2 Material en Methods

5.2.1 Materials

The sample consisted of 40 dry human skulls obtained from the collection of the Department of Orthodontics and Oral Biology of the Radboud University Nijmegen Medical Centre. The skulls were selected from a larger sample according to the following criteria: the presence of permanent upper and lower incisors; the presence of first permanent upper and lower molars; and the presence of a reproducible, stable occlusion. The mandible was related to the skull based on the position of the condyle in the fossa and maximum occlusal interdigitation. The mandibular position was fixed with broad tape from the ipsilateral temporal bone around the horizontal ramus of the mandible to the contralateral temporal bone.

5.2.2 Radiography

Each skull was positioned in the cephalostat (Cranex Tome Ceph; Soredex, Tuusula, Finland) by fixing it between the ear rods. The ear rods were placed in the pori acoustici externi and the Frankfurt Horizontal plane was placed horizontally, parallel to the floor. Cephalometric radiographs were taken according to the following radiographic settings. For larger skulls (n=30), the adult settings were chosen: 70 kV, 10 mA, 0.6 s. For the smaller skulls (n=10), the child settings were chosen: 70 kV, 10 mA, 0.5 s (Figure 5.1A). The viewbox software (dHAL Software, Kifissia, Greece) was used to identify conventional cephalometric hard tissue landmarks and to calculate distances and angles.

The same skulls were placed in the I-Cat CBCT scanner (Imaging Sciences, Hatfield, PA, USA) on a foam platform with the Frankfurt Horizontal plane parallel to the floor. The skulls were placed in the centre of the CBCT scanner using the midline light beam to coincide with the midsagittal plane. The CBCT scan was taken for all skulls in the extended height mode: 129 kVp, 47.74 mA, 40 s with a resolution of 0.4 voxel. A 3D model of each skull was constructed (Figure 5.1B) from the CBCT data using Maxilim (Medicim, Sint-Niklaas, Belgium). This same software was used to analyse the constructed 3D models cephalometrically.

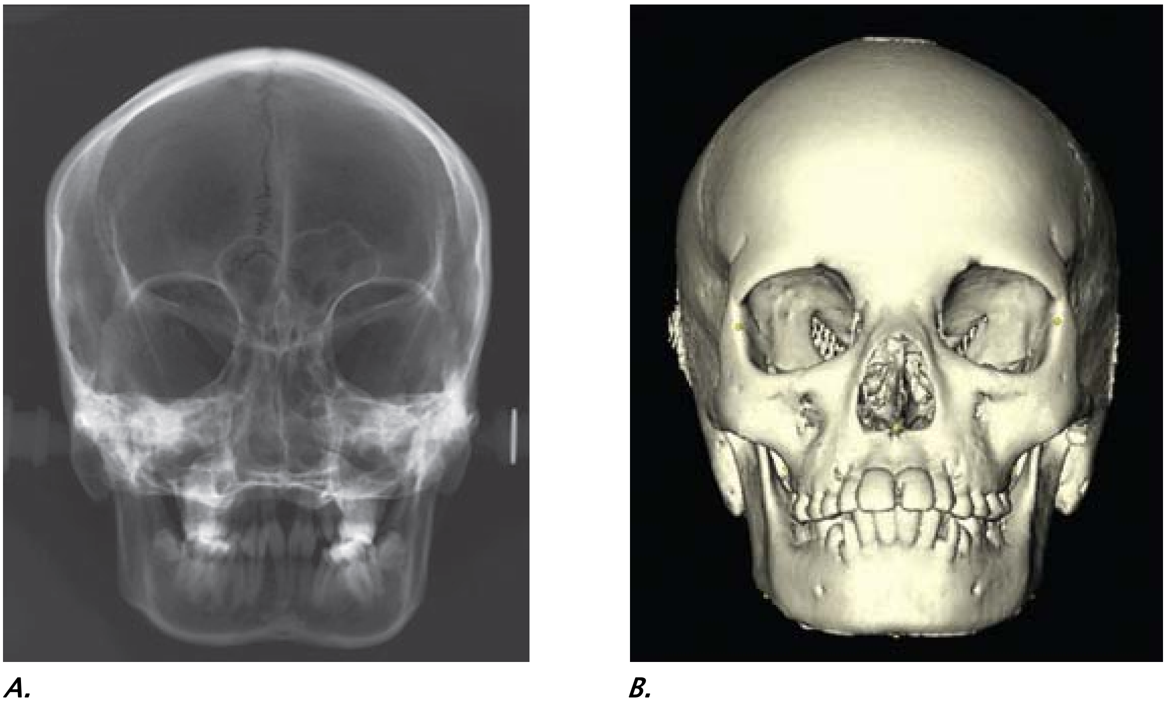
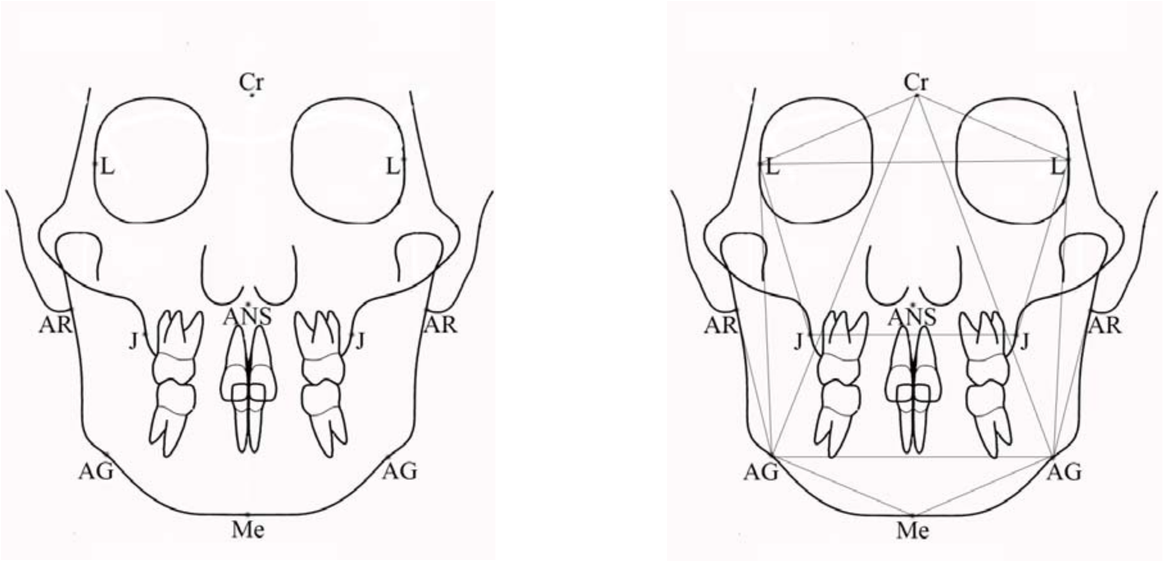


Figure 5.1 *Cephalometric frontal radiographs of the same skull. (A) Conventional radiograph. (B) Cone beam computed tomography (CBCT)-constructed three-dimensional (3D) model.*

5.2.3 Cephalometry

For the cephalometric analysis, 10 conventional hard-tissue cephalometric landmarks (Figure 5.2 and Table 5.1) were identified. Twelve widely used cephalometric variables (nine angles and three linear ratios) were calculated in Viewbox for the 2D measurements and in Maxilim for the 3D measurements (Table 5.2). All images were measured in random order.



A.

B.

Figure 5.2 *(A) Schematic representation of the landmarks that were identified. (B) Angles that were measured. The landmarks are defined in Table 5.1.*

Table 5.1 *Anatomical landmarks used in this study.*

AGl	Antegonion left	The antoganial notch at the lateral inferior margin of the antegonial protuberances on left side.
AGr	Antegonion right	The antoganial notch at the lateral inferior margin of the antegonial protuberances on right side.
AR	Articulare	The point of intersection of the dorsal contours of the processus articularis mandibulae and the pharyngeal part of the clivus. Both on the left and on the right side.
Jl	Jugale left	At the jugal process the intersection of the outline of the maxillary tuberosity and the zygomatic buttress on the left side.
Jr	Jugale right	At the jugal process the intersection of the outline of the maxillary tuberosity and the zygomatic buttress on the right side.
Ll	Lateral orbital margin left	The most lateral point of the orbital cavity on the left side.
Lr	Lateral orbital margin right	The most lateral point of the orbital cavity on the right side.
ANS	Anterior Nasal Spine	The tip of the anterior nasal spine
CR	Crista Galli	Most superior point at its intersection with the sphenoid
ME	Menton	The most inferior point of the symphysis of the mandible, as seen on the lateral jaw projection

Table 5.2 Cephalometric variables.

R ME-AG	Ratio between line ME-AG left and line ME-AG right
R J-ANS	Ratio between line J left-ANS and line J right-ANS
R CR-L	Ratio between line CR-L left and line CR-L right
ME/AGl/CR	Angle between line ME-left AG and line left AG-CR
ME/AGr/CR	Angle between line ME-right AG and line right AG-CR
AGl/ME/AGr	Angle between line ME-left AG and line ME-right AG
Jl/Jr/Ll	Angle between the line J left- J right and line J left-L left
Jl/Jr/Lr	Angle between the line J left- J right and line J right-L right
AGl/AGr/Ll	Angle between the line AG left- AG right and line AG left-L left
AGl/AGr/Lr	Angle between the line AG left- AG right and line AG right-L right
AGl-AGr/Ll-Lr	Angle between the line AG left-AG right and line left L-right L
Ll/CR/Lr	Angle between the line left L-CR and line right L-CR

5.2.4 Statistical analysis

For both the conventional frontal cephalometric radiographs and the CBCT-constructed frontal cephalometric radiographs, the same operator (OV) marked the landmarks on all 80 images five times, each time with a time interval of 1 wk. The mean value and standard deviation of these five measurements were used for the statistical analysis. The intra-observer reliability was calculated by means of the Pearson correlation coefficient for the first and second measurements. For each measurement, the standard error was calculated and compared with the standard error of the same measurement in the other group. Paired t-tests were performed to compare the means of corresponding. measurements on the two cephalometric radiographs of the same skull.

5.3 Results

Intra-observer reliability for both the conventional frontal cephalometric radiographs and the CBCT constructed 3D model was acceptable for most measurements. The correlation coefficient between the first and second measurements ranged from 0.23 to 0.99 (average = 0.71) for the conventional frontal radiographs and from 0.42 to 0.93 (average = 0.79) for the 3D models (see Table 5.3).

Table 5.3 *Intra-observer reliability expressed as Pearson's Correlation coefficient for first and second measurements and duplicate measurement error for 40 cases with 95 % confidence interval (CI). P-value relates to the test for statistically significant difference between the two methods.*

	Conventional			**3D model**			
		Duplicate measurement error			Duplicate measurement error		***P-value for error***
	Reliability	**Error**	**95% CI**	**Reliability**	**Error**	**95% CI**	
R CR–L:	0.23	0.02	0.02 – 0.02	0.88	0.02	0.01 – 0.20	0.021
R J–ANS:	0.49	0.04	0.04 – 0.04	0.62	0.03	0.03 – 0.04	0.009
R ME–AG:	0.84	0.03	0.03 – 0.04	0.42	0.03	0.03 – 0.03	0.105
AGl/AGr/Ll-Lr (°)	0.67	0.95	0.84 – 1.05	0.44	0.94	0.83 – 1.04	0.439
AGl/AGr/Ll (°)	0.96	0.72	0.64 – 0.80	0.81	0.63	0.56 – 0.70	0.052
AGl/AGr/Lr (°)	0.89	0.72	0.64 – 0.80	0.82	0.72	0.64 – 0.80	0.489
AGl/ME/AGr: (°)	0.99	1.20	1.06 – 1.33	0.92	1.16	1.03 – 1.28	0.333
Jl/Jr/LL (°)	0.51	2.28	2.03 – 2.54	0.89	1.09	0.96 – 1.21	<0.001
Jl/Jr/Lr (°)	0.64	2.20	1.95 – 2.44	0.87	0.92	0.82 – 1.02	<0.001
Ll/CR/Lr (°)	0.34	4.18	3.71 – 4.64	0.93	1.22	1.09 – 1.36	<0.001
ME/AGl/CR (°)	0.99	0.89	0.79 – 0.99	0.93	0.76	0.67 – 0.84	0.032
ME/AGr/CR (°)	0.99	0.66	0.59 – 0.73	0.91	0.88	0.78 – 0.98	<0.001

The duplicate measurement error for the CBCT constructed 3D model was significantly smaller for six measurements (R CR-L, R J-ANS, Jl/Jr/Ll, Jl/Jr/Lr, Ll-CR-Lr, ME/AGl/CR; see Table 5.2 for definitions of these anatomical variables) compared with the standard error of the conventional frontal cephalometric radiographs. For the conventional frontal radiographs this was the case for one measurement (ME/AGr/CR). For five measurements there were no statistically significant differences between both types of radiographs (AGl-AGr/Ll-Lr, R CR-L, R ME-AG, AGl/AGr/Ll, AGl/AGr/Lr, Gonial Angle l; see Table 5.2 for definitions of these anatomical variables). The reproducibility of the measurements on the CBCT-constructed 3D model was therefore higher than the reproducibility of the measurements on conventional frontal radiographs.

There was a statistically significant difference between the conventional frontal cephalometric radiographs and the CBCT-constructed 3D model for 11 out of 12 measurements (Table 5.4). For the measurement AGl/AGr/Ll, no statistically significant difference was found. Although the average difference for those measurements between the two methods was clearly statistically significant (all P values < 0.01), for most of them the actual mean average difference for repeated measurements ranged from 0.02 to 0.12 for the ratios. For the angles these average differences ranged from 0.15° to 39.66°.

Table 5.4 *The mean difference between corresponding measurements taken on conventional frontal radiographs and CBCT-constructed 3D models with 95 % confidence interval (CI), corresponding P-value and reliability expressed as Pearson's Correlation coefficient.*

	Difference Conv–CBCT	**95% CI**	**P-value**	**Reliability**
R CR–L:	0.02	0.00 – 0.03	0.010	-0.150
R J–ANS:	-0.03	-0.05 – -0.01	0.002	-0.302
R ME–AG:	0.12	0.10 – 0.14	<0.0001	-0.234
AGl/AGr/Ll-Lr (°)	-0.93	-1.37 – -0.49	<0.0001	0.273
AGl/AGr/Ll (°)	2.03	1.55 – 2.50	0.533	0.789
AGl/AGr/Lr (°)	0.15	-0.34 – 0.64	0.0001	0.683
AGl/ME/AGr: (°)	39.66	34.71 –44.61	<0.0001	-0.130
Jl/Jr/LL (°)	-1.73	-2.47 – -0.98	<0.0001	0.549
Jl/Jr/Lr (°)	1.30	0.65 – 1.94	<0.0002	0.655
Ll/CR/Lr (°)	33.04	31.03 –35.04	<0.0001	0.174
ME/AGl/CR (°)	16.34	14.40 –18.28	<0.0001	0.716
ME/AGr/CR (°)	11.76	10.49 –13.02	<0.0001	0.820

5.4 Discussion

In this study, twelve widely used cephalometric measurements on conventional frontal radiographs and CBCT-constructed 3D models of dry human skulls were compared. We used dry skulls because it is not considered to be ethical to expose patients twice to radiation from both a conventional radiograph and a CBCT. In this way, we obtained two images that were completely comparable. The largest error in cephalometric studies is the error in landmark identification[13] and each landmark exhibits a characteristic pattern of error that contributes to measurement inaccuracy[14]. Images from dry skulls do not suffer from distortion caused by soft tissues. This reduces the chance of errors in landmark identification because it makes accurate localization of bony landmarks easier. Testing the reliability of soft tissue measurements is, of course, not possible.

In a previous study our group showed that the position of the patient in frontal radiology plays an important role in the outcome of a cephalometric analysis because the measurements are influenced by tilt or rotations of the head[11]. The position of the patient in a CBCT scanner is, for 3D angular measurements, not that important because rotation along the long axis or the sagittal axis is not of any influence on angles measured. In this study each skull was only placed in the cephalostat once and the same image was traced five times. This approach was chosen because the biggest error in cephalometric studies is the error in landmark identification[13] and we wanted to eliminate other factors that could influence the identification of landmarks. In a clinical situation the repeated positioning of the patient in a cephalostat or a CBCT scanner is probably more variable than the single positioning of a skull in a study design. This may have resulted in an underestimation of the error. Further research must show whether this is of significant influence.

For all measurements, except one (AGl/AGr/Ll), statistically significant differences were found between the conventional frontal cephalometric radiographs compared with CBCT-constructed 3D models. For four of these measurements (AGl/ME/AGr, Ll/CR/Lr, ME/AGl/CR, ME/AGr/CR) these differences ranged from 11.76° to 39.66° and are well beyond any reasonable clinically acceptable range, as described by Hajeer et al.[15]. The question arises: What caused these large differences? This is most obvious in the AGl/ME/AGr angle and can best be explained if we take a closer look at this angle. In 2D the landmarks needed to measure this angle are all in one tomographic plane and the angle measured is around 120°. In 3D these three landmarks are in different tomographic planes and therefore the angle measured is completely different, on average around 80°. This angle clearly shows that comparing 2D and 3D cephalometric measurements should be performed with great caution and one should be very careful when interpreting the results. Comparable results were found in a similar study when comparing 2D lateral radiographs with 3D models. Nevertheless, the mean differences for the AP radiographs were much larger than for lateral radiographs. The reason for this is that landmarks for AP cephalometry are located in more different tomographic planes compared with those for lateral cephalometry.

In this study, all measurements were performed by one observer. The question remains whether this observer made a systematic error. The standard errors in Table 5.3 are acceptable. Systematic errors in the identification of landmarks are the same for both types of radiographs and therefore do not have any influence on reproducibility. It is therefore justified to have one observer for this type of study.

Five repetitions of the measurements were undertaken to allow estimation of the variability of each landmark for each skull. That is where the number of repetitions of the measurements pays off. For determining the intra-observer reliability, however, per definition only two measurements are needed. Statistically there is no reason to suspect a different intra-observer reliability between the first and second measurement series compared with, for example, the second and third or the third and fourth measurement series. Therefore, it does not give relevant additional information. This is why we choose to mention only the reliability of the first two series of measurements in our results. The mean value of all five repeated measurements and their variance, however, was used for further statistical analysis.

In general, orthodontists and maxillofacial surgeons are experienced in the use and interpretation of conventional frontal cephalometric radiographs (Figure 1A). However, tracing a 3D model (Figure 1B) is very different and landmarks have to be well defined in all three dimensions.

Conventional cephalometry is a 2D representation of a 3D structure. This has certain disadvantages. Now that it is possible to make a 3D model of the skull, it is also possible to perform a 3D cephalometric analysis[12,16]. In such an analysis, the actual anatomical structures can be identified more realistically than in a 2D projection. In 2D anterior posterior radiology, positioning of the patient can result in major difficulties. As long as a 2D projection of 3D scans is used for analysis, positioning of the patient remains an important factor. If a 3D model is made and a 3D analysis is performed, it is likely that positioning of the patient has no effect on the measurements made during a 3D cephalometric analysis. Future research needs to confirm this hypothesis. Therefore, there is a need to further develop and test the measurements made in new 3D-cephalometric analyses.

It can be concluded that there is a clinically relevant difference between angular measurements performed on conventional frontal cephalometric radiographs, compared with measurements on CBCT-constructed 3D models. Tracings of 3D models are therefore not suitable for longitudinal research in cases where there are only 2D records from the past.

5.5 References

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Chapter 6

Measurements on 3D models of human skulls derived from two different cone beam CT scanners

O.J.C. van Vlijmen
F.A. Rangel
S.J. Bergé
E.M. Bronkhorst
A.G. Becking
A. M. Kuijpers-Jagtman

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Abstract

Purpose: The aims of this study were to compare measurements on three-dimensional (3D) models of human skulls derived from two different cone beam CT scanners (CBCT) and to evaluate if the used hardware can influence the performed measurements.

Materials and Methods: CBCT scans of 40 dry human skulls with both the I-Cat™ and the Iluma™ cone beam CT scanners were made. From the CBCT scans, 3D models were constructed. One operator identified 19 landmarks five times on both types of 3D models with a time interval of 1 week.

Results: Intra-observer reliability was high for most measurements. There was a statistically significant and clinically relevant difference for some measurements between constructed 3D models of the same skull from the two different CBCT devices.

Conclusions: Used hardware for scanning might influence the measurements performed. This means that care should be taken when interpreting measurements made on CBCT 3D models derived from different CBCT devices.

6.1 Introduction

In the last decade, we have seen a paradigm shift towards a three-dimensional (3D) approach for orthodontic and orthognathic analysis and treatment planning. Conventional records like facial photographs, plaster casts, or traditional frontal and lateral cephalometry, which have been in use since the 1930s[1,2], have been replaced by 3D photographs, digital dental casts and 3D cone beam CT (CBCT)[3-5]. Integration of these new 3D records eventually will lead to a virtual head of the patient, which can be used for case analysis and treatment planning in the virtual operating room[6].

CBCT technology has seen a huge increase of its applications, and the number of publications on this topic grows every week. CBCT has reduced radiation compared with a multislice CT scan[7,8] and therefore can be used for a wider range of patients. Nevertheless, a CBCT scan is still not suitable for the routine orthodontic patient[4]. However, for patients with craniofacial anomalies, orofacial clefts or orthognathic cases, the CBCT has many benefits.

Recently, it has been shown[9-13] that conventional lateral cephalometric radiographs, which may still be considered as the “gold standard”, can be compared with constructed lateral cephalometric radiographs from CBCT scans, and thus, the latter can be used for longitudinal research in cases where there are conventional radiographic records from the past. In a similar study on frontal radiographs, some differences between conventional and constructed images for CBCT scans were found[14]. These differences were caused by different positioning of the skulls in both X-ray devices. When constructing two-dimensional (2D) images from 3D data, the patient positioning is of utmost importance, but when performing sole 3D cephalometry, the positioning of the patient is of no importance. In two other studies from our group in which we investigated whether conventional radiographs could be compared with 3D models of human skulls, differences between both methods were found, showing that comparison of 2D and 3D records cannot be recommended[15,16].

Multiple studies have been done on comparison of conventional 2D with constructed 2D out of 3D cephalometry[9-13] or comparing 2D with 3D cephalometry[15,16], but at present, to our knowledge, there is no study concerning the comparison of 3D models from two different CBCT devices. At present, there are many CBCT devices on the market, all with their own possibilities and limitations. The aim of this study was to evaluate whether measurements on 3D models of human skulls derived from two different

CBCT scans are comparable and moreover if the choice of device used has an influence on the performed measurements.

6.2 Material en Methods

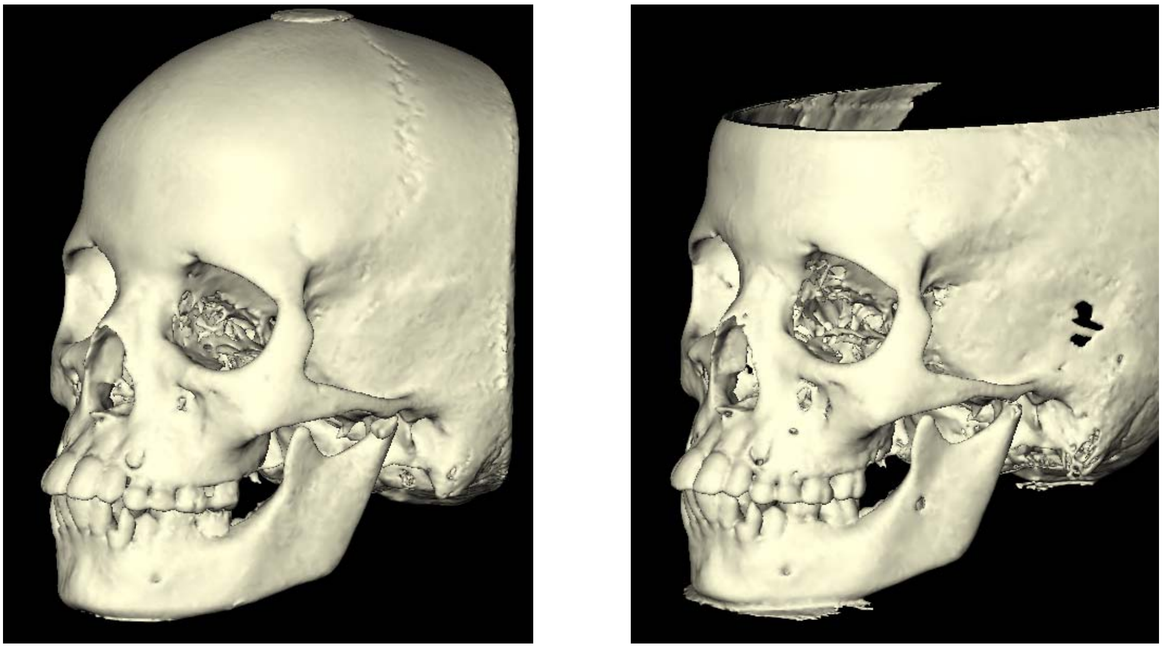
6.2.1 Materials

The sample consisted of 40 dry human skulls obtained from the collection of the Department of Orthodontics and Oral Biology of the Radboud University Nijmegen Medical Centre. The skulls were selected from a larger sample according to the following criteria: presence of permanent upper and lower incisors, presence of first permanent upper and lower molars and presence of a reproducible, stable occlusion. The mandible was related to the skull based on the position of the condyle in the fossa and maximum occlusal interdigitation. The mandibular position was fixed with broad tape from the ipsilateral temporal bone around the horizontal ramus of the mandible to the contralateral temporal bone.

6.2.2 Radiography

Each skull was positioned in the Iluma Cone Beam CT scanner (Imtech, Ardmore, OK, USA) and in the I-Cat CBCT scanner (Imaging Sciences International, Inc. Hatfield, PA, USA). The skulls were placed on a foam platform in the I-Cat and on a Perspex layer in the Iluma with the Frankfurt Horizontal plane parallel to the floor, in the centre of the CBCT scanner using the midline light beam to coincide with the midsagittal plane. A CBCT scan was taken of all skulls with both devices. The following settings were used; for the Iluma 120 kVp, 3.8 mA s, 20 s with a resolution of 0.3 voxel. For the I-Cat 129 kVp, 47.74 mA s, 40 s with a resolution of 0.4 mm/voxel.

Two 3D models of each skull were constructed (Figure 6.1A, B), one from the I-Cat CBCT data and one from the Iluma CBCT data. The 3D models were constructed with Maxilim® (Medicim, Sint-Niklaas, Belgium). This same software was used to analyse the constructed 3D models by identifying landmarks on the actual 3D reconstructed models.



A. ***B.***

Figure 6.1 *CBCT-constructed 3D models of the same skull. (A) Three-dimensional model from the I-Cat. (B) Three-dimensional model from the Iluma.*

6.2.3 Measurements

For the morphometric analysis, 19 hard tissue landmarks (Table 6.1) were identified on the 3D models. Fourteen widely used cephalometric variables (12 angles and two linear ratios) were calculated using Maxilim® (Table 6.2).

Table 6.1 Anatomical landmarks used in this study.

S	Sella	Centre of sella turcica
N	Nasion	Most anterior limit of the frontonasal suture on the frontal bone
A	A - point	Deepest bony point on the contour of the premaxilla below ANS
B	B - point	Deepest bony point of the contour of the mandible above pogonion
NSL	Nasion sella line	Line from point S to point N
NSP	Nasion sella plane (3D)	Plane constructed by projecting NSL on the medial plane
MP	Mandibular plane (3D)	Plane between left Gonion, right Gonion and Gnathion
NP	Palatal plane (3D)	Plane constructed by projecting the line through point ANS and PNS on the medial plane
ANS	Anterior Nasal Spine	The tip of the anterior nasal spine
PNS	Posterior Nasal Spine	The most posterior point at the sagittal plane on the bony hard palate
GN	Gnathion	Most anterior inferior point of the bony chin
ME	Menton	The most inferior point of the symphysis of the mandible, as seen on the lateral jaw projection
GOl	Gonion left	Most posterior inferior point of the angle of the mandible on left side
GOr	Gonion right	Most posterior inferior point of the angle of the mandible on right side
BOP	Bisected occlusal plane (3D)	Plane connecting the vertical midpoint between Is and Li and the mesial contact between the first molars on left side and first molar on the right side
AGl	Antegonion left	The antoganial notch at the lateral inferior margin of the antegonial protuberances on left side.
AGr	Antegonion right	The antoganial notch at the lateral inferior margin of the antegonial protuberances on right side.
Is	Incision Superius	The incisal tip of the most anterior upper incisor
Ii	Incision Inferius	Incisal point of the most prominent medial mandibular incisor
Ll	Lateral orbital margin left	The most lateral point of the orbital cavity on the left side.
Lr	Lateral orbital margin right	The most lateral point of the orbital cavity on the right side.
CR	Crista Galli	Most superior point at its intersection with the sphenoid

Table 6.2 Cephalometric variables.

SNA	Angle between line SN and line NA
SNB	Angle between line SN and line NB
NSL / NL	Angle between line SN and line ANS-PNS
NSL / ML	Angle between line SN and line GnGo
NL / ML	Angle between line ANS to PNS and the line from GN to GO
NSL / BOP	Angle between the line from S to N and the occlusal plane
R CR -L	Ratio between line CR-L left and line CR-L right
R ME -AG	Ratio between line ME-AG left and line ME-AG right
Me/AGl/CR	Angle between line ME-left AG and line left AG-CR
Me/AGr/CR	Angle between line ME-right AG and line right AG-CR
AGr/AGl/Ll	Angle between the line AG left- AG right and line AG left-L left
AGl/AGr/Lr	Angle between the line AG left- AG right and line AG right-L right
AGl/ME/AGR	Angle between line ME-left AG and line ME-right AG
Ll/CR/Lr	Angle between the line left L-CR and line right L-CR

6.2.4 Statistical analysis

For both the 3D models derived from the Iluma CBCT scanner and from the I-Cat CBCT scanner, the same operator (OV) marked the landmarks on all 80 3D models five times, each time with a time interval of 1 week. The intra-observer reliability was calculated by means of the Pearson correlation coefficient for the first and second measurement. The mean value and standard deviation of the five measurements performed were used for the statistical analysis. For each measurement, the duplicate measurement error was calculated and compared with the duplicate measurement error of the same measurement for the other device. Because the standard deviations of the measurement errors were skewed, nonparametric statistics were performed. Wilcoxon signed ranks tests were performed to compare the means of corresponding measurements on the two 3D models of the same skull.

6.3 Results

Intra-observer reliability, expressed as Pearson correlation coefficient, for the first and second measurements ranged between 0.42 and 0.98 with an average of 0.89 for the I-Cat measurements and between 0.43 and 0.99 with an average of 0.91 for the Iluma measurements (see Table 6.3). The duplicate measurement error for the I-Cat CBCT-constructed 3D models was significantly smaller for two measurements (NSL/NL, Ll-CR-Lr) as compared with the standard error of the measurements on the Iluma CBCT-constructed 3D models (see Table 6.3). The duplicate measurement error for the Iluma CBCT-constructed 3D models was significantly smaller for five measurements (SNB, R CR-L, NL/ML, NSL/BOP and AGl/AGr/Lr) as compared with the standard error of the measurements on the I-Cat CBCT-constructed 3D models. For seven measurements, there were no statistical significant differences regarding the measurement error between both types of radiographs (SNA, R ME-AG, NSL/NL, AGr/AGl/Ll, AGl/ME/AGr, ME/AGl/CR and ME/AGr/CR). Reproducibility of the measurements on the Iluma CBCT-constructed 3D models was therefore higher compared with the reproducibility of the I-Cat CBCT-constructed 3D models.

Table 6.3 *Intra-observer reliability expressed as Pearson's Correlation coefficient for first and second measurements and mean duplicate measurement error for repeated measurements of 40 cases with their corresponding P-value according to Wilcoxon signed ranks test.*

	Reliability		**Duplicate Measurement Error**		
	I-Cat	**Iluma**	**I-Cat**	**Iluma**	***P-values***
SNA (°)	0.87	0.92	1.10	0.89	0.068
SNB (°)	0.84	0.94	1.05	0.64	0.014
R CR – L	0.88	0.93	2.27	1.26	0.003
R ME – AG	0.42	0.43	8.33	15.81	0.259
NL / ML (°)	0.98	0.99	0.66	0.40	0.001
NSL / BOP (°)	0.92	0.90	2.39	1.45	0.008
NSL / ML (°)	0.87	0.86	1.26	1.37	0.010
NSL / NL (°)	0.82	0.92	1.19	0.82	0.056
AGr/AGl/Ll (°)	0.81	0.94	0.39	0.24	0.265
AGl/AGr/Lr (°)	0.82	0.87	0.51	0.35	0.004
AGl/ME/AGR (°)	0.92	0.83	1.33	2.68	0.056
Ll/CR/Lr (°)	0.93	0.93	1.50	2.90	0.001
ME/AGl/CR (°)	0.93	0.89	0.57	0.87	0.648
ME/AGr/CR (°)	0.91	0.90	0.77	1.09	0.872

A statistically significant difference was found between the I-Cat CBCT-constructed 3D models and the Iluma CBCT-constructed 3D models for eight out of 14 measurements (Table 6.4). Though the differences for these eight measurements (SNA, R Cr-L, R ME-AG, NL/ML, NSL/ML, NSL/NL, AGr/AGl/Ll and AGl/AGr/Lr) between the two devices was clearly statistically significant (all P values <0.05); for most of them, the actual mean average difference for repeated measurements was small, ranging from 0.27° to 0.95°. For the angles NL/ML and NSL/ML, the difference between both methods was more substantial, with values of 2.56° and 3.21°, respectively.
For the ratios, the average differences were statistically significant and ranged from 1.46% to 1.84%. For six measurements (SNB, NSL/BOP, AGl/Me/AGr, Ll/CR/Lr, Me/AGl/CR and Me/AGr/CR), no statistically significant differences were found.

Table 6.4 *The mean difference between corresponding measurements taken on the I-Cat 3D model and on the Iluma 3D model with 95 % confidence interval, corresponding P-value and reliability, expressed as Pearson's Correlation coefficient.*

	Difference I-Cat – Iluma	**95% CI**	**P-value**	**Reliability**
SNA (°)	0.60	0.19 – 1.02	0.005	0.922
SNB (°)	0.32	-0.28 – 0.92	0.287	0.789
R CR – L	1.46	0.89 – 2.04	<0.001	0.867
R ME – AG	-1.84	-2.92 – -0.76	0.001	0.565
NL / ML (°)	-2.56	-2.94 – -2.08	<0.001	0.959
NSL / BOP (°)	0.17	-0.75 – -1.09	0.714	0.776
NSL / ML (°)	-3.21	-3.72 – -2.70	<0.001	0.909
NSL / NL (°)	-0.65	-1.27 – -0.20	0.044	0.781
AGr/AGl/Ll (°)	-0.27	-0.46 – -0.08	0.007	0.945
AGl/AGr/Lr (°)	-0.95	-1.16 – -0.73	<0.001	0.927
AGl/ME/AGR (°)	0.59	-0.19 – 1.37	0.136	0.816
Ll/CR/Lr (°)	-0.97	-2.53 – 0.59	0.216	0.592
ME/AGl/CR (°)	0.29	-0.14 – 0.73	0.180	0.929
ME/AGr/CR (°)	-0.12	-0.56 – 0.31	0.571	0.935

6.4 Discussion

In this study, 14 widely used cephalometric measurements on CBCT-constructed 3D models of dry human skulls derived from two different CBCT devices were compared. Dry skulls were used since it is not considered to be ethical to expose patients twice to radiation. In this way, two models were obtained that were utterly comparable.

The largest error in 2D and 3D cephalometric studies is the error in landmark identification[17,18], and each landmark exhibits a characteristic pattern of error that contributes to measurement inaccuracy[19,20]. Images from dry skulls are not affected by any distortion caused by soft tissues. This reduces the chance of errors in landmark identification because it makes an accurate localisation of bony landmarks easier. On the other hand, testing the reliability of the real clinical setting, i.e. soft tissue measurements, is not possible.

In this study, all measurements were performed by one observer. The question remains whether this observer made a systematic error. The duplicate measurement errors in Table 3 are acceptable. Since the stability of the new 3D measurements and comparison between two CBCT devices is the focus of the article, using a consensus approach would be favourable if a comparison with a gold standard was to be made. But, such a gold standard is not available. Furthermore, possible systematic errors in the identification of landmarks would be the same for both types of 3D models and therefore would not have any influence on the reproducibility. Averaging/combining the measurements of more observers would lead to underestimation of the true variability of the measurements. It is therefore justified to have one observer for this type of study.

In a previous study, it was shown that the position of the skull in frontal radiology, where a 2D image is obtained from a 3D data set, plays an important role in the outcome of a cephalometric analysis since the measurements are influenced by tilt or rotations[14]. The position of the patient in a CBCT scanner for 3D measurements is not that important since rotation along the long axis or the sagittal axis is not of any influence on angles or distances measured. In this study, each skull was placed in both CBCT scanners once, and from both data sets, a 3D model was constructed. Both 3D models were analysed five times. This approach was chosen because the biggest error in cephalometric studies is the error in landmark identification[17], and we wanted to eliminate other factors that could influence the identification of landmarks. In a clinical situation, the repeated positioning of the patient in a CBCT scanner is probably more variable than the single positioning of a skull in a study protocol. Nevertheless, positioning of the patient is of little to no importance when working in 3D only.

There was a difference in resolution between both CBCT scanners: a voxel size of 0.3 mm for the Iluma and voxel size of 0.4 mm for the I-Cat. At the time this investigation was performed, the extended height scans used in this study had a pre-set voxel size by the CBCT scanner, which could not be altered. Therefore, the difference in voxel size for both scans could not be avoided. The difference between both scanners is 0.1 mm per voxel; therefore, it is highly unlikely that this has any influence on the measurements performed and no clinical significance is to be expected.

Five repetitions of the measurements were undertaken to allow estimation of the variability of each landmark for each skull. That is where the amount of repetitions of measurements pays off. For determining the intra-observer reliability, however, per definition only two measurements are needed. Statistically, there is no reason to suspect a different intra-observer reliability between first and second measurement series compared with, e.g. the second and third, or third and fourth. Therefore, additional intra-observer reliabilities do not give any relevant additional information. This is why only the reliability of the first two series of measurements is mentioned in our results. The mean value of all five repeated measurements, however, was used for further statistical analysis.

Because the measurement errors were skewed, the measurement error is influenced by outliers, making the mean measurement error less suited for comparisons between methods. Therefore, the Wilcoxon signed ranks tests were used to compare the measurement error between the two methods.

For eight out of 14 measurements (Table 6.4), statistically significant differences between the I-Cat and the Iluma CBCT-constructed 3D models were found. For five of these measurements, these differences were smaller than or similar to the standard error for these measurements and therefore of no clinical significance. For AGl/AGr/Lr (degrees), the difference was with 0.95° larger than the standard error, but still within clinical acceptable range. For the measurements NL/ML and NSL/ML, the differences were respectively 2.56° and 3.21°, which are larger than the standard error of these measurements and in our opinion beyond a reasonable clinical acceptable range.

The question of what might have caused these differences arises. Maybe one or several landmarks used to calculate these variables were differently placed in both types of 3D models. Since other measurements for which the same landmarks are used do not display any differences between both types of 3D models, the difference for NL/ML and NSL/ML must be caused by the Gonion landmark. A possible explanation for this is that while making a 3D reconstruction (Figure 1A, B) a part of the angulus mandibulae is reconstructed differently. During the acquisition of the scan, voxels are awarded different Hounsfield units (HU). When a 3D model is constructed, these HU values are used to differentiate between hard tissues, soft tissues and air. During the acquisition, a voxel can only be awarded one HU value. Due to the size of the voxels, it often happens that not all space in the voxel is filled with the same tissue. For instance, when an image is acquired, only 75% of the voxel is filled with bone and the other 25% is filled with air or soft tissue. Since the voxel can only have one value, the value is awarded to the tissue which is most present in the voxel. So, the area where there is no bone can be seen as bone in the constructed 3D model since the voxel has the HU value of bone. If the skulls were positioned exactly the same in both CBCT devices, this would not be a problem since these mistakes would be made in both scans. However, since the positioning of the skulls will not be exactly the same for both devices, in the 3D constructed models, small differences can appear between the I-Cat model and the Iluma model. This can result in minor differences in the positioning of Gonion, which leads to another orientation of the mandibular plane and therefore different measurements. Thus, different HU values necessary for reconstruction of different types of CBCT 3D models can cause differences in the 3D models.

6.5 Conclusion

There are statistical significant differences between some angular measurements performed on I-Cat CBCT constructed 3D models compared with Iluma-constructed 3D models. Two of these measurements had a clinically relevant difference. This means that care should be taken when interpreting measurements made on CBCT 3D models derived from different CBCT devices.

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Chapter 7

Evidence supporting the use of cone-beam computed tomography in orthodontics

O.J.C. van Vlijmen
M.A.R. Kuijpers
S.J. Bergé
J.G.J.H. Schols
T.J.J. Maal
K.H. Breuning
A. M. Kuijpers-Jagtman

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Abstract

Background: The authors conducted a systematic review of cone beam computed tomography (CBCT) applications in orthodontics and evaluated the level of evidence to determine whether the use of CBCT is justified in orthodontics.

Types of Studies Reviewed: The authors identified articles by searching the Cochrane Library, PubMed, MEDLINE, Embase, Scopus and Cumulative Index to Nursing and Allied Health Literature databases. They searched the articles' reference lists manually for additional articles and had no language limitations. They did not search the gray literature. Inclusion criteria were CBCT use in orthodontics and that the participants be human. The lowest level of evidence accepted for inclusion was a case series with five or more participants. The authors evaluated the studies' methodological quality according to 13 criteria related to study design, measurements and statistical analysis.

Results: The authors identified 550 articles, and 50 met the inclusion criteria. Study topics included temporary anchorage devices, cephalometry, combined orthodontic and surgical treatment, airway measurements, root resorption and tooth impactions, and cleft lip and palate. The methodological quality averaged 53 percent (range, 15-77 percent) of the maximum score.

Clinical Implications: The authors found no high-quality evidence regarding the benefits of CBCT use in orthodontics. Limited evidence shows that CBCT offers better diagnostic potential, leads to better treatment planning or results in better treatment outcome than do conventional imaging modalities. Only the results of studies on airway diagnostics provided sound scientific data suggesting that CBCT use has added value. The additional radiation exposure should be weighed against possible benefits of CBCT, which have not been supported in the literature. In future studies, investigators should evaluate the effects of CBCT on treatment procedures, progression and outcome quantitatively.

7.1 Introduction

In the last two decades, two-dimensional (2D) images, such as facial photographs or traditional frontal and lateral cephalometric radiographs, which have been used since the 1930s[1,2], have been replaced in part by three-dimensional (3D) photographs and 3D cone beam computed tomography (CBCT) scan images[3-5]. The number of articles regarding CBCT applications has increased since its introduction into orthodontics. We have noticed that the available literature regarding CBCT in databases such as PubMed grows weekly. This increase may have been fueled in part by misinformation regarding its safety and efficacy. CBCT is an image acquisition technique that uses a cone shaped x-ray beam. Similar to an orthopantogram, the x-ray beam is aimed at a detector. A pair of source-detector devices rotates around the patient to produce a series of 2D images. These images are reconstructed on a computer to form a 3D data set. Dedicated CBCT scanners for the oral and maxillofacial region were pioneered in the late 1990s[6]. Interest in this imaging technique for use in the oral and maxillofacial region has increased.

Investigators of previous studies that applied CBCT and authors of narrative reviews that discussed the possibilities and limitations of CBCT[7-9] have described the potential for the use of CBCT in orthodontics. For example, CBCT can help in determining the best temporary anchorage device (TAD) location, in the planning for and outcomes evaluation of combined orthodontic and surgical treatment, and in the diagnosing of and treatment planning for complex cases such as those involving cleft lip and palate (CLP). CBCT also can provide 3D cephalometry, 3D evaluations of the temporo-mandibular joint and 3D information regarding the locations of impacted teeth. Manufacturers of CBCT devices have advertised the benefits of using 3D technology, but these claims have not been supported adequately. To our knowledge, no investigators have conducted a systematic review whose results support the use of CBCT in orthodontics. We conducted a systematic review to assess the use of CBCT in orthodontics and to determine what level of evidence is available to support the use of CBCT in orthodontic diagnosis and treatment planning.

7.2 Methods

7.2.1 Information sources

To identify publications, we conducted an electronic database search. We searched the reference lists of articles manually for additional literature. We set no language limitations, and we did not attempt to explore the gray literature.

We searched the following databases:

- PubMed (from Jan. 1, 1966, to March 15, 2010);
- MEDLINE (from Jan. 1, 1966, to March 15,2010);
- Embase Excerpta Medica (from Jan. 1, 1980, to March 15, 2010);
- Scopus (from Jan. 1, 1996, to March 15, 2010);
- Cumulative Index to Nursing and Allied Health Literature (CINAHL) (from Jan. 1, 1982, to March 15, 2010);
- Cochrane Library (from Jan. 1, 1993, to March 15, 2010).

7.2.2 Search strategy

We developed the search strategy and selected the databases with the help of a senior librarian who specialized in health sciences.

The search strategy focused on the terms “Cone Beam CT” and “Orthodontics.” We used both free text words in the title and abstract (TIAB) and Medical Subject Headings (MeSH) terms. For PubMed and the Cochrane Library, the following search sequence we selected was “Orthodontics”[MeSH] OR “Orthodontic*” AND “Cone-Beam Computed Tomography”[MeSH] OR “cone beam” OR “computed tomography”[TIAB] OR “volume ct”[TIAB] OR “cbct”[TIAB] OR “volumetric ct”[TIAB].

For MEDLINE, the search sequence we selected was “Orthodontics” or Orthodontic* and “Cone-Beam Computed Tomography” or “cone beam” or “computed tomography” or “volume ct” or “cbct” or “volumetric ct.”

For Embase, the search sequence we selected was “Orthodontics” or Orthodontic* and “Cone-Beam Computed Tomography” or “cone beam” or “computed tomography” or “volume ct” or “cbct” or “volumetric ct.”

For Scopus, the search sequence we selected was “Cone Beam” and “orthodontics.”

For CINAHL, the search sequence we selected was “Orthodontics” or “Orthodontic” or “Orthodontics+”[MeSH heading (mh)] And “Computed Tomography” or “Tomography, X-Ray Computed+”[mh] or “volume ct” or "cbct" or "volumetric ct" or "Cone-Beam Computed Tomography" or "cone beam" or "computed tomography."

7.2.3 Study selection

In the first step of the screening process, two observers (O.J.C.V.,A.M.K.-J.) independently screened the retrieved records on the basis of TIAB. They included articles that involved a study regarding CBCT requested for orthodontic purposes and articles that involved human participants. The lowest level of evidence accepted for inclusion was a case series with a sample size of five or more. They excluded reviews, letters and case reports from the study. They classified articles as included, excluded or unclear after reviewing only the abstract. The observers resolved any differences regarding which articles to include or exclude by achieving consensus. In the second step of the screening process, they obtained the full articles for those articles classified as included or unclear because the title or abstract did not present enough relevant information. Any articles that might have been of interest for our review underwent the first and second steps of the screening.

7.2.4 Grading of methodological quality

The observers (O.J.C.V., M.A.R.K.) independently assessed the methodological quality of the selected articles according to a scoring system developed by Lagravere and colleagues[10] and later adapted by Gordon and colleagues[11]. This system for scoring the methodology of clinical trials is based on 15 criteria addressing study design, performed measurements and statistical analysis. We adapted the scoring system by removing two criteria to make it suitable for our systematic review and scored using the remaining 13 criteria (Box 7.1). For each study, we reported the quality scores by criterion and averaged the scores as percentages. We rated mean quality (mQ) as follows: mQ < 60 percent = poor quality; 60 percent ≤ mQ ≤ 70 percent = moderate quality; mQ > 70 percent = good quality.

Box 7.1 Methodological scoring. √: Fulfills satisfactorily the methodological criteria. O: does not fulfill the methodological criteria. NA: not applicable.

I. Study Design (total = 6; response: √, o)
A. Objective — objective clearly formulated
B. Sample size — considered adequate
C. Sample size — estimated before collection of data
D. Selection criteria — clearly described
E. Baseline characteristics — similar baseline characteristics
F. Randomization — stated
II. Study measurements (total = 3; response: √, o, NA)
G. Measurement method — appropriate to the objective
H. Masked measurement method — masking
I. Reliability — adequate level of agreement
III. Statistical analysis (total = 4; response: √, o, NA)
J. Statistical analysis — appropriate for data
K. Confounders — confounders included in analysis
L. Statistical significance level — P value stated
M. Confidence intervals provided

7.3 Results

A Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram[12] provides an overview of the article selection process (Figure 7.1). The database search revealed 364 articles listed in PubMed, 179 articles listed in MEDLINE, 83 articles listed in Scopus, 60 articles listed in Embase, and 95 articles listed in CINAHL. We found no studies listed in the Cochrane Library. Our manual search of the articles' reference lists revealed five additional articles of interest. After the observers excluded 236 duplicate articles, they reviewed the remaining 550 articles. They excluded 456 of these articles because they did not meet the inclusion criteria. The observers reviewed the full text of 94 articles in the second step of the screening process. They then excluded 44 articles because they did not meet the inclusion criteria. Common reasons for exclusion were that the study involved the use of a multislice computed tomographic (CT) scanner, did not involve human participants, had an inadequate sample size or was a review article.

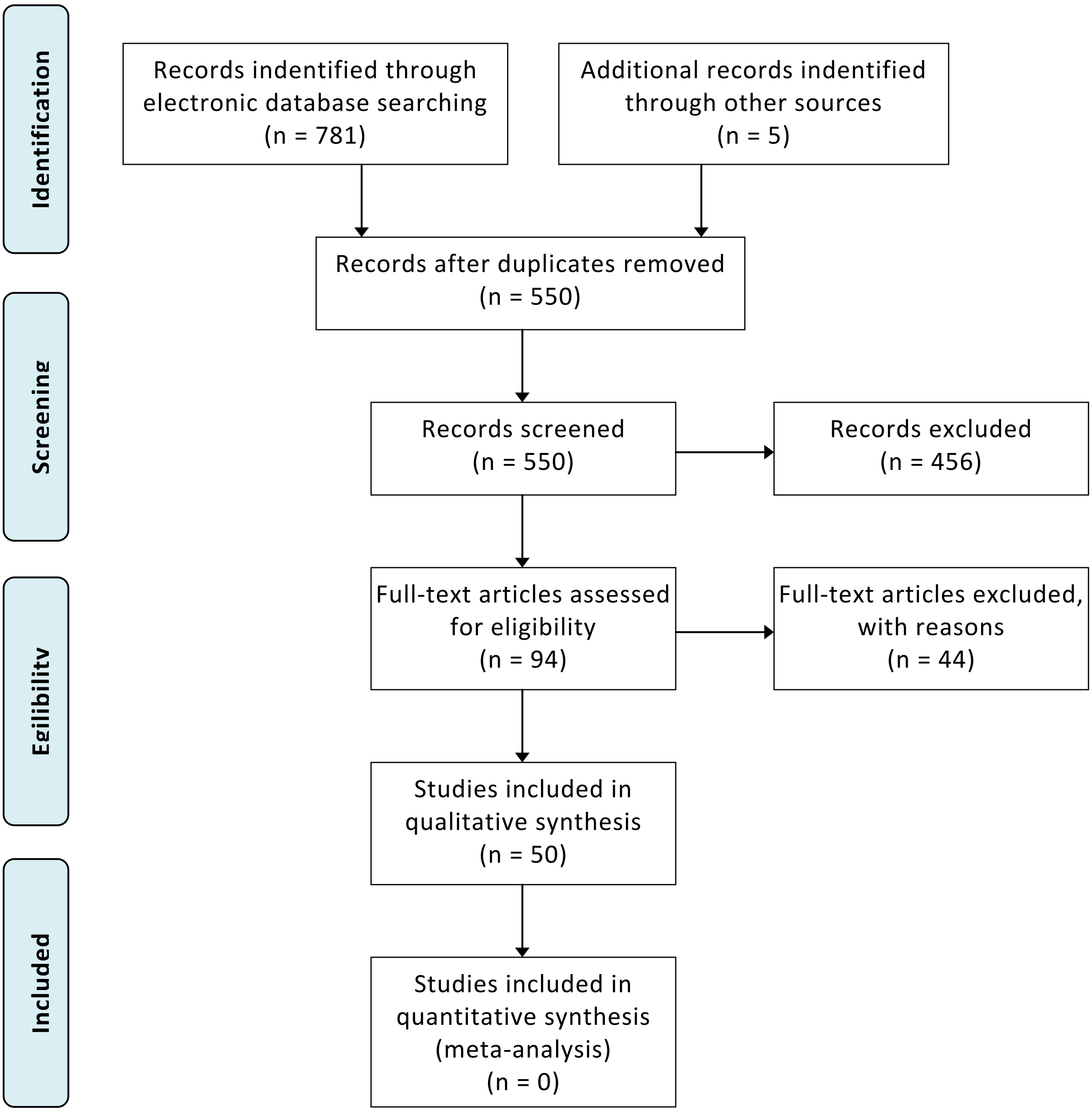

Figure 7.1 *PRISMA Flow Diagram.*

Our selection process resulted in 50 fulltext articles. We categorized these 50 studies by study topic as follows: 13 studies regarding placement of TADs, 10 studies regarding cephalometry, six studies regarding combined orthodontic-surgical treatment, five studies regarding airway measurements, six studies regarding root resorption and tooth positioning, three studies regarding CLP and seven studies regarding various other subjects. The observers evaluated the 50 articles by conducting methodological quality assessments. The assessment scores ranged from 15 to 77 percent of the maximum score (13) (average, 53 percent). We categorized the score for each study according to study type.

In the 13 studies regarding TADs, investigators used CBCT to assess interradicular space, cortical bone thickness and palatal bone thickness to determine the best location for TAD placement (Table 7.1)[13-25]. The methodological quality scores ranged from 33 to 77 percent (average, 58 percent).

Table 7.1 Methodological quality scores for studies on TADs. √: Fulfilled satisfactorily the methodological criteria. O: Did not fulfill the methodological criteria. NA: Not applicable.

Authors	**Year**	**Methodological score**													**Total**
		Design						Measurements			Statistical analysis				
		A	**B**	**C**	**D**	**E**	**F**	**G**	**H**	**I**	**J**	**K**	**L**	**M**	
Poggio et al.	2006	√	√	o	o	o	o	√	o	√	√	NA	o	o	42%
Gracco et al.	2006	√	√	o	√	o	o	√	o	o	√	o	√	o	46%
King et al.	2006	√	√	o	√	√	o	√	o	o	√	√	√	√	69%
Palomo et al.	2007	√	√	o	o	√	o	√	o	NA	o	o	o	o	33%
Gracco et al.	2007	√	√	o	√	o	√	√	√	√	√	√	√	o	77%
King et al.	2007	√	√	o	√	√	o	√	o	√	√	√	√	√	77%
Ono et al.	2008	√	√	o	o	√	o	√	o	NA	√	o	√	o	50%
Gracco et al.	2008	√	√	o	√	o	o	√	o	o	√	√	√	o	54%
Kim et al.	2009	√	√	o	√	√	o	√	o	√	√	o	√	o	62%
Park et al.	2009	√	√	o	√	√	o	√	o	√	√	o	√	o	62%
Kim et al.	2009	√	√	o	√	√	o	√	o	√	√	√	√	o	69%
Kau et al.	2010	√	√	o	o	√	o	√	o	o	√	√	√	√	62%
Park et al.	2010	√	√	o	o	√	o	√	o	NA	√	o	√	o	50%

In the 10 studies regarding cephalometry, investigators analyzed the differences between CBCT and conventional cephalometry, head orientation, orientation of 3D images and the anthropometric analyses (Table 7.2) [26-35]. The methodological quality scores ranged from 15 to 77 percent (average, 52 percent).

Table 7.2 *Methodological quality scores for studies on cephalometry. √: Fulfilled satisfactorily the methodological criteria. O: Did not fulfill the methodological criteria. NA: Not applicable.*

Authors	**Year**	**Methodological score**													**Total**
		Design						Measurements			Statistical analysis				
		A	**B**	**C**	**D**	**E**	**F**	**G**	**H**	**I**	**J**	**K**	**L**	**M**	
Lagravére et al.	2005	√	√	o	o	o	o	o	o	√	o	o	o	o	23%
Lagravére et al.	2006	√	√	o	o	o	o	o	o	o	o	o	o	o	15%
Cataneo et al.	2008	√	√	o	√	o	o	√	√	√	√	√	√	o	69%
Kumar et al.	2008	√	√	o	o	√	o	√	o	√	√	o	√	o	54%
Ludlow et al.	2009	√	√	o	o	√	o	√	o	o	√	o	√	o	46%
Cevidanes et al.	2009	√	√	o	o	√	√	√	o	√	√	o	√	o	62%
Chien et al.	2009	√	√	o	√	o	√	√	√	√	√	o	√	√	77%
Gracco et al.	2009	√	√	o	√	√	o	√	o	o	√	o	√	o	54%
Swasty et al.	2009	√	√	o	√	√	o	√	o	√	o	√	√	o	62%
Grauer et al.	2010	√	√	o	√	o	o	√	o	o	√	√	√	o	54%

In the six studies regarding orthodontic surgical treatments, investigators described 3D CBCT evaluations of surgically assisted rapid maxillary expansion, voxel-based superimposition of pretreatment and posttreatment 3D models and condylar position after orthodontic surgical treatment (Table 7.3) [36-41]. The methodological quality scores ranged from 33 to 69 percent (average, 57 percent).

Table 7.3 *Methodological quality scores for studies on combined surgical treatment. √: Fulfilled satisfactorily the methodological criteria. O: Did not fulfill the methodological criteria. NA: Not applicable.*

Authors	**Year**	**Methodological score**													**Total**
		Design						Measurements			Statistical analysis				
		A	**B**	**C**	**D**	**E**	**F**	**G**	**H**	**I**	**J**	**K**	**L**	**M**	
Cevidanes et al.	2005	√	√	o	o	√	o	√	o	√	√	√	√	o	62%
Rungcharassaeng et al.	2007	√	√	o	√	√	o	√	o	√	√	√	√	o	69%
Cevidanes et al.	2007	√	√	o	o	√	o	√	o	o	√	o	√	o	46%
Garret et al.	2008	√	√	o	o	√	o	√	o	√	√	√	√	o	62%
Swennen et al.	2009	√	√	o	o	o	o	√	o	NA	√	o	o	o	33%
Kim et al.	2010	√	√	o	√	√	o	√	o	NA	√	√	√	o	67%

In the five studies regarding airway measurements, investigators focused on assessments of airway volume in three dimensions and comparisons between the airway area in two dimensions and the airway volume in three dimensions (Table 7.4)[42-46]. The methodological quality scores ranged from 42 to 69 percent (average, 55 percent).

Table 7.4 *Methodological quality scores for studies on airway. √: Fulfilled satisfactorily the methodological criteria. O: Did not fulfill the methodological criteria. NA: Not applicable.*

Authors	**Year**	**Methodological score**													**Total**
		Design						Measurements			Statistical analysis				
		A	**B**	**C**	**D**	**E**	**F**	**G**	**H**	**I**	**J**	**K**	**L**	**M**	
Aboudara et al.	2003	o	√	o	√	√	o	√	o	NA	√	o	o	o	42%
Grauer et al.	2009	√	√	o	√	o	o	√	o	o	√	√	√	√	62%
Tso et al.	2009	√	√	o	√	o	√	√	o	o	√	o	o	o	46%
Aboudara et al.	2009	√	√	o	√	√	o	√	o	√	√	√	√	o	69%
Kim et al.	2010	√	√	o	√	√	o	√	o	o	√	NA	√	o	58%

In the six studies regarding root resorption and tooth position before and during orthodontic treatment, investigators used CBCT to assess the location of unerupted teeth, impacted teeth, root resorption, proximity of adjacent teeth and alveolar width in the area of an impacted tooth (Table 7.5)[47-52]. In addition, investigators compared panoramic radiographs with CBCT images in the evaluation of root proximity and root resorption. The methodological quality scores ranged from 38 to 69 percent (average, 55 percent).

Table 7.5 *Methodological quality scores for studies on root resorption and tooth impaction √: Fulfilled satisfactorily the methodological criteria. O: Did not fulfill the methodological criteria. NA: Not applicable.*

Authors	**Year**	**Methodological score**													**Total**
		Design						Measurements			Statistical analysis				
		A	**B**	**C**	**D**	**E**	**F**	**G**	**H**	**I**	**J**	**K**	**L**	**M**	
Walker et al.	2005	√	√	o	o	√	o	√	o	NA	√	NA	o	o	45%
Liu et al.	2008	√	√	o	√	√	o	√	o	√	√	NA	√	o	67%
Zang and Kuang	2008	√	√	o	o	o	o	√	o	o	√	√	o	o	38%
Dudic et al.	2009	√	√	o	o	√	o	√	√	o	√	o	√	o	54%
Leuzinger et al.	2010	√	√	o	o	√	o	√	√	√	√	o	√	√	69%
Lund et al.	2010	√	√	o	o	√	o	√	o	√	√	o	√	o	54%

In the three studies regarding CLP, investigators used CBCT to assess 3D bone volume of the alveolus after bone grafting, morphology of the maxilla and displacement of the canine adjacent to the cleft (Table 7.6)[53–55]. The methodological quality scores ranged from 31 to 67 percent (average, 53 percent).

Table 7.6 *Methodological quality scores for studies on CLP. √: Fulfilled satisfactorily the methodological criteria. O: Did not fulfill the methodological criteria. NA: Not applicable.*

Authors	**Year**	**Methodological score**													**Total**
		Design						Measurements			Statistical analysis				
		A	**B**	**C**	**D**	**E**	**F**	**G**	**H**	**I**	**J**	**K**	**L**	**M**	
Hamada et al.	2005	√	√	o	o	√	o	√	o	o	o	o	o	o	31%
Schneiderman et al.	2009	√	√	o	√	√	o	√	o	NA	√	√	√	o	67%
Oberoi et al.	2010	√	√	o	o	√	o	√	o	o	√	√	√	√	62%

The investigators of the seven studies regarding various other subjects addressed incidental findings with CBCT, the quality of CBCT images, and the justification and indication for CBCT (Table 7.7, page 247)[56–62]. The methodological quality scores of these articles ranged from 23 to 69 percent (average, 46 percent).

Table 7.7 Methodological quality scores for studies on various subjects. √: Fulfilled satisfactorily the methodological criteria. O: Did not fulfill the methodological criteria. NA: Not applicable.

Authors	**Year**	**Methodological score**													**Total**
		Design						Measurements			Statistical analysis				
		A	**B**	**C**	**D**	**E**	**F**	**G**	**H**	**I**	**J**	**K**	**L**	**M**	
Holberg et al.	2005	√	√	o	√	o	o	√	o	√	√	√	√	√	69%
Korbmacher et al.	2007	√	√	o	√	√	o	√	o	√	√	√	√	o	69%
Cha et al.	2007	√	√	o	o	√	o	√	o	o	√	√	o	o	46%
Huntjens et al.	2008	√	√	o	o	o	o	√	o	o	√	o	o	o	31%
Maal et al.	2008	√	√	o	o	o	o	√	o	o	√	√	√	o	46%
Kim et al.	2009	√	√	o	o	o	o	√	o	o	√	√	o	o	38%
Kau et al.	2010	√	√	o	o	o	o	√	o	o	o	o	o	o	23%

7.4 Discussion

The use of CBCT is increasing[7], but clinical guidelines based on a solid scientific foundation are lacking. We conducted this systematic review to investigate the use of CBCT in orthodontics, as well as to evaluate the level of available evidence so we could provide a basis for when to use CBCT for orthodontic purposes.

As we were searching and selecting articles for this review, it often was unclear from the articles' abstracts whether multislice CT or CBCT was used. We expected this lack of clarity with older articles, as CBCT did not exist before the late 1990s. However, even in more recent articles, this distinction often was not clear in the abstract. This underlines the importance of providing well-written, structured abstracts for scientific publications.

The scoring system for methodological quality, developed by Lagravere and colleagues[10] and later adapted by Gordon and colleagues[11], has been used repeatedly in systematic reviews in orthodontics. In contrast with their studies, which included only clinical trials, we included case series with a sample size of five or more participants and studies with a higher level of evidence. We adapted the scoring system to reflect the change in inclusion criteria. We removed the criteria "prospective study design" and "dropouts included in statistical analysis" from the criteria list, since a prospective study design is not a fundamental quality criterion for the study types included in our review and a dropout analysis is not relevant for studies whose investigators assessed results at only one moment in time. We scored the included articles using the 13 criteria (Box 7.1). The quality score was expressed as an averaged percentage. Although we did not validate the quality as a percentage in this method of expression, we show detailed quality scores per criterion in Tables 7.1 through 7.7. Lagravere and colleagues[10] and Gordon and colleagues[11] reported on the effects of rapid maxillary expansion. They found an average score of 50 percent and 49 percent, respectively, for the quality of the articles they included in their studies. We found similar average scores of methodological quality for the studies we included in our review. The overall average methodological quality score in our review was 53 percent (range, 15 to 77 percent). In most articles, we obtained satisfactory scores for criteria A, B, G and J (Box 7.1). However, we almost never obtained satisfactory scores for criteria C, F and H, which are crucial for high quality studies. In addition to the overall limited quality of the articles included in our review, many studies lacked originality. Different research groups performed comparable studies on the same subject. Although a repetition of high-quality studies is justified, since different investigators can obtain different results, the repetition of studies of low methodological quality, even when findings are corroborated, does not lift the present knowledge to a higher level.

We divided the studies in our review into seven categories according to study topics. Investigators often discussed the advantages of and potential for CBCT in these articles, but little attention was given to the actual benefit of using CBCT for either the clinician or the patient when compared with the use of conventional 2D imaging.

For example, it can be concluded from the results of the studies regarding TAD placement that CBCT allowed for better visualization of the entire volume of a proposed implant site compared with 2D radiology[21,24]. The results of the studies showed that the hard palate offers several suitable sites for TAD insertion[17,18]; the paramedian palate is a promising region for implant placement when a midpalatal suture should be avoided[15]; there is sufficient interradicular space for TAD placement between the second premolar and the first molar in the buccal alveolar bone of the maxilla, between the molars in the palatal alveolar bone, and between the first premolar and the second molar in the mandibular buccal alveolar bone[22]; and the initial point for TAD placement in buccal alveolar bone should be near the mucogingival junction and at less than a 45-degree angulation to the long axis of the tooth[21]. Although the results of all of these studies provided more insight into the best locations for TAD placement, none of the results indicated that using CBCT in TAD placement led to better results (for example, less chance of hitting a root of an adjacent tooth or the TAD's having better stability and a longer life span compared with the use of clinical judgment only [that is, visual inspection and palpation] in combination with a 2D radiograph).

In studies regarding cephalometry, CBCT enabled investigators to obtain 3D measurements of craniofacial morphology. An anthropometric cross-sectional analysis by Swasty and colleagues[34] regarding mandibular morphology showed that the mandibular cortical bone was thickest at the base on the buccal side. People between the ages of 10 and 19 years had thinner cortical bone and decreased mandibular height in comparison with people in other age groups. The mandible continued to mature in people aged 40 to 49 years, and after that period, it decreased in thickness. In longitudinal studies, investigators compared previous 2D records with new 3D records for the same patient. For these studies, it is important to determine whether it is valid to compare a 2D projection from a 3D scan with a conventional 2D cephalometric radiograph. The results of a study in which investigators compared conventional cephalograms and CBCT-generated cephalograms showed that CBCT-generated cephalograms could replace conventional radiographs of the head region successfully[28]. In addition, the results of another study showed that the measurements from CBCT-generated cephalograms were similar to those from conventional cephalograms[29]. The results of two studies showed differences between conventional and CBCT-generated cephalograms, but their methodological quality was insufficient[31,32]. Chien and colleagues[32] found that the mean error of landmark identification was larger on 2D radiographic images than it was on 3D CBCT images. Cevidanes and colleagues[31] suggested that the orientation of the head in CBCT images may affect both the reliability of the measurements and the relative anatomical location, and, therefore, the patient's head orientation may influence diagnosis and treatment planning. Two-dimensional cephalometry has been used to aid treatment planning for decades. To our knowledge, however, no study investigators have compared 3D cephalometry with 2D cephalometry in human participants to determine which method is more effective in planning orthodontic treatment.

In studies regarding combined orthodontic and surgical treatment, 3D models from CBCT images have provided valid assessments of craniofacial structures. Different patterns of ramus and condylar remodeling were identified on CBCT images after orthognathic surgery[36]. Kim and colleagues[41] found that the condylar position in the glenoid fossa changed from a concentric to an anterior position after mandibular surgery. Garrett and colleagues[39] found that rapid maxillary expansion produced an increase in nasal width and a decrease in maxillary sinus width. Rungcharassaeng and colleagues[37] reported that rapid maxillary expansion caused the tipping of the buccal crown and reductions of both buccal bone thickness and buccal marginal bone levels in the maxillary posterior teeth. In addition, these changes were correlated with patient's age, appliance expansion and patient's initial buccal bone thickness. The results of a systematic review by Plooij and colleagues[63] showed that image fusion and, particularly, that the 3D virtual head provided accurate, realistic tools for treatment planning. No studies have been conducted to investigate whether planning orthognathic treatment by means of 3D imaging has led to better treatment results than does planning orthognathic treatment by means of 2D imaging, but developing an effective computer-based approach to perform orthognathic surgery has the potential to improve the current approaches. This process takes time and might come to pass in the near future.

In studies regarding airway measurements, conventional lateral head radiographs allowed clinicians to determine the size of the airway area. This size can be of interest in the treatment of patients with deviating jaw relationships, craniofacial anomalies or sleep apnea. As the airway is a complex dynamic 3D structure, CBCT imaging could enhance diagnostics. Aboudara and colleagues[45] reported a correlation between the airway area shown in two dimensions and the airway volume shown in three dimensions; the larger the area, the larger the volume. Similar areas on the lateral cephalometric radiographs, however, did not automatically correspond to similar volumes measured by means of CBCT; that is, the airway area shown in two dimensions did not reflect the airway volume shown in three dimensions. Therefore, we do not recommend that operators rely on only 2D information for assessing airway measurements. Grauer and colleagues[43] found that airway shape, but not airway volume, differed among patients with different anteroposterior jaw relationships.

In studies regarding root resorption after orthodontic treatment, investigators often obtained an orthopantomogram to check root angulation and detect root resorption. Bouwens and colleagues[64] mentioned that a panoramic radiograph can distort tooth position and inclination, and the magnification can vary on different parts of the image. Thus, panoramic radiographs have limitations when used for this purpose. In contrast, the 3D view of a CBCT image can reveal true root angulations. Leuzinger and colleagues[51] compared panoramic radiographs and CBCT images from the same patients for root proximity. They found that root contacts generally were overestimated when evaluated by means of a panoramic radiograph. Similarly, Bouwens and colleagues[64] found an overall difference in root angulations as measured by means of panoramic radiographs and CBCT images. No study results, however, have shown that root contacts or thin interdental alveolar bone has any long-term effect on periodontal health. On the contrary, in 1987, Årtun and colleagues[65] reported that teeth were not predisposed to more rapid periodontal breakdown when roots were in close proximity. Furthermore, in 1986 Årtun and colleagues[66] found that marginal periodontal breakdown was unrelated to the thickness of bone between the roots in anterior areas. Therefore, it is not known whether a panoramic radiograph or even a CBCT scan is needed to add clinical value concerning root angulation.

In orthodontics, the use of CBCT is promoted by its manufacturers in the area of tooth impaction. However, only two of the 50 articles in our review concerned tooth impaction, and they had average methodological quality. Liu and colleagues[48] found that resorption of adjacent permanent incisors occurred when impacted canines were in close contact with the incisors, which is common in canine impaction. The scientific data, however, did not support the manufacturers' presumptions that 3D localization of impacted teeth could reduce treatment time and facilitate a more accurate exposure procedure.

The results of studies regarding CLP indicated that patients with CLP would be expected to benefit from 3D diagnostics, owing to the 3D nature of this anomaly. Unfortunately, the available evidence did not support this assumption. No studies have been published in which researchers compared 2D and 3D contributions to diagnosis of and treatment planning for patients with orofacial clefts. Schneiderman and colleagues[55] conducted a preliminary study regarding a set of 18 new CBCT measurements used for patients with unilateral CLP. These measurements could be the foundation for larger-scale prospective studies. Oberoi and colleagues[54] conducted a CBCT study regarding the canine eruption path in patients with CLP. They found that most canines on both the cleft and noncleft sides of the mouth moved incisally, facially and mesially during eruption.

The seven studies regarding various other subjects included two with acceptable methodological quality. Korbmacher and colleagues[57] assessed the feasibility of using CBCT for various orthodontic indications. They considered CBCT use to be justified in cases of tooth impaction or for assessing the location of third molars before surgical removal. In our systematic review, however, we did not find any scientific evidence to support these assumptions. Without the appropriate evidence, CBCT cannot be considered a clinical guideline for those indications.

In our view, for simple cases, normal digital photographs, models and a panoramic radiograph can provide sufficient information for clinicians to make a diagnosis and plan treatment. Accidental findings discovered by viewing CBCT images or 2D radiographs are unlikely to change treatment plans, although research has not confirmed this hypothesis. Incidental findings more commonly are found on a CBCT image than on a lateral head radiograph or a panoramic radiograph. Cha and colleagues[58] reported the rate of incidental findings on CBCT images was 24.6 percent. These incidental findings are more likely to be noticed by experienced CBCT users. It remains unknown if these findings will cause orthodontists to alter their treatment plans and, if they do, to what degree. Unfortunately, Cha and colleagues[58] did not comment on this in their article.

Holberg and colleagues[56] examined the quality of CBCT images with that of multislice CT images. They found that, in contrast to multislice CT, metal artifacts were nearly undetectable in CBCT images. On the other hand, multislice CT images offered better image quality of the dental and surrounding structures than do CBCT images. Nevertheless, obtaining multislice CT images requires higher amounts of radiation than does obtaining CBCT images for the same volume[56]. The use of CBCT technology reduces the patient's exposure to ionizing radiation compared with the use of multislice CT technology, but it causes significantly more radiation exposure than do the conventional radiographic imaging procedures routinely used in orthodontics[67,68]. There are radiation dose variations among different CBCT units, since the dose depends on the field of view, scan time, milliampere setting, peak kilovoltage, voxel size, sensor sensitivity and number of images obtained. The 2007 International Commission on Radiological Protection's[69] (ICRP's) recommended effective dose for conventional 2D imaging used in orthodontics ranges from 14.2 to 24.3 microsieverts for a panoramic radiograph and from 5.1 to 5.6 μSv for a conventional cephalometric radiograph[70]. The radiation dose for CBCT ranges from 19 to 1,073 μSv, depending on the CBCT unit and the field of view[68,71,72]. The radiation dose for a multislice CT scan of the maxillofacial region varies from 474 to 1,410 μSv (measured according to ICRP 2007 tissue-weighting factors)[73,74]. A review by Brenner and Hall[75] focused on the increasing number of CT scans performed, the associated radiation dose and the consequent risk of developing cancer in adults and in children. This last group of patients is relevant to the field of orthodontics, because a large proportion of patients in that field are children or adolescents. Brenner and Hall[75] concluded that when patients undergo two or three CT scans, they receive a radiation dose to their organs that is in a range that is correlated directly with a statistically significant increase in the risk of developing cancer.

The average dose of background radiation for all people on earth is approximately 2.4 millisieverts per year[76]. Taking a commercial airline flight exposes a person to higher radiation levels than those they are exposed to when spending the same amount of time at sea level. Flying at an altitude of 10,000 meters leads to a radiation dose of as much as 5 μSv per hour; a one-way flight from London (UK) to New York City would expose a person to around 40 μSv[77,78]. A week of skiing in the mountains would expose a person to approximately 15 μSv[77]. There is no known health effect of background radiation, but higher doses of radiation can cause serious health issues. The U.S. Nuclear Regulatory Commission has stated that “although radiation may cause cancers at high doses ... , currently there are no data to establish unequivocally the occurrence of cancer following exposure to low doses and dose rates ... below about ... 100 mSv[79].” On the basis of the results of epidemiologic studies regarding the survivors of the atomic bombings of Hiroshima and Nagasaki (Japan) the ICRP has estimated the fatal cancer risk as 5 percent per sievert exposure in a population of all ages[69]. In 2010 recommendations, the European Committee on Radiation Risk (ECRR) estimated the fatal cancer risk as 10 percent per sievert[80]. Therefore, of every 10 people according to the ECRR estimates or 20 people according to the ICRP estimates exposed to 1,000 mSv, one person could be expected to develop fatal cancer. If the linear hypothesis, which assumes that the relationships between high levels of radiation and its adverse effects also apply to low levels of radiation, is true, it would mean that per 1 μSv of exposure the risk of developing fatal is one in 10 million people according to the ECRR guidelines and in one in 20 million according to the ICPR guidelines. For a CBCT exposure of approximately 200 μSv, the associated risk of developing fatal cancer is one in 50,000 according to ECRR estimates and one in 100,000 according to ICRP estimates.

There are no large-scale epidemiologic studies of the risk of developing cancer associated with CBCT scans. We may expect that the relationship between the number of CBCT images and cancer risk will be less obvious than that for CT, because CBCT requires lower doses of ionizing radiation than does CT. Nevertheless, the As Low As Reasonably Achievable (ALARA) principle should be honored at all times. For each patient, the clinician should weigh the potential benefits of a CBCT scan against the chance of causing cancer. Although the chance may be small, it is never negligible.

All radiographic examinations, including CBCT, must be justified for each patient by means of a risk-benefit analysis. On the basis of our review, there is no justification for obtaining both 2D radiographic images and a CBCT image, one shortly after the other, or for routinely obtaining CBCT images in orthodontics. The European Academy of Dentomaxillofacial Radiology's[81] clinical practice guidelines and the SEDENTEXCT project's guidelines[82] are sources of information for the use of CBCT in dentistry, and they offer guidance for good dental practice.

7.5 Conclusion

There is no high-quality evidence regarding the benefits of CBCT use in orthodontics. The application of CBCT in orthodontics can be justified in some cases, but it is not always the answer to all clinical problems. Limited evidence has been found that CBCT offers better diagnostic potential, leads to better treatment planning and results in better treatment outcomes than do conventional 2D imaging modalities. Only the results of the studies regarding airway measurement provided sound scientific data to suggest that CBCT may provide added diagnostic value (Table 7.4) [42-46]. The additional radiation exposure associated with a CBCT scan compared with that associated with a conventional 2D radiograph should be weighed in each case against the possible benefits, which have not been supported in the literature. It is likely that more benefits of CBCT will be shown to be advantageous compared with those of 2D radiography and that the diagnostic possibilities will increase. Research is needed to elucidate the efficacy, efficiency and cost effectiveness of CBCT use in orthodontic diagnosis and treatment planning. This requires quantification of the effects of CBCT on treatment procedures, progression and outcome.

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Chapter 8

General Discussion and a glimpse in to the future

8.1 Introduction

The first decade of CBCT in orthodontics has passed and brought significant changes. CBCT has expanded the diagnostic possibilities and changed the way we are looking at patients. In this thesis five methodological studies and one systematic review on the evidence for the use of CBCT in orthodontics are included. The methodological studies (Chapter 2 to 5) were performed to determine whether different 2D and 3D image modalities can be compared. The study described in Chapter 6, aimed to determine whether images obtained from two different CBCT devices are comparable. Finally, a systematic review (Chapter 7) was performed to assess the level of evidence for the use of CBCT in orthodontics.

In the next paragraphs the results of these studies are discussed, concentrating on the aims previously set out in the first chapter. At the end of this chapter in paragraph 8.7, future perspectives of CBCT applications for the orthodontic specialty, are explored.

8.2 Lateral cephalometry

8.2.1 Measurement errors

For the comparison of 2D and 3D cephalometry, dry skulls were used in all four studies. This provides an excellent opportunity to indentify bony landmarks, since there is no interference of soft tissues[1]. When tracing images of actual patients, soft tissues might increase the chance of errors in localization of landmarks, resulting in a larger error. A unique study done by Fourie[2] did use human cadaver heads to simulate the clinical situation as much as possible. However, human cadaver heads for scientific purposes are scarce. To compare different image modalities as described in Chapter 2 to 4, a big group of subjects would be needed. Therefore it was not possible to use human cadaver heads. Instead dry skulls were used in all four studies comparing 2D and 3D cephalometry.

Cephalometric measurements are prone to errors. Each cephalometric landmark exhibits a characteristic pattern of error that contributes to measurement inaccuracy. There are studies that question the ability to detect a true treatment effect with 2D cephalometrics[1,3], since the error for landmark positioning is possibly larger than the smallest detectable difference for the associated measurements. Localization of landmarks is considered to be the biggest error in cephalometric studies[4]. Adding a third dimension with the use of CBCT, might result in an increase of this error. However, different studies show different results. Some studies report a consistent and reproducible landmark identification in 3D for a majority of anatomical landmarks[5,6]. Accurate measurements can be acquired on real size images and without anatomical superimpositions[7]. Some landmarks can even be identified with greater precision on a 3D model compared to a 2D radiograph and show a smaller measurement error in 3D[8-10]. Apparently for these landmarks, the 3D CBCT model leads to a more precise identification of traditional cephalometric landmarks. In 3D, planes can be measured instead of a projection of a plane which in 2D is represented by a line. Superimposition of bilateral landmarks, as seen in a 2D radiograph, does not exist in 3D as the actual anatomical structures can be identified instead of a 2D projection[10]. Other landmarks however, show a greater variability, probably because of an inadequate definition of the landmarks in the third dimension[10]. Further developing and applying new definitions describing these landmarks in all three dimensions, is needed. Training of the operator in performing a 3D analysis seems to be important as well to get consistent and reproducible results[6]. Increasing the resolution by using a smaller voxel size on the other hand, does not result in greater accuracy and is therefore not of much help[3].

For the correct statistical interpretation of measurements, especially in longitudinal cephalometric research, the measurement error that contributes to measurement inaccuracy should always be taken into consideration. Each individual landmark has its own characteristic pattern or envelope of error[11,12] and calculation of the smallest detectable difference could be a solution to discriminate between measurement errors and actual measured differences[13].

8.2.2 Comparability of image modalities

The studies described in this thesis did not specifically look at error of landmark identification, emphasis was on comparability of different image modalities. The methodological studies showed that a 2D lateral projection of the 3D volumetric data is necessary if 2D records need to be compared to 3D records. Comparisons between conventional frontal radiographs and frontal projections of the 3D volumetric data, conventional 2D images and 3D models, and 3D models from different CBCT scanners is not accurate. This is crucial information for longitudinal research in cases where part of the records are in 2D and another part in 3D. Another conclusion was that there is a need to develop and test new 3D-cephalometric analyses. First off all, because there are newly defined 3D landmarks and second, since there are no data available that can be used as normative values for 3D cephalometric measurements.

Analysing a patient in 3D requires a different way of thinking. When analysing 3D data over time, it is possible to perform 3D superimpositions on which calculations of volumetric data instead of linear and angular comparisons are possible. Changes in volume then represent changes in the patient's facial structures. Also mirroring a part of the 3D model offers options to analyse the data set in another way then what is common in 2D analyses. Differences between right and left side of the patient's face can then easily be displayed. The need for reference values of angular measurements can be avoided this way[14].

8.3 Frontal cephalometry in 3D

Malocclusions and craniofacial deformities even more so, are three-dimensional conditions. Also before a 3D analysis became available, clinicians were interested in the 3D characteristics of patients. Assessment of frontal cephalometric radiographs together with lateral cephalometric radiographs could give an impression of the 3D condition. Frontal radiographs can be of particular importance in cases of dentalveolar- and facial asymmetries, dental and skeletal crossbites, and functional mandibular displacements[15].

The studies in this thesis concerned with frontal cephalometry proved that conventional frontal cephalometric radiographs cannot be compared with either constructed frontal radiographs from 3D data nor with a 3D model itself. Unlike in lateral cephalometry, where positioning of the patient in the CBCT device is of little importance (as long as the midsagittal plane is coinciding with the midline light beam of the CBCT device) in frontal cephalometry correct positioning of the patient is of vital importance as shown in Chapter 4. A small tilt in head position leads to considerable distortion in cases where 2D images are constructed from the 3D data set. This is caused by localisation of most landmarks in different tomographic planes and therefore these images are more susceptible to geometric distortion. This influences the cephalometric measurements significantly.

With the expanding possibilities in available software, it is now possible to orient the 3D model of the patient's head in a desired position before generating a 2D radiograph from the 3D data set. Then the only challenge remaining is to standardize the orientation of the 3D data set before generating a 2D radiograph. On the other hand, since the use of frontal cephalometry in orthodontics has reduced to virtually nil over the past years, it is not very likely that studies combining 2D conventional and 2D CBCT constructed frontal radiographs will be performed in the future.

It is generally accepted now that in cases of dentoalveolar- and facial asymmetries and dental and skeletal crossbites, the use of 3D models of the facial skeleton, can provide better insight into the transverse dimensions of the maxillofacial complex than 2D radiographs. Numerous studies on this topic have been published the past years[16-18]. These studies show that 3D CBCT provides an excellent opportunity to evaluate effects of expansion therapy in all three planes of space. If a 3D CBCT diagnosis of the transverse dimension actually leads to better diagnostics and therewith better treatment plans and treatment results, is, as yet, not scientifically proven.

8.4 Different CBCT machines

In the study described in Chapter 6 a statistically significant and clinically relevant difference was found for measurements on different 3D models of the same skull constructed from CBCT scans by different CBCT devices. A possible explanation for the differences found, could be that while making a 3D reconstruction of the skull the part of the mandible containing point Gonion is reconstructed differently in both devices. During the acquisition of the scan, voxels are awarded different HU values. When not all space in a voxel is filled with the same tissue, the HU value awarded to the voxel is that of the tissue which is most present in that voxel. This way an area where there is no bone, can be seen as bone in the constructed 3D model and vice versa. If the skulls are positioned exactly the same in both CBCT devices, there would be no differences between both 3D models. Since the positioning of the skulls will not be identical, this can be a source of error. Another source of error can be a difference in X-ray beam inhomogeneity of the different CBCT devices. This also can result in small differences between the two 3D models. This means that hardware used for CBCT scanning can influence the landmark identification on a 3D model and therefore can influence the measurements performed. So when interpreting measurements made on 3D models derived from different CBCT devices, care should be taken.

Since the introduction of the first CBCT device dedicated to the oral and maxillofacial region in 1997[19], many other CBCT devices have become available. The first CBCT scanner dedicated to the oral and maxillofacial region was the Italian NewTom-9000 by Quantitative Radiology. The entire maxillofacial volume was imaged with a diameter of 13 cm while the patient was scanned in supine position. It was not possible to collimate the scan to the region of interest. Now there are approximately 40 CBCT devices dedicated to the oral and maxillofacial region on the market worldwide[20]. All modern CBCT devices for this purpose scan the patient in a sitting position, reducing the size of the CBCT device dramatically. An essential difference between CBCT devices is the field of view, which can range from a small FOV of several cubic centimetres like in the J Morita 3D Accuitomo, to the largest available FOV able to capture the whole head of the patient, e.g. a field of view of 25 x 25 x 30 cm in the Hitachi CB MercuRay[21]. Because of continuing development of the flat panel detectors, they have become more sensitive and thus require less radiation. It is also possible to collimate the scan to the exact region of interest reducing the radiation even further. The PaX-Zenith3D by Vatech America for example, which became available in 2010, has a fully adjustable field of view (FOV) ranging from 5 x 5 x 5 cm to 24 x 24 x 19 cm[22]. All available CBCT devices have different characteristics and therewith different applications. Depending on the application of CBCT within the practice setting a choice between the available devices can be made on basis of the desired FOV, along with other characteristics such as: radiation exposure, resolution and voxel size, size of the CBCT device, reconstruction time of the 3D model, file size of the 3D data set, wheel chair accessibility and costs.

8.5 Radiation exposure

Since the introduction of the CBCT in dentistry there has been a lot of discussion and uncertainty about the radiation associated with a CBCT scan. To make a CBCT scan x-rays are used. X-rays are produced by firing electrons over a high potential difference between the cathode and the anode where X-ray photons are emitted[23]. X-rays are part of the electromagnetic spectrum which covers a wide range of radiation from radio waves (low energy) at one end to gamma rays (high energy) at the other. Part of this spectrum consists of ionising radiation, including gamma rays, X-rays, alpha and beta particles and other heavy ions[24]. Ionising radiation has enough energy to eject an electron from an atom, forming ions in the material or tissue through which the radiation interacts. Direct ionization in tissues produces free radicals, which are atoms containing unpaired electrons. Free radicals tend to be very chemically reactive and can easily damage DNA. Ionizing radiation may also directly damage DNA by ionizing or breaking down DNA molecules itself. Cells which experience DNA damage may either repair the damage, go through the process of cell apoptosis or experience a DNA mutation that is passed on by means of successive cell divisions. This mutation may lead to pre-mature aging of the cell or uncontrolled cell divisions resulting in a neoplasm[25].

Because of potential hazardous effects of ionizing radiation on living tissues, the radiation exposure to a human being e.g. because of medical reasons, should be kept As Low As Reasonably Achievable (ALARA). Every radiation dose of any magnitude, no matter how small, involves a certain degree of detrimental effects like an increased risk of genetic mutations. The associated effective dose of a medical examination is measured using the 2007 International Commission on Radiological Protection (ICRP) tissue-weighting factors. The effective dose for frequently used conventional 2D radiographs and CBCT scans are mentioned in the discussion part of Chapter 7.

Human exposure to radiation sources has always existed and ever will. The natural environment has always been radioactive and accounts for up to 85% of the annual human radiation dose[26,27]. This radiation is emitted from various natural sources[28]. Radiation can also arise from human activities. This accounts for up to 15% of the public's exposure every year. Radiation from medical procedures accounts for far most exposure arising from human activities[27]. Radiation from nuclear power plant disasters like Chernobyl in April 1986 and Fukushima in March 2011, or radiation due to fallout from nuclear weapons testing, account for less than 1% of the annual human dose. The constantly present radiation in the environment from natural sources and nuclear industry, is called background radiation. Background radiation is the main source of exposure for most people, and provides some perspective on radiation exposure from medical procedures.

The average dose of background radiation for all persons on earth is around 2.4 mSv/yr (or 2400 µSv/yr), ranging between 1 and 10 mSv/yr, depending on the geology and altitude people live[26]. Taking a commercial airline trip exposes you to higher (mainly cosmic) radiation levels then spending the same time at sea level. Flying at 10.000m leads to a dose up to 5 µSv /h. Airline personnel therefore receives an annual dose well over the average of 2.4 mSv/yr. The average annual dose for airline personnel is about 5 to 10 mSv/yr, depending on flight duration and route[29]. A single radiation dose to humans of more than 1 Sv causes acute radiation syndrome, but not immediate death. Above 1 Sv the severity of illness increases with the dose, ultimately with a single dose at once of 10 Sv or more being fatal to all humans within a few weeks.

Although the radiation of CBCT compared to 2D radiology is an issue, a CBCT does offer new diagnostic possibilities. CBCT can be used in a wider range of patients in comparison to MSCT because of lower radiation doses. In some cases the CBCT can even replace a MSCT scan, e.g. for the radiographic follow-up of orthognathic or trauma cases. However, there is a limit for the use of CBCT because of the CBCT technique's susceptibility to artefacts such as scatter, increased noise level and poor soft-tissue visibility which influences the image quality and diagnostic accuracy. This means that still an indication for MSCT exist, where there are extensive fractures with suspicion of craniocerebral (soft tissue) trauma as well as where there is suspicion of bone tumours with soft tissue participation. Consequently in cases of neoplasms in the soft tissues or cases with functional temporomandibular joint symptoms, magnetic resonance imaging (MRI) is preferable to CBCT[30].

8.6 CBCT in orthodontics

Despite the increasing popularity of CBCT in orthodontics and its advantages over routine radiography for orthodontic patients, the effects of information derived from these CBCT images in altering diagnosis and treatment decisions, has not been confirmed[31,32]. At present, there is only limited evidence for the use of CBCT in orthodontics and this evidence only exists for a certain patient category[32]. This means that it is still difficult to develop evidence based guidelines for the use of CBCT for orthodontic purposes.

In 2008 the European Academy of Dentomaxillofacial Radiology (EADMFR) devised a set of 20 “Basic Principles” to act as core standards for the use of CBCT imaging in dentistry. The beginning of that year also marked the kickoff of the SEDENTEXCT project, an EU project aimed at improving the safety and efficacy of CBCT in dentistry. The project is a collaboration between six European universities and a British enterprise. The work plan aimed to find solutions to the challenge of a new x-ray imaging modality becoming available to the large community of dentists, medical physicists and other stakeholders in Europe. The final report of the project, that was delivered in June 2011, contains evidence based guidelines for the use of CBCT in maxillofacial imaging. These guidelines confirm that CBCT for orthodontic purposes should be used in selected cases only. Guidelines for CBCT images for orthodontic purposes are[33]:

1. All CBCT examinations must be justified on an individual basis by demonstrating that the potential benefits to the patients outweigh the potential risks. CBCT examinations should potentially add new information to aid the patient’s management. A record of the justification process must be maintained for each patient.
2. CBCT should not be selected unless a history and clinical examination have been performed. Routine or screening imaging is unacceptable practice.
3. CBCT may be indicated for the localised assessment of an impacted tooth (including consideration of resorption of an adjacent tooth) where the current imaging method of choice is MSCT or where lower dose conventional dental radiography fails to provide the information required. The use of CBCT units offering only large volumes (craniofacial CBCT) requires very careful justification and is generally discouraged.
4. Where the current imaging method of choice for the assessment of cleft palate patients is MSCT, CBCT may be preferred if radiation dose is lower. The smallest volume size compatible with the situation should be selected because of reduced radiation dose.
5. CBCT is not normally indicated for planning the placement of temporary anchorage devices in orthodontics.
6. Large volume CBCT should not be used routinely for orthodontic diagnosis.
7. For complex cases of skeletal abnormality, particularly those requiring combined orthodontic/surgical management, large volume CBCT may be justified in planning the definitive procedure, particularly where MSCT is the current imaging method of choice.
8. Limited volume, high resolution CBCT may be indicated in selected cases of suspected, or established, inflammatory root resorption or internal resorption, where three-dimensional information is likely to alter the management or prognosis of the tooth.
9. CBCT may be indicated for pre-surgical assessment of an unerupted tooth in selected cases where conventional radiographs fail to provide the information required.

10. CBCT is indicated where bone information is required, in orthognathic surgery planning, for obtaining three-dimensional datasets of the craniofacial skeleton.

For each indication a correct scanning protocol should be determined in such a way that ALARA can be honoured. The need to image other types of cases should be made on a case-by-case basis, following an assessment of benefits versus associated radiation risks[31].

Taken the popularity of CBCT and the increase in technological knowledge, one can expect that in a few years from now 3D superimposition of CBCT scans will be common knowledge and will have replaced 2D superimposition completely for certain patient categories. It remains questionable however, whether a 3D CBCT data set can be used in the same way as a lateral cephalometric radiograph is used nowadays, that is: comparing measurements to standard values for the patient's ethnic group. This is caused by the absence of reference data for 3D cephalometry, which for 2D cephalometry, are available from longitudinal growth studies. Obtaining longitudinal CBCT scans of a growing non-orthodontic child in order to obtain a series of 3D CBCT data sets to build those reference values, is not possible because of radiation hygiene. 3D CBCT reference data of non treated individuals will therefore not become available. More emphasis should be put on non-ionizing imaging for orthodontic purposes such as 3D stereophotogrammetry. The utility of these 3D images needs to be investigated further to enable the clinician to use them for treatment planning and treatment evaluation.

8.7 Glimpse into the future and directions for future research

About thirty years after the introduction of cephalometrics in orthodontics, the first study on accuracy of landmarks was published in 1960[34]. In 1971 a comprehensive study in this perspective, showed that commonly used landmarks deviated from their generally accepted definitions[35]. Since then the need of cephalometric radiographs for orthodontic patients has been questioned. Already in 1986 Van der Linden and Boersma wrote in their book *Diagnosis and Treatment Planning in Dento-facial Orthopedics*[36]: "Nowadays, it is not necessary to take a lateral skull radiograph of the average patient who presents himself for orthodontic treatment. In fact, only a limited number of cases will actually need such a radiograph, i.e., patients with markedly abnormal faces and extreme anomalies and particularly those cases where disturbed facial growth seems evident, or may be expected, such as some Class II and Class III anomalies and cleft lip and palate patients. If combined orthodontic and surgical correction is contemplated, then lateral and often other skull radiographs are indispensable. This also applies for anomalies with a marked component of asymmetry." Since then studies have been performed questioning the need for cephalometric radiographs in orthodontics[37]. Recent research has confirmed findings that lateral cephalometric radiographs probably have no added value for treatment planning of orthodontic patients[38,39]. Despite these studies, a lateral cephalometric radiograph is at present, still part of the orthodontic records protocol in most orthodontic clinics. Further implementation of non invasive 3D records, such as 3D stereo photogrammetry, could result in abandoning lateral cephalometry in the vast majority of orthodontic patients, but the clinical utility of these 3D images should be investigated thoroughly. On the other hand, for complex cases where there might be an indication for obtaining lateral cephalometric radiographs, it is likely that the use of lateral cephalometry for treatment planning will be abandoned soon and will be replaced by CBCT.

CBCT together with other 3D techniques have only found their way into dentistry and its specialties for about a decade now. Ongoing efforts are undertaken to further enhance clinical applications and investigate, utilize and combine CBCT applications with other 3D applications in the years ahead. Ultimately this should result in a virtual 3D patient head, which can fast and easily be visualized. The limiting factor for widespread use of CBCT in orthodontics at this point is the radiation dose. Further technical development of CBCT devices and flat panel detectors will reduce the radiation dose further. Also fully adjustable collimation of the radiation beam to the desired FOV, will contribute to lowering the radiation dose. When the dose of a CBCT for the lower part of the face is in the range of the present radiation dose of a panoramic radiograph, it is possible that the only records needed for treatment planning of an orthodontic patient are a CBCT scan and a colour (3D) photograph of the patient's face. Impression taking for dental casts and other orthodontic records may become redundant. The CBCT and photograph of the patient's face combine into a 3D virtual head of the patient, which is then available for comprehensive diagnosis, treatment planning and treatment simulation on the computer screen[40]. Three-dimensional treatment simulation, which already is available now, but at present is not more than a rough estimation, will improve and ultimately turn into a good predictor. It will be possible to show patients real time 3D results of different treatment options on a chair side 3D tablet computer. Also planning of multidisciplinary cases can be made quicker, more efficient and with greater precision. Besides these applications the 3D data could also be used for the production of indirect bonding trays for accurate bracket placement, individualised brackets, wires and appliances made accurately from 3D data in the computer.

Before this 3D virtual patient and treatment simulations can become reality, current software has to be improved and new software has to be developed. To accomplish this, studies are needed that enable software developers to eliminate artefacts in the part of the CBCT scan containing the teeth. Other studies that need to be performed are studies that validate the treatment predictions in order to further improve the treatment outcome estimations.

There is an overwhelming amount of studies concerning CBCT in the literature and the publications on this topic increase weekly. But the evidence for the clinical use of CBCT for the purpose of treatment planning is still lacking. Studies showing that diagnosis and treatment planning utilizing CBCT records indeed lead to better treatment results, have not been published. Because of this continuing lack of evidence of clinical benefits of CBCT in orthodontics and because of radiation hygiene, it might be possible that other 3D image modalities will further expand their clinical applications, e.g. 3D stereophotogrammetry with integrated digital dental models in the correct anatomical position as described by Rangel[41]. For the everyday orthodontic patient for example, the only records that will be made in the future could be a panoramic radiograph, a set of digital dental casts and a 3D stereo photograph. The latter fused together with the dentition in the correct anatomical position in relation to the rest of the face. This brings us back to where Van Loon started in 1915 with his "Cubus Craniofurus" with one important difference though, today's "Cubus Cranioforus" is digital. Future studies need to establish the value of this 3D fused data set of dentition and face for orthodontic diagnosis and treatment planning.

8.8 References

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Chapter 9

Summary

Summary

For longitudinal studies it is essential to be able to compare records made at different points in time. About 15 years ago three dimensional (3D) cone beam computer tomography (CBCT) has been introduced into the field of orthodontics. CBCT has expanded the diagnostic possibilities for orthodontic patients and has changed the way diagnosis and treatment plans for certain patient categories are made. Nowadays, these patients will be documented in 3D. If longitudinal evaluation is indicated those 3D records need to be compared with older two dimensional (2D) records. For further application of CBCT technology within the field of orthodontics, it is important to develop evidence based guidelines. At first, it is important to know which evidence is currently available for the use of CBCT for orthodontic purposes. Therefore the aim of this thesis was to investigate the comparability of 2D and 3D images and to assess the level of evidence for the use of CBCT in orthodontics.

Chapter one explains the background of the thesis. The history of early attempts to make an orthodontic diagnosis in three dimensions is described as well as a brief history of cephalometrics in the orthodontic field. Also the introduction of CT and CBCT is described. The basic principles of CBCT are explained and possible indications for CBCT in the field of orthodontics are presented.

In **chapters two to five** of this thesis, four methodological studies performed on dry human skulls are worked out. The aim of these studies was to determine whether different 2D and 3D image x-ray modalities of the facial skeleton can be compared. The first two studies are concerned with lateral cephalometry and the latter are concerned with frontal cephalometry. **Chapter two** describes a study in which measurements on conventional lateral cephalometric radiographs were compared to measurements on CBCT-constructed lateral cephalometric radiographs taken from human skulls. **In chapter three**, measurements on conventional lateral cephalometric radiographs were compared to 3D measurements on 3D models of human skulls. **Chapter four** describes a study in which measurements on conventional frontal radiographs are compared to measurements on CBCT-constructed frontal cephalometric radiographs. Finally, in **chapter five**, measurements on conventional frontal radiographs were compared to measurements on 3D models of human skulls derived from CBCT scans.

These four methodological studies proved that only a 2D lateral projection of the 3D volumetric data set can be compared to a conventional 2D lateral cephalometric radiograph. Comparison between conventional frontal radiographs

and frontal projections of the 3D volumetric data and comparison of conventional 2D images and 3D models, is not accurate. This is crucial information for longitudinal research in cases where part of the records are in 2D and a another part of the records is in 3D.

Chapter six describes a study which investigated whether the used hardware influences the performed measurements. Images obtained from two different CBCT devices were compared. Thereto CBCT scans of 40 dry human skulls were made with both the i-CAT™ and the Iluma™ cone beam CT device. From the CBCT scans 3D models were constructed and cephalometric measurements were performed repeatedly. The results showed that hardware used for making a CBCT might influence the measurements. It was concluded that care should be taken when interpreting measurements made on CBCT 3D models derived from different CBCT devices.

In **Chapter seven** a systematic review on the evidence for the use of CBCT in orthodontics is described. Articles were identified by searching the Cochrane library, PubMed, Medline, Embase, Scopus and CINHAL. Articles up to March 2010 were reviewed and the methodological quality was evaluated. From the systematic review of the literature it was concluded that only a few studies have quantified the assumed advantages of CBCT in orthodontics. Only for the analysis of airway volume scientific evidence was available, suggesting that CBCT provided added value. Future research is needed to elucidate the efficacy, efficiency and cost effectiveness of using CBCT in orthodontic diagnosis and treatment planning. Future studies should quantitatively evaluate the effects of CBCT on diagnostic and treatment procedures, progression and outcome.

Chapter eight is the general discussion. In this chapter the results of the studies performed for this thesis are discussed, concentrating on the aims set out in the first chapter. At the end of the chapter suggestions for future research are given and future perspectives of CBCT applications for the orthodontic specialty are explored.

Chapter 10

Samenvatting

Samenvatting

Voor longitudinale studies is het essentieel om records die gemaakt worden op verschillende tijdstippen te kunnen vergelijken. Bijna 15 jaar geleden werd driedimensionale (3D) cone beam computer tomografie (CBCT) geïntroduceerd binnen de orthodontie. CBCT heeft de diagnostische mogelijkheden voor orthodontische patiënten verruimd en heeft de manier waarop een diagnose en behandelplan tot stand komen voor bepaalde patiëntencategorieën veranderd. Deze patiënten worden tegenwoordig in 3D gedocumenteerd. Maar in een longitudinaal onderzoek moeten deze 3D data worden vergeleken met oudere 2D gegevens. Voor de verdere toepassing van CBCT technologie binnen de orthodontie, is het belangrijk om evidence-based richtlijnen voor het gebruik van CBCT voor orthodontische doeleinden te ontwikkelen. In eerste instantie moeten we daarom weten welk wetenschappelijk bewijs momenteel beschikbaar is voor toepassingen van CBCT in de orthodontie. Het doel van het onderzoek beschreven in dit proefschrift is daarom de vergelijkbaarheid te onderzoeken van 2D en 3D röntgenbeelden van het hoofd en na te gaan voor welke toepassingen van CBCT in de orthodontie wetenschappelijk bewijs bestaat.

In **Hoofdstuk één** wordt uitleg gegeven over de achtergrond van het proefschrift. De eerste pogingen om een driedimensionale orthodontische diagnose te stellen worden beschreven, evenals de invoering van cefalometrie binnen de orthodontie. Ook de introductie van CT en CBCT wordt besproken. De basisprincipes van CBCT worden toegelicht en mogelijke indicaties van CBCT binnen de orthodontie worden beschreven.

In de **hoofdstukken twee tot en met vijf** van dit proefschrift worden vier methodologische studies beschreven die zijn uitgevoerd op menselijke schedels. Het doel van deze onderzoeken was om te bepalen of de verschillende 2D en 3D beeldvormen kunnen worden vergeleken. De eerste twee onderzoeken houden zich bezig met laterale cefalometrie en de laatste twee betreffen frontale cefalometrie. **Hoofdstuk twee** beschrijft een studie waarin metingen op conventionele laterale schedelröntgenfoto's worden vergeleken met metingen op geconstrueerde laterale schedelröntgenfoto’s uit CBCT scans. In **hoofdstuk drie** worden metingen op conventionele laterale schedelröntgenfoto’s vergeleken met metingen op 3D CBCT modellen van menselijke schedels. **Hoofdstuk vier** beschrijft een onderzoek waarin metingen op conventionele frontale schedelröntgenfoto's zijn vergeleken met metingen op CBCT geconstrueerde frontale schedelröntgenfoto's. Tenslotte worden in **hoofdstuk vijf** metingen op conventionele frontale schedelröntgenfoto's vergeleken met metingen op 3D CBCT modellen van menselijke schedels.

Deze vier methodologische studies toonden aan dat voor vergelijking van conventionele 2D laterale schedelröntgenfoto's met nieuwe 3D data, een tweedimensionale laterale projectie van het 3D volume noodzakelijk is. Vergelijking van conventionele frontale schedelröntgenfoto's met frontale projecties van de 3D data en vergelijking van conventionele 2D beelden met 3D modellen, is niet nauwkeurig genoeg. Dit is cruciale informatie voor longitudinaal onderzoek wanneer een deel van de records bestaat uit 2D data en een deel uit 3D data.

Hoofdstuk zes beschrijft een studie waarin onderzocht is of de gebruikte hardware invloed heeft op de uitgevoerde metingen. Beelden verkregen uit twee verschillende CBCT scanners werden hiervoor vergeleken. 40 CBCT scans van menselijke schedels werden gemaakt met zowel de i-CAT™ als de Iluma™ CBCT scanner. Van beide typen CBCT scans werden virtuele 3D modellen geconstrueerd waarop cefalometrische metingen werden uitgevoerd die meerdere malen werden herhaald. De resultaten toonden aan dat het type CBCT scanner van invloed kan zijn op de metingen. Hieruit valt te concluderen dat men voorzichtig moet zijn bij het interpreteren van metingen die met verschillende CBCT scanners zijn gemaakt.

In **hoofdstuk zeven** is een systematische literatuuronderzoek beschreven over beschikbaar wetenschappelijk bewijs voor gebruik van CBCT binnen de orthodontie. Artikelen tot en met maart 2010 werden gezocht in de Cochrane Library, PubMed, Medline, Embase, Scopus en CINHAL. De geselecteerde artikelen en hun methodologische kwaliteit werden beoordeeld. Het systematische literatuur onderzoek toonde aan dat slechts enkele studies de veronderstelde voordelen van CBCT voor orthodontische doeleinden gekwantificeerd hebben. Alleen voor het bestuderen van het volume van de luchtweg, bestaat er wetenschappelijk bewijs dat suggereert dat CBCT daadwerkelijk een toegevoegde waarde heeft. Er is verder onderzoek nodig dat de effecten van CBCT op orthodontische diagnostiek en behandeling kwalitatief moeten evalueren. Toekomstig onderzoek moet uitwijzen of het gebruik van CBCT in orthodontische diagnostiek en behandelplanning daadwerkelijke effectief en efficiënt is en zal inzicht moeten geven in de kosteneffectiviteit van de procedure.

Hoofdstuk acht is de algemene discussie. In dit hoofdstuk worden de resultaten van de studies uitgevoerd in dit proefschrift besproken, toegespitst op de doelstellingen genoemd in het eerste hoofdstuk. Aan het eind van het hoofdstuk worden suggesties voor toekomstig onderzoek gegeven en worden toekomstperspectieven geschetst voor verdere toepassingen van CBCT binnen de orthodontie.

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The acknowledgements. Not uncommon to be the part of a PhD thesis most read. So for you who start to read here, I challenge you to return to chapter 8 and at least read through the discussion. You might even find it interesting!

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The author was born in the St Radboud Hospital in Nijmegen The Netherlands on Friday the 4th of April 1980, the 95th day of that year. After finishing his secondary school at the Canisius College Mater Dei in Nijmegen in 1998, he started his undergraduate dental education later that year at the Katholieke Universiteit Nijmegen. During his study, he went to Nepal several times with the Nepal Oral Health Society for dental camps in rural areas of Nepal. From July to October of 2002 the author went to the Universiteit Stellenbosch in South Africa as an elective student, where he participated in clinical work in the department of orthodontics and the department of maxillofacial surgery. Since then he has visited South Africa on many occasions and maintained close ties with the colleagues he met and worked with during that time. In July 2003 he graduated as a dentist and started his professional career in dentistry. After working in general dentistry in several practices domestically and abroad, he started the postgraduate programme in orthodontics at the Radboud University Nijmegen Medical Centre in 2005, which he completed in July 2009. Since then Olivier worked part time at the Department of Orthodontics and Craniofacial Biology on the research for this thesis which was supported by the Dutch Technology Foundation STW, which is part of the Netherlands Organisation for Scientific Research (NWO) and partly funded by the Ministry of Economic affairs, Agriculture and Innovation (project number 10315).

At present Olivier works in several practices as an orthodontist and plans to open his own orthodontic office in the Nijmegen area within the coming years.

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