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Correlation between gray values of cone-beam computed tomograms and Hounsfield units of computed tomograms: A systematic review and meta-analysis

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ABSTRACT

Purpose: The aim of this review was to systematically analyze the available literature on the correlation between the gray values (GVs) of cone-beam computed tomography (CBCT) and the Hounsfield units (HUs) of computed tomography (CT) for assessing bone mineral density.

Materials and Methods: A literature search was carried out in PubMed, Cochrane Library, Google Scholar, Scopus, and LILACS for studies published through September 2021. *In vitro*, *in vivo*, and animal studies that analyzed the correlations GVs of CBCT and HUs of CT were included in this review. The review was prepared according to the PRISMA checklist for systematic reviews, and the risk of bias was assessed using the Quality Assessment of Diagnostic Accuracy Studies tool. A quantitative analysis was performed using a fixed-effects model.

Results: The literature search identified a total of 5,955 studies, of which 14 studies were included for the qualitative analysis and 2 studies for the quantitative analysis. A positive correlation was observed between the GVs of CBCT and HUs of CT. Out of the 14 studies, 100% had low risks of bias for the domains of patient selection, index test, and reference standards, while 95% of studies had a low risk of bias for the domain of flow and timing. The fixed-effects meta-analysis performed for Pearson correlation coefficients between CBCT and CT showed a moderate positive correlation ($r = 0.669$; 95% CI, 0.388 to 0.836; $P < 0.05$).

Conclusion: The available evidence showed a positive correlation between the GVs of CBCT and HUs of CT. ***(Imaging Sci Dent 2022; 52: 133-40)***

KEY WORDS: Tomography, X-ray Computed; Cone-Beam Computed Tomography; Bone Density; Reproducibility of Results

Introduction

Bone mineral density (BMD) evaluation at implant placement sites is essential to ensure adequate primary stability. Computed tomography (CT) has been accepted as the gold standard for BMD evaluation because it displays consistent Hounsfield units (HUs), as X-ray attenuation values can be accurately calibrated with a standard HU scale based on the reference density values of air (−1,000 HU), pure water (0 HU), and cortical bone density values ranging +1,000 HU.[1] However, the high radiation dose of CT limits its application for diagnosis in dentistry.[2,3]

Cone-beam computed tomography (CBCT) scans are commonly employed in dental practice and can be used for bone density assessment, as they provide adequate resolution with less radiation than CT and a shorter acquisition period.[4-7] Nonetheless, the use of CBCT for bone density evaluation remains questionable, as it lacks standardized voxel values and relies on grayscale differences set by the manufacturer.[8,9] Some studies have suggested that CBCT

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can be used as a reliable substitute for CT and affirmed its reliability.[5,10-12] González-García and Monje[13] were the first to compare CBCT and micro-CT for assessing bone microstructure in the maxilla prior to implant placement and found a high positive correlation, suggesting that CBCT is a reliable method. Conversely, others have raised concerns regarding the effectiveness and reproducibility of CBCT.[7,14-16] These conflicting results may be due to different study designs and methodology used for density estimation; hence, a systematic evaluation of the available literature is warranted.

A recent systematic review by Eguren et al.[17] in 2021 reported on whether the gray values (GVs) of CBCT could be translated to HUs in multidetector CT (MDCT) and concluded that sufficient evidence was not available to suggest that GVs in CBCT could be converted to HUs in MDCT. Hence, the present review aimed to systematically analyze all available literature and report whether the GVs of CBCT can be correlated with the HUs of CT for assessing BMD.

Materials and Methods

The research question of this review was "Do the GVs of CBCTs have any correlation with the HUs of CTs for measuring BMD?" This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. The review protocol was registered in the PROSPERO database (CRD42021254775).

A literature search was performed using specific search strategies in various electronic databases including PubMed, Cochrane Library, Google Scholar, Scopus, and LILACS to identify studies published through September 2021. Information sources in the gray literature were also performed. Key words were customized for each database. In PubMed, a search was performed using the following keywords: (computed tomography, cone beam [MeSH Terms]) AND (computed tomography scanners, x ray [MeSH Terms])) OR (multislice computed tomography [MeSH Terms])) OR (multidetector computed tomography [MeSH Terms])) AND (correlation studies [MeSH Terms])) OR (validity and reliability [MeSH Terms])) OR (comparative studies [MeSH Terms])) AND (in vitro [MeSH Terms])) OR (in vivo [MeSH Terms])) OR (animal use [MeSH Terms]). The Cochrane Library was searched with the following keywords: "CBCT scan" AND "computed tomographic" AND "correlation" AND "animal studies" AND "in vitro" AND "In vivo". In Google Scholar, the search keywords were: "Correlation" AND "CBCT AND CT" AND "in vitro studies or animal studies or In vivo studies". In LILACS, the search keywords were: (CBCT OR Cone Beam Computed Tomography [Abstract words] and Computed Tomography OR CT [Abstract words] and Correlation OR Reliability [Abstract words] and In vitro OR Animal studies [Abstract words]). In Scopus, the search was: (correlation OR comparison OR reliability OR accuracy AND CBCT OR cone-beam AND computed AND tomography AND computed AND tomography OR CT OR MSCT AND in vitro OR animal OR in vivo).

A complementary manual search was also done in the following journals: *Dentomaxillofacial Radiology, The British Journal of Radiology, European Journal of Radiology, American Journal of Orthodontics and Dentofacial Orthopedics, European Journal of Orthodontics, Journal of Clinical Orthodontics, Seminars in Orthodontics, and Angle Orthodontics*. The bibliographies of the included full-text articles were also searched for relevant studies. No restrictions were set on the language or date of publication when searching the electronic databases. Duplicates were eliminated manually. Initially, the titles of all studies identified were screened by 2 independent authors and irrelevant studies were excluded. The screened studies were then evaluated according to the eligibility criteria. The full texts were then procured for the articles that fulfilled the inclusion criteria mentioned below.

The PICOS (population, intervention, comparison, outcome, study design) format was used to formulate the clinical question with defined inclusion and exclusion criteria, as follows: population: animal, *in vitro*, and *in vivo* studies; intervention: GVs of CBCT, comparison: Hounsfield units (HUs) of multislice CT (MSCT) or spiral CT; outcomes: correlation, comparison, reliability, and accuracy between the GVs of CBCT and HUs of CT.

In vivo, *in vitro*, and animal studies that evaluated correlations between the GVs of CBCT and HUs of CT were included. Reviews, personal opinions, conference papers, abstracts, letters, studies without reference standards, and studies that used other devices such as dual-energy X-ray absorptiometry, ultrasonography, magnetic resonance imaging, and micro-CT were excluded. The primary outcome assessed was the correlation between the GVs of CBCT and HUs of CT. All studies meeting the selection criteria were included in the review. Studies were selected according to the PRISMA guidelines mentioned in the PRISMA flow chart (Fig. 1). The data required for analysis were extracted by both reviewers (AS and RKJ) independently. A third

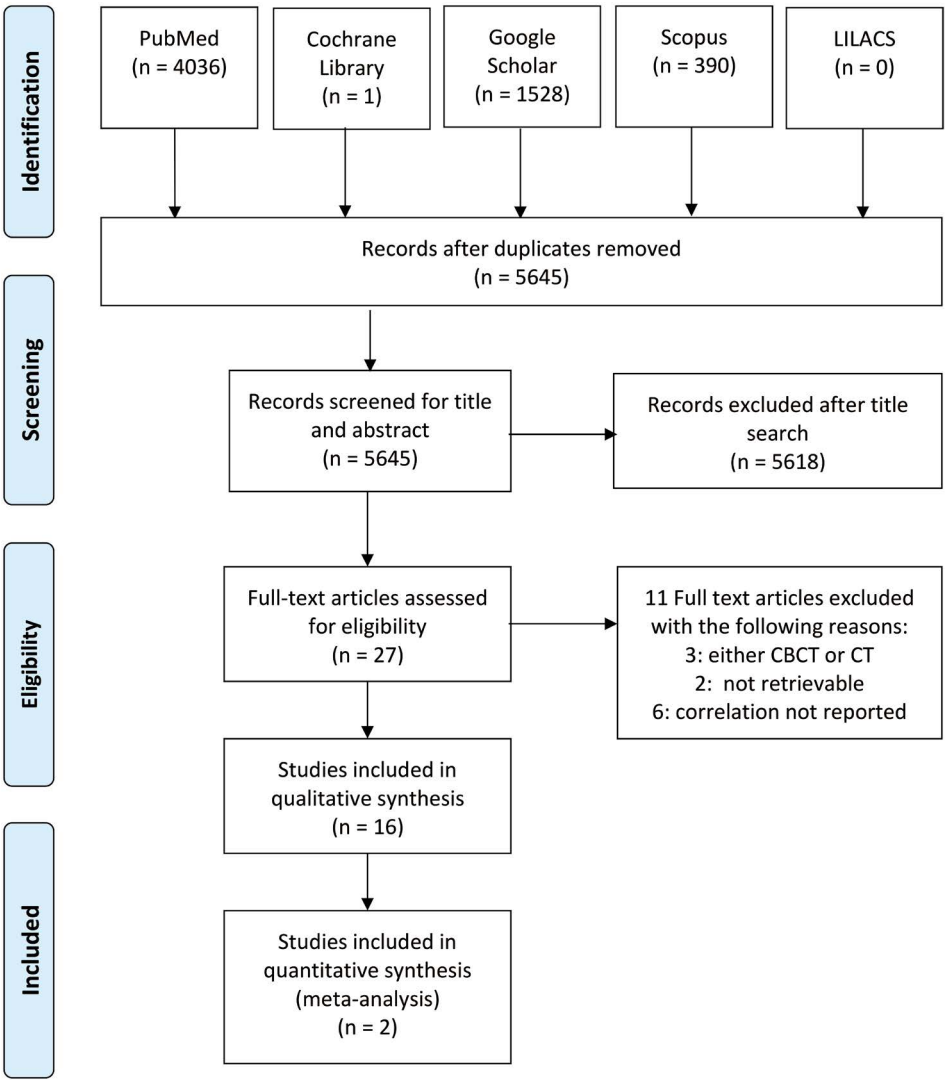


Fig. 1. Preferred Reporting Items for Systematic Reviews (PRISMA) flow chart for study selection.

reviewer (RN) verified each study before being eligible for final consideration. When disagreements among reviewers could not be resolved, a fourth reviewer (AB) was consulted.

The studies included in the review were subjected to a risk of bias assessment with the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) checklist (Fig. 2). The QUADAS-2 tool comprises 4 domains: patient selection, index test, reference standard, and flow and timing. The first 3 domains were assessed in terms of concerns regarding applicability, and every domain was assessed in terms of risk of bias. Signaling questions were included to help judge the risk of bias. If a study is judged as "low" in all domains relating to bias or applicability, then it is appropriate to have an overall judgment of "low risk of bias" or "low concern regarding applicability" for that study. If a study is judged "high" or "unclear" in 1 or more domains, then potential for bias or "concerns regarding applicability may exist. Two authors (AS and RKJ) evaluated the risk of bias independently and a fourth author (AB) was consulted to resolve any disagreements. The Cohen κ test was used to assess the level of agreement between the reviewers; a κ coefficient value of 0.933 was obtained, which was suggestive of very high agreement.

The meta-analysis was conducted using MedCalc version 15.2 (www.medcalc.org) to pool correlation coefficients. The Pearson correlation coefficients from the included studies were pooled and analyzed to produce a forest plot. Heterogeneity across the studies was assessed using the I^2 test. An I^2 value greater than 40% was considered high.

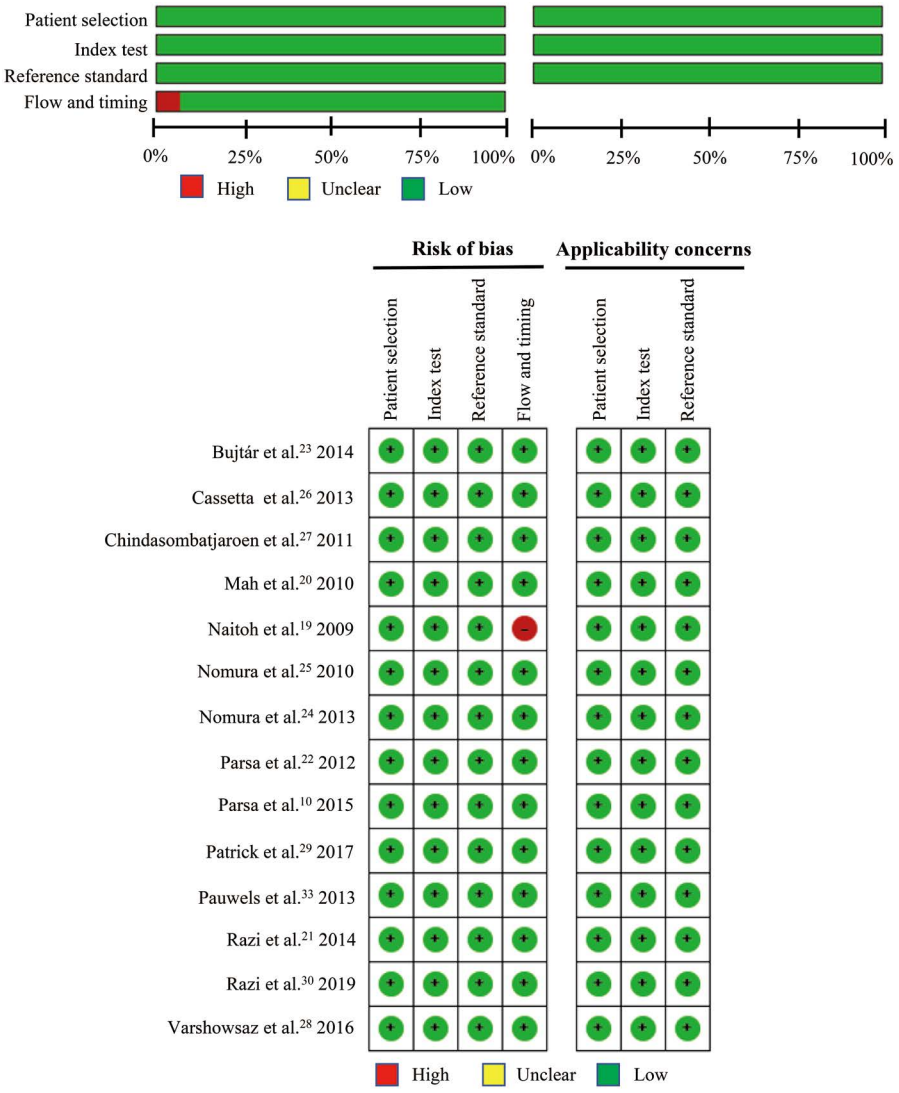


Fig. 2. Risk of bias summary assessed using Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2).

The Pearson correlation coefficients were interpreted as low (0.1 to 0.3), moderate (0.4 to 0.7) and strong (0.8 to 1).[18]

Results

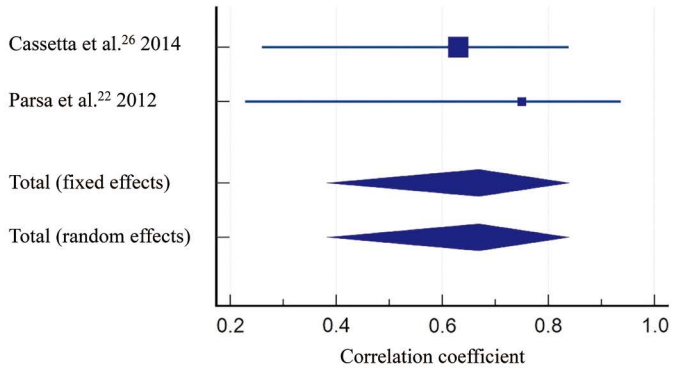
The electronic search identified a total of 5,955 studies. After removing duplicates, there were a total of 5,645 articles, which were then subjected to title screening. After screening the titles, 5,618 studies were excluded and remaining 27 studies were evaluated for eligibility. After excluding 11 studies that did not meet the eligibility criteria, 14 studies were included for qualitative analysis and only 2 studies were subjected to quantitative analysis. Figure 1 depicts the PRISMA flow diagram for studies selected in this systematic review.

Risk of bias and applicability assessment of the included studies

All included studies had low risks of bias for the domains of patient selection, index test, and reference standards all included studies; hence, applicability concerns were low for them. For the domain of flow and timing, 95% of studies had a low risk of bias, except for an *in vivo* study by Naitoh et al.[19] where correlations were analyzed between images of 2 systems taken at different intervals, which might have influenced the study results. The overall risk of bias of the included studies was deemed to be low (Fig. 2).

Qualitative analysis

Twelve of the 14 included studies were *in vitro* studies, while 2 were *in vivo* studies. Six out of the 12 *in vitro* stud-



Meta-analysis: correlation

Variable for studies	Study
Variable for number of cases	N N
Variable for correlation coefficients	Correlation Coefficient Correlation Coefficient

Study	Sample size	Correlation coefficient	95% CI	z	P	Weight (%)	
						Fixed	Random
Parsa et al., 2012	10	0.750	0.228 to 0.937			29.17	29.17
Cassetta et al., 2014	20	0.630	0.260 to 0.839			70.83	70.83
Total (fixed effects)	30	0.669	0.388 to 0.836	3.963	<0.001	100.00	100.00

Fig. 3. Forest plot of the meta-analysis with a fixed-effects model.

ies[20-25] used linear regression to assess the correlations between CBCT GVs and CT HUs. Five of these studies[20-24] reported strong linear correlations, while 1 study[25] reported that CBCT could be used to estimate the BMD from voxel values, but the relationship was non-linear ($R^2 = 0.982$).

Four out of the 12[10,11,26,27] *in vitro* studies reported using Pearson correlation coefficients to assess the correlation between CBCT GVs and CT HUs, and all 4 of these studies[10,11,26,27] reported statistically significant linear correlations ($P < 0.05$).

The CBCT GVs and CT HUs were compared using 1-way analysis of variance in 2[28,29] of the 12 *in vitro* studies. One study[29] reported that large-volume (160 mm × 130 mm) CBCT was more reliable in measuring GVs of only hypodense structures ($P > 0.05$) with reference to the HUs of MSCT than in measuring hyperdense structures ($P < 0.05$). Moreover, another study[28] reported that CBCT was unreliable for measuring BMD ($P < 0.05$).

Out of 14 studies, 2 studies[18,29] were *in vivo* studies that reported that GVs of CBCT could be used to evaluate bone density as there exists a high level of correlation between GVs of CBCT and HUs of CT.

Meta-analysis

Two studies[22,26] assessing the same parameters with a sample size of 30 each were included in the meta-analysis. Due to the absence of significant heterogeneity across the included studies, an analysis was carried out using a fixed-effects model. A forest plot was produced after pooling data on Pearson correlation coefficients of CBCT and MSCT. The results indicated that there was a moderate positive correlation between CBCT and MSCT ($r = 0.669$; 95% CI, 0.388 to 0.836; $P < 0.05$) (Fig. 3).

Discussion

To the authors' knowledge, this is the first systematic review to investigate the existing literature on the correlation between the GVs of CBCT and HUs of CT in a systematic manner. This review included all available literature, including *in vitro*, *in vivo*, and animal studies up to September 2021, and the results revealed a strong correlation between the GVs of CBCT and the HUs of CT scans. The conclusions of this review are supported by the high quality of evidence, since the included studies all had a low risk of bias and a quantitative analysis also revealed a moderately good correlation ($r = 0.669$).

The equipment employed and the methodological criteria used for reporting the outcomes differed among the studies included in the review. Four of the 14 stud-

ies[20,21,26,28] have compared the GVs of CBCT with CT, 8 studies[10,11,19,22-25,27,29] between CBCT and MSCT/MDCT, and 1 study[19] compared CBCT with spiral CT. Although the imaging geometry of the equipment utilized in the included studies varied, most of the included studies indicated that there was a strong correlation between the GVs of CBCT and HUs of MSCT, MDCT, or spiral CT.

In order to convert CBCT linear attenuation coefficients into HUs, a prediction equation model or conversion ratio must be applied to GVs. Mah et al.[20] proposed a standard conversion formula with an effective energy of 63 keV, which was as follows: $HU = (\mu_{material} - \mu_{water})/(\mu_{water}) \times 1000$. Cassetta et al.[26] also gave the following conversion ratio: values of CT = 0.7 × values of CBCT. Parsa et al.[22] proposed another equation: HU = 0.67 × voxel gray value from CBCT − 171.80. Meanwhile, other studies[21,24,25,27,30] have calculated the GVs of CBCT from linear regression equations. It was possible to derive HUs using density conversion factors from these results. However, these equations were derived by using different materials of known densities and are unique to each CBCT machine. Consequently, these equations may only be applicable to densities within the spectrum of materials used in these studies. To compare the diagnostic accuracy of CBCT to CT in various density ranges, a variety of materials and concentrations of media were employed to reconstruct hard and soft tissues.[11,20,23-25,27,28] Among these studies, only Mah et al.[20] used standard phantoms with appropriate consideration of the production process. Some[10,22,26,29] only assessed the hard tissues using dry mandibles, while 1 study[21] used a sheep's head to analyze hard and soft tissues. Out of 12 *in vitro* studies, studies involving only phantoms with materials, particularly that by Mah et al.,[20] exhibited high correlation coefficients ($R^2 = 0.999$), which could be related to the lack of a soft tissue effect on the results and standard phantoms.

Different exposure and reconstruction parameters such as tube voltage, tube current, field of view (FOV) size, and voxel size can affect CBCT GVs in reconstructed images, which may subsequently have an impact on the correlation between GVs and HUs for measuring BMD.[31,32] Three studies found that CBCT had higher GVs than CT, which can be attributed to differences in image acquisition methods, increased noise levels, beam hardening, and scattered radiation, which were more in CBCT.[10,22,26] Contrastingly, 1 study[27] noted that the GVs in CBCT were considerably lower than the HUs of CT in various exposure parameters owing to distinctions in the algorithms used to compute images as well as detector configurations between the 2 machines. Varshowsaz et al.[28] and Nomura et al.[25] compared the reliability of CBCT with CT for measuring BMD under different image acquisition settings and found that CBCT was not reliable, since GVs can be affected by image acquisition settings or any other X-ray dose. In most current CBCT systems, the kVp is fixed, but the tube current (mA) and exposure time(s) can vary depending on the desired image quality and patient size. Hence, it is appropriate to incorporate automatic exposure control via real-time feedback to optimize patient dose and minimize manual error in CBCT imaging to obtain high correlations without any discrepancies in GVs and HUs.[33]

With regard to the correlation between GVs and HUs for assessing BMD, voxel size seemed to be more important than kVp because it may have an impact on image resolution during assessment. Generally, smaller voxels lead to a higher image resolution; however, this might cause noise and necessitate more irradiation. By contrast, a larger voxel size may minimize noise, but it may impair the ability to discriminate between anatomical features with precision.[34] Out of 14 studies, 1 study by Pauwels et al.[11] compared correlation at different voxel sizes ranging from 0.125 to 0.4 mm by using 13 CBCT devices with 2 protocols of MSCT and found that the correlation was greater than 0.98 between GVs of CBCT and HUs of CT. Hence, they claimed that voxel size had no impact on the correlation between GVs and HUs.

FOV size is another aspect that influences the correlation between GVs and HUs, since the amount and distribution of densities within the FOV and outside the FOV may shift the GVs. Two of the 14 studies investigated the influence of FOV on the correlation between GVs and HUs. Pauwels et al.[11] compared correlations for different volumes of FOVs by using 13 CBCT devices with 2 protocols of MSCT and showed a GV-HU correlation greater than 0.98; however, for small FOVs of 3 CBCT devices, poor correlations (below 0.8) were found when scanning each material separately. They claimed that this might be related to the algorithm employed for the reconstruction process, which usually enhances image contrast when determining GVs. Patrick et al.[29] studied bone densities for both hypodense and hyperdense structures in different FOVs on CBCT and found that only large-FOV GVs of hypodense structures were more reliable with MSCT. Hence, it is recommended that CBCT imaging should be performed with a FOV larger than the patient's diameter in order to obtain GVs that are equivalent to HUs when assessing BMD. However, the determination

of GVs is specific to the scanner, depending on the calibration of the devices.

Identifying the region of interest (ROI) at the measurement site is another important factor that can alter CBCT GVs, which may subsequently have an impact on the correlations between GVs and HUs. Nine studies[11,19,21,23-25,27,29,30] relied on observers to manually locate the ROI, as well as the orientation and location of the site between the 2 scans. However, this method is much less reliable due to observer error, which may result in discrepancies at the measurement sites. In 5 studies[10,20,22,26,28] included in this systematic review, the assessment of the ROI in the measurement site was done with the aid of image analysis software, thus avoiding potential human error. Mah et al.[20] believed that human error is inevitable in selecting the ROI. However, no specific strategy for the exact selection of the ROI in various settings has been proposed, with the exception of a study by Naitoh et al.,[19] who stressed that equal points were selected by manual observations. As a result, the reliability of the reviewers' findings should be viewed with caution.

Even though the *in vivo* studies included in this review showed a high degree of correlation between the 2 systems, there existed significant heterogeneity in the methodology. Naitoh et al.[19] reported strong correlations using images of 2 systems that were taken at different intervals; however, the scatter plots showed variations of up to about 200 GV from the fitted line.

Although a good correlation between GVs of CBCT and HUs of CT was noted, the results of the present review cannot be directly extrapolated to clinical practice due to some limitations. The limitations of this review are mainly due to the heterogeneity in the methodology among included studies. The included studies had different *in vitro* set-ups, and both animal studies and *in vivo* studies were included. The diagnostic efficacy of CBCT can vary with different exposure parameters, different software programs employed, post-acquisition adjustments, and various thresholding procedures in image evaluation.

Within the limitations of the review, both qualitative and quantitative assessments showed a positive correlation between the GVs of CBCT and HUs of CT. The GVs of CBCT could be used for a quantitative estimate of bone density before implant-related procedures.

Acknowledgments

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Conflicts of Interest: None

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