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Artificial Intelligence for Detecting Cephalometric Landmarks: A Systematic Review and Meta-analysis

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Abstract

Using computer vision through artificial intelligence (AI) is one of the main technological advances in dentistry. However, the existing literature on the practical application of AI for detecting cephalometric landmarks of orthodontic interest in digital images is heterogeneous, and there is no consensus regarding accuracy and precision. Thus, this review evaluated the use of artificial intelligence for detecting cephalometric landmarks in digital imaging examinations and compared it to manual annotation of landmarks. An electronic search was performed in nine databases to find studies that analyzed the detection of cephalometric landmarks in digital imaging examinations with AI and manual landmarking. Two reviewers selected the studies, extracted the data, and assessed the risk of bias using QUADAS-2. Random-effects meta-analyses determined the agreement and precision of AI compared to manual detection at a 95% confidence interval. The electronic search located 7410 studies, of which 40 were included. Only three studies presented a low risk of bias for all domains evaluated. The meta-analysis showed AI agreement rates of 79% (95% CI: 76–82%, $I^2=99\%$) and 90% (95% CI: 87–92%, $I^2=99\%$) for the thresholds of 2 and 3 mm, respectively, with a mean divergence of 2.05 (95% CI: 1.41–2.69, $I^2=10\%$) compared to manual landmarking. The menton cephalometric landmark showed the lowest divergence between both methods (SMD, 1.17; 95% CI, 0.82; 1.53; $I^2=0\%$). Based on very low certainty of evidence, the application of AI was promising for automatically detecting cephalometric landmarks, but further studies should focus on testing its strength and validity in different samples.

Keywords Artificial intelligence · Cephalometric landmarks · Dentistry · Deep Learning · Computer vision

Introduction

Artificial intelligence (AI) is an innovative technology that allows digital systems to learn from experience, adapt to it, and perform tasks often performed by humans [1]. The advent of AI positively impacted data and medical sciences, allowing efficient analysis of large data banks [2]. The clinical application of AI has been growing and showing promising results in diagnosis [3, 4], monitoring [5, 6], and treatment of diseases [6, 7].

The application of AI in dentistry is recent and based predominantly on computer vision techniques [1], which use automatic segmentation and analysis to manage large medical image banks for a precise and efficient diagnosis [8]. Recent studies have focused on the application of AI for studying diagnoses of caries [9], oral cancer [10], gingivitis [11], radiolucent lesions of the mandible [12], root fractures [13], and orthodontic treatment [14]. The results of these

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studies have suggested that AI has space for growth, with the potential to improve dental care at lower costs and for the benefit of patients [1].

Technology has been extensively recommended for orthodontic clinical practice, with digital imaging examinations, 3D scanners, and intraoral cameras, which facilitate the scanning, sharing, and storing of the data collected [14]. However, analyzing these data is still slow and time-consuming [15]. For instance, the manual cephalometric analysis performed by orthodontists requires time and professional experience. In this scenario, AI has stood out for identifying cephalometric landmarks of orthodontic interest, making this task faster and less susceptible to human error [16]. Previous studies have shown a high accuracy of AI for detecting several cephalometric landmarks, with up to 98% agreement towards manual annotation [17] and at shorter times [18, 19].

However, the existing literature on the practical application of AI for detecting cephalometric landmarks of orthodontic interest in digital images (two- or three-dimensional) is heterogeneous, with different software and programming for this purpose, and without consensus regarding accuracy and precision. A recent systematic review and meta-analysis [20] found a 79% agreement, considering a margin of error of up to 2 mm for manual detection. However, this review included one specific AI system, excluding other critical automatic detection systems.

Therefore, this systematic review of the literature evaluated studies that assessed the level of agreement between AI, regardless of system, with the human registration for annotating cephalometric landmarks in digital imaging examinations (two- or three-dimensional).

Materials and Methods

Protocol Registration

The protocol of this systematic review was produced according to the PRISMA-P (Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols) guidelines [21] and registered in the PROSPERO database (http://www.crd.york.ac.uk/PROSPERO) (CRD42021246253). The review was reported according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) [22] guidelines and performed according to the JBI Manual for Evidence Synthesis [23].

Research Question and Eligibility Criteria

The eligibility criteria of this review were based on the following research question, created according to the PIRD framework (Population, Index test, Reference test, and Diagnosis): Is artificial intelligence (I) accurate to confirm cephalometric landmarks (D) manually detected (R) in digital imaging examinations of the general population (P)?

Inclusion Criteria

- Population: Two- or three-dimensional digital imaging examinations (teleradiography and computed tomography, respectively) applied to the general population, without restrictions of age and sex
- Index test: Automatic detection with artificial intelligence (different available approaches such as handcrafted, deep learning, or hybrid methods) with sufficient information on software calibration and databases
- Reference test: Manual/conventional detection by expert professionals
- Diagnosis: Detection of any cephalometric landmark of orthodontic significance, as long as explained in the study
- Study design: Diagnostic accuracy studies

There were no restrictions on language or year of publication.

Exclusion Criteria

- Literature reviews, letters to the editor/editorials, personal opinions, books/book chapters, case reports/case series, pilot studies, preprint studies not yet submitted for peer-reviewing, congress abstracts, and patents
- Studies with non-digital imaging examinations (conventional cephalograms)
- Studies that did not compare automatic and manual landmarking
- Studies with imaging examinations of *post-mortem* skulls and individuals with syndromes and cleft lip.

Sources of Information and Search

The electronic searches were performed until November 2021 in the Embase, IEEE Xplore, LILACS, MedLine (via PubMed), SciELO, Scopus, and Web of Science databases. OpenGrey and ProQuest were used to partially capture the “gray literature” to reduce the selection bias. The MeSH (Medical Subject Headings), DeCS (Health Sciences Descriptors), and Emtree (Embase Subject Headings) resources were used to select the search descriptors. Moreover, synonyms and free words composed the search. The Boolean operators “AND” and “OR” were used to improve the research strategy with several combinations. The search strategies in each database were made according to their respective syntax rules (Table 1). The results obtained in the primary databases were initially

Table 1 Database search strategies

Databases	Search strategy (November 2021)
Main databases	
Embase http://www.embase.com	#1 "cephalometry"/exp OR "cephalometry"
	#2 "artificial intelligence"/exp OR "artificial intelligence" OR "image processing"/exp OR "image processing" OR "machine learning"/exp OR "machine learning" OR "deep learning"/exp OR "deep learning" OR "artificial neural network"/exp OR "artificial neural network" OR "knowledge base"/exp OR "knowledge base"
	#1 AND #2
LILACS https://lilacs.bvsalud.org/	#1 (MH:cephalometry OR "cephalometric landmark*" OR "cephalometric analysis" OR "cephalometric measurements")
	#2 (MH: "artificial intelligence" OR MH:"image processing, computer-assisted" OR MH:"machine learning" OR MH:"deep learning" OR MH:"neural networks, computer" OR "convolutional neural network" OR "neural network model" OR "connectionist model" OR MH: "knowledge bases" OR "automated localization" OR "automated detection" OR "automatic localization" OR "automatic detection")
	#1 AND #2
PubMed http://www.ncbi.nlm.nih.gov/pubmed	#1 Cephalometry[Mesh] OR "Cephalometric Landmark*"[tw] OR "Cephalometric Analysis"[tw] OR "Cephalometric Measurements"[tw]
	#2 "Artificial Intelligence"[Mesh] OR "Image Processing, Computer-Assisted"[Mesh] OR "Machine Learning"[Mesh] OR "Deep Learning"[Mesh] OR "Neural Networks, Computer"[Mesh] OR "Convolutional Neural Network"[tw] OR "Neural Network Model"[tw] OR "Connectionist Model"[tw] OR "Knowledge Bases"[Mesh] OR "Automated Localization"[tw] OR "Automated Detection"[tw] OR "Automatic Localization"[tw] OR "Automatic Detection"[tw]
	#1 AND #2
SciELO https://scielo.org/	("Artificial Intelligence" OR "Image Processing, Computer-Assisted" OR "Machine Learning" OR "Deep Learning" OR "Neural Networks, Computer" OR "Convolutional Neural Network" OR "Neural Network Model" OR "Connectionist Model" OR "Knowledge Bases" OR "Automated Localization" OR "Automated Detection" OR "Automatic Localization" OR "Automatic Detection")
Scopus http://www.scopus.com/	#1 TITLE-ABS-KEY cephalometry OR "cephalometric landmark*" OR "cephalometric analysis" OR "cephalometric measurements"
	#2 TITLE-ABS-KEY "artificial intelligence" OR "image processing, computer-assisted" OR "machine learning" OR "deep learning" OR "neural networks, computer" OR "convolutional neural network" OR "neural network model" OR "connectionist model" OR "knowledge bases" OR "automated localization" OR "automated detection" OR "automatic localization" OR "automatic detection"
	#1 AND #2
Web of Science http://apps.webofknowledge.com/	#1 TS = (cephalometry OR "cephalometric landmarks" OR "cephalometric landmarking" OR "cephalometric measurements")
	#2 TS = ("artificial intelligence" OR "image processing, computer-assited" OR "machine learning" OR "deep learning" OR "neural networks, computer" OR "convolutional neural network" OR "neural network model" OR "knowledge bases" OR "automated localization" OR "automated detection" OR "automatic localization" OR "automatic detection")
	#1 AND #2
IEEE Xplore https://ieeexplore.ieee.org/	#1 "ALL METADATA": cephalometry OR "cephalometric landmarks" OR "cephalometric landmarking" OR "cephalometric analysis" OR "cephalometric measurements"
	#2 "ALL METADATA": "artificial intelligence" OR "image processing, computer-assisted" OR "machine learning" OR "deep learning" OR "neural networks, computer" OR "convolutional neural network" OR "neural network model" OR "connectionist model" OR "knowledge bases" OR "automated localization" OR "automated detection" OR "automatic localization" OR "automatic detection"
	#1 AND #2
Gray literature	
OpenGrey http://www.opengrey.eu/	(cephalometry OR "cephalometric landmarks") AND ("artificial intelligence" OR "machine learning" OR "deep learning" OR "neural network" OR "automatic localization" OR "automatic detection")
ProQuest https://www.proquest.com/	(cephalometry OR "cephalometric landmarks") AND ("artificial intelligence" OR "machine learning" OR "deep learning" OR "neural network" OR "automatic localization" OR "automatic detection")

exported to the EndNote Web™ software (Thomson Reuters, Toronto, Canada) for cataloguing and removing duplicates. The "gray literature" results were exported to Microsoft Word (Microsoft™, Ltd, Washington, USA) for manually removing duplicates.

Study Selection

After removing duplicates, the results were exported to the Rayyan QCRI software (Qatar Computing Research Institute, Doha, Qatar) to begin selecting the studies. Two reviewers (GQTB and MTCV) read the titles of the studies (first phase) and excluded those unrelated to the topic. In the second phase, the abstracts of the studies were assessed with the initial application of the eligibility criteria. The titles that met the objectives of the study but did not have abstracts available were fully analyzed in the next phase. In the third phase, the potentially eligible studies were fully read to apply the eligibility criteria. If the full texts were not found, a bibliographic request was performed to the library database (COMUT) and an e-mail was sent to the corresponding authors to obtain the texts. Full-text studies published in languages other than English or Portuguese were translated. Two reviewers independently performed all phases, and in case of doubt or disagreement, a third reviewer (LRP) was consulted to make a final decision.

Data Collection

The full texts of the eligible studies were analyzed, and the data were extracted for the following information: study identification (author, year, country, study location, and the application of ethical criteria), sample characteristics (the number of imaging examinations used for training and testing and type of imaging examination), collection and processing characteristics (software used for automatic detection, the number and name of cephalometric landmarks analyzed, the number of professionals participating in manual detection, and the number of times manual detection was performed), and main results (intra- and inter-examiner results, mean differences in millimeters between manual/conventional and automatic landmarking, and the level of agreement of AI with the human registration of landmarks). In the case of incomplete or insufficient information, the corresponding author was contacted via e-mail.

An author (GQTB) extracted all the aforementioned data, and a second reviewer (MTCV) performed a cross-examination to confirm the agreement among the data extracted. Any disagreement between the reviewers was solved with discussions with a third reviewer (LRP).

Risk of Bias Assessment

Two authors (GQTB and WAV) independently assessed the risk of individual bias in the eligible studies with QUADAS-2 [24]. This tool includes four domains: patient selection, index test, reference standard, and flow and timing. Each domain is evaluated for the risk of bias, and the first three domains are also evaluated for applicability concerns. Each domain can be classified as a "high risk," "uncertain risk," and "low risk." The evaluators solved their divergences with a discussion, and when there was no consensus, a third author (LRP) was consulted to make a final decision.

Data Synthesis

The meta-analysis was performed with the R software, version 4.2.0, for Windows (R Foundation for Statistical Computing, Vienna, Austria), aided by the meta and metafor packages. For inclusion in the meta-analysis, the studies should present one of the following outcomes: (1) the proportion of cephalometric landmarks correctly identified with AI within the thresholds of 2 or 3 mm (agreement) and (2) the mean divergence between cephalometric landmarking with AI and manual landmarking, in millimeters.

For the first outcome, individual studies were combined in the meta-analysis with the random-effects model by Dersimonian-Laird, logit transformation, and the inverse variance method, and the results were described in percentage (%) of agreement. For the second outcome, considering that the studies used different methods and formulas to determine the mean divergence between AI and manual landmarking, the present review used the standardized mean difference (SMD) as an effect measure, with a respective 95% confidence interval, using the inverse variance method. For this outcome, the closer to 0 the SMD, the more precise the automatic identification of the cephalometric landmark. Whenever possible, the individual results of each dataset were considered for studies using more than one dataset in their samples. The weights of each study in the meta-analytical analyses were calculated considering the total number of imaging examinations and cephalometric landmarks analyzed in each study. The heterogeneity among studies was assessed with tau-squared statistic (t^2) and I^2 and classified as low ($I^2 < 50\%$), moderate ($I^2 = 50\%$ to 75%), and high ($I^2 > 75\%$).

The mean divergence between AI and manual detection of cephalometric landmarks was also individually investigated. For this analysis, the cephalometric landmarks were selected based on those used in the IEEE 2015 ISBI Grand Challenge #1: Automated Detection and Analysis for Diagnosis in Cephalometric X-ray Image [25].

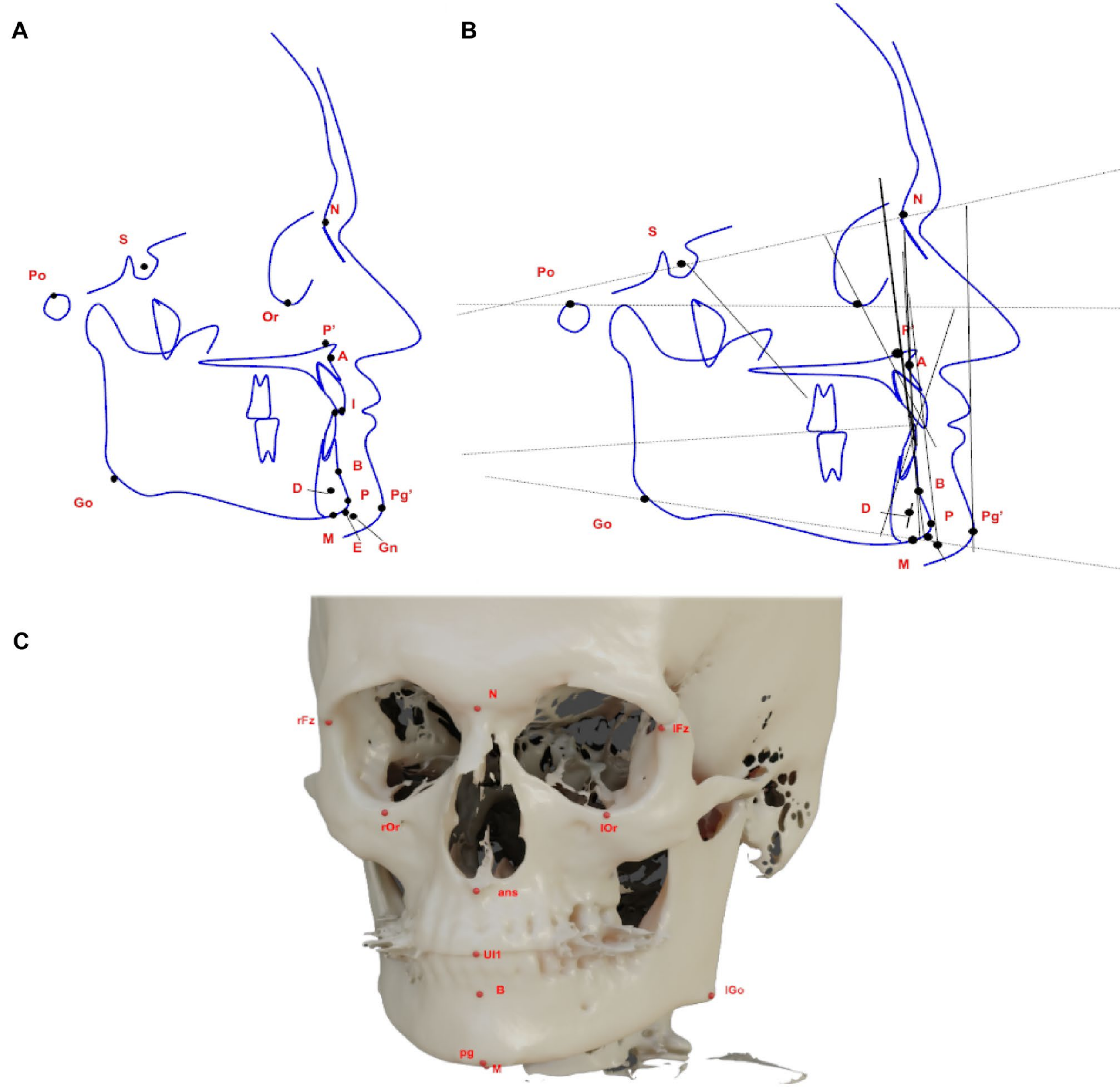


Fig. 1 Schematic representations of 2D and 3D cephalometric analysis. **A** Examples of landmark placement; **B** linear and angular measurements based on the most common landmarks; **C** representation of 3D landmark placement

Figure 1 shows an example of landmarks placement in 2D cephalometric schematic representation (Fig. 1A), how it serves as a reference for many angular and linear analyses for diagnosis purposes (Fig. 1B), and those landmarks in a 3D analysis (Fig. 1C).

The subgroups were analyzed considering the image (2D vs. 3D) and AI system (handcrafted vs. deep learning) used in the assessment. The publication bias was evaluated with a visual inspection of funnel plot asymmetry and the Egger test.

Assessment of the Certainty of Evidence

The certainty of evidence was assessed with the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) tool. The GRADEpro GDT software (http://gdt.guidelinedevelopment.org) summarized the results. The assessment was based on study design, risk of bias, inconsistency, indirect evidence, imprecision, and publication bias. The certainty of evidence can be classified as high, moderate, low, or very low [26].

Results

Study Selection

In the first phase of study selection, 7410 results were found distributed in nine electronic databases, including the "gray literature." After removing duplicates, 4401 results remained for analysis. A careful reading of the titles excluded 4129 results. Two hundred seventy-two studies remained for the reading of abstracts. Of these, 141 studies were excluded after applying the eligibility criteria. The 131 remaining results were fully read, of which 91 were excluded (Supplementary Table 1). Forty studies [17–19, 27–63] were included in the qualitative analysis. Figure 2 presents the details of the search, identification, inclusion, and exclusion of studies.

Characteristics of Eligible Studies

The studies were published between 2005 and 2021 and performed in 12 different countries, with 26 studies in Asia [17–19, 30–35, 39, 43–49, 51, 52, 54, 55, 57, 59, 60, 62, 63], nine in Europe [27–29, 36, 40, 50, 56, 58, 61], and five in America [37, 38, 41, 42, 53]. The total sample included 12,601 imaging examinations, with 11,029 digital teleradiographs and 1572 cone beam computed tomographs (CBCTs).

The studies used different methods for automatically detecting cephalometric landmarks, highlighting those related to the big groups of AI: handcrafted and deep learning. The imaging examinations of the included studies detected several landmarks, ranging from 10 [28, 29] to 93 [59] cephalometric landmarks per study. The following

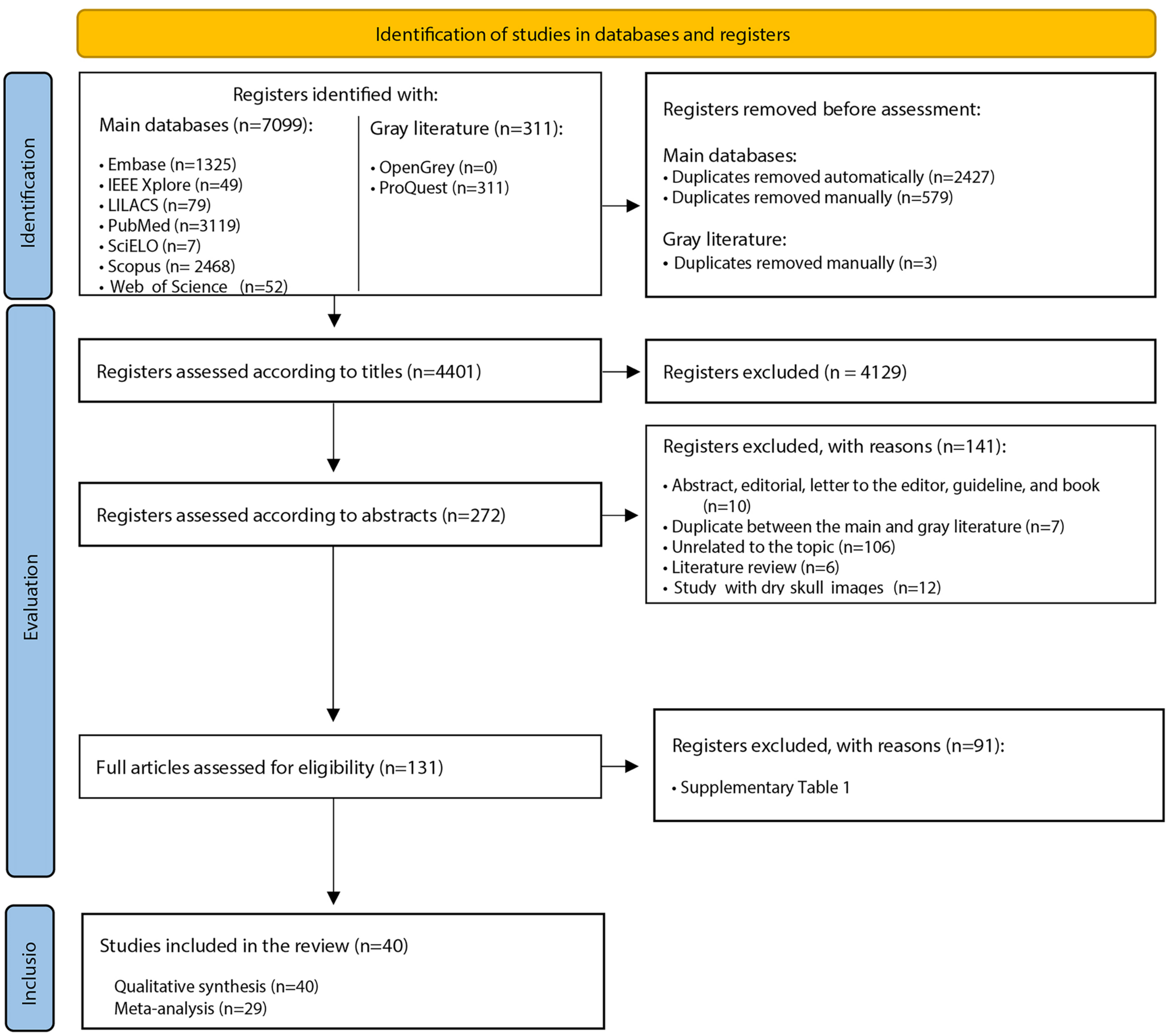


Fig. 2 Flowchart of the search, identification, and selection of eligible studies

landmarks were the most used for detection: nasion (90.7% of studies), gonion (88.4%), pogonion (86.0%), menton (83.7%), orbitale (81.4%), sella (76.7%), anterior nasal spine (72.1%), gnathion (72.1%), porion (69.8%), posterior nasal spine (67.4%), upper incisal incision (53.5%), articulare (48.8%), lower incisal incision (46.5%), supramentale (46.5%), upper lip (46.5%), lower lip (46.5%), subspinale (44.2%), soft tissue pogonion (39.5%), and subnasale (39.5%). Table 2 details the main information of each eligible study.

Risk of Individual Bias in the Studies

Table 3 presents detailed information on the risk of bias in the eligible studies. Only three studies [31, 32, 40] presented a low risk of bias for all domains evaluated with QUADAS-2. Most studies presented a high risk of bias for the domains of patient selection (80%—32/40) and reference test (65%—26/40). Regarding the applicability assessment, the results were similar to those of the risk of bias assessment.

Specific Results of the Eligible Studies

The overall mean distance (mean error) between automatic detection and manual landmarking ranged between 1.03 ± 1.29 [62] and 2.59 ± 3.45 mm [31] in two-dimensional imaging examinations (teleradiographs) and between 1.88 ± 1.10 mm [43] and 7.61 ± 3.61 mm [47] in three-dimensional imaging examinations (computed tomographs). The lower the mean error, the better the precision of the method used for automatic detection.

The overall agreement rate of the automatic detection for a margin of error up to 2 mm (clinically acceptable) ranged between 43.75 [31] and 88.49% [53] for two-dimensional imaging examinations. For three-dimensional imaging examinations, the variation was between 64.16% [43] and 87.13% [62]. The higher the agreement rate within the margin of error up to 2 mm, the better the performance of the method used for automatic detection. Supplementary Table 2 presents the quantitative results and the main outcomes of the eligible studies.

Synthesis of Results and Meta-analysis

For assessing the agreement between AI and manual detection considering a margin of error of 2 mm, the meta-analysis obtained a summarized effect of 79% (95% CI: 76–82%) with high heterogeneity ($I^2 = 99\%$). The subgroup analyses showed similar proportions between the digital images (2D = 79%; 95% CI 76–82% vs. 3D = 74%; 95% CI 30–95%) (Fig. 3A) and AI systems (handcrafted = 77%; 95% CI 71–83% vs. deep learning = 79%; 95% CI 76–83%) (Fig. 3B). There was no asymmetry in the funnel plot (Fig. 4), which was confirmed with the Egger test ($p = 0.6187$).

Considering a margin of error of 3 mm, agreement was 90% (95% CI: 88–92%) with high heterogeneity ($I^2 = 99\%$). The subgroup analyses for this outcome also showed similar accuracy between the images (Fig. 5A) and AI systems (Fig. 5B). The analysis of funnel plot asymmetry (Fig. 6) and the Egger test ($p = 0.0718$) did not detect a publication bias.

The meta-analysis to verify the divergence of the position between cephalometric landmarking with AI and manual landmarking showed an SMD of 2.05 (95% CI: 1.41–2.69) with low heterogeneity ($I^2 = 10\%$). The subgroup analyses showed similar divergences between the digital images (2D = 1.51; 95% CI 1.37–1.65 vs. 3D = 2.89; 95% CI 1.01–4.77) (Fig. 7A) and AI systems (handcrafted = 1.83; 95% CI 1.44–2.22 vs. deep learning = 2.23; 95% CI 0.18–4.27) (Fig. 7B). The analysis of funnel plot asymmetry (Fig. 8) and the Egger test ($p = 0.8883$) did not detect a publication bias.

This study also investigated the divergence between cephalometric landmarking with AI and manual landmarking for each cephalometric landmark. Hence, the landmarks with the lowest divergences were menton (SMD, 1.17; 95% CI, 0.82; 1.53), subnasale (SMD, 1.07; 95% CI, 0.69; 1.46), and gnathion (SMD, 1.27; 95% CI, 0.95; 1.58). The subgroup analyses showed that 2D images were more precise in identifying the sella, supramentale, gnathion, lower incisal incision, and posterior nasal spine landmarks. Considering the AI systems, deep learning was more precise in identifying nine of the 19 landmarks analyzed (Table 4).

Certainty of Evidence

The certainty of evidence of the three outcomes (accuracy for the margin of error of 2 and 3 mm and divergence of the position between cephalometric landmarking with AI and manual landmarking) was classified as very low (Table 5).

Discussion

This systematic review with meta-analysis aimed to evaluate the use of artificial intelligence (AI) for detecting cephalometric landmarks in digital imaging examinations and compare it to manual landmarking. The results showed that the agreement between AI and manual detection ranged from 79 to 90% according to the margin of error, and the mean divergence was 2.05 compared to manual landmarking.

Using AI to identify cephalometric landmarks is a great innovation in clinical practice. The development of reliable and automated tools to detect and perform cephalometric analysis have great repercussion for the clinician as it speeds,

Table 2 Main characteristics of the eligible studies

Authors, year (country)	Imaging examination	Mean age ± SD (age group)	Number of training/testing radiographs	Source of radiographs	Cephalometric landmarks detected	Number of experts involved in manual landmarking	Intra- and inter-examiner test	Specific artificial intelligence method used	General classification of the artificial intelligence used
Giordano et al., 2005 (Italy)	Cephalograms	nr	97/26	nr	8	2 (orthodontists)	nr	Cellular neural networks	Handcrafted
Leonardi et al., 2009 (Italy)	Cephalograms	14.8 ± nr (10–17)	nr/41	Orthodontic Department of Policlinico, University Hospital of Catania, Italy	10	5 (orthodontists)	Intra and inter	Cellular neural networks	Handcrafted
Vucinic et al., 2010 (Serbia)	Cephalograms	14.7 ± nr (7.2–25.6)	Modified leave-one-out/60	Orthodontic Department of the Dental Clinic, University of Novi Sad, Serbia	17	1	Intra	Active appearance models	Handcrafted
Tam and Lee, 2012 (Japan)	Cephalograms	nr	1/20	Dental clinic	20	2	nr	Two-stage rectified point translation transform	Handcrafted
Shahidi et al., 2013 (Iran)	Cephalograms	nr	nr/40	Private oral and craniofacial radiology center	16	3 (orthodontists)	Intra and inter	Template-matching method or edge detection technique	Handcrafted
Shahidi et al., 2014 (Iran)	Cone Beam Computed tomography	nr (10–43)	8/20	Oral and maxillofacial radiology center in Shiraz	14	3 (2 orthodontists and 1 radiologist)	Intra and inter	Combined approach: feature-based and voxel similarity-based	Handcrafted
Gupta et al., 2015 (India)	Cone Beam Computed tomography	nr	nr/30	Postgraduate Orthodontic Clinic of All India Institute of Medical Sciences	20	3 (orthodontists)	Intra and inter	Knowledge-based algorithm with extraction through a VOI	Handcrafted
Tam and Lee, 2015 (Japan)	Cephalograms	nr	0/80	nr	20	2	nr	Two-stage rectified point transform	Handcrafted

Table 2 (continued)

Authors, year (country)	Imaging examination	Mean age ± SD (age group)	Number of training/testing radiographs	Source of radiographs	Cephalometric landmarks detected	Number of experts involved in manual landmarking	Intra- and inter-examiner test	Specific artificial intelligence method used	General classification of the artificial intelligence used
Vasamsetti et al., 2015 (India)	Cephalograms	nr	9/37	Center for Dental Education and Research of All India Institute of Medical Sciences, India	24	3 (orthodontists)	nr	Optimized template matching algorithm	Handcrafted
Codari et al., 2016 (Italy)	Cone Beam Computed tomography	nr (37–74)	nr/18	SST Dentofacial Clinic, Italy	21	3 (radiologists)	Intra and inter	Adaptive cluster-based segmentation followed by an intensity-based registration	Handcrafted
Lindner et al., 2016 (Japan)	Cephalograms	$27 \pm$ nr (7–76)	150/400	nr	19	2 (orthodontists)	Intra and inter	Fully automatic landmarking annotation system	Handcrafted
Zhang et al., 2016 (United States)	Cone Beam Computed tomography	nr	30/41	nr	15	nr	Intra and inter	Segmentation-guided partially-joint regression forest model	Handcrafted
Arik et al., 2017 (United States)	Cephalograms	nr	450/750	IEEE ISBI 2014 and 2015 dataset	19	2 (orthodontists)	Intra and inter	Convolutional neural networks	Deep learning
Lee et al., 2017 (South Korea)	Cephalograms	nr	150/150	IEEE ISBI 2015 dataset	19	2 (orthodontists)	nr	End-to-end deep learning system based on convolutional neural networks	Deep learning
De Jong et al., 2018 (Netherlands)	Cone Beam Computed tomography	nr (16–54)	Leave-one-out/39	Oral and Maxillofacial Surgery Department at Erasmus, Netherlands	33	3	Intra and inter	2D Gabor wavelets and ensemble learning	Handcrafted
Montufar et al., 2018a (Mexico)	Cone Beam Computed tomography	nr	Leave-one-out/24	Public dataset of virtual skeleton database from the Swiss Institute	18	2	Intra	Active shape models	Handcrafted

Table 2 (continued)

Authors, year (country)	Imaging examination	Mean age ± SD (age group)	Number of training/testing radiographs	Source of radiographs	Cephalometric landmarks detected	Number of experts involved in manual landmarking	Intra- and inter-examiner test	Specific artificial intelligence method used	General classification of the artificial intelligence used
Montufar et al., 2018b (Mexico)	Cone Beam Computed tomography	nr	Leave-one-out/24	Public dataset of virtual skeleton database from the Swiss Institute	18	2	Intra	Hybrid approach with active shape models	Handcrafted
Neelapu et al., 2018 (India)	Cone Beam Computed tomography	nr	nr/30	Postgraduate orthodontic clinic database	20	3 (orthodontists)	Intra and inter	Algorithm based on boundary definition of the human anatomy	Handcrafted
Wang et al., 2018 (China)	Cephalograms	nr (6–60)	150/315	IEEE ISBI 2015 Challenge dataset and database of Peking University	19 or 45	2 (orthodontists)	Intra and inter	Multiresolution decision tree regression voting	Handcrafted
Chen et al., 2019 (China)	Cephalograms	nr	150/250	IEEE ISBI 2015 dataset	19	2 (orthodontists)	nr	Attentive feature pyramid fusion and regression-voting	Handcrafted
Dai et al., 2019 (China)	Cephalograms	nr	100/200	Dataset of the Automatic Cephalometric X-Ray Landmark Detection Challenge	19	2	nr	Adversarial encoder-decoder networks	Deep learning
Kang et al., 2019 (South Korea)	Cone Beam Computed tomography	24.22 ± 2.91	18/9	Data from a previous study	12	2 (radiologists)	Intra and inter	Three-dimensional convolutional neural networks	Deep learning
Lee et al., 2019 (South Korea)	Cone Beam Computed tomography	24.22 ± 2.91	20/7	Data from a previous study	7	2 (radiologists)	nr	Deep learning	Deep learning
Nishimoto et al., 2019 (Japan)	Cephalograms	nr	153/66	Gathered via the Internet with Image Spider	10	nr	nr	Convolutional neural network with convolutional and dense layers	Deep learning

Table 2 (continued)

Authors, year (country)	Imaging examination	Mean age ± SD (age group)	Number of training/testing radiographs	Source of radiographs	Cephalometric landmarks detected	Number of experts involved in manual landmarking	Intra- and inter-examiner test	Specific artificial intelligence method used	General classification of the artificial intelligence used
Payer et al., 2019 (Austria)	Cephalograms	nr	150/250	IEEE ISBI 2015 dataset	19	2 (orthodontists)	nr	Convolutional neural network based on spatial configuration-net	Deep learning
Kim et al., 2020 (South Korea)	Cephalograms	nr	1675/400	Own dataset of two medical institutes	19 or 23	2 (orthodontists)	nr	Stacked hourglass deep learning model	Deep learning
Lee et al., 2020 (South Korea)	Cephalograms	nr	150/250	IEEE ISBI 2015 dataset	19	2 (orthodontists)	Intra and inter	Bayesian convolutional neural networks	Deep learning
Li et al., 2020 (United States)	Cephalograms	nr	150/250	IEEE ISBI 2015 dataset	19	2 (orthodontists)	nr	Global-to-local cascaded graph convolutional networks based on deep adaptive graph	Deep learning
Ma et al., 2020 (Japan)	Cone Beam Computed tomography	nr	58/8	Database of the University of Tokyo Hospital	13	1 (orthodontist)	nr	Patch-based deep neural networks with a three-layer convolutional neural network	Deep learning
Moon et al., 2020 (South Korea)	Cephalograms	nr	2200/200	PACS server at Seoul National University Dental Hospital	19, 40, or 80	1 (orthodontist)	Intra and inter	Deep learning system: modified you-only look-once	Deep learning
Noothout et al., 2020 (Netherlands)	Cephalograms	nr	150/250	IEEE ISBI 2015 dataset	19	2 (orthodontists)	Intra and inter	Fully convolutional neural network	Deep learning
Oh et al., 2020 (South Korea)	Cephalograms	nr	150/250	IEEE ISBI 2015 dataset	19	2	Inter	Local feature perturbator with anatomical configuration loss	Deep learning
Qian et al., 2020 (China)	Cephalograms	nr	150/250	IEEE ISBI 2015 dataset	19	2 (orthodontists)	Intra and inter	Multi-Head Attention Neural Network with multi-head and attention part	Handcrafted

Table 2 (continued)

Authors, year (country)	Imaging examination	Mean age ± SD (age group)	Number of training/testing radiographs	Source of radiographs	Cephalometric landmarks detected	Number of experts involved in manual landmarking	Intra- and inter-examiner test	Specific artificial intelligence method used	General classification of the artificial intelligence used
Song et al., 2020 (Japan)	Cephalograms	nr	150/350	IEEE ISBI 2015 dataset and own dataset	19	2 (orthodontists)	nr	Convolutional Neural Network based on extracted ROI patches	Deep learning
Wirtz et al., 2020 (Germany)	Cephalograms	nr	150/250	IEEE ISBI 2015 dataset	19	2 (orthodontists)	nr	Coupled Shape Model refined with a Hough Forest	Handcrafted
Yun et al., 2020 (South Korea)	Cone Beam Computed tomography	24.22 ± 2.91	230/25	Data from a previous study	93	1	nr	Convolutional Neural Network with Variational Autoencoder	Deep learning
Zeng et al., 2020 (China)	Cephalograms	nr	150/250	IEEE ISBI 2015 dataset	19	2 (orthodontists)	nr	Cascaded Convolutional Neural Network	Deep learning
Huang et al., 2021 (Germany)	Cephalograms	nr	150/250	IEEE ISBI 2015 dataset	19	nr	nr	Fully automated deep learning method combining LeNet-5 and ResNet50	Deep learning
Kim et al., 2021 (South Korea)	Cone Beam Computed tomography	nr	345/85	PACS database at Kyung Hee University Dental Hospital	15	1 (orthodontist)	Intra	Multistage Convolutional Neural Network	Deep learning
Kwon et al., 2021 (South Korea)	Cephalograms	nr	150/100	IEEE ISBI 2015 dataset	19	2 (orthodontists)	nr	Multistage Convolutional Neural Network with Probabilistic Approach	Deep learning

SD standard deviation (years), *nr* not reported in the study

Table 3 Risk of bias assessed with QUADAS-2

Author, year	Risk of bias				Applicability		
	Patient selection	Index test	Reference test	Flow and timing	Patient selection	Index test	Reference test
Giordano et al., 2005	H	L	H	H	H	L	H
Leonardi et al., 2009	U	L	U	L	L	L	U
Vucinic et al., 2010	U	L	U	L	U	L	U
Tam and Lee, 2012	H	U	H	L	H	U	H
Shahidi et al., 2013	L	L	L	L	L	L	L
Shahidi et al., 2014	L	L	L	L	L	L	L
Gupta et al., 2015	H	L	L	L	H	L	L
Tam and Lee, 2015	H	U	H	L	H	L	H
Vasamsetti et al., 2015	H	L	U	L	H	L	U
Codari et al., 2016	H	L	U	L	H	L	U
Lindner et al., 2016	H	L	H	L	H	L	H
Zhang et al., 2016	H	L	H	L	H	L	H
Arik et al., 2017	H	L	H	L	H	L	H
Lee et al., 2017	H	L	H	L	H	L	H
De Jong et al., 2018	L	L	L	L	L	L	L
Montufar et al., 2018a	H	L	L	L	H	L	L
Montufar et al., 2018b	H	L	L	L	H	L	L
Neelapu et al., 2018	H	L	L	L	H	L	L
Wang et al., 2018	H	L	H	L	L	L	L
Chen et al., 2019	H	L	H	L	H	L	H
Dai et al., 2019	H	L	H	L	H	L	H
Kang et al., 2019	L	L	U	L	L	L	U
Nishimoto et al., 2019	H	L	H	L	H	L	H
Payer et al., 2019	H	L	H	L	H	L	H
Lee et al., 2019	H	H	H	L	H	H	H
Kim et al., 2020	H	L	U	L	H	L	U
Lee et al., 2020	H	L	H	L	H	L	H
Li et al., 2020	H	L	H	L	H	L	H
Ma et al., 2020	H	H	H	L	H	H	H
Moon et al., 2020	U	L	U	L	U	L	U
Noothout et al., 2020	H	L	H	L	H	L	H
Oh et al., 2020	H	L	H	L	H	L	H
Qian et al., 2020	H	L	H	L	H	L	H
Song et al., 2020	H	L	H	L	H	L	H
Wirtz et al., 2020	H	L	H	L	H	L	H
Yun et al., 2020	H	H	H	L	H	H	H
Zeng et al., 2020	H	L	H	L	H	L	H
Huang et al., 2021	H	H	H	H	H	H	H
Kim et al., 2021	U	L	H	L	U	L	H
Kwon et al., 2021	H	L	H	L	H	L	H

H high risk, *U* unclear risk, *L* low risk

standardizes, and enhance the process. The studies included in this systematic review showed that AI can perform an automatic identification in under one minute, which would make this step more practical for dentists and allow faster orthodontic planning. Another advantage of AI reported in the eligible studies is that because it is an automated tool, the identification of cephalometric landmarks would not be susceptible to human error. Those findings may influence the decision to transition from traditional methods to upcoming technologies, such as the ones reported.

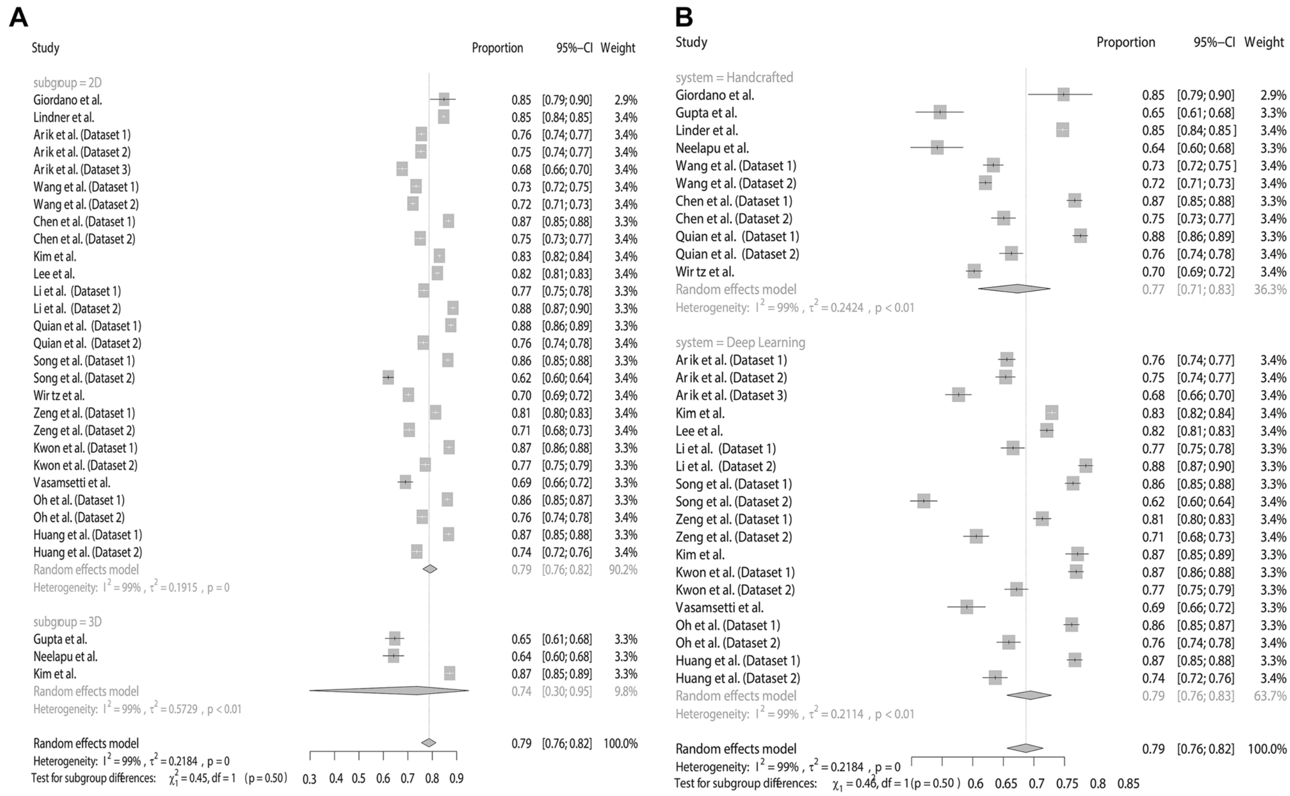


Fig. 3 Agreement of AI and manual landmarking considering a margin of error of 2 mm. **A** Subgroup analysis according to images. **B** Subgroup analysis according to AI

The meta-analysis results showed that the agreement rates between AI and manual detection in identifying cephalometric landmarks were 79% and 90%, considering the margins of error of 2 and 3 mm, respectively, with a mean divergence of 2.05. These data may be promising, as some studies affirm that even when two experts perform manual landmarking, there may be divergences over 1 mm [18, 64, 65]. The data of the present review are similar to those of another previous meta-analysis, which found 80% agreement and a divergence of 0.05 for a margin of error of 2 mm. Different from the review by Schwendicke et al., this new review included all types of AI presented in the literature, aiming to extend the evidence. Moreover, only studies using digital imaging examinations were included because these images have extensive clinical use. Even with the differences indicated, the application of AI shows good accuracy for cephalometric landmarking. However, when considering a margin of error of 2 mm clinically acceptable [52, 58], AI has space for improvement because the higher the margin of error, the better the results.

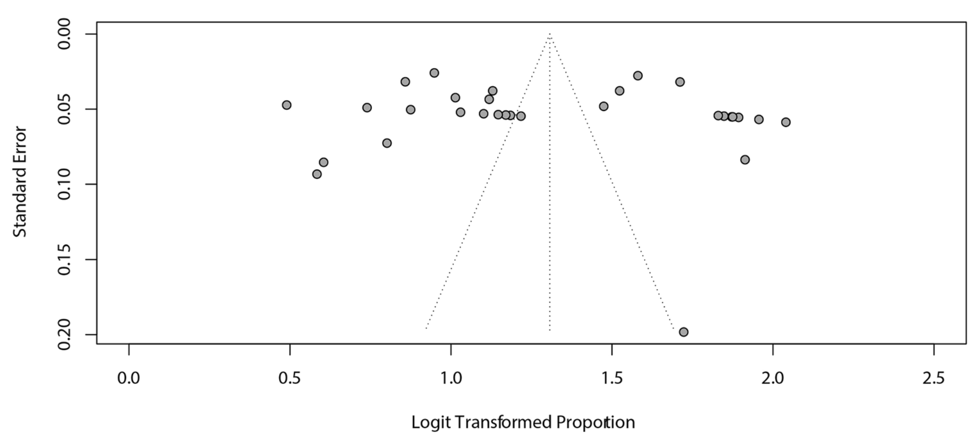


Fig. 4 Assessment of the risk of publication bias for the agreement of AI and manual landmarking, considering a margin of error of 2 mm

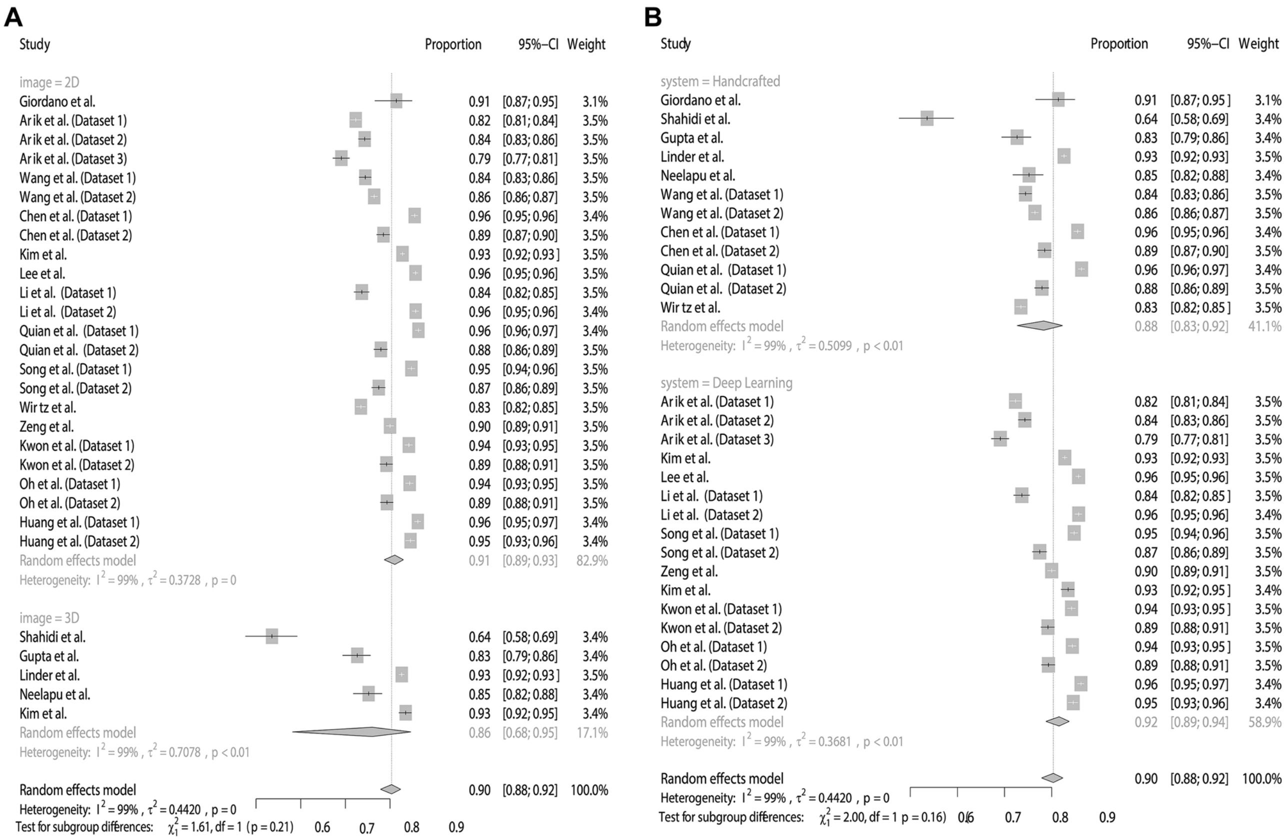
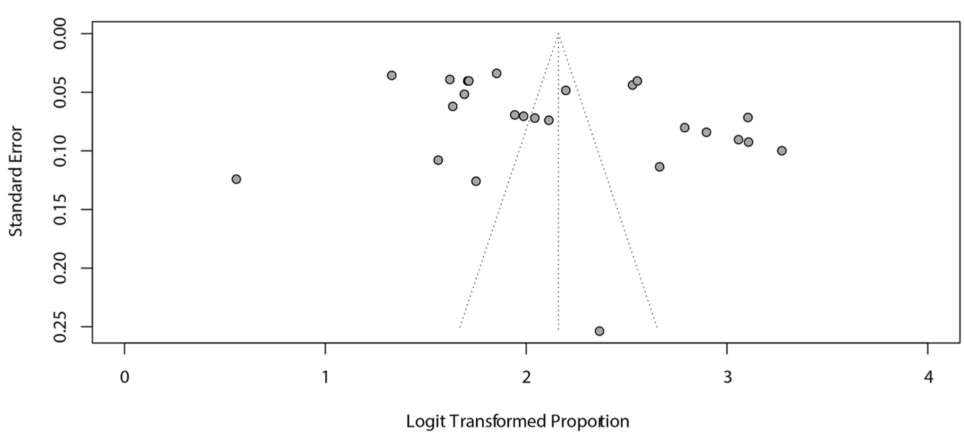


Fig. 5 Agreement of AI and manual landmarking considering a margin of error of 3 mm. **A** Subgroup analysis according to images. **B** Subgroup analysis according to AI

The individual analysis of cephalometric landmarks showed a high variety of mean divergences between AI and manual detection of each landmark. For instance, the results of the meta-analysis showed that the subnasale landmark had a lower divergence, while the gonion landmark had a divergence higher than 2 mm. This result may be justified by the inherent challenge of cephalometric landmarking either with AI or manually [65, 66]. Previous studies showed potentially significant variations among experienced examiners when identifying some landmarks [18, 67]. These results are explained by the difficult visualization of these landmarks due to their anatomical position, which may depend on the head position at the time of examination, changes due to the radiography device, and quality and overlap of structures in imaging examinations [52]. Moreover, landmarks located in bone margins may

Fig. 6 Assessment of the risk of publication bias for the agreement of AI and manual landmarking, considering a margin of error of 3 mm



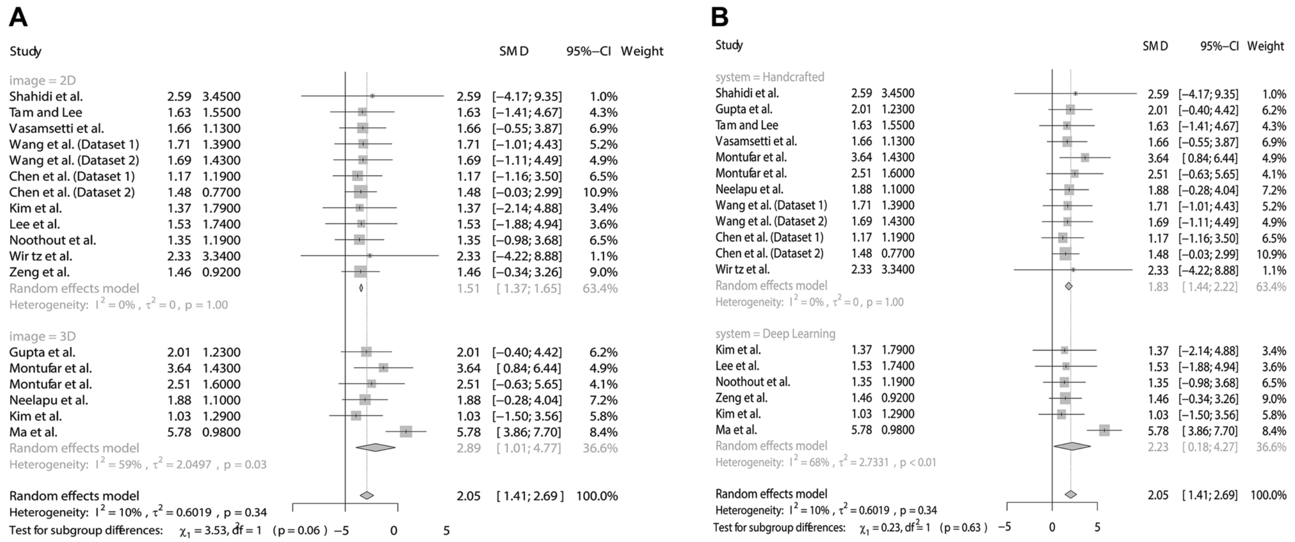


Fig. 7 Divergence of the position between cephalometric landmarking with AI and manual landmarking. (**A**) Subgroup analysis according to images. (**B**) Subgroup analysis according to AI

represent a challenge for AI identification [18]. In this context, considering that the evaluation of cephalometric landmarks does not have a definite gold standard and depends on manual assessments, these errors and difficulties may be transferred to the interpretations of results presented by AI. This may be characterized as one of the significant limitations of the current evidence on the accuracy of AI in identifying cephalometric landmarks [18].

Cephalometry is the reference examination in orthodontics, mostly used to diagnose facial skeletal morphology, predict growth, and plan and assess orthodontic treatment results [68]. However, this assessment uses two-dimensional images of a three-dimensional structure, causing errors in the projection and identification of structures [68]. To overcome these limitations, studies have proposed the transition from cephalometric analysis in 2D images to 3D images, using cone-beam computed tomography [53]. The advantages of using 3D images for this task include the precise identification of anatomical structures, prevention of geometric distortion of the image, and the ability to evaluate complex facial structures [69]. Considering these practical differences, this meta-analysis performed subgroup analyses to assess the influence of the type of image on the accuracy of AI. The results showed that using 2D images resulted in a lower divergence between AI and manual identifications for specific landmarks (sella, supramentale, gnathion, lower incisal incision, and posterior nasal spine). However, the overall assessment of the results showed similar accuracy levels of AI landmark placement in 2D or 3D images. However, these results may be justified by the fact that 3D images were used in in a reduced number of samples, making the results for this subgroup imprecise. It is also important to highlight that these subgroup analyses are only exploratory, and their results should be interpreted with caution.

Fig. 8 Assessment of the risk of publication bias for the divergence analysis between AI and manual landmarking

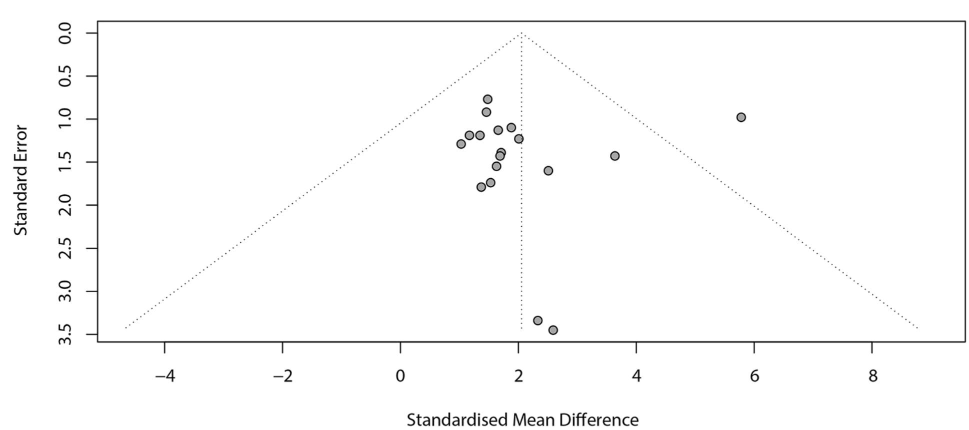


Table 4 Meta-analysis results of the individual precision of cephalometric landmarks, based on the ISBI 2015 challenge

Cephalometric landmark	# of studies	Overall summary mean (95% CI)	Overall I^2 test	Subgroup summary mean (95% CI)—type of image	I^2 subgroups	Subgroup difference test	Subgroup summary mean (95% CI)—type of AI	I^2 subgroups	Subgroup difference test
Sella	11	1.55 (1.02; 2.08)	0%	2D, 1.13 (0.93; 1.32)	0%	$p<0.01$	Handcrafted: 1.92 (1.26; 2.57)	0%	$p<0.01$
				3D, 2.69 (1.48; 3.90)	0%		Deep learning: 0.92 (0.72; 1.12)	0%	
Nasion	17	1.44 (1.10; 1.79)	0%	2D, 1.43 (1.08; 1.78)	0%	$p=0.94$	Handcrafted: 1.56 (1.12; 1.99)	0%	$p=0.22$
				3D, 1.45 (0.80; 2.10)	0%		Deep learning: 1.14 (0.36; 1.91)	0%	
Orbitale	14	2.12 (1.61; 2.62)	0%	2D, 1.94 (1.43; 2.45)	0%	$p=0.32$	Handcrafted: 2.63 (2.04; 3.22)	0%	$p=0.03$
				3D, 2.44 (1.37; 3.51)	0%		Deep learning: 1.63 (0.49; 2.77)	0%	
Porion	13	1.76 (1.01; 2.50)	20%	2D, 1.22 (0.64; 1.80)	0%	$p=0.04$	Handcrafted: 1.94 (0.36; 3.53)	33%	$p=0.99$
				3D, 2.98 (1.08; 4.88)	42%		Deep learning: 1.95 (0.93; 2.97)	4%	
Subspinale	12	1.96 (1.55; 2.37)	0%	2D, 1.66 (1.31; 2.00)	0%	$p=0.10$	Handcrafted: 2.25 (1.73; 2.76)	0%	$p<0.01$
				3D, 2.32 (1.15; 3.50)	0%		Deep learning: 1.45 (1.00; 1.89)	0%	
Supramentale	14	2.11 (1.69; 2.53)	0%	2D, 1.63 (1.18; 2.08)	0%	$p=0.03$	Handcrafted: 2.28 (1.79; 2.77)	0%	$p=0.08$
				3D, 2.38 (1.66; 3.10)	97%		Deep learning: 1.57 (0.45; 2.68)	0%	
Pogonion	11	1.47 (0.98; 1.96)	0%	2D, 1.26 (1.10; 1.43)	0%	$p=0.21$	Handcrafted: 1.93 (1.34; 2.53)	0%	$p<0.01$
				3D, 1.87 (0.56; 3.18)	0%		Deep learning: 0.91 (0.34; 1.48)	0%	
Menton	13	1.17 (0.82; 1.53)	0%	2D, 0.95 (0.82; 1.09)	0%	$p=0.17$	Handcrafted: 1.31 (0.88; 1.73)	0%	$p=0.23$
				3D, 1.43 (0.59; 2.28)	23%		Deep learning: 0.86 (-0.04; 1.76)	0%	

Table 4 (continued)

Cephalometric landmark	# of studies	Overall summary mean (95% CI)	Overall I^2 test	Subgroup summary mean (95% CI)—type of image	I^2 subgroups	Subgroup difference test	Subgroup summary mean (95% CI)—type of AI	I^2 subgroups	Subgroup difference test
Gnathion	11	1.27 (0.95; 1.58)	0%	2D, 0.98 (0.80; 1.15)	0%	$p<0.01$	Handcrafted: 1.43 (1.03; 1.82)	0%	$p<0.01$
				3D, 1.85 (1.32; 2.39)	0%		Deep learning: 0.92 (0.62; 1.22)	0%	
Gonion	13	2.42 (2.04; 2.79)	0%	2D, 2.12 (1.44; 2.79)	0%	$p=0.17$	Handcrafted: 2.63 (2.20; 3.07)	0%	$p<0.01$
				3D, 2.60 (2.11; 3.10)	0%		Deep learning: 1.82 (1.43; 2.22)	0%	
Lower incisal incision	10	1.92 (1.23; 2.60)	20%	2D, 1.20 (0.94; 1.46)	0%	$p<0.01$	Handcrafted: 2.50 (1.68; 3.32)	0%	$p<0.01$
				3D, 2.66 (1.22; 4.11)	34%		Deep learning: 0.99 (0.62; 1.36)	0%	
Upper incisal incision	13	1.32 (0.94; 1.71)	0%	2D, 1.01 (0.80; 1.23)	0%	$p=0.11$	Handcrafted: 1.76 (1.26; 2.25)	0%	$p<0.01$
				3D, 1.79 (0.84; 2.74)	0%		Deep learning: 0.90 (0.69; 1.12)	0%	
Upper Lip	6	1.69 (1.00; 2.37)	0%	N/A	N/A	N/A	Handcrafted: 1.23 (0.62; 1.84)	0%	$p=0.14$
							Deep learning: 1.99 (-0.10; 4.09)	10%	
Lower Lip	6	1.47 (0.95; 1.99)	0%	N/A	N/A	N/A	Handcrafted: 1.24 (0.47; 2.00)	0%	$p=0.34$
							Deep learning: 1.66 (0.08; 3.24)	0%	
Subnasale	5	1.07 (0.69; 1.46)	0%	N/A	N/A	N/A	Handcrafted: 1.51 (-0.15; 3.18)	0%	$p=0.16$
							Deep learning: 0.96 (0.71; 1.22)	0%	
Soft tissue pogonion	5	2.07 (1.05; 3.10)	100%	N/A	N/A	N/A	Handcrafted: 1.81 (1.22; 2.40)	0%	$p=0.39$
							Deep learning: 2.60 (-1.30; 6.51)	22%	
Posterior nasal spine	11	1.44 (0.99; 1.89)	0%	2D, 1.10 (0.85; 1.36)	0%	$p<0.01$	Handcrafted: 1.91 (1.35; 2.47)	0%	$p<0.01$
				3D, 2.32 (1.45; 3.19)	0%		Deep learning: 0.98 (0.58; 1.39)	0%	

Table 4 (continued)

Cephalometric landmark	# of studies	Overall summary mean (95% CI)	Overall I^2 test	Subgroup summary mean (95% CI)—type of image	I^2 subgroups	Subgroup difference test	Subgroup summary mean (95% CI)—type of AI	I^2 subgroups	Subgroup difference test
Anterior nasal spine	11	1.53 (1.01; 2.05)	0%	2D, 1.62 (1.05; 2.20)	0%	$p = 0.86$	Handcrafted: 1.82 (1.00; 2.63)	0%	$p = 0.10$
				3D, 1.54 (0.27; 2.81)	33%		Deep learning: 1.16 (0.54; 2.05)	0%	
Articulare	5	1.51 (1.11; 1.90)	0%	N/A	N/A	N/A	Handcrafted: 1.48 (-0.02; 2.97)	0%	$p = 0.90$
							Deep learning: 1.52 (0.92; 2.13)	0%	

Another subgroup analysis performed in this meta-analysis was the comparison between the types of AI used in the studies. Among the algorithms used in computer vision techniques, handcrafted systems use specific techniques to extract different characteristics from the images, such as texture, color, and object margins, to later compose the feature vector, which is used by different machine-learning algorithms. In turn, deep learning systems are considered the most recent AI technology and use an artificial neural network with several layers of depth that learn characteristics directly from observing input images, using a pyramid approach [70]. The present study did not find differences in both subgroups for overall accuracy or

Table 5 Summary of finding (SoF) for the proportion of cephalometric landmarks correctly identified with AI, and the mean divergence from manual landmarking

Certainty assessment								**Certainty**
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirect Evidence**	**Imprecision**	**Other considerations**	**Relative effect (95% CI)**	
Agreement between cephalometric landmarking with AI and manual landmarking (Threshold 2 mm)								
19	Diagnostic accuracy studies	Very serious[a]	Serious[b]	Not serious	Not serious	Publication bias not detected	Proportion: 0.79 (0.76;0.82)	⨁◯◯◯ Very Low
Agreement between cephalometric landmarking with AI and manual landmarking (Threshold 3 mm)								
19	Diagnostic accuracy studies	Very serious[a]	Serious[b]	Not serious	Not serious	Publication bias not detected	Proportion: 0.90 (0.88;0.92)	⨁◯◯◯ Very Low
Divergence between cephalometric landmarking with AI and manual landmarking								
15	Diagnostic accuracy studies	Very serious[a]	Not serious	Not serious	Serious[c]	Publication bias not detected	SMD: 2.05 (1.41;2.69)	⨁◯◯◯ Very Low

Evidence levels of the GRADE workgroup

High certainty: strongly confident the true effect is close to the effect estimate

Moderate certainty: moderately confident in the effect estimate. The true effect might be close to the effect estimate, but it might be substantially different

Low certainty: limited confidence in the effect estimate. The true effect might substantially differ from the effect estimate

Very low certainty: little confidence in the effect estimate. The true effect will probably substantially differ from the effect estimate

CI confidence interval, *SMD* standardized mean difference

[a]High risk of bias in majority of the included studies—downgraded by two levels

[b]High and unexplained heterogeneity ($I^2 > 75\%$)—downgraded by one level

[c]Large confidence interval—downgraded by one level

mean divergence between AI and manual detections, but deep learning provided lower divergences in nine of the 19 landmarks analyzed. Deep-learning algorithms are more accurate for specific landmarks, probably because the positions of the landmarks are easier to identify, facilitating learning by the artificial neural network, which justifies the previous results. However, these results must be interpreted very cautiously because this is only a subgroup analysis.

The results of the meta-analysis in this review should be interpreted critically and cautiously because only three [31, 32, 40] of the 40 studies included had a low risk of bias. This finding shows that, although extensive, the existing literature is limited by studies that may present some distortion in their results. According to the risk of bias analysis, patient selection was the domain in which most studies showed deficiencies, considering that few studies described in detail the sample selected and were not representative of the population. Another important source of bias was the description of the reference test. Considering it was a manual and examiner-dependent analysis, the studies should detail the form of manual identification of cephalometric landmarks and describe the type of calibration of evaluators, the number of assessments performed, and intra- and inter-examiner reliability. In this context, further studies should follow guidelines such as the CONSORT-AI and SPIRIT-AI [71] to perform and report AI analyses.

Among the limitations of this review, the low certainty of evidence stands out because of the high risk of bias in the eligible studies. Another limitation is the heterogeneity of analyses, especially for accuracy, probably because of the different methodologies and programming for AI identification and the heterogeneity of the datasets used. However, this is the most comprehensive systematic review with meta-analysis on using AI to identify cephalometric landmarks of orthodontic interest and the first to perform individual analyses for each cephalometric landmark.

Conclusion

AI shows good agreement for landmark placement on both 2D and 3D images and may assist in the final manual identification or confirmation of the positions for cephalometric landmarks, making this task faster and more precise. Further studies should be performed to expand the datasets used to include a more representative population, with study models of lower risks of biases, and aiming to overcome the limitations of the lack of a gold standard to identify cephalometric landmarks.

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Data Availability The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed Consent For this type of study, formal consent is not required.

Conflict of Interest The authors declare no competing interests.

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