Dentomaxillofacial Radiology (2022) 51, 20210335

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SYSTEMATIC REVIEW

CBCT in dental age estimation: A systematic review and meta analysis

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Objectives: This study aimed to investigate the reproducibility of dental age estimation methods in cone beam computed tomography (CBCT) and the correlation between dental (DA) and chronological (CA) ages.
Methods: The scientific literature was searched in six databases (PubMed, Scopus, LILACS, Web of Science, SciELO, and OATD). Only observational studies were selected. Within each study, the outcomes of interest were (I) the quantified reproducibility of the method (κ statistics and Intraclass correlation coefficient); and (II) the correlation (r) between the dental and chronological ages. A random-effect three-level meta-analysis was conducted alongside moderator analysis based on methods, arch (maxillary/mandibular), population, and number of roots.
Results: From 671 studies, 39 fulfilled the inclusion criteria, with one study reporting two different methods. The methods used in the studies were divided into metric (n = 17), volumetric (n = 20), staging (n = 2), and atlas (n = 1). All studies reported high examiner reproducibility. Group 1 (metric and volumetric) provided a high inverse weighted r ($\delta = -0.71$, CI [-0.79,–0.61]), and Group 2 (staging) provided a medium-weighted r ($\delta = 0.49$, CI [0.44, 0.53]). Moderator analysis on Group one did not show statistically significant differences between methods, tooth position, arch, and number of roots. An exception was detected in the analysis based on population (Southeast Asia, $\delta = -0.89$, CI [-0.94,–0.81]).
Conclusion: There is high evidence that CBCT methods are reproducible and reliable in dental age estimation. Quantitative metric and volumetric analysis demonstrated better performance in predicting chronological age than staging. Future studies exploring population-specific variability for age estimation with metric and volumetric CBCT analysis may prove beneficial.
Dentomaxillofacial Radiology (2022) **51**, 20210335. doi: 10.1259/dmfr.20210335

Cite this article as: Merdietio Boedi R, Shepherd S, Mânica S, Franco A. CBCT in dental age estimation: A systematic review and meta analysis. *Dentomaxillofac Radiol* (2022) 10.1259/dmfr.20210335.

Keywords: Cone Beam Computed Tomography; Age Determination by Teeth; Forensic dentistry; radiology; systematic review

Introduction

The development of diagnostic and therapeutic radiology in medicine have opened opportunities and potential advantages in Forensic Odontology. These improvements have enabled new perspectives in dental age estimation, in particular improvements in data acquisition, image fidelity, and visualization of structures.[1] Greater access to the detail of complex anatomical structures, such as the human teeth, has allowed analytics such as linear regressions[2] and forensic statistic modelling.[3] It is however important to note that these advances in radiological techniques must be matched by skills development in viewing and interpreting the resultant images. As contemporary forensic

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Received 19 July 2021; revised 21 December 2021; accepted 21 December 2021; published online 07 January 2022

odontology changes, forensic odontologists need to change.[4]

Forensic odontology has benefited mainly from the use of periapical[5] and panoramic radiographs[6] but with the advanced imaging, the cone beam computed tomography (CBCT), was introduced to the forensic practice. The advantage of CBCT over intraoral periapical and panoramic imaging in dental age estimation comes from the availability of three-dimensional multiplanar navigation, allowing more detailed observation of morphological features. Among these features are pulp chamber size that demonstrates time-dependent reduction in volume following the progressive deposition of secondary dentin. This phenomenon has great value in the estimation of age of adults.[7,8] Children and juvenile populations are different and are usually studied by means of developmental parameters such as dental staging[9] and measurements of tooth ratios.[9]

It must be emphasized that CBCT made significant contributions Forensic Odontology.[10–12] Studies have highlighted the application of CBCT for human identification,[10] bite-mark analysis,[12,13] and dental age estimation[14–17] among other disciplines. As the literature grows, new evidence is presented that raises ever more pertinent questions. Consequently, systematic reviews and meta-analyses have become more common as a tool to extract data and build evidence-based answers. Between 2017 and 2021, several systematic reviews on dental age estimation were published.[8,18–20] The studies had in common the stratified population targeted for dental age estimation. In other words, Sehrawat et al.,[19] Yusof et al,[18] and Franco et al[20] revisited age estimation studies in children and adolescents, while Marroquin et al investigated adults.[8] The outcomes of the previous systematic reviews were able to indicate best-fitting methods for a specific population,[20] and the overall performance of a single method in populations worldwide.[18] Hence, the present study is justified to bridge the gap of systematic reviews of techniques from CBCT images, namely metric, volumetric, and staging analyses. Some of these analyses—especially volumetric—are described in the literature as time-consuming and suboptimal for application in practice,[8] deserving a deep and dedicated look that could lead to evidence-based answers to whether they are reproducible and reliable enough for dental age estimation.

In order to further understand whether accurate dental age estimation is possible using CBCT, the objective of this systematic review was to investigate the intra- and interobserver reproducibility and the *r*-value between visualized 3D dental parameters and the chronological age (CA). The set research question was: Are CBCT methods reproducible and reliable for dental age estimation?

Methods and materials

Eligibility criteria

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used.[21] The research question stated in the previous section was established based on population (P), exposure (E), comparison (C), and outcome (O) as follows: p = human population; E = the CBCT methods used for dental age estimation (*i.e.,* metric/volumetric, staging); C = the CA; and O = the quantified reproducibility and the *r*-value between the dental and CA (O).

Information sources

An electronic search (16 April 2021–19h April 2021) was performed in five databases to find out primary data: PubMed, Scopus, LILACS, Web of Science, and SciELO. Grey literature was collected from Open Access Theses and Dissertation (OATD) to reduce publication bias.

Search strategy

Search strings were built based on Medical Subject Headings (MeSH), Descriptors in Health Sciences (DeCS), and Emtree terms using associated key words (Table 1) combined with Boolean operators (*i.e.,* "AND" and "OR") and truncation (*) strategies. The keywords were associated with dental age estimation and CBCT using database-specific terms, synonyms, and their variations.

Selection process

Study eligibility was based on the following inclusion criteria: *in vivo* studies providing reproducibility and *r*-value between dental parameters and CA using CBCT, no restriction for population, year of publication or language were applied. The exclusion criteria included other means of CT imaging (*i.e.,* Multidetector CT), studies including populations with known systemic diseases and dental anomalies, books, book chapters, editorials, letters to the editor, case reports, case series, abstract, and systematic reviews.

Study selection was performed by a main reviewer supervised by two others—all forensic odontologists. The acquired data were registered in EndNote 20 (Thomson Reuters, Toronto, Canada). Within the software, different folders were created to allocate studies based on their database of origin. The first study selection was done by automatic duplicate detection using an EndNote built-in function and reviewed manually by the main examiner. The remaining studies were exported to Microsoft Excel 365 (Microsoft Ltd, Washington, USA) using tab-delimited output tools in EndNote 20 and then curated manually. Based on the title and abstract information, the second study selection phase was performed. Titles and abstracts not related to the topic of interest were promptly excluded. In case of doubts, the article was maintained in the sample and progressed to the next phase. Every article removed during the progressive

Table 1 The query for database search

DATABASE	***SEARCH STRATEGY***	***n***
PubMed	((“Cone-Beam Computed Tomography”[Mesh] OR CBCT OR “Cone Beam Computed Tomography” OR “Cone Beam CT”) AND (Dentition[Mesh] OR tooth OR teeth OR dental) AND (“Age Determination by Teeth”[Mesh] OR “age estima*” OR “age determination” OR “age assessment” OR “dental age”))	57
Scopus	ALL ((“Cone Beam Computed Tomography” OR “Cone-Beam Computed Tomography” OR “Cone Beam CT” OR CBCT) AND (“Age Determination” OR “Age Assessment” OR “Age estimation”) AND (dental OR dentition OR tooth OR teeth))	532
LILACS	(“cone beam computed tomography” OR “cone beam computerized tomography” OR “cone beam computer assisted tomography” OR CBCT OR “cone beam CT”) AND (“age measurement” OR “age estimation” OR “age determination” OR “dental age”) AND tooth OR teeth OR dentition	6
SciELO	(“cone-beam computed tomography” or “CONE BEAM COMPUTED TOMOGRAPHY” or “CONE BEAM CT” or CBCT) AND (“AGE estimation” or “AGE DETERMINATION” or “AGE DETERMINATION” or “AGE ASSESSMENT”) AND (tooth or teeth or dentition)	3
Web of Science	ALL=((“Cone Beam Computed Tomography” OR “Cone-Beam Computed Tomography” OR “Cone Beam CT” OR CBCT) AND (“Age Determination” OR “Age Assessment” OR “Age estimation”) AND (dental or dentition or tooth or teeth))	71
Open Access Theses and Dissertation	“dental age estimation” OR “age determination” OR “age assessment” OR “age estimation” AND “cone-beam computed tomography” OR “CONE BEAM COMPUTED TOMOGRAPHY” OR “CONE BEAM CT” OR CBCT	2

Boolean operator [Mesh] indicates that the keyword needs to be pulled from MeSH and all its derivatives.
Boolean operator asterisk, or wildcard truncation, (*) indicates that the search results may be displayed if the previous query requirement was met (i.e., “age estima*” requesting a search within age estima*tion* or age estimat*ive*)

selection was noted separately. Subsequently, the third study selection was accomplished by evaluating the full texts to check for their eligibility. Articles that remained after full-text exclusions underwent data collection process.

Data collection

Data to be collected consisted of authors’ names, year of publication, studied population, sample size, age range, observed tooth/teeth, CBCT device, software for image analysis, method for age estimation, the (intra- and interobserver) reproducibility of the reported method and the *r*-value between the assigned independent variable and the CA. In case of unclear data reported in the eligible studies, e-mails were sent to the corresponding authors requesting clarification.

Study risk of bias assessment

The selected studies were assessed with risk of bias assessment by Joanna Briggs Institute (JBI) for cross-sectional studies.[22] Each study was classified by two observers (RMB and AF) using the critical appraisal checklist, with positive answer divided into 49%, 50–70%, and above 70% for high, moderate, and low risk of bias. Furthermore, the eligible studies underwent analysis with Begg’s rank correlation test to investigate if publication bias was present.[23]

Meta-analysis

A meta-analysis was designed to estimate the mean and variance of underlying effects between multiple studies with the same research question. This goal was achieved by integrating studies’ reports in dedicated statistical analyses.[24] In this meta-analysis, the primary effect size used was the *r*-value. Fisher *r-to-z* transformation was used to convert *r* into a normal metric value.[25] Furthermore, the authors relied on a random-effects model to assume that the effect size of interest is distributed due to the influence of study characteristics.[26] Normally, methods for handling effect size dependency are to treat the effect size independently (*i.e.,* coming from a different study); to take the average measure of multiple effect sizes; or even may select only one effect size per study.[27] These common approaches will lead to information loss and false independence, implying a questionable homogeneity within the study. To avoid these problems, a three-level meta-analysis model was applied. This model is an optimal approach to deal with effect size dependency using three levels of the model: variance of reported effect size, the variance of effect size within a study, and variance between studies.[28] Due to this approach, two types of heterogeneity measures were used, variance due to difference within studies (T_w^2 , I_w^2) and the difference between studies (T_b^2, I_b^2).

Synthesis methods

RStudio with metaphor statistical package was used in this study.[29,30] RStudio is open-source statistical software capable of advanced analysis in multiple fields of statistics. For a three-level meta-analysis, we used the rma.mv function via the metaphor package. Further adjustment using the Restricted Maximum Likelihood as an estimator, and Knapp and Hartung’s adjustment were undertaken to reduce the number of unjustified

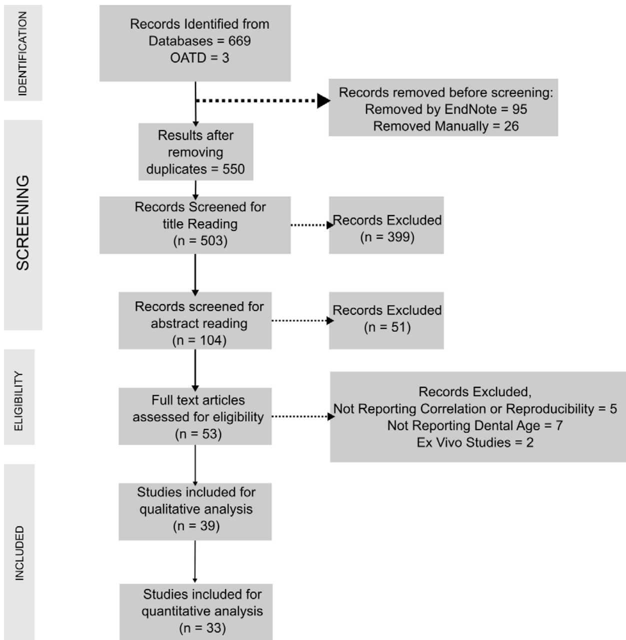

Figure 1 PRISMA flowchart for the systematic review

significant result due to the *Z* distribution.[31] Considering that the *r*-value has two separate directions in this study (negative *r*-value for inverse relation with CA, and positive *r*-value for linear relation with CA), we separated the analysis between them. Group 1 consisted of studies with a negative *r*-value, and Group 2 consisted of studies with a positive *r*-value. Subgroup analyses (also called moderator analysis) with categorical variables were conducted to investigate the effects of a potential moderator variable. Categorical moderators used in this analysis are methods (volumetric, metric), arch (maxillary or mandibular tooth), population (European, West Asia, East Asia, etc.), and number of roots (single or multiradicular tooth).

Certainty assessment

Two reviewers independently performed the analysis in each of the meta-analysis results based on their certainty using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) tool, which rated the studies within high, moderate, low, and very low certainty.[32]

Results

The initial literature search resulted in 671 studies, with 121 duplicates. An initial exclusion based on article type resulted in 503 studies. A total of 399 studies were excluded having reviewed the titles due to the absence of any relevance to the current research question. After reviewing the abstracts, 53 studies remained for full-text reading. Exclusion resulted from the following: use of periapical radiographs (n = 7), not reporting dental age estimation (n = 10), use of other means of CT (n = 9), use of panoramic radiographs (n = 14), use of lateral cephalometric radiographs (n = 1), literature reviews (n = 2), use of magnetic resonance imaging (n = 1), use of subjects with systemic/local conditions/diseases (n = 3), and use of *ex-vivo* samples (n = 4). The final sample included 39 studies for the qualitative analysis and 33 studies for quantitative analysis (Figure 1).

Study characteristics

The results of the qualitative analysis can be found in Tables 2 and 3. The first eligible study using CBCT for dental age estimation was conducted in 2006.[67] Across 39 studies, 40 methods were reported, with one study using two different methods.[33] Dental age estimation methods were metric (n = 17),[14,33,35,36,40,41,43,45–47,49,51,55,57,63–65] volumetric (n = 20),[2,11,16,33,34,37–39,42,48,50,53,54,56,58–62,67] staging (n = 2),[44,52] and atlas.[66]

Twenty-two studies reported reproducibility values with inter- and intraclass correlation coefficient,[2,11,14,16,35,37–39,41–43,46,49–51,53,59–61,63–65] one study reported technical error measurement,[57] two studies reported Cronbach's α,[33,66] and one study reported Cohens' κ.[66] All studies reported high agreement between and within the observers regardless of the reproducibility measurement used. The intraclass correlation coefficient reported ranged from 0.592 to 0.981 for metric and 0.856 to 0.998 for volumetric analysis. Interclass correlation coefficient ranged from 0.798 to 0.93 for metric and 0.63 to 1 for volumetric analysis. Three studies reporting reproducibility values by means of *t*-test[36,47,67] and one by *r*-value[58] were detected.

In metric methods, the *r*-value ranged from −0.094 to −0.978, while in volumetric methods, it ranged from −0.24 to −0.985. Staging methods had a variation from 0.44 to 0.575. Five studies were conducted using East-Asian populations,[36,38,50,55,61] six studies used European populations,[2,34,37,54,64,67] three studies used North African population,[16,43,58] two studies used South American populations,[53,56] five studies used South Asian populations,[11,41,42,47,52] seven studies used Southeast Asian populations,[39,44,48,51,57,60] nine studies used West Asian populations,[33,35,45,46,49,59,62,63,65] one study only reported the population ethnicity,[66] and one study did not report the population origin.[40] When it comes to arch position, seven studies used mandibular teeth,[35,40,44,48,51,52,64] twenty used maxillary teeth,[11,14,33,36,38,39,42,43,46,47,49,50,53–56,60,61,63,65] and twelve used both arches..[2,16,34,37,41,45,57–59,62,66,67] Single-rooted teeth were used in twenty eight studies ,[2,11,14,33,34,36–39,42–47,49,50,53–60,62,65,67] while seven studies used multirooted teeth,[16,35,41,48,51,61,63] and four studies used both single and multirooted teeth.[40,52,64,66]

Risk of bias in eligible studies

Two studies had a moderate risk of bias,[47,63] while the other studies revealed low risk of bias (Table 4). The most common bias that affected the studies was not addressing the validity and reliability of the measured

Table 2 Summary of the included studies

Study ID	*Authors*	*Population*	n	*Age Range*	*Tooth Sample*
1	Yang et al. 2006[33]	Belgian	19	23–70	U1, U2, U3, L1, L2, L3, L4
2	Wu et al. 2016[34]	Chinese	420	15–84	U1
3	Nemsi et al. 2017[35]	Tunisian	120	22–67	U3, U5
4	Helmy et al. 2020[17]	Egyptian	187	21–50	U7 L7
5	Rai et al. 2016[36]	Indian	60	20–85	U3
6	Pinchi et al. 2015[2]	Italian	148	10–80	21
7	Elgazzar et al. 2020[37]	Egyptian	200	15–60	U3 L3
8	Yang et al. 2020[38]	Chinese	230	8,18–19,92	21 23
9	Biuki et al. 2017[39]	Iranian	122	13–70	U1 U2 U3 L1 L2 L3
10	Ceena Denny et al. 2021[40]	Indian	100	-	U6 U7 L6 L7
11	Salemi et al. 2020[41]	Iranian	300	14–60	13
12	Molina et al. 2021[42]	Spanish	107	14–70	U1 U2 U3 L1 L2 L3 L4 L5
13	Penaloza et al. 2016[43]	Malaysian	101	15–75	U1 U2 U5 L2 L3 L4
14	Koh et al. 2017[44]	Malaysian	284	Above 20	L4
15	Asif et al. 2019a[45]	Malaysian	73	15–23	L8
16	Al-Omoush et al. 2020[46]	Jordanian	135	18–63	U8
17	Archana et al. 2018[9]	Indian	100	12 - Above 18	U8 L8
18	Doni et al. 2021[47]	-	160	20–70	L5 L6
19	Gulsahi et al. 2018[48]	Turkish	204	Above 15	U1 U2 U3 L3 L4 L5
20	Haghanifar et al. 2019[49]	Iranian	377	20–69	U1 U3 L1 L3
21	Andrade et al. 2019[50]	Brazilian	116	13–70	U1 U3
22	Farhadian et al. 2019[51]	Iranian	300	14–60	U3
23	Kazmi et al. 2019[52]	Pakistan	717	15–65	23 33
24	Asif et al. 2019b[53]	Malaysian	300	16–65	U3 11
25	Kazmi et al. 2021[12]	Pakistan	717	15–65	23 33
26	Star et al. 2011[54]	Belgian	111	10–65	U1 U2 U3 U4 U5 L1 L2 L3 L4 L5
27	Alsoleihat et al. 2017[55]	Jordanian	155	18–58	L8
28	De Angelis et al. 2015[56]	Italian	91	15–85	13
29	Adisen et al. 2018[57]	Turkish	131	17–75	U3
30	Zhan et al. 2020[58]	Chinese	392	16–76	21 22 23
31	Asif et al. 2018[59]	Malaysian	110	16–65	U1
32	Zhang et al. 2019[60]	Chinese	414	20–65	L8
33	Oscandar et al. 2018[61]	Indonesian	180	6–50	L6
34	Porto et al. 2015[62]	Brazilian	72	22–70	U1
35	Asif et al. 2020[15]	Malaysian	191	7–14	U3
36	Różyło-Kalinowska et al. 2020[63]	Polish	121	5–13	31 32 33 34 35 36 37
37	Ugur Aydin et al. 2019[64]	Turkish	120	14–75	U1
38	Lee et al. 2017[65]	South Korean	224	20–77	13
39	Buchanan 2019[66]	Hispanic	250	8.5–20.7	Left or Right Region

L, Lower; U, Upper.
Number notation in Tooth Sample follows the Federation Dentaire Internationale (FDI) numbering.

outcome—which is related to the presence/absence of methods' reproducibility. Begg's rank correlation test indicated that publication bias was not present in our systematic review ($p > 0.05$).

Meta-Analysis

Table 5 contains the multilevel meta-analysis results. Across 33 studies, there were 179 observations. Group 1 consisted of 31 studies with 170 nested effect sizes, and Group Table 6 2 consisted of two studies with nine nested effect sizes. Group 1 includes metric and volumetric studies provides a high inverse weighted r ($\delta = -0.71$, CI [-0.79,–0.61]) with high certainty. Group 2had the staging methods and revealed a medium-weighted r ($\delta = 0.49$, CI [0.44, 0.53]) with moderate certainty due to small number of studies

Considerable heterogeneity was observed in between study analysis for Group 1 ($T_b^2 = 0.24$, $I_b^2 = 0.85$), and a small heterogeneity was observed within the study

Table 3 Continuation on Included Studies Characteristics

Study ID	*Device*	*Software*	*Method*	*Parameters*	r *n*	*Min* r	*Max* r	*ICC*	
								Inter	*Intra*
1	3D Accuitomo	iDixel	V	Pulp Tooth Ratio	1	-	−0.54	-	-
2	Galileos	-	M	Kvaal Method	7	0.69	0.86	-	-
3	Galileos	Galileos Viewer	M	Pulp Dentine Ratio	3	−0.84	−0.85	0.976	0.993
4	PlanMeca	ITK-SNAP 3.8	V	Pulp Chamber Volume	6	−0.69	−0.82	0.917	0.979
5	Kodak 9000	KODAK Dental Imaging Software 6.8	M	Pulp Tooth Ratio	1	-	0.42	-	-
6	Scanora 3D	OnDemand 3D	V	Pulp Tooth Ratio	1	-	−0.76	0.99	-
7	Cranex 3D	ITK-SNAP 3.8	V	Pulp Chamber Crown Ratio	4	−0.90	−0.96	-	-
8	PlanMeca	MIMICS 21.0	V	Pulp Tooth Ratio	6	−0.67	−0.88	0.989	0.973
9	NewTom VG	MIMICS 10.01	V	Pulp Tooth Ratio	13	0.53	0.85	-	-
10	Promax 3D	-	M	Tooth Coronal Index	1	-	−0.65	0,592–0,730	-
11	Cranex 3D	OnDemand 3D	M	Pulp Tooth Ratio	24	−0.16	−0.61	-	0.94
12	Promax 3D	Planmeca Romexis 2.3.1 .R	V	Pulp Crown Ratio	3	−0.40	−0.60	-	0,63–0,83
13	Kodak 9000-3D; i-CAT	OSIRIX	M	Kvaal Method	41	−0.21	−0.65	-	-
14	i-CAT	i-CAT Vision	S	Gustafson Method modified by Olze	4	0.44	0.62	-	-
15	i-CAT	MIMICS	M	Open Apices Surface Area	1	-	−0.92	-	0.9
16	-	OnDemand 3D	M	Pulp Tooth Ratio	1	-	−0.52	-	0,91–0,93
17	-	Planmeca Romexis	S	Demirjian	5	0.48	0.56	-	-
18	Scanora 3D	OnDemand 3D	M	Tooth Coronal Index	2	−0.09	−0.18	-	-
19	Kodak CS9300	3D DOCTOR	V	Pulp Tooth Ratio	6	0.15	0.53	0,81–0,9	0,85–0,93
20	Cranex 3D	OnDemand 3D	M	Pulp Tooth Ratio	16	−0.33	−0.76	-	-
21	KODAK K9500	ITK-SNAP 3.4	V	Pulp Volume	2	−0.87	−0.88	0,994–0,9998	0,994–1
22	Cranex 3D	OnDemand 3D	M	Pulp Tooth Ratio	8	−0.16	−0.78	0.99	0.99
23	Promax 3D	Planmeca Romexis	V	Pulp Volume	2	−0.51	−0.51	0,912–0,965	0,945–0,995
24	i-CAT	MIMICS	V	Pulp Tooth Ratio	6	0.68	0.84	0.968	0.945
25	Promax 3D	Planmeca Romexis	V	Pulp Tooth Ratio	2	−0.64	−0.66	0,8–0,9	0.9
26	Scanora 3D	Simplant Pro	V	Pulp Tooth Ratio	12	−0.24	−0.88	-	-
27	-	-	M	Pulp Tooth Ratio	1	-	−0.36	-	0,85–0,87
28	i-CAT	OSIRIX	V	Pulp Tooth Ratio	3	−0.51	−0.70	-	-

(Continued)

Table 3 (Continued)

Study ID	*Device*	*Software*	*Method*	*Parameters*	r *n*	*Min* r	*Max* r	*ICC*	
								Inter	*Intra*
29	Promax 3D	3D DOCTOR	V	Pulp Tooth Ratio	1	-	−0.49	-	-
			M	Kvaal Method	1	-	−0.33	-	-
30	Promax 3D	MIMICS	V	Pulp Tooth Ratio	6	−0.78	0.81	0,932–0,975	0,946–0,987
31	i-CAT	MIMICS	V	Pulp Tooth Ratio	2	−0.80	−0.88	0.982	0.914
32	Pax-Zenith 3D	"Open Source"	V	Pulp Enamel Ratio	3	−0.63	−0.69	0.856	0,911–0,937
33	Vatech	ITK-SNAP 3.6	V	Pulp Chamber Volume	2	−0.98	−0.99	-	-
34	i-CAT NG	i-CAT Workstation; DentalSlice	V	Pulp Tooth Ratio	2	−0.39	−0.55	-	-
35	i-CAT	MIMICS 21.0; 3-Matics	M	Open Apices Surface Area	4	−0.97	−0.98	0.902	0.931
36	NewTom 5G XL	NNT	M	Cameriere Open Apices Ratio	0	-	-	0,711–0,981	0,798–0,988
37	i-CAT	inVivo 5	M	Pulp Tooth Ratio	1	-	−0.62	-	0.869
38	-	OnDemand 3D	M	Pulp Tooth Ratio	3	−0.60	−0.73	-	-
39	CB MercuRay	Anatomage	A	London Atlas	-	-	-	-	-

A, Atlas; ICC, Intra-Class Correlation Coefficient for Inter-and Intra-observer; M, Metric; Max *r*, Maximum r value reported; Min *r*, Minimum *r* value reported; S, Staging; V, Volumetric; *r* n, Number of correlation coefficient (r) reported.
Study ID corresponds with Table 2.

(T_w^2 = 0.13, I_w^2 = 0.03) with significant Q test. Group 2 does not appear to have any heterogeneity between and within the study concluded with an insignificant Q test.

Moderator analysis
Table 6 displays the overall analysis conducted for the moderator variables for Group 1, all with high certainty except for population analysis with low certainty of evidence due to indirectness from the included studies.[68] Due to a small number of included studies (n = 2), moderator variable analysis was not conducted in Group 2. There is no significant difference in r-values between methods, tooth position in arch and number of roots. In the population analysis, Southeast Asian study populations significantly differ among other populations (δ = −0.89, CI [-0.94,–0.81]).

Discussion

The results show a promising capability of CBCT in dental age estimation. This tool was especially useful for the detailed volumetric measurement of morphological dental features of adults. However, the European Commission Guidelines on CBCT for dental and maxillofacial radiology discourages the use of CBCT in daily dental practice without a proper justification and ideal image optimisation.[69] Furthermore, guidelines describing the best practice for the use of CBCT in forensic dental identification and dental age estimation are not available. These guidelines would be fundamental for forensic examination of the living and could be helpful to aid researchers and forensic odontologists to conceptualisz the methods and their application while still considering limitations and biosafety.

This systematic review and meta-analysis were designed to review the reliability and reproducibility of age estimation methods using CBCT. In general, high agreement was found in inter- and intraobserver analyses in each eligible study. Besides ICC approach to quantify reproducibility, alternative methods consist of technical error measurement,[70] Cronbach's α[71] (for continuous variables) and Cohens' κ (categorical variables)[72]—these tests were detected throughout the eligible papers.[33,57,66] However, another important finding is that multiple studies used different methods, namely t-tests[36,47,67] and r-values.[58] These methodological decisions could reduce the reliability of the method. Streiner reports this as a type III error, which is "*getting the right answer to a question that no one is asking*".[73] On the same note, using the r-value will mask the systematic

Table 4 Risk of Bias Assessment by Joanna Briggs Institute for Cross-Sectional Study

Study ID	*Q1*	*Q2*	*Q3*	*Q4*	*Q5*	*Q6*	*Q7*	*Q8*	*Total*
1	✓	✓	✓	✓	✓	✓	x	✓	87,50%
2	✓	✓	✓	✓	✓	✓	x	✓	87,50%
3	✓	✓	✓	✓	✓	✓	✓	✓	100,00%
4	✓	✓	✓	✓	✓	✓	✓	✓	100,00%
5	x	✓	✓	✓	x	x	x	✓	50,00%
6	x	✓	✓	✓	✓	✓	✓	✓	87,50%
7	✓	✓	✓	✓	✓	✓	x	✓	87,50%
8	✓	✓	✓	✓	✓	✓	✓	✓	100,00%
9	✓	✓	✓	✓	✓	✓	x	✓	87,50%
10	✓	x	✓	✓	✓	✓	✓	✓	87,50%
11	✓	✓	✓	✓	✓	✓	✓	✓	100,00%
12	✓	✓	✓	✓	✓	✓	✓	✓	100,00%
13	✓	✓	✓	✓	✓	✓	✓	✓	100,00%
14	✓	✓	✓	✓	✓	✓	x	✓	87,50%
15	✓	✓	✓	✓	✓	✓	✓	✓	100,00%
16	✓	x	✓	✓	x	x	✓	✓	62,50%
17	✓	✓	✓	✓	✓	✓	x	✓	87,50%
18	✓	x	✓	✓	✓	✓	x	✓	75,00%
19	✓	✓	✓	✓	✓	✓	✓	✓	100,00%
20	✓	✓	✓	✓	✓	✓	x	✓	87,50%
21	✓	✓	✓	✓	✓	✓	✓	✓	100,00%
22	✓	✓	✓	✓	✓	✓	✓	✓	100,00%
23	✓	✓	✓	✓	✓	✓	✓	✓	100,00%
24	✓	✓	✓	✓	✓	✓	✓	✓	100,00%
25	✓	✓	✓	✓	✓	✓	✓	✓	100,00%
26	✓	✓	✓	✓	✓	✓	x	✓	87,50%
27	✓	✓	x	✓	✓	✓	✓	✓	87,50%
28	✓	✓	✓	✓	✓	✓	x	✓	87,50%
29	✓	✓	✓	✓	✓	✓	✓	✓	100,00%
30	✓	✓	✓	✓	✓	✓	✓	✓	100,00%
31	✓	✓	✓	✓	✓	✓	✓	✓	100,00%
32	✓	✓	✓	✓	✓	✓	✓	✓	100,00%
33	✓	✓	x	✓	✓	✓	x	✓	75,00%
34	✓	✓	x	✓	✓	✓	x	✓	75,00%
35	✓	✓	✓	✓	✓	✓	✓	✓	100,00%
36	✓	✓	✓	✓	✓	✓	✓	✓	100,00%
37	✓	✓	✓	✓	✓	✓	✓	✓	100,00%
38	✓	✓	✓	✓	✓	✓	x	✓	87,50%
39	✓	✓	✓	✓	✓	✓	✓	✓	100,00%

Q1. Were the criteria for inclusion in the sample clearly defined?
Q2. Were the study subjects and the setting described in detail?
Q3. Was the exposure measured in a valid and reliable way?
Q4. Were objective, standard criteria used for measurement of the condition?
Q5. Were confounding factors identified?
Q6. Were strategies to deal with confounding factors stated?
Q7. Were the outcomes measured in a valid and reliable way?
Q8. Was appropriate statistical analysis used?

bias since a large difference between the observation will not be detected as long as there is a consistent error in the measurement.[72]

Our findings concerning the correlation between observed dental parameters and CA revealed high- and medium-weighted *r*-values for Group 1 (metric and volumetric) and Group 2 (staging). Studies that used the metric analysis used ratio-based measurements to overcome the angular distortion and to promote a systematization of the selection of measurement units (*i.e.,* centimetres and millimetres) in each analysis. On the contrary, in volumetric studies, the methods depend on the capability and performance of the software. The earliest study by Yang et al. (2006) was conducted in a semi-automatic software.[67] In the later studies, researchers commonly use region-growing tools and greyscale-threshold based volumetric analysis, which provide an automated segmentation,[16,60] three-dimensional masking to incorporate further analysis,[51] and a less time-consuming process.[34] Improvements in software used in volumetric studies should be encouraged to allow more accurate detected of anatomic limits by distinguishing adjacent voxels on an image. Whilst the variety of software available offers multiple possibilities of choice, this variety also serves to increase the methodological heterogeneity across studies. Forensic-dedicated freeware are encouraged so researchers can contribute with inputs and plug-ins to fulfil the experts' needs in practice.

Volumetric assessment in CBCT relies heavily on the voxel size.[74] CBCT image acquired with small voxel size may produce a higher fidelity image,[75] but also may increase radiation dose depending on protocol.[76] This side-effect might contradict the need for high-resolution images to create an accurate volumetric rendering in CBCT. Pauwels et al. (2015) stated that to preserve image quality, a lower radiation dose can be effectively achieved by selecting a smaller field of view.[77] Oenning et al. (2018) proposed a new approach following the concept of image acquisition with radiation dose "As Low as Diagnostically Acceptable being Indication-oriented and Patient-specific" (ALADAIP).[78] ALADAIP principle creates a new perspective in dental imaging and moves imaging science to create a standard based on the clinical needs and patient care.[79] Hence, an alternative dental age estimation method in CBCT needs to be explored with lower radiation dose, especially in the late adolescence and early adulthood—a time interval in which the number of age estimation requests to investigate the age of majority (16 and 18 in most countries) increases. In this context, forensic experts must know that the younger the individuals, the higher risk of radiation-induced biological effects.[80] This is one of the reasons why panoramic radiographs remain the most common image of choice for age estimation of children and adolescents. When it comes to the deceased, radiation dose is not relevant,[81] but the lack of standardized protocols for (CB)CT image

Table 5 Results of Three-Level Meta-Analysis in Correlation Coefficient between Dental Parameters and Chronological Age

	n *(ES)*		*95% CI*		*Q(df)*	T^2_w	I^2_w	T^2_b	I^2_b	*Certainty Rating*[a]
Group 1	31(170)	−0.71	−0.79	−0.61	6173.5615(169)	0.04	0.13	0.24	0.85	⊕⊕⊕⊕ High
Group 2	2 (9)	0.49	0.44	0.53	4,7412(8)	0	0	0	<0.01	⊕⊕⊕ Moderate

95% CI, confidence interval; ES, number of effect sizes ; n, number of studies.
δ = weighted average effect size;
Q(df) = Q test for homogeneity and degrees of freedom
T2= estimated systematic variance in within (w) or between (b) studies
I2= percentage of systematic variance of the overall observed variance in within (w) or between (b) studies.
[a]Certainty is rated following the GRADE Certainty Assessment

acqusition for age estimation reflects the heterogeneous scenario in Forensic Odontology.

A deeper look into the results was feasible by means of a three-level meta-analysis. More specifically, the analysis of Group 1 showed a high inverse-weighted *r* of −0.71 (CI [-0.79,–0.61]). However, through the moderator analysis, no difference was observed between metric and volumetric assessments and the other *a priori*-defined moderating variables. In the present meta-analysis, statistically significant differences were detected involving population-specific comparisons of samples. Specifically, individuals from Southeast Asia differed significantly from other populations. This event might be explained by the amount of reported effect size (n = 56) in the study and the use of a novel technique proposed by the authors (-0.92 to −0.98).[14,51] Oscandar et al. (2018) and Helmy et al. (2020) also acquired high inverse *r*-value, ranging from −0.98 to −0.99[57] and −0.69 to −0.82,[16] respectively. Although this moderating variable was significant, it needs to be interpreted carefully.

It is important to note that employing a staging method for a specific modality creates a better model rather than metric or volumetric measurements in developing dentition.[82] Furthermore, the moderator analysis was limited on explaining the variability in Group 1 due to the small number of studies in Group 2. Considering the heterogeneity present in Group 1, future studies might seek to more thoroughly explore this issue since there is an underlying cause of high heterogeneity (I_b^2 = 0.85). Other recommendations for future studies include the need to set proper statistic methods to quantify the reproducibility in dental age estimation studies (to avoid neglecting systematic errors), and the need

Table 6 Results of Three-Level Meta-Analysis in Correlation Coefficient between Dental Parameters and Chronological Age.

	n*(ES)*		*95% CI*		T^2_w	R^2_w	T^2_b	R^2_b	*Certainty Rating**
Methods									
Volumetric	18(64)	−0.75	−0.84	−0.62	0.04	0.00	0.24	0.03	
Metric	13(106)	−0.66	−0.79	−0.47					⊕⊕⊕⊕ High
Arch									
Mandibular	4 (6)	−0.81	−0.93	−0.53	0.04	0.00	0.25	0.03	
Maxillary	18(79)	−0.71	−0.81	−0.57					⊕⊕⊕⊕ High
Both	9 (85)	−0.68	−0.82	−0.44					
Population									
East Asian	4 (18)	−0.73	−0.87	−0.48	0.04	0.01	0.1499	0.49	
European	5 (20)	−0.60	−0.79	−0.30					
North African	3 (13)	−0.86	−0.94	−0.68					
South American	2 (4)	−0.73	0.91	−0.34					⊕ Low
South Asian	3 (5)	−0.61	−0.83	−0.22					
Southeast Asian[b]	6 (56)	−0.89	−0.94	−0.81					
West Asian	7 (52)	−0.49	−0.69	−0.23					
Number of Roots									
Single-rooted	24(154)	−0.70	−0.78	−0.59	0.04	0.00	0.23	0.01	⊕⊕⊕⊕ High
Multi rooted	6 (14)	−0.82	−0.91	−0.64					

95% CI, confidence interval; ES, number of effect sizes; n, number of studies.
δ = weighted average effect size;
Q(df) = Q test for homogeneity and degrees of freedom
T2= estimated systematic variance in within (w) or between (b) studies
R2= percentage of systematic variance of the overall observed variance in within (w) or between (b) studies.
[a]Certainty is rated following the GRADE Certainty Assessment
[b]significant value ($p < 0.05$)

to standardize the protocols of observational studies following uniform guidelines, such as STROBE.

Conclusion

There is high evidence that CBCT methods are reproducible and reliable in dental age estimation. Volumetric and metric methods presented a high certainty of evidence with the highest weighted *r*-value for dental age estimation with no significant difference. High certainty was also observed in the moderator analysis variables, except for population due to the indirectness of evidence. The assessment of volumetric morphological characteristics using CBCT provides a significant improvement in the accuracy of dental age estimation in adults. The eligible articles revealed lack of standardized methods, especially when it comes to the quantification of examiner reproducibility.

Acknowledgment

The author would like to thank Dr Muhammad Khan Asif, Rehman College of Dentistry and Dr Gavin Revie, University of Dundee for their respective study data and Dr Holger Steinmetz, Leibniz-Institute for Psychology for the statistical support.

Funding

This work was supported by Ministry of Education and Culture, Universitas Diponegoro No.497/UN7.P/HK/2021.

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