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Comprehensive investigation of long-term side effects of cone beam computed tomography used for orthodontic treatment modalities in young children: Systematic review and meta- Analysis

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Abstract
The purpose of our systematic review and meta-analysis was to investigate long term side effects of cone beam computed tomography investigations used regularly now a days in orthodontic treatment modalities. 6 studies were included in the meta analysis finally excluding articles which didn't meet our inclusion criteria. The results concluded that the cone beam computed tomography imaging highlighted a critical concern regarding the increasing use in paediatric orthodontics. Younger age groups (5-10 years) exhibit significantly higher percentages of risk of cancer compared to older age groups.

Keywords: Cone beam computed tomography, orthodontic treatment, long-term side effects, young children

Introduction

In the realm of orthodontics, the use of imaging techniques plays a crucial role in diagnosis, treatment planning and monitoring progress. Traditionally, two-dimensional (2D) radiographs, such as panoramic and cephalometric X-rays, have been the standard for assessing dental and skeletal structures. However, the field is undergoing a significant shift with the introduction and increasing adoption of three-dimensional (3D) imaging modalities, most notably cone-beam computed tomography (CBCT). This transition marks a move towards more comprehensive and accurate diagnostic capabilities, offering a wealth of information that surpasses the limitations of traditional 2D radiographs. Cone beam computed tomography technology provides a volumetric representation of the craniofacial structures, allowing clinicians to visualize teeth, bone and soft tissues in three dimensions. This eliminates the inherent distortions and superimpositions present in 2D images, leading to more precise measurements and a more thorough understanding of the patient's unique anatomy.

The benefits of CBCT in orthodontics are numerous. CBCT enables the detection of impacted teeth, supernumerary teeth, perforations, root resorption, and other dental anomalies with greater accuracy. This level of details surpasses what is achievable with traditional twodimensional X-rays. Furthermore, it also provides detailed information about the temporomandibular joints (TMJ) and airway, aiding in the diagnosis of TMJ disorders and sleep apnoea, a condition characterized by interrupted breathing during sleep. Beyond diagnosis, CBCT greatly improved treatment planning. The 3D models generated by the scans allow clinicians to precisely plan the treatment in various different procedures. This includes the optimal placement of dental implants, ensuring they are positioned correctly within the bone for maximum stability and function. CBCT is also instrumental in creating surging guides, which are used during implant surgery to ensure accurate placement. In orthodontics, the 3D visualization allows for precise planning of appliance placement, such as braces or aligners, leading to more effective and efficient treatment. Moreover, CBCT facilitates the prediction of treatment outcomes by allowing clinicians to visualize the potential changes in tooth position and jaw structure. It also helps in the evaluation of potential risks associated with difference treatment options, allowing for more informed decision making.

While any X-rays procedure involves some level of radiation exposure, advancements in CBCT technology have significantly reduced the effective dose compared to traditional CT scans. This reduction in radiation exposure makes CBCT a safe and viable option for orthodontics and dental imaging, particularly when the benefits of the detailed information outweigh the minimal risk. Finally, these 3D images generated by the scans are easily shared with patients, providing them with a clear and comprehensive understanding of their condition. This visual representation allows patients to better grasp the complexities of their dental or orthodontic issue and the rationale behind the proposed treatment plan. This improved understating fosters better patient engagement and cooperation, leading to more successful treatment outcomes.

Over the past few decades, the sue of dental cone-beam computed tomography (CBCT) has become increasingly prevalent, even in paediatric dentistry. In many clinical scenarios, CBCT has become the preferred method for oral and maxillofacial radiology (Dworschak *et al.*2017) [1]. However, it's important to acknowledge that CBCT scans generally involve higher absorbed doses compared to conventional X-ray examinations (Pauwels *et al.*2010) [2]. This raises a crucial concern, particularly in children.

Children are known to be more susceptible to the carcinogenic effects of ionizing radiation. This heightened sensitivity stems from their rapidly developing tissues and organs. Furthermore, their longer life expectancy increases the potential for long-term consequences, such as the development of radiation-induced cancer later in life (Chodick *et al.*2007) [3]. Therefore, the question of cancer risk associated with diagnostic medical exposure to ionizing radiation, especially from dental CBCT scans, is particularly relevant and warrants careful consideration in the paediatric population. To minimize radiation exposure, orthodontists should adhere to the "As Low as Reasonably Achievable"

principle, involving the use of the lowest possible radiation dose necessary to obtain diagnostic-quality images. This can be achieved by optimizing equipment settings, selecting appropriate imaging protocols, etc. Additionally, it is essential to weigh the benefits of CBCT against the potential risks for each patient. In many cases, a traditional radiograph may be sufficient for diagnostic purposes.

The current study aimed to estimate the side effects of the use of Cone beam computed tomography X-rays in young children for orthodontic treatment by utilizing the systematic review and meta-analysis will help assess the risk of frequency of scans and higher organ dosage. Therefore, orthodontist can harness the power of CBCT while ensuring the safety and well-being of their patients. A systematic review explores the usage of CBCT techniques and Meta-analysis was utilized to combine the results of several studies and provide a synthesized result. This helps to identify differences between studies, underlying factors, and potential biases. By pooling data from various studies, meta-analysis offers valuable insights to address research questions and identify knowledge gaps.

Methodology

1. /Search Strategy and Selection Criteria

To initiate our systematic review, we precisely defined the research topic and conducted a thorough literature search, focusing on published articles and unpublished thesis containing pertinent English content that examine cone-beam computed tomography, orthodontic treatment, and cancer risk in children. Adhering to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines (Shamseer *et al*., 2015) [4] ensures a rigorous and transparent review process. To identify the relevant studies, we systematically searched reputable databases including PubMed, Springer, Google Scholar, Science Direct, Biomed Central, CeRA, Krishikosh, and other published sources. We also utilized Zotero 5.0 and Rayyan QCR, two web-based tools for this purpose.

We followed strict inclusion and exclusion criteria, studies lacking examination cone-beam computed tomography, orthodontic treatment, and cancer risk, and extracted information on authors, study period, sample size, species, and country.

2. Quality assessment of studies

Two reviewers independently rated the quality of the studies by utilizing structured questionnaires with 8 items, following the modified risk of bias tool, the scale was determined using the Kappa Index, and each study was rated on a Likert scale ranging from 1 to 5, and the average score was calculated as the final score. The agreement between the authors was quantified using Aiken's V Index. If the Aiken V Index was greater than 0.7, the study quality was considered confirmative and acceptable (Ashwini *et al*., 2024) [5].

$$V = \frac{\sum S}{n(c-1)}$$

Where,

Aiken V = Validity index;

S = Scores assigned by each rater minus the lowest score used.

$S = r - l_o$; r = rater category selection score; l_o = lowest scores in the scoring category. c = Maximum score on the grading scale. n = number of raters.

V value ranges from 0 to 1, where 1 denotes that the rater has given 100% consent in the structured question included.

3. Data analysis

3.1 Systematic review

The systematic review was developed to ensure objectivity and transparency in the collection and evaluation of information from published articles. By following established PRISMA guidelines, quality and credibility were enhanced, promoting a more robust and evidencebased approach within the domine.

3.2 Meta-analysis

Meta-analysis is to combine the results of several studies and provides a synthesized result
(Normand, 2005) [6].

3.2.1 Forest and funnel plots

This plot is typically used to display data cone-beam computed tomography, orthodontic treatment, and cancer risk and is often used in subject area reviews to summarize previously published findings. Whereas funnel plots are scatterplots that display the treatment effects of individual studies against a measure of study size.

3.2.2 Fixed-effects model and random-effects model

The fixed effect model is a statistical method to estimate a single, common effect size across studies, assuming differences are due to chance (sampling error), rather than genuine variations in the true effect size. This model is most suitable for homogeneous studies.

The random effect model is a statistical technique used to account for heterogeneity among the studies by recognizing that the effect size can differ due to factors such as populations, interventions, and methodological approaches. This model provides a robust and generalized estimate of the overall effect.

3.2.3 Heterogeneity indices

To assess heterogeneity among studies, the I^2 index was used. The I^2 ranging from 0 % to 100%, indicates heterogeneity levels, value below 50 % suggests minimal heterogeneity, above 50% indicates moderate to substantial heterogeneity, and 95% reflects significant heterogeneity. A random effect model was employed to account for notable heterogeneity among the studies. The size of the squares in the forest plots represented study weight, and I^2 statistics, quantified variability, τ to estimate study variance. In Cochrane reviews, the chisquare [χ^2] test was employed to determine the statistical significance of heterogeneity. A Pvalue less than 0.05 from the test indicated significant heterogeneity (Ashwini *et al*. 2024) [5].

3.2.4 Publication bias

Publication bias is an eminent issue in systematic review and meta-analysis, as it can affect the accuracy of the findings. Published studies often favour positive results, leading to an overrepresentation of confirmatory tests. To evaluate publication bias in our selected studies, we used a funnel plot, which visualized heterogeneity. In this plot, the

Y-axis represents the standard error, and the X-axis shows the Arcsine transformation of the study proportion (Ashwini *et al*. 2024) [5]. With no publication bias, studies with higher precisions tend to cluster near the normal line, while those with lower precision are more evenly distributed, creating a funnel shape.

3.3 Meta-regression, subgroup analysis

Meta-regression is to examine how study characteristics affect both estimates and variability within the study. Factors such as sample size, detection techniques, species, and regions were analysed through meta-regression to quantify the heterogeneity with P-values below 0.05 from the univariate analysis were retained (Ashwini *et al*. 2024) [5].

Subgroup analysis is a technique used in meta-analysis to examine heterogeneity by stratifying data into more specific groups. Our study posited that the studies we included were not all from the same population but rather from various subgroups, each with its overall effect. This investigates the related heterogeneity for sample size, detection techniques, species, and regions.

Results

1. Data extraction

An extensive literature search was executed using various keywords, including "cone-beam computed tomography" "orthodontic treatment" "cancer risk" and "children", along with Boolean operators [or and not] asterisk* and quotation marks [" "] were utilized to refine the search. This initial phase in the collection of 80 articles using Google Scholar, PubMed, NCBI, and ResearchGate to identify both national and international articles. A total of 47 studies were initially earmarked for primary scrutiny. After eliminating the 27 duplicates and irrelevant articles, 20 remained for further screening. A thorough review of titles and abstracts led to the exclusion of 10 additional studies. Two authors independently reviewed the complete texts of the rest 10 articles using Aiken's Index to evaluate study quality. An additional 4 studies were excluded due to outliers. Ultimately, 6 articles were included to conduct a meta-analysis (Fig 2).

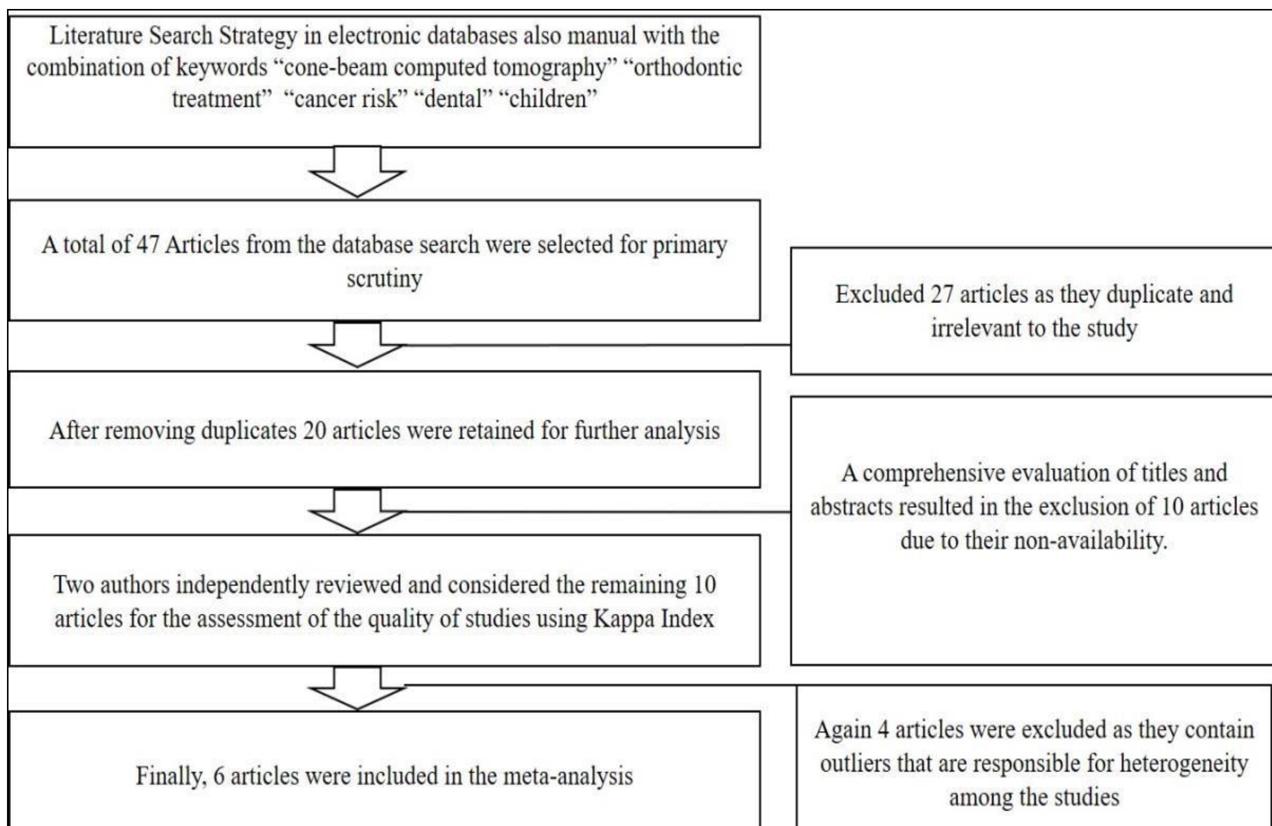


Fig 1: Schematic Illustration of articles selection for Systematic Review

2. Quality assessment of studies

Two independent reviewers rated the 6 articles using a Likert scale (1-5) to determine their relevance. The average score was designated as the final score. Inter-rater reliability was assessed using the Kappa Statistics (Table 1) and agreement between the two reviewers' ratings was measured using Aiken's Index (Ashwini *et al*.2024) [5], a value greater than 0.7 was considered to have acceptable quality. Consequently, 6 articles were included to conduct a meta-analysis.

3. Publication bias

The funnel plot (Fig.3) portrays the publication bias, although it is relatively minor. This bias is more pronounced in smaller studies, which tend to report larger effect sizes compared to larger studies. The study highlights the importance of meta-regression and sub-group analysis to improve the accuracy of reported cone-beam computed tomography in orthodontics patients. This analysis considered the factors such as sample size, diagnostic tests, species, and geographical regions. This plot revealed no publication bias (p-value > 0.05).

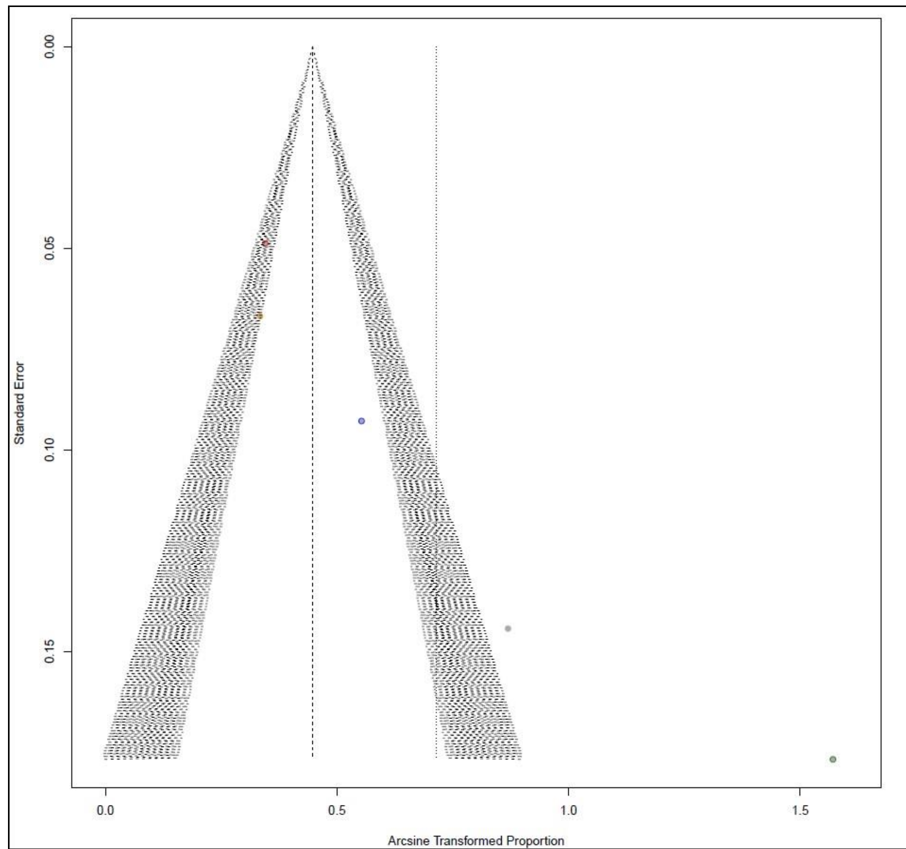


Table 1: Interrater agreement testing between two raters in using the risk of bias tool

Sl.no Validation procedures	Author 1*	Authors 2*	KAPPA (95 % CI)
External validation			
1 Was the study's target population representative of the national population concerning relevant variables?	4.00	5.00	0.8[0.27-0.98]
2 How were the samples selected, randomly, or was the census undertaken?	5.00	5.00	0.8[0.27-0.98]
3 Was the probability of bias minimal?	5.00	5.00	0.8[0.27-0.98]
4 Internal validation			
5 Was the data collected directly from the subjects?	4.00	4.00	0.75[0.22-0.98]
6 Was an acceptable case definition used in the study	4.00	4.00	0.75[0.22-0.98]
7 Was the used study methods to measure parameter valid and reliable	4.00	4.00	0.75[0.22-0.98]
8 Was the same mode of data collection used?	5.00	5.00	0.75[0.22-0.98]
9 Summary of the overall risk of the study bias	5.00	5.00	

3.1 Systematic review

The systematic review was developed to ensure objectivity and transparency in the collection and evaluation of information from published articles. By following established PRISMA guidelines, quality and credibility were enhanced, promoting a more robust and evidencebased approach within the domine (Table 2).

Table 2: CBCT diagnosis on organs using organ doses causing cancer

Authors	Organ doses	Results	Side effects
Jha *et al.*2020[7]	105	The mean lifetime fractional ratio (LFR) was 14.28% for children and 0.91% for adults; this indicated that the risk to children was 16 times the risk to adults. For median exposure settings, the mean LFR was 5.25% and 0.58% for children and adults, respectively	The risk of cancer decreases with increasing age.
Yeh and Chen. 2018[8]	29	Organs with the reference at 83.0cm, and measured with their coordinating from75.0 to92.5cm	Individual cancer risk estimates as a function of gender and age are small, the concern about the risks from dental CBCT is related to the rapid increase in its use for orthodontic practice, especially in children's patients.
Felice *et al.*2019[9]	8	3-dimensional projections of X-ray images, and cone beam computed tomography (CBCT) has resulted in a large application in dentomaxillofacial imaging, even in children. CBCT uses ionizing radiation that may cause damage to the DNA	Children are at the greatest carcinogenesis risk due to their higher tissue radiosensitivity and their longer life expectancy compared to adult
Najjar *et al.*2013[10]	8.67 (i-CAT full head 0.3 mm) 13.08 (i-CAT maxilla 0.2 mm) 6.82 (i-CAT maxilla 0.4 mm)	significantly higher equivalent radiation doses to children compared with adults, ranging from a 117% average ratio of equivalent dose to 341%.	CBCT scans adult settings on both phantoms resulted in radiation doses to the head and neck organs with heads higher

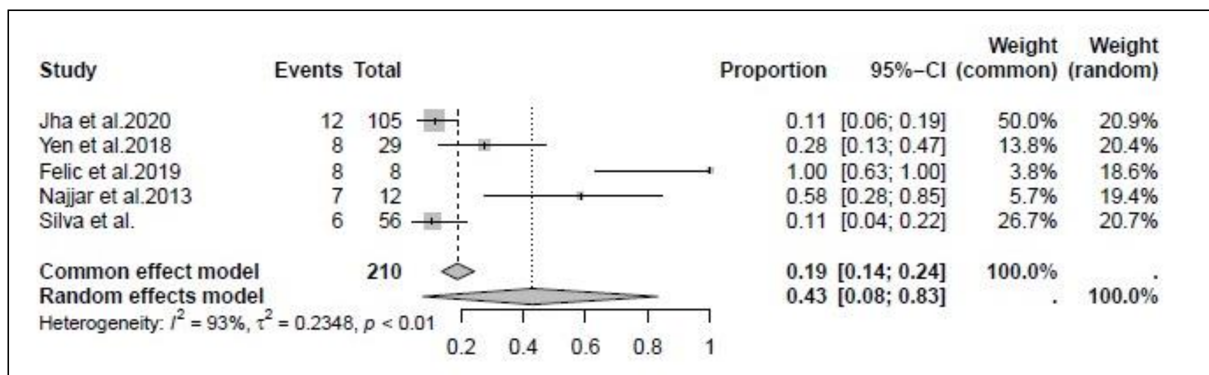
	15.75 (i-CAT mandible 0.2 mm 8.28 (i-CAT mandible 0.4 mm 8.18 (i-CAT full head 7.8 mm 24.6 (i-CAT maxillamandible 40 sec)		in the child compared with the adult	
Silva et al [11].	56.2	The thyroid gland received the lowest organ dose (13.1 µSv) during conventional panoramic and lateral cephalometric imaging. The highest mean organ dose (15,837.2 µSv) was received by the neck skin from the multi-slice CT. The effective dose was also lower for the panoramic and lateral cephalometric device (10.4 µSv), and highest for the multi-slice CT (429.7 µSv).	From a radiationprotection point of view, conventional images still deliver the lowest doses to patients.	

3.2 Meta-analysis

Meta-analysis is to combine the results of several studies and provides a synthesized result (Normand, 2005) [6].

3.2.1 Forest plot

The forest plot summarizes the results of multiple studies that investigated a specific outcome, likely a binary outcome (e.g., success/failure, presence/absence). Each horizontal line represents a single study, with the square indicating the point estimate of the outcome and the horizontal line representing the 95% confidence interval. The plot highlights the variability in individual study results. The random effect model provides a more conservative estimate of 43 %, stating the success rate of cone beam computed tomography in orthodontics patients.



Individual cancer risk estimates as a function of gender and age are small, the concern about the risks from dental CBCT is related to the rapid increase in its use for orthodontic practice, especially in children's patients. The study presents data on the risk of exposure to certain factors (likely radiation, given the content of CBCT and cancer risk) across different age groups. The data suggests a clear age-related trend in exposure risk. Younger age groups (510 years) exhibit significantly higher percentages of risk compared to older age groups. This trend aligns with the general understanding that younger individuals are more susceptible to the long-term effects of radiation exposure. The gender ratio is maintained at 1:1 across all age groups, indicating that both genders are equally exposed to the risk factors. The total average number of cases remains constant across all age groups, suggesting that the overall exposure level is similar. However, the distribution of risk within these groups varies, with younger individuals bearing a higher proportion of the risk.

These findings highlight the importance of minimizing radiation exposure, especially for younger patients. While CBCT is a valuable diagnostic tool, it should be used judiciously and with the lowest possible organ dose.

Orthodontists should carefully consider the need for CBCT in each case, weighing the potential benefits against the cancer risks. By adopting best practices and adhering to guidelines for radiation protection, clinicians can help mitigate the long-term health consequences associated with CBCT exposures.

Discussion

Cone-beam CT (CBCT) was introduced in the market to bring a solution to the disadvantages of conventional CT in Europe in 1998 (NewTom QR-DVT 9000, Quantitative Radiology Srl, Verona, Italy) and in the USA in 2001 (Coskun and Kaya.2018) [12]. Cone-beam computed tomography (CBCT) has revolutionized the field of orthodontics by providing detailed threedimensional images of the oral and maxillofacial region. While CBCT offers several advantages over traditional two-dimensional radiographs, enabling more precise diagnosis and treatment planning, it is important to acknowledge the potential risks of radiation exposure. For example, instead of focusing on the vertical and transverse dimensions, malocclusions generally are described by using anteroposterior terminology (which may seem awkward to a clinician who does not practice orthodontics, because clinical malocclusion is a 3-D manifestation), which may be why most orthodontic appliances are targeted to result in anteroposterior correction. Furthermore, many orthodontic treatment procedures are geared toward resolving conditions that cannot be appraised adequately by using conventional twodimensional (2-D) radiographs. For example, dentoalveolar limits of tooth movement, particularly in attempts at non-extraction expansion treatments, cannot be determined without 3-D imaging. In addition, many relationships of the craniofacial complex, such as the position of the mandibular condyles in the temporomandibular fossa concerning the occlusal scheme and the association of airway abnormalities to craniofacial

morphology, cannot be evaluated with conventional imaging approaches [16]. Advanced CBCT software applications also can be used to quantify airway space (relevant for sleep apnoea cases), perform superimpositions of objects at different time points to semi quantitatively visualize changes (e.g., mandibular growth, temporomandibular joint, airway), and generate digital dental models to streamline the workflow in the orthodontic clinics [17].

Unlike patients receiving implants or endodontic treatment, most orthodontic patients are children who are particularly sensitive to ionizing radiation. Cone-beam computed tomography (CBCT) carries risks and benefits in orthodontics (Abdelkarim 2016) [13]. While the radiation dose from CBCT is relatively low, repeated exposure, especially in young patients, can increase the cumulative risk of cancer. Felice *et al.*2019 [9] found that Children are at the greatest carcinogenesis risk due to their higher tissue radio sensitivity and their longer life expectancy compared to adults. The risk is particularly concerning for children and adolescents, as their cells are more sensitive to radiation and their lifespan is longer, increasing the potential for long-term effects. Yen and Chen 2018 [8] stated that individual cancer risk estimates as a function of gender and age are small, the concern about the risks from dental CBCT is related to the rapid increase in its use for orthodontic practice, especially in children's. Najjar *et al.*2013 [10] revealed that CBCT scans with adult settings on both phantom heads resulted in higher radiation doses to the head and neck organs in the child compared with the adult. To minimize radiation exposure, orthodontists should adhere to the "As Low as Reasonably Achievable" principle, involving using the lowest possible radiation dose necessary to obtain diagnostic-quality images. This can be achieved by optimizing equipment settings, selecting appropriate imaging protocols, etc. The study found no benefit in terms of changes in treatment plans for patients when the reason for obtaining a CBCT scan was to examine for abnormalities of the temporomandibular joint or airway, or crowding. Orthodontic participants who own CBCT machines or use CBCT scans frequently in practice reported significantly more diagnosis and treatment plan changes and greater confidence after viewing the CBCT scans (Hodges *et al.*2012) [14]. Additionally, weighing the benefits of CBCT against the potential risks for each patient is essential. In many cases, a traditional radiograph may be sufficient for diagnostic purposes. Silva *et al.* stated that from the radiation-protection point of view, conventional images still deliver the lowest doses to patients. CBCT has replaced conventional lateral cephalograms and panoramic images as the most commonly ordered imaging for comprehensive orthodontic patients (Halazonetis.2012) [15].

Our study results are in line with the above studies stating that the success rate of CBCT found that 43% across the studies included and highlighted a critical concern regarding the increasing use of cone-beam computed tomography in paediatric orthodontics. While CBCT offers valuable diagnostic information, its use necessitates careful consideration of the potential radiation risks, particularly in young patients. Our study reveals an age-related trend in exposure risks. Younger age groups (5-10 years) exhibit significantly higher percentages of risk compared to older age groups. This finding aligns with established scientific principles that underscore the heightened sensitivity of young individuals to the long-term effects of ionizing radiation [18]. While the total number of cases remains constant across age groups, suggesting a similar overall exposure level, the distribution of risk within these groups is skewed. Younger patients bear a disproportionately higher share of the radiation burden. This observation underscores the need for stringent justification and optimization protocols for CBCT use in paediatric orthodontics. The gender ratio is the same (1:1) across all age groups indicating that both males and females are equally exposed to the risk factors associated with CBCT. However, this does not negate the importance of conserving individual patient factors, including gender, when assessing the risk-benefit ratio of CBCT.

Conclusion

Cone-beam computed tomography (CBCT) has become increasingly popular in orthodontic practice, providing detailed 3D images that can aid in diagnosis and treatment planning, enhancing diagnostic accuracy, and outcome assessment. However, its use, especially in paediatric patients, raises concerns about potential radiation exposure. While the radiation dose from a single CBCT scan is relatively low, repeated exposure, particularly in young patients with longer life expectancies and higher tissue radio sensitivity, can increase the cumulative risk of cancer. Therefore, it's crucial to adhere to strict clinical guidelines, employ dose optimization techniques, and explore alternative diagnostic methods whenever possible to minimize radiation exposure in paediatric orthodontic care. Thereby, to mitigate these risks, orthodontists should adhere to the ALARA principle, minimizing radiation exposure by optimizing equipment settings and selecting appropriate imaging protocols. In many cases, traditional radiographs may suffice for diagnostic purposes. However, when CBCT is deemed necessary, careful consideration of the patient's individual needs and potential benefits versus risks is crucial. While CBCT can provide valuable diagnostic information and improve treatment outcomes, it should use judiciously and only when clinically justified. By balancing the benefits and risks, orthodontists can ensure the safe and effective use of CBCT in their practice.

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