Radiographic and diagnostic approaches for mandibular asymmetries in orthodontic practice: a narrative review
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\section{Abstract}
Mandibular asymmetry refers to dimensional differences between the left and right sides of the mandible in terms of size, form and volume. This condition may result in problems with functionality as well as appearance. Early intervention is often deemed optimal for addressing mandibular asymmetry; however, there is a lack of consensus regarding the diagnostic approach and strategy for identifying asymmetries in developing individuals. The purpose of this narrative review (NR) is to provide a clinician-focused update on the radiographic techniques for identifying mandibular asymmetries in orthodontic patients. Selective database searches were conducted until November 2023 to assess the available literature on mandibular asymmetry diagnosis. A health-sciences librarian developed a search strategy utilizing appropriate terms associated with mandibular asymmetry diagnosis. The databases used were Web of Science, Embase, Scopus, Lilacs and PubMed. Fifty-two studies were included in this review and data regarding the evaluation of mandibular asymmetries were presented with a narrative approach delineating clinical indications based on retrieved findings. There is no unanimous consensus on the method for diagnosing mandibular asymmetries. Cone beam computed tomography emerges as the preferred examination method for diagnosing mandibular asymmetry, thanks to the assessment of a 3D structure with a 3D image. However, the use of only orthopantomography could be advisable as a first-line diagnostic tool in children due to less radiation exposure.

\textbf{Keywords} Mandibular asymmetry; Orthodontics; Radiographic diagnosis

\section{1. Introduction}
Facial asymmetry occurs in 34–38.6% of patients with dento-facial deformities \cite{1} as opposed to 23% in the orthodontic population \cite{2}. Every subject exhibits a dominant half-face, predominantly the right side in 80% of cases, with equal distribution across sexes and age groups \cite{3}. Additionally, with 40–80% of cases affecting the lower third of the face, this area is the most commonly affected by facial asymmetry \cite{1, 4}. The increased frequency of lower facial asymmetry has been attributed to the mandible’s mobility and longer growth period than that of the maxilla \cite{5}.

Mandibular asymmetry can arise from a misalignment between the midface and the mandible (positional asymmetry) or differences in size and shape between the two halves of the mandible (shape asymmetry) \cite{6}. Multifactorial mandibular asymmetry is linked to cleft lip and palate, posterior crossbite, temporomandibular disorder (TMD), and various skeletal patterns \cite{7-12}. In particular, congenital asymmetry can be caused by hypoplasia or hyperplasia of the ramus and condyle \cite{13}, while acquired asymmetry is linked to tumors, infections, rheumatoid arthritis, osteoarthritis of the temporomandibular joint, and myogenic issues like myospasm, persistent muscle shortening, splinting, or occlusal interferences \cite{13-15}.

Mandibular asymmetry may potentially benefit from early detection and treatment, according to some research findings \cite{16}. It is imperative for orthodontists to evaluate this condition since one of the primary treatment objectives is to achieve facial symmetry and balance, reflecting the overall harmony of the face and jaw \cite{14}. A preliminary evaluation would include a detailed facial and soft-tissue analysis with specific focus on the chin’s center, the lip commissures’ leveling, and the bilateral symmetry of the mandibular body contours and gonial angles. Additionally, smile and occlusal examinations should determine whether the dental midlines align with the facial midlines, the occlusal plane’s inclination, and the degree of gingival exposure on both sides \cite{17}.

The secondary level diagnosis of mandibular asymmetry involves the radiographic assessment of hard tissues. Before the advent of 3D (three dimensional) imaging radiology, 2D (two dimensional) imaging were used to assess skeleton-facial asymmetry, including posteroanterior (PA) cephalograms, submentovertex and orthopantomography (OPT). However, 2D radiographic imaging present inherent limitations that can lead
to underestimate the presence of skeletal asymmetry [18]. The advent of Computed tomography (CT) and Cone beam Computed tomography (CBCT) has added the third dimension to the skeletal evaluation thereby overcoming the limitations associated with 2D radiography [19]. In addition, it has been proposed the usage of other methods of diagnosis, such as Magnetic resonance imaging (MRI), scintigraphy, single photon emission computed tomography (SPECT), photos or laterolateral teleradiography (TELE LL). Such radiographic tools, both 2D and 3D, have been tested and validated for the analysis of facial asymmetry under specific conditions [18, 20, 21].

However, as far as the actual evidence is concerned, there are not studies in literature that provide a comprehensive overview of the radiological technologies involved in the analysis of mandibular asymmetry, neither a definitive protocol for selecting the appropriate radiographic tool for diagnosis of mandibular asymmetries in growing subjects. Consolidating this information would aid pediatric dentists and orthodontists in selecting the appropriate radiographic tool, as suggested by the authors of this review.

In this regard, the present systematic-narrative hybrid review (HR) aims to offer a clinician-focused update on the methods for radiological diagnosis of mandibular asymmetries in orthodontic patients during growth. This review intends to comprehensively analyze various methods across different domains to provide a thorough understanding of the available diagnostic approaches.

2. Materials and methods

The current manuscript’s structure complies with the essential elements of the recommended SR methodology [22].

2.1 Research question

To delineate the scope of the search strategy, we formulated a central research question that orthodontists could reference for guidance: “What are the appropriate radiological methods for diagnosing mandibular asymmetries according to evidence-based medicine?”.

2.2 Justification

The rationale for conducting the current NR (narrative review) stemmed from the lack of a thorough and comprehensive overview in the literature concerning the diagnostic method of mandibular asymmetries in orthodontic patients during growth. The search procedures and inclusion/exclusion criteria for this purpose are based on the consolidated methodology for Systematic Reviews (SRs) [23], and the selected articles underwent analysis using a narrative approach [22].

2.3 Eligibility criteria

With the exception of reviews, all research on mandibular asymmetries diagnostic techniques in orthodontics was taken into account. The language was unrestricted and the publication year was limited from 2013 to 2023, to consider only the most up-to-date diagnostic methods. Studies were included if they met the following criteria outlined according to the PICO format: studies conducted in growing human subjects (Participants); studies analyzing mandibular asymmetry using radiographic examination (Intervention), studies evaluating different type of radiographic tools used for the diagnosis of mandibular asymmetry (Comparison), mandibular asymmetry calculated via 2D or 3D dataset (Outcomes).

2.4 Literature sources and search parameters

To assess the corpus of current literature on the subject, multiple database searches were carried out through November 2023. The development of a search strategy that incorporated all discovered keywords and free-standing terms was aided by a health sciences librarian. The Web of Science, Embase, Scopus, Lilacs and PubMed databases were utilized. Additionally, further research was conducted to validate each source of evidence listed in the reference list. The results of customizing the search approach for each database are presented in Table 1.

2.5 Data cleaning

2.5.1 Study selection

Following the retrieval of search results from each electronic database, the citations were imported into EndNote X9, a reference manager program developed by ClarivateTM, London, UK. Reports that were duplicates were eliminated, and articles that provided updates or preliminary findings were only assessed once. Two authors, V.R. and S.L.R., independently screened all titles and abstracts retrieved from the databases before proceeding to read the full texts of relevant studies. Any discrepancies in the assessment of study eligibility were resolved through consultation with an additional author, L.R. The degree of agreement between the two reviewers has been assessed using Cohen’s kappa statistics.

2.5.2 Data extraction

In order to gather the characteristics and outcomes (study design, sample size and objectives) needed for the subsequent literature analysis, two authors (S.L.R. and V.R.) created a data extraction form. We had discussed any discrepancies with L.R., another author reviewer. Cohen kappa statistics has been employed to evaluate the degree of concurrence between the two authors.

2.6 Information synthesis

The findings from the selected papers had to be presented narratively to comply with the suggested method for HRs [22]. A methodology derived from previous studies published by other researchers was used to report the results [24]. To better address clinical indications, the results were organized and discussed into distinct domains that included all the data retrieved from the included studies.
3. Results

After deleting duplicate files, the reviewers focused on 1429 out of the 1553 citations generated by the search strategy. Following the reading of the abstracts and titles, 1274 papers in total were eliminated, leaving 155 articles for full-text assessment. Following a comprehensive analysis of these articles, 52 studies were deemed suitable for evaluation. The remaining 103 articles were excluded for various reasons: 6 of them were systematic reviews, 1 was case control, 8 were reviews, 2 were books and 86 had a topic not compatible with the study. Table 2 presents the characteristics of the included studies, while Fig. 1 provides an overview of the research selection process.

Moreover, the chosen articles required to clarify the efficacy model of Fryback and Thornbury: therapeutic efficacy, diagnostic thinking efficacy, diagnostic accuracy efficacy, or any combination of the aforementioned [25]. They proposed a hierarchical model in which demonstrating efficacy at each lower level is necessary but not sufficient to guarantee efficacy at higher levels. Level 1 addresses the technical quality of the images, whereas Level 2 deals with the diagnostic accuracy, sensitivity and specificity related to the image interpretation. Level 3 examines whether the information alters the diagnostic reasoning of the referring physician. Such a shift is a necessary precondition for Level 4 efficacy, which deals with the impact on the patient treatment plan. Level 5 efficacy studies assess the impact of information on patient outcomes. Level 6 evaluations, in the end, consider the advantages and disadvantages of a diagnostic imaging technology for society.

<table>
<thead>
<tr>
<th>Database</th>
<th>Search format</th>
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<tbody>
<tr>
<td>PubMed</td>
<td>((&quot;cbct&quot;(All Fields) OR (&quot;imaging, three dimensional&quot;(MeSH Terms) OR (&quot;imaging&quot;(All Fields) AND “three dimensional”(All Fields)) OR “three-dimensional imaging”(All Fields) OR (&quot;3d&quot;(All Fields) AND “imaging”(All Fields)) OR “3d imaging”(All Fields)) OR (&quot;radiography, panoramic&quot;(MeSH Terms) OR (“radiography”(All Fields) AND “panoramic”(All Fields)) OR “panoramic imaging”(All Fields) OR “panoramic radiography”(All Fields) OR “orthopantomographies”(All Fields) OR “orthopantomography”(All Fields)) OR (“edrecolomab”(Supplementary Concept) OR “edrecolomab”(All Fields) OR “panorex”(All Fields)) OR (&quot;radiography, panoramic&quot;(MeSH Terms) OR (&quot;radiography&quot;(All Fields) AND “panoramic”(All Fields)) OR “panoramic imaging”(All Fields) OR “panoramic radiography”(All Fields) OR “orthopantomographies”(All Fields) OR “orthopantomography”(All Fields)) OR (“radiography”(All Fields) AND “orthopantomographies”(All Fields)) OR (“orthopantomography”(All Fields)) OR (“panoramic imaging”(All Fields) OR “panoramic radiography”(All Fields) OR “orthopantomographies”(All Fields) OR “orthopantomography”(All Fields)) OR (&quot;antero-posterior&quot;(All Fields) AND (“cephalogram”(All Fields) OR “cephalograms”(All Fields))) OR (&quot;axial&quot;(All Fields) OR “axially”(All Fields) OR “axials”(All Fields) AND (“cephalometry”(All Fields) OR (“cephalometry”(All Fields) AND “2d”(All Fields) AND (“image”(All Fields) OR “image s”(All Fields) OR “images”(All Fields) OR “imaged”(All Fields) OR &quot;imager”(All Fields)) OR “imaging”(All Fields) OR “imaging s”(All Fields) OR “imagings”(All Fields)) OR (&quot;diagnosable”(All Fields) OR “diagnosi”(All Fields) OR “diagnosis”(MeSH Terms) OR “diagnosis”(All Fields) OR “diagnosis”(All Fields) OR (“diagnosis”(All Fields) OR “diagnose”(All Fields) OR “diagnosed”(All Fields) OR “diagnoses”(All Fields) OR “diagnosing”(All Fields) OR “diagnosis”(MeSH Subheading))) AND (&quot;mandible”(MeSH Terms) OR “mandible”(All Fields) OR “mandibular”(All Fields) OR (“asymmetries”(All Fields) OR “asymmetric”(All Fields) AND (&quot;orthodontal”(All Fields) OR “orthodontic”(All Fields) OR “orthodontical”(All Fields) OR “orthodontics”(All Fields)) AND (&quot;young”(All Fields) OR “youngs”(All Fields)))) AND (y_10(Filter))</td>
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<tr>
<td>Embase via Ovid</td>
<td>((cbct or 3d imaging or orthopantomography or panorex or panoramic radiography or antero-posterior cephalogram or axial cephalometry or 2d imaging or diagnosis) and (mandibular asymmetry and orthodontics and young)).</td>
</tr>
<tr>
<td>Web of science</td>
<td>(ALL = (((cbct OR (3d imaging) OR (orthopantomography) OR (panorex) OR (panoramic radiography) OR (antero-posterior cephalogram) OR (axial cephalometry) OR (2d imaging) OR (diagnosis)))) AND ALL = (((mandibular asymmetry) AND (orthodontics) AND (young))</td>
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<tr>
<td>Scopus</td>
<td>(cbct OR (3d AND imaging) OR (orthopantomography) OR (panorex) OR (panoramic AND radiography) OR (antero-posterior AND cephalogram) OR (axial AND cephalometry) OR (2d AND imaging) OR (diagnosis)) AND ((mandibular AND asymmetry) AND (orthodontics) AND (young)) AND PUBYEAR &gt; 2012 AND PUBYEAR &lt; 2024</td>
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<tr>
<td>Liliacs</td>
<td>(((cbct OR (3d imaging) OR (orthopantomography) OR (panorex) OR (panoramic radiography) OR (antero-posterior cephalogram) OR (axial cephalometry) OR (2d imaging) OR (diagnosis)) AND ((mandibular asymmetry) AND (orthodontics) AND (young))</td>
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<tr>
<td>Author/year</td>
<td>Sample</td>
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<tr>
<td>Agrawal, 2015</td>
<td>10 patients</td>
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<td>Ajmera, 2022</td>
<td>21 patients</td>
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<tr>
<td>Ajmera, 2023</td>
<td>21 patients</td>
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<tr>
<td>Alhazmi, 2023</td>
<td>131 patients</td>
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<td>Alkis, 2023</td>
<td>100 patients</td>
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<tr>
<td>Bal, 2018</td>
<td>776 patients</td>
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<tr>
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<td>104 patients</td>
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<td>Cavagnetto, 2021</td>
<td>133 patients</td>
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<tr>
<td>Chan, 2017</td>
<td>200 patients</td>
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<td>Espinosa, 2023</td>
<td>40 patients</td>
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<tr>
<td>Fan, 2022</td>
<td>120 patients</td>
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<tr>
<td>Faryal, 2022</td>
<td>118 patients</td>
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<tr>
<td>García-Sanz, 2017</td>
<td>6 cadavers</td>
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<td>Goto, 2014</td>
<td>40 patients</td>
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<tr>
<td>Ha, 2022</td>
<td>120 patients</td>
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<tr>
<td>Hasebe, 2019</td>
<td>166 patients</td>
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<td>Hlatcu, 2023</td>
<td>214 patients</td>
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<td>Huang, 2017</td>
<td>32 patients</td>
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<td>Huang, 2023</td>
<td>125 patients</td>
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<td>Kim, 2016</td>
<td>56 patients</td>
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<td>Kim, 2019</td>
<td>60 patients</td>
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<td>Lemos, 2014</td>
<td>10 patients</td>
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<tr>
<td>Leonardi, 2019</td>
<td>48 patients</td>
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<tr>
<td>Leonardi, 2020</td>
<td>57 patients</td>
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<td>Author/year</td>
<td>Sample</td>
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<tr>
<td>Leonardi, 2021</td>
<td>40 patients</td>
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<tr>
<td>Li, 2023</td>
<td>95 patients</td>
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<td>Lim, 2018</td>
<td>43 patients</td>
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<tr>
<td>Lima, 2018</td>
<td>40 patients</td>
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<tr>
<td>Liu, 2019</td>
<td>56 patients</td>
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<td>Lopezb, 2016</td>
<td>61 patients</td>
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<tr>
<td>Macri, 2022</td>
<td>1 patient</td>
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<tr>
<td>Malik, 2020</td>
<td>61 patients</td>
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<tr>
<td>Marques, 2023</td>
<td>96 patients</td>
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<tr>
<td>Miresmaeili, 2021</td>
<td>30 patients</td>
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<tr>
<td>Nolte, 2015</td>
<td>132 patients</td>
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<td>Author/year</td>
<td>Sample</td>
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<tr>
<td>Nolte, 2016</td>
<td>74 patients</td>
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<tr>
<td>Nur, 2016</td>
<td>88 patients</td>
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<tr>
<td>Oh, 2020</td>
<td>30 patients</td>
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<tr>
<td>Paknahad, 2018</td>
<td>60 patients</td>
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<tr>
<td>Park, 2013</td>
<td>67 patients</td>
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<tr>
<td>Pradnahan, 2023</td>
<td>126 patients</td>
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<tr>
<td>Rakauskatie, 2020</td>
<td>160 patients</td>
</tr>
<tr>
<td>Ryu, 2015</td>
<td>85 patients</td>
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<tr>
<td>Shetty, 2022</td>
<td>150 patients</td>
</tr>
<tr>
<td>Silvestrini-Biavati, 2014</td>
<td>28 patients</td>
</tr>
<tr>
<td>Takahashi-Ichikawa, 2013</td>
<td>20 patients</td>
</tr>
<tr>
<td>Tam, 2023</td>
<td>50 patients</td>
</tr>
</tbody>
</table>
The data are presented in a narrative review format, establishing domains to aid comprehension for clinicians (OPT, PA cephalogram, CBCT, other methods).

Eleven studies [26–36] focused on the usage of OPT to detect mandibular asymmetries, either alone or in conjunction with other diagnostic methods, such as teleradiography or CBCT. According to various studies [26, 30], through linear and angular measurements made in the radiography, it is possible to assess mandibular asymmetry, in particular on the vertical plane. An asymmetry index (AI) was proposed in 1988 by Habets [20] to assess the dimensions asymmetries of the mandibular ramus and condyle in panoramic radiographs (PR). Given that the asymmetry index may be computed using routine PR obtained, several studies based on this guide the diagnosis or a first screening tool in children [27–29, 31, 33–36].

In one study [32] the screening for mandibular asymmetry was made through an image processing software, ImageJ, to automate and facilitate measurements, avoiding clinician error. Four studies [26, 27, 37, 38] evaluated the usage of PA cephalograms to achieve a mandibular asymmetry diagnosis. Through linear and angular measurements, one study [26] reported the importance of this radiographic technique as a primary diagnostic tool. This statement is corroborated by other articles [27, 38], which used the asymmetry index to identify mandibular discrepancies. The identification of valid landmarks is one of the principal problems of 2D imaging. To address this issue, one study [37] associated the PA cephalograms with lateral cephalograms and orthopantomography, both of them routine exams for an orthodontic patient.

The LL cephalometric exam was proposed in one study [39] to obtain mandibular asymmetry diagnosis. Another study [40], instead, used MRI 3D images, which proved to be effective in evaluating both the deviated and nondeviated side especially in early disease stages because it allows an excellent evaluation of the disc, especially in early disease. MRI employs non-ionizing radiation; and does not entail significant biological side effects. Four studies [41–44] assessed the use of SPECT. While three of these studies [41–43] concluded that SPECT was not beneficial, one study [44] found it to be more effective than scintigraphy for the diagnosis of condylar hyperplasia. Moreover, five studies [36, 45–48] proposed the usage of CT scans, in particular, one of them [45] focused on PET/CT instead of the SPECT for diagnosing active growth of the condyle. Mandibular asymmetries have been evaluated by a 3D vector system [46], with successful results. According to three studies [36, 47, 48], CT is an appropriate diagnostic tool for mandibular asymmetries, because it provides 3D imaging of 3D structures, but the high biological cost should be evaluated.

The usage of CBCT was assessed in thirty-one studies [5, 6, 18, 21, 33, 49–73], aiming to obtain a 3D image with a lower biological cost than spiral CT [49]. These articles proposed various ways to evaluate mandibular asymmetry, ranging from adapting asymmetry index or linear measurements, to volume analysis, superimposition of models and reverse engineer mirroring. In a recent study [51], the authors employed four methods, on the same CBCT, to evaluate asymmetry:

<table>
<thead>
<tr>
<th>Author/year</th>
<th>Sample</th>
<th>Method</th>
<th>Type of study</th>
<th>Objective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teng, 2021</td>
<td>40 patients</td>
<td>CBCT</td>
<td>Retrospective study</td>
<td>The purpose of this study was to examine mandibular symmetry, the occlusal plane, and their relationships using CBCT images in individuals with high-angle skeletal class III malocclusion and jaw deformity.</td>
</tr>
<tr>
<td>Thiesen, 2018</td>
<td>120 patients</td>
<td>CBCT</td>
<td>Retrospective study</td>
<td>The purpose of this study was to use CBCT to evaluate the features that affect skeletal Class I individuals with mandibular asymmetry.</td>
</tr>
<tr>
<td>Tun, 2021</td>
<td>50 patients</td>
<td>CT</td>
<td>Retrospective study</td>
<td>The purpose of this study was to assess the glenoid fossa’s three-dimensional location and its connection to asymmetrical condylar translational movement in order to look into the morphological and functional implications on mandibular asymmetry.</td>
</tr>
<tr>
<td>Tun, 2022</td>
<td>50 patients</td>
<td>CT</td>
<td>Retrospective study</td>
<td>The purpose of this study was to assess the three-dimensional morphology of the temporomandibular joint and its correlation with asymmetric condylar mobility in individuals with mandibular asymmetry.</td>
</tr>
<tr>
<td>You, 2018</td>
<td>50 patients</td>
<td>CBCT</td>
<td>Retrospective study</td>
<td>This study used CBCT to examine the morphologic characteristics of skeletal units in the mandibles of patients with mandibular retrognathism and facial asymmetry.</td>
</tr>
</tbody>
</table>

OPT = Orthopantomography; CBCT = Cone-Beam Computed Tomography; PA = Postero-Anterior Cephalogram; SPECT = Single Photon Emission Computed Tomography; LL = Latero-Lateral Cephalogram; MRI = Magnetic Resonance; PET/CT = Positron Emission Tomography/Computed Tomography.
asymmetry index, clinically derived midline, Procrustes analysis (PA), and modified Procrustes analysis (MPA). Unlike Procrustes analysis (PA), which used all face landmarks for aligning the original and reflected 3D configurations, MPA was created so that the superimposition was based only on 4 stable landmarks (bilateral orbitale and porion). The authors discovered that, similar to AI, the clinically derived midline (CM) and modified Procrustes analysis (MPA) were able to fully identify asymmetry, particularly in the mandibular region. In contrast, Procrustes analysis produced different outcomes in cases where the chin and mandible midline were symmetric. Another technique involves the usage of mirrored 3D overlaid models [74], which is based on the creation of a virtual 3D mandible and a mirrored counterpart, landmark identification and then measuring linear distances and models. The reverse engineering software method of superimposition and mirroring has been proposed by various authors [18, 61, 62] enabling the assessment of morphological symmetry of
any anatomical structure or treatment effectiveness. To assess Euclidean distances between the surfaces of superimposed anatomical structures, 3D bone structures from CBCT scans are mirrored and then superimposed. Using a method known as “surface-to-surface” analysis, the software also enables the evaluation of the morphological differences between superimposed structures in various colors on a 3D color map by varying the tolerance levels. Two studies [5, 21] focused not only on hard tissue asymmetry but also on soft tissue one, reporting that the combination of these conditions should be considered for developing an accurate treatment plan.

4. Discussion

Pediatric dentists and orthodontists are called to possess a comprehensive expertise in diagnosing of facial asymmetry in growing subjects. In this regard, clinicians should be able to identify all the features involved in the process of asymmetry, analyzing disharmony both qualitatively and quantitatively. Skeletal asymmetry might involve a single structure, however, it could affect the structures of antagonist basal bone as growth compensation process [24]. Concerning facial structures, the mandible is the jaw mostly affected by asymmetries, with maxillary asymmetric growth occurring as compensatory mechanism to maintain function and occlusion [60]. Mandibular asymmetries might involve the condyle, ramus, mandibular body and symphysis, all of which might experience changes in size, volume or position. In all these circumstances, radiographic examination represents a fundamental step in the diagnostic process of skeletal asymmetry since it allows to discriminate and to distinguish the structures and relative area/regions affected.

To the best of our knowledge, this is the first contribute in the literature that provides an updated detailed description of the radiographic tools usable for implementing the diagnosis of mandibular asymmetry, providing the rationale for clinical usability according to the evidence retrieved from included studies. In this regard, various methods have been explored, each with its own merits and limitations.

4.1 OPT

Since OPT is the standard preliminary radiographic record for orthodontic purpose, it may be utilized as a screening radiographic tool to identify the need for more in-depth radiographic studies and to detect early vertical mandibular asymmetries [30]. Indeed, OPT can assess condyle or ramus height vertically with acceptable consistency and reliability [75, 76] making it suitable for preliminary detection of condylar or ramal asymmetry. However, OPT has limitations, including limited resolution and susceptibility to picture distortion, magnification, and the superposition of anatomic structures [75, 77]. Considering that posterior structures (i.e., condyle and ramus) are subjected to less vertical distortion compared to anterior regions, high-quality OPT can be considered a non-invasive, acceptable diagnostic tool for screening vertical asymmetry of the mandible [20, 78]. However, a standardized protocol, which involves two aspects, is warmly encouraged to avoid reduction of diagnostic accuracy. Firstly, it is impor-

tant that the distance between the film and the X-ray tube’s focus point is the same in order to avoid vertical amplification [79]. Secondly, head posture during x-ray acquisition must be standardized since there is evidence [78] that a 10 mm shift in head position could result in a 6% vertical size difference. Such posture discrepancy can influence the analysis of asymmetry, especially considering that, according to Habets [20], mandibular posterior vertical asymmetry is defined as asymmetry index values higher than 3%.

The utilization of Habets’ Asymmetry Index [20], which focuses on linear and angular measurements, can enhance the precision of assessing mandibular conditions, providing orthodontists with a quantitative tool to evaluate the severity and direction of asymmetries. This index can be evaluated by direct tracing with a pencil, or with a computer software [32]. The benefit of the study presented is that it enables simultaneous evaluation of mandibular measures in individuals, facilitating the differential diagnosis of morphological and functional mandibular asymmetries.

4.2 PA cephalogram

The PA cephalogram has long been utilized in orthognathic and orthodontic diagnosis, as well as in surgical planning, to examine the transverse dimension of the craniofacial skeleton and dentoalveolar structures, hence to address asymmetry [24, 80]. In one study [27] PA cephalometric analysis in orthodontics has been compared with orthopantomography as a diagnostic tool for mandibular asymmetries, using the asymmetry index. When the measurement values were entered into the AI formula, the results did not indicate a significant difference between the PR and PA cephalogram images, suggesting that both methods can be used for diagnosis. However, measurements such as the condylar height (CH), ramus height (RH), and CH + RH showed statistically significant differences on the right and left sides in panoramic radiographs (PR) and posteroanterior cephalometric radiographs (PACR) [27]. Another study [26] compared PA cephalometry with OPT using linear and angular measurements, concluding that there is a strong diagnostic correlation between the two methods. Therefore, the combination of both techniques allows for initial diagnostic screening. Nevertheless, as for panoramic radiograph, also posteroanterior teleradiography is a 2D image of 3D structures, and the head position has a significant impact on the vertical dimension, making it unsuitable for distance measurements [80].

4.3 Latero-lateral cephalogram

In this section of the discussions, studies referring to diagnostic methods of mandibular asymmetry not commonly employed are evaluated. A lateral cephalogram can contribute to the diagnosis, follow-up, and management of various dentoalveolar deformities and growth anomalies by evaluating interactions among the skull, face, and teeth [81]. However, due to the overlap of the two sides’ structures and superimposed pictures, the lateral cephalogram is unable to compare the orofacial features on the right and left [30].
4.4 Computed tomography methodologies

The 3D anatomical reconstruction ensures excellent visualization of both hard and soft tissues and, consequently, allows for a better definition of the discrepancy of the same structure between both sides. In assessing facial asymmetry, CT scans offer high-resolution images that allow for precise visualization of different areas of the mandible facilitating the identification of asymmetrical growth patterns, structural abnormalities, and deviations from normal anatomical configurations. By employing cross-sectional imaging, CT facilitates the examination of specific regions such as the condyle, ramus, mandibular body, and symphysis, elucidating alterations in size, volume, and position. However, CT has two main limitations for the primary identification of mandibular asymmetry in growing subjects. Firstly, CT does not fully adhere to the ALARA (As Low As Reasonably Achievable) principle due to the inherent high exposure to ionizing radiation, which poses potential biological risks in pediatric populations [74]. Secondly, CT is not an ideal imaging modality for detailing and characterizing soft tissues. CT primarily excels in imaging dense structures such as bones due to its reliance on X-rays, which are more effectively absorbed by dense materials. Soft tissues, being less dense, may appear less distinct on CT scans, making it challenging to discern detailed features or subtle variations in soft tissue structures. Also, CT is more susceptible to artifacts that compromise the clarity and accuracy of soft tissue representations, impacting the precision of facial soft tissue analysis [21].

Positron Emission Tomography-Computed Tomography (PET-CT) and Single Photon Emission Computed Tomography (SPECT) are imaging modalities that involve the injection of a radiopharmaceutical tracer which accumulates in areas with increased metabolic activity, such as regions of high cell turnover, inflammation and metabolism. Both imaging systems evaluate the dynamic aspects of mandibular asymmetry which could be crucial for differentiating between developmental asymmetries and acquired asymmetries due to trauma or pathological conditions. However, both methods also have limitations, including lower spatial resolution compared to anatomical imaging modalities like CT [21] or MRI [40]. In this regard, three studies [41–43] reported that SPECT is not sufficient to achieve the diagnosis of mandibular asymmetry and should be employed in conjunction with other imaging techniques to provide a more comprehensive assessment of mandibular asymmetry. These findings, again, arise concern related to adherence to the ALARA principle, as the use of multiple imaging modalities may increase radiation exposure.

4.5 CBCT

Although CBCT generates higher radiation exposure compared to single conventional 2D radiographic examinations (OPT, PA), the radiation dose is lower than all additional radiographic examinations necessary for complete orthodontic records, with the advantage of providing more detailed diagnostic data on asymmetry [82, 83]. The American Academy of Oral and Maxillofacial Radiology and the SedentexCT guidelines recommend using CT scans to evaluate facial asymmetry [84, 85]. Moreover, with technological progress, it is possible to reduce the Field of View (FOV) of the CBCT and consequently reduce the amount of radiation. For this reason, most of the studies available in the literature addressing mandibular asymmetry are related to the usage of CBCT technology.

Several studies [54–56, 86] have confirmed a high degree of repeatability of CBCT for assessing asymmetry, achieving good diagnostic outcomes. However, the conclusions drawn from the studies were only based on 2D linear and/or angular measurements of the mandibular, ramus, and condyle. The problem of using 2D measurements of 3D dataset has been recently emphasized since linear measurements can underestimate the true diameter of any curved surface [18, 87]. In this regard, the concept of integrating volumetric data with surface analysis obtained from sophisticated 3D imaging systems has been introduced for analyzing 3D dataset from both quantitative and qualitative perspective [18, 58]. In particular, recent studies [18, 61, 62, 88] demonstrated that reverse engineering software enables a detailed assessment or the monitoring of treatment progress of morphological symmetry of any anatomical structure. Specifically, 3D bone structures derived from CBCT scans can be mirrored and overlaid, allowing for the measurement of Euclidean distances or root mean squared (RMS) differences between the surfaces of the anatomical structures [50]. The mirroring process is performed after identifying the anatomical plane that serves as a reference for the models’ speculation. Subsequently, the models are registered using a “Best-fit alignment” algorithm, and a surface analysis is performed and visualized with a color map that highlights differences between both anatomical sides (right-to-left or left-to-right) [18]. Different levels of tolerance are applied through a technique known as “surface-to-surface” analysis, facilitating the identification and characterization of asymmetries with precision.

4.6 Acute and chronic TMJ disorders and asymmetry

Disorders of the temporomandibular joint (TMJ) can be transient or chronic. Acute illnesses are transient and usually go away on their own or with little medical intervention. Treatment for chronic diseases might be more complicated and have a longer duration. Symptoms of TMD (temporomandibular joint disorder) can include pain, jaw dysfunction, and joint noises. Another acute condition could be trauma of TMJ, which could be seen through OPT firstly, but for a better imaging evaluation CT or MRI is recommended [40].

With a female-to-male ratio of 3–6:1, juvenile idiopathic arthritis (JIA) refers to a set of disorders characterized by joint inflammation (arthritis) [53]. A tiny, asymmetrical, and hypoplastic mandible, a skeletal open bite, a short mandibular ramus, an elevated gonial angle, and anterior facial convexity are among the classic indicators of inflammation present in the affected joints. It has been suggested that the primary underlying causes of maxillomandibular growth abnormalities are chronic inflammation and gradual disruption of the condylar cartilage during mandible development. Affected condyles have a shorter and frequently asymmetric mandibular ramus [89]. Patients with JIA frequently exhibit indications of
erotion and flattening of the condylar head, varying in severity. There are differences in the degree of functional limitations according to how much of the condylar head has been affected by the articular injury, ranging from minor erosions and osteophytes to conditions in which the condylar head is completely absent [53]. Using two-dimensional (2D) cephalometric studies, dentofacial development deviation in JIA with TMJ involvement has been well-described [90]. However, compared to 2D methods, 3D imaging offers a better visibility of dentofacial features [91]. Over the past 20 years, 3D imaging techniques have become more common in the assessment and follow-up of dentofacial development due to the advent of cone-beam computed tomography (CBCT) in the field of dentistry [53].

Moreover, the diagnosis and follow-up of TMJ chronic disorder such as internal derangement could be done with MRI, with no biological side effect into the patient.

4.7 Clinical implications

In light of the findings retrieved from the included studies, pediatric dentists and orthodontists should follow an appropriate clinical strategy when using radiological tools for the diagnosis of mandibular asymmetry. In this regard, after clinical facial and occlusal examination, a preliminary detailed analysis of 2D data retrieved from OPT is necessary to discriminate potential signs of asymmetry and to identify the area/regions involved. CBCT scans are encouraged as a second level of investigation, due to several advantages: (1) the ability to perform measurements in the three dimensions in each investigated area, (2) obtain volumetric reconstruction and volumetric data for side-to-side comparison, (3) integrate volumetric data with the analysis of side-to-side surface dataset, aiding in distinguishing the area mostly involved by the developing asymmetry. PET-CT and SPECT should only be considered if active pathological conditions are suspected.

The results discussed in this narrative are based on a limited number of studies, with heterogenous methodological design. In this regard, the topic of diagnosing mandibular asymmetry appears to be underestimated in literature. Future studies are warmly encouraged to evaluate and compare the diagnostic effectiveness of different radiographic imaging systems for detecting different mandibular asymmetric conditions.

5. Conclusions

According to current knowledge, there is no unanimous consensus on the method for diagnosing mandibular asymmetries. The objective of this literature review is, therefore, to provide a practical guide for clinicians to easily diagnose this condition. CBCT appears to be the preferred examination method, thanks to the assessment of a 3D structure with a 3D image. However, clinicians should consider the biological cost, namely the radiation exposure rate to which a young patient would be subjected. Therefore, in cases of mild asymmetries, the use of only orthopantomography might be advisable as a primary diagnostic tool in children.

AVAILABILITY OF DATA AND MATERIALS

The data of the present manuscript are available upon request to the corresponding author.

AUTHOR CONTRIBUTIONS

VR—formal analysis; SLR—wrote the manuscript and performed the research; MC—visualization; RL—provided help and advice; ALG—designed the research study and made revision. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

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