REVIEW ARTICLE

Systematic review with hierarchical clustering analysis for the fractal dimension in assessment of skeletal bone mineral density using dental radiographs

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Abstract

Objectives To systematically review the relationship between the fractal dimension (FD) on jaw bones and skeletal bone mineral density (BMD), focusing on the different methodologies and results in the existing literature.

Methods An electronic literature search was performed to identify articles that evaluated the relationship between the mandibular and maxillary FD and BMD up to February 2014. After selecting the articles, a hierarchical clustering analysis was performed to verify the dissimilarity of the studies. The following variables were grouped into clusters, and assessed for reliability of the cluster distribution: kind of study, method for calculating FD, relationship between FD and low BMD, digital imaging, and kind of dental radiography. The relative frequencies of the categories of variables were calculated and compared.

Results Only 15 studies were selected and three clusters were obtained. Most articles were in the third cluster, and primarily consisted of clinical studies that used the box-counting method to calculate FD on panoramic radiographs. A significant association was found for the variable relationship between FD and low BMD and the clusters. Most of the clinical studies were performed on trabecular bone, but three studies found differences in FD between individuals with normal mandibular cortex and individuals with cortical porosity.

Conclusions The kind of study, method for calculating FD, relationship between FD and low BMD, and imaging modality should be better standardized to minimize the controversies found in published studies. The performance of FD on the cortical and trabecular bone for osteoporosis screening deserves further investigation.

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Introduction

Fractal analysis, a mathematical method for describing and analyzing complex shapes and structural patterns, has been adapted to the study of various natural structures and bio-signals [1]. Fractal analysis is expressed numerically as the fractal dimension (FD). The FD of a process measures its complexity, spatial extent, or space-filling capacity and is related to the shape and dimensionality of the process. If the theoretical FD of a set exceeds its topological dimension, the set is considered to have fractal geometry. The main attraction of fractal geometry stems from its ability to describe the irregular or fragmented shapes of natural features as well as other complex objects that traditional Euclidean geometry fails to analyze. Fractal geometry is widely used in image analysis problems in general and especially in the medical field [2–5].

Trabecular bone has a branching pattern that exhibits fractal properties such as statistical self-similarity and lack of well-defined scale. Because of this phenomenon, application of fractal geometry and measurement of FD can be used to determine the trabecular complexity and bone structure [6–8]. The applicability and relevance of fractal geometry to medical image analysis are justified by the fact that statistical self-similarity can hardly be verified in biological objects imaged with finite resolution [5]. Therefore, algorithms have been developed to quantify the textural properties of an image for evaluating certain bone diseases, such as osteoporosis [9–16].

Osteoporosis is a disease characterized by reduced bone strength and increased susceptibility to fractures per se or secondary to a minor trauma. The bone strength primarily reflects the integration of bone density and quality [17]. Currently, osteoporosis diagnosis and staging are based on the identification of different risk factors, the most important being low bone mineral density (BMD) of the femur or lumbar spine [18].

BMD is routinely determined by dual-energy X-ray absorptiometry (DXA) [19]. Although BMD is a strong determinant of bone strength [20], many patients without densitometric diagnosis are at increased risk of fractures, and a high percentage of fractures occurs in patients with osteopenia or normal BMD T-scores [21]. Consequently, other important factors need to be taken into account for proper assessment of fractures, such as clinical risk factors as well as the macroarchitecture and microarchitecture of bone [22].

One of the most important factors contributing to bone strength is its complex structure [6]. Consequently, fractal analysis of plain radiographs has been employed to assess the trabecular bone structure and biomechanical properties at several bone sites [10–16, 22]. One study found that the relationship between FD analysis and elastic properties of bone was stronger than that with BMD [23]. Other studies demonstrated that inclusion of fractal measures, in addition to BMD, improved the predictions of strength and elastic modulus values [16, 22, 23].

Few studies have analyzed the trabecular pattern on dental radiographs of osteoporotic patients [24–37], following the FD approach. Nevertheless, several previous studies have demonstrated that dental imaging could be strongly positioned as a way to screen for osteoporosis, given that it is applied to a large fraction of the older population annually in private practices and public health clinics [24–40]. These studies revealed reduced mandibular cortical and alveolar BMD, decreased alveolar bone height, increased porosity of mandibular alveolar and inferior cortical bone, erosion and reduced width of the inferior border of the mandible, and altered trabecular patterns in maxillary and mandibular bone in osteoporotic patients.

Although fractal analysis has been proven to be efficient in evaluating bone quality at several bone sites, there is no scientific evidence for application of FD analysis for the same purpose in the jaw bones. This article offers a systematic review and analysis of published information in the area, focusing on the different methodologies and results in the existing literature.

Materials and methods

Literature search and selection of articles

An electronic literature search was performed in the Pub-Med interface of Medline (National Library of Medicine), Scopus Database, and Web of Science to identify as many articles as possible that applied FD analysis in the assessment of skeletal BMD using dental imaging modalities up to February 2014. The inclusion criteria used for the initial selection of appropriate articles from the published abstracts consisted of combinations of the following keywords: (1) fractal and bone mineral density, (2) fractal and osteoporosis, (3) fractal and jaws, and (4) fractal and mandibular. The initial eligibility of potential studies was determined by reading the title and abstract of each article identified by the search engine using the criteria mentioned above. All articles that appeared to meet the inclusion criteria based on their abstracts were selected and collected. The first electronic search resulted in 204 different abstracts. The final selection was completed after eliminating duplicated articles, reviews of the literature, and articles that were not related to osteoporosis and FD
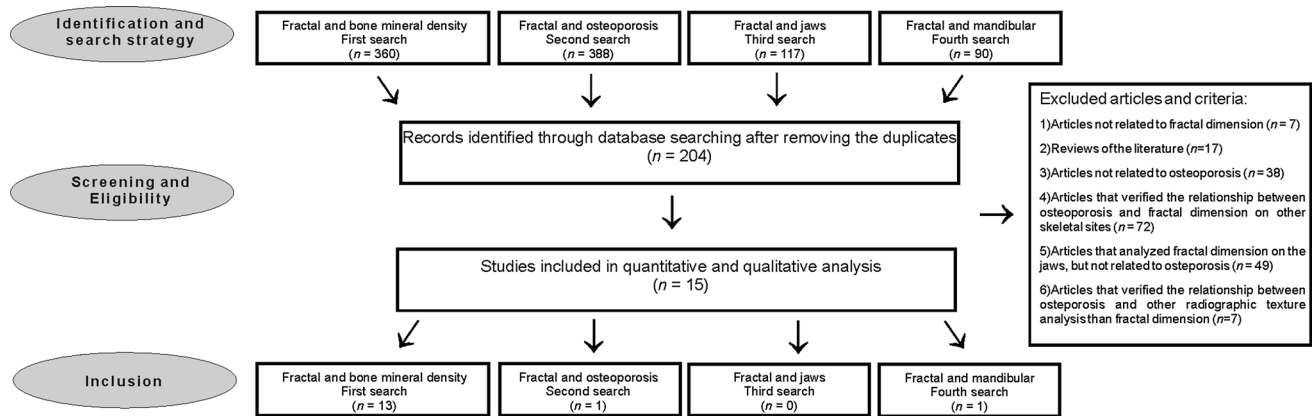
Fig. 1 Flowchart of the study selection procedure

analysis of the jaws. Figure 1 shows a flowchart of the study selection procedure.

Statistical analyses

A meta-analysis of the data in the selected studies was not attempted because of the variations in study design, methodology, imaging modality, and method for calculating FD.

After selecting and reading the articles, a hierarchical clustering analysis according to Ward's method was performed to verify the dissimilarity of the studies, using the chord distance. For this purpose, five variables were defined for each study: (1) kind of study (in vitro, in vivo with patients, in vivo with animals), (2) method for calculating FD (power spectrum method, caliper method, box-counting method, dilation method), (3) relationship between FD and low BMD (increase in FD, decrease in FD, absence of change/correlation), (4) kind of digital image (direct using digital technologies/receptors, indirect using analog techniques/scanned images), and (5) kind of dental radiography [intraoral, extraoral, intraoral and extraoral, cone-beam computed tomography (CBCT)]. Subsequently, the aforementioned variables were grouped into clusters, and assessed for reliability of the cluster distribution by the cophenetic correlation coefficient. The relative frequencies of the categories of variables were calculated and compared by clusters using the χ^2 test and Fisher's exact test. All statistical analyses were performed with XLStat 2010 software (Addinsoft, New York, NY). Values of $p < 0.05$ were considered to indicate statistical significance for all tests.

Results

After a complete analysis of the articles, only 14 articles met all of the inclusion criteria [24–37]. One article contained two different experiments, and was thus considered as two different studies [24]. The study designs, objectives, main results, and conclusions related to the FD are shown in Table 1. Table 2 shows the technical parameters of the FD calculations in the selected articles. Reading of the selected articles further demonstrated that the sizes and locations of the regions of interest (ROIs) were not standardized, as can be seen in Fig. 2.

Three different clusters were obtained after testing the dissimilarity of the selected articles. The third cluster was composed of nine articles [28, 30–37], while the remaining articles were divided into the first [24, 26] and second [25, 27, 29] clusters. Figure 3 shows a dendrogram of the dissimilarity of the clusters of the selected articles.

The first cluster was mainly composed of studies that used digitized intraoral radiographs and the power spectrum method for calculating FD, and the FD increased in most of the studies of this cluster. The second cluster was also mainly composed of studies that used digitized intraoral radiographs, but the caliper method was chosen for calculating FD. In most of the studies in the second cluster, the relationship between the FD and BMD was not significant. The third cluster primarily consisted of clinical studies (in vivo) that used the box-counting method to calculate FD on panoramic radiographs.

Figure 4 demonstrates the relationships between the five variables defined for each study and the clusters. Regarding the type of study (Fig. 4a), a higher frequency of in vivo studies in patients was present in the third cluster (88.9 %), but there were no associations between the other categories of studies and the other clusters ($p = 0.210$).

Regarding the variable relationship between FD and low BMD (Fig. 4b), a significant association was found with the clusters ($p = 0.044$). An increase in FD was observed in the articles in the first cluster (100 %). An absence of correlation was observed in 67 % of articles in the second cluster. Conversely, FD decreased with low BMD in most of the studies in the third cluster (55.6 %).

Table 1 Search results: study design, population characteristics, objectives, main fractal dimension results, and conclusions

Authors and reference number	Study design; Population characteristics	Objectives	FD main results	Main conclusions
Ruttmann et al. 1992 [24]	First experiment in vitro. Radiographs of two human mandibles before and after decalcification, considering five bone segments in each mandible	To verify whether the fractal model is an adequate descriptor of the peridental bone pattern represented on intraoral radiographs, and whether the FD is independent of the X-ray projection angle	FD was higher in the molar region compared with the incisor and premolar regions. Decalcification increased the FD, irrespective of the X-ray projection angle	FD can be applied to non-standardized intraoral radiographs and may have potential for application in the clinical diagnosis of osteoporotic or other age-related changes in bone structure
Ruttmann et al. 1992 [24]	Second experiment in vivo. Analysis of FD in six premenopausal and six postmenopausal women	To verify whether preexisting periapical radiographs can differentiate between premenopausal and postmenopausal women by FD calculation	FD was higher in postmenopausal women	
Southard et al. 1996 [25]	In vitro. Ten human maxillary alveolar bone processes with progressive decalcification	To examine radiographic FD changes in maxillary anterior and posterior alveolar bone processes during simulated osteoporosis, and to determine whether FD is insensitive to small changes in radiographic projection angles in the maxilla	A strong correlation was found between generalized demineralization and decreasing FD	Although FD is promising for detecting simulated osteoporosis, the sensitivity to small X-ray angular changes renders its clinical use questionable
Law et al. 1996 [26]	In vivo. Bone measurements (FD, microdensitometry, pixel intensity, and panoramic analysis of cortical thickness at the gonial angle) on dental radiographs of 64 women with osteoporosis and 47 women with normal BMD (control group)	To compare four methods for estimating bone density from dental radiographs with one another and with quantitative computed tomography and single-photon and dual-photon absorptiometry	FD was significantly higher on radiographs from the osteoporotic group than on those from the control group (3.24 vs. 3.19)	Pixel intensity appears to be more effective than the other three methods to distinguish between radiographs from the osteoporotic and control groups, although FD and microdensitometry are also effective. One method alone cannot be used to diagnose osteoporosis
Southard et al. 2000 [27]	Animal model in vivo. Twelve adult female white rabbits divided into four groups receiving different dosages of cortisone acetate for 4 weeks	To examine the mandibular bone density and radiographic textural changes and the relationship between mandibular and spinal BMDs in an osteoporotic rabbit model	A moderate negative correlation ($r = -0.61$) was found between mandibular FD and cumulative glucocorticoid dose. Weak or insignificant correlations were found between mandibular or spinal BMD and mandibular FD	Although there is a moderate correlation between mandibular interdental bone density and spinal density, FD is not related to spinal density. Mandibular FD decreases with cumulative steroid dose, but is not significantly related to either mandibular or spinal density
Bollen et al. 2001 [28]	In vivo. FD on panoramic and periapical radiographs of 281 older patients (> 60 years of age). Of the 281 patients, 20 were edentulous and had no periapical radiographs. Based on the image quality, periapical FD was calculated in 199 subjects and panoramic FD in 261 images	To compare FD from periapical radiographs with FD from panoramic radiographs, to correlate FD with cortical thickness and morphology, and to correlate FD with a reported history of osteoporotic fractures	FD was higher in subjects with a history of osteoporotic fractures, and also in patients with a thinner and severely eroded mandibular cortex. FD measured on panoramic radiographs was lower than FD measured on periapical radiographs	FD increases when bone mass decreases. Panoramic radiographs can be used as a possible alternative to periapical radiographs for measurement of FD

Table 1 continued

Authors and reference number	Study design; Population characteristics	Objectives	FD main results	Main conclusions
Southard et al. 2001 [29]	In vivo. Thirty-seven healthy women aged 20–78 years	To determine the correlations between FD of the maxillary and mandibular alveolar processes and bone density of the spine, hip, radius, and alveolar processes	Significant correlations were found between maxillary and mandibular alveolar processes and FD. No significant relationships were found between the maxillary alveolar process or mandibular alveolar process FD and the density of any postcranial regions	FD is not related to the density of the spine, hip, or radius. Conversely, FD is related to the alveolar process density
Yaşar and Akgünlü 2006 [30]	In vivo. Forty-eight postmenopausal women aged 40–64 years. BMD was measured with DXA of the lumbar spine	To evaluate the relationships among osteoporosis, body mass index, age, number of teeth, FD, and panoramic-based mandibular indices (cortical width, cortical index, panoramic mandibular index, mandibular crest resorption degree)	The mean FD was slightly higher in osteoporotic patients (1.4) than in patients with normal BMD (1.38), but the difference was not statistically significant	Cortical width, panoramic mandibular index, mandibular crest resorption degree, number of mandibular teeth, and FD do not lend themselves to the diagnosis of osteoporosis. The cortical index is a useful oral sign in screening for osteoporosis
Tosoni et al. 2006 [31]	In vivo. Fifty-four panoramic images of normal and potentially osteoporotic perimenopausal and postmenopausal women	To compare pixel intensity values and FD of the mandibular bone in specific regions on digital panoramic images of normal, osteopenic, and osteoporotic perimenopausal and postmenopausal women	For all FD measurements, there were no significant differences between the normal and osteopenic populations	Osteoporotic changes in mandibular canine/premolar cancellous bone can be detected by the pixel intensity
Yasar and Akgunlu 2008 [32]	In vivo. Fifty-two panoramic images of patients aged 40–64 years	To evaluate whether FD and lacunarity can discriminate patients with different MCI classifications	The mean FD was higher in patients classified as C3 (1.715) than in patients classified as C1 (1.66)	FD can differentiate C1 mandibular cortical shape from both C2 and C3, but cannot differentiate C2 from C3. FD and lacunarity are quantitative measurements and do not have observer dependency as radiomorphometric indices based on panoramic radiographs
Hua et al. 2009 [33]	In vitro. Nineteen human mandibular dry bone specimens used for creation of artificial bone lesions ($n = 5$) or decalcification ($n = 12$) to simulate osteoporosis, and as controls ($n = 2$)	To investigate the accuracy of FD and morphometry for bone quality assessment measured by DXA	A significant positive correlation was found between FD and BMD. When performing 3D fractal analysis based on the trabecular bone alone, the calculated FD increased after osteoporosis simulation	Fractal analysis and bone area measurement seem to have potential for bone quality assessment on CBCT images
Alman et al. 2011 [34]	In vivo. Total sample size of 241 subjects (188 males and 53 females). Of these, 56 subjects with panoramic images taken within 6 months of DXA were used in the analysis	To assess the diagnostic capability of the FD and mandibular cortical width in identifying men and women with decreased BMD	The mean FD was significantly higher in men (1.73) than in women (1.69). The optimal cut-off point for FD was found to be 1.72, with a sensitivity of 73.1 % and specificity of 70 %	FD measured on panoramic radiographs is a good surrogate measure of skeletal BMD in both men and women

Table 1 continued

Authors and reference number	Study design; Population characteristics	Objectives	FD main results	Main conclusions
Roberts et al. 2013 [35]	In vivo. Total of 663 women aged 40–70 years	To verify whether image texture features, based on co-occurrence matrices and FD, can be considered as potential biomarkers of osteoporosis	There was a strong association between image texture features and osteoporosis at the femoral neck, and a moderate association with osteoporosis at other skeletal sites	Image texture features can be considered as potential biomarkers for osteoporosis. However, FD is a less effective texture feature
Oliveira et al. 2013 [36]	In vivo. Seventy-three panoramic radiographs of postmenopausal women	To evaluate the relative efficacy of mandibular trabecular bone in detecting osteoporotic-associated bone changes in panoramic radiographs	Osteoporotic patients had significantly lower FD values than women with normal BMD. FD had a strong correlation with pixel intensity	Analysis of the mandibular trabecular bone by FD and pixel intensity is effective for detecting osteoporotic changes
Sindeaux et al. 2014 [37]	In vivo. Total of 133 panoramic radiographs from 49 men aged > 60 years and 84 postmenopausal women	To verify whether FD on the mandibular trabecular and cortical bone and mandibular cortical width differ between patients with normal BMD and osteoporosis	Differences were found in the FD values on mandibular cortical bone between patients with normal BMD and osteoporosis, but not in the FD values of trabecular bone	Cortical bone measurements (mandibular cortical width and FD) can be considered as auxiliary tools to refer patients for DXA examination

FD fractal dimension, *BMD* bone mineral density, *DXA* dual-energy X-ray absorptiometry

As shown in Fig. 4c, there was a strong association ($p < 0.001$) between the power spectrum method of calculating FD and cluster 1 (100 %), the caliper method and cluster 2 (100 %), and the box-counting method and cluster 3 (88.9 %), but no association was found between the dilation method and the clusters.

No association was found between the kind of digital image (digitized or direct digital images) and the clusters ($p = 0.238$), although scanned images were used in all articles in the first cluster and 67 % of articles in the second cluster. Conversely, the direct method was used in 67 % of studies in the third cluster (Fig. 4d).

Most of the studies in the first and second clusters used intraoral radiographs, while 67 % of articles in the third cluster were based only on panoramic radiographs (Fig. 4e). However, no significant association was found between the kind of dental radiographs and the clusters ($p = 0.127$).

Discussion

To the best of our knowledge, the present study is the first systematic review with the aim of discussing the little available evidence about the relationship between mandibular and maxillary FD and skeletal BMD. First, only a few articles related to this subject were found. Of the 204 articles initially found, only 14 met the inclusion criteria [24–37]. As one article had two different experiments (in vitro and in vivo), we decided to consider this article as two different studies for quantitative and qualitative analyses [24].

Some authors have stated that fractal analysis of radiographs at different skeletal sites appears to be a promising tool for assessment of trabecular bone structure, biomechanical properties, and skeletal status, and these measures could play a complementary role in addition to BMD in the examination of osteoporosis and skeletal status [10–16]. Regarding the application of FD analysis to the jaws, a previous study stated that, among several methods developed to estimate the alveolar bone density from dental radiographs, fractal analysis appears to hold the greatest promise as an inexpensive and readily available method [41].

In our systematic review, we made an attempt to collate, compare, and discuss the methodologies and results of different studies that calculated FD on the jaw bones and related it to skeletal BMD. Reading of the selected articles revealed significant heterogeneity. Variations in the study design, methodology, imaging modality, and method for calculating FD precluded a meta-analysis of the data in the selected studies. A comparison of the findings was also difficult because of the significant

Table 2 Technical parameters for fractal dimension calculation in the selected articles

Authors and reference numbers	Imaging modality	Digital conversion	Image size	ROI selection	ROI size	Fractal analysis method
Ruttimann et al. 1992 [24]	Radiographs taken with periapical films and different angle degrees	Video camera with charge-coupled device: JavelinJE2362®	512 × 512 pixels	Peridental alveolar mandibular bone between roots	128 × 128 pixels	Power spectrum method
Ruttimann et al. 1992 [24]	Preexisting periapical radiographs	Video camera SCSeries®	512 × 512 pixels	Peridental alveolar maxillary bone between roots	64 × 64 pixels	Power spectrum method
Southard et al. 1996 [25]	Radiographs taken with periapical films and different angle degrees	Flatbed scanner Imapro®	–	–	21 × 21 pixels	Caliper method
Law et al. 1996 [26]	Periapical, occlusal, and panoramic radiographs	Flatbed scanner, scanning ROIs	64 × 64 pixels (about 2 × 2 mm)	Area between the roots of the premolar and molar so that no tooth structure was included	64 × 64 pixels	Power spectrum method
Southard et al. 2000 [27]	Direct digital radiographs of rabbit hemimandibles	N/A	Non-standardized	Mandibular ROIs from the three most distal interdental bony regions on each left and right hemimandible	–	Caliper method
Bollen et al. 2001 [28]	Periapical and panoramic radiographs	Flatbed scanner Artiscan®	600 dpi	Periapical radiographs: area between the lateral incisor and canine (left and right, upper and lower). Panoramic radiographs: below the left and right lower canine and first premolar	–	Dilation method
Southard et al. 2001 [29]	Four maxillary anterior and two posterior periapical radiographs and two posterior vertical bitewing radiographs	Flatbed scanner Imapro®	Spatial resolution of 0.042 mm	Interdental regions, at least 2.5 mm apical to the crest bone	–	Caliper method
Yaşar and Akgünlü 2006 [30]	Direct digital panoramic and periapical radiographs from the mandibular premolar–molar region	N/A	–	Between second premolar and first molar teeth	23 × 155 pixels	Box-counting method

Table 2 continued

Authors and reference numbers	Imaging modality	Digital conversion	Image size	ROI selection	ROI size	Fractal analysis method
Tosoni et al. 2006 [31]	Direct digital panoramic radiographs	N/A	Matrix of 2200 × 934 pixels	Three ROIs: (1) anterior to the mandibular angle, superoinferiorly centered between the upper and lower cortical borders and anteriorly aligned with the anterior cortex of the ramus, (2) in the body of the mandible, limited superiorly by the tooth apices and inferiorly by the mandibular inferior border, (3) in the trabecular bone, 2 mm anterior to the mental foramen and 2 mm superior to the superior cortical boundary of the inferior border	(1) 100 × 100 pixels, (2) Varying in relationship to the shape of the mandibular body, (3) 50 × 50 pixels	Box-counting method
Yasar and Akgunlu 2008 [32]	Panoramic radiographs	Flatbed scanner	300 dpi	Mandibular cortex, ROI extending in the mediolateral direction from the mental foramen	Varying in relationship to the shape of the mandibular cortex	Box-counting method
Hua et al. 2009 [33]	CBCT images	N/A	N/A	Whole bone (cortical and trabecular bone) or only the trabecular bone. 2D and 3D fractal analysis	Varying in relationship to the shape and size of the specimen	Box-counting method (2D analysis) and cube-counting method (3D analysis)
Alman et al. 2011 [34]	Direct digital panoramic radiographs	N/A	–	Between and apical to the roots of the first molar and second premolar	64 × 64 pixels	Box-counting method
Roberts et al. 2013 [35]	Direct digital panoramic radiographs from different devices	N/A	–	Mandibular cortex, between the antegonion and the mental foramen on both sides of the image, and in the superior basal bone above the cortex	–	Box-counting method
Oliveira et al. 2013 [36]	Direct digital panoramic radiographs	N/A	265 dpi	Two ROIs on each side: (1) on the mandibular angle, below the mandibular canal, posteriorly to the molar region, (2) on the mandibular body, below the apex of the canine, right anteriorly to the mental foramen	230 × 130 pixels	Box-counting method

Table 2 continued

Authors and reference numbers	Imaging modality	Digital conversion	Image size	ROI selection	ROI size	Fractal analysis method
Sindeaux et al. 2014 [37]	Panoramic radiographs	Flatbed scanner Epson Expression®	600 dpi	Five ROIs, three from the trabecular bone and two from the cortical bone of the mandible: (1) in the trabecular bone, 2 mm anterior to the mental foramen, (2) in the trabecular bone, 2 mm anterior to the mental foramen, inside the first ROI, (3) in the trabecular bone, 2 mm inferior to the mental foramen, (4) an irregular shape in the basal cortical bone, distal to the mental foramen extending toward a line traced along the anterior border from the ascending ramus down to the lower border of the mandible, (5) an irregular shape in the basal cortical bone, distal to the mental foramen extending 2 mm	(1) 100 × 100 pixels, (2) 50 × 50 pixels, (3) 50 × 50 pixels, (4) and (5) Varying in relationship to the shape of the mandibular cortex	Box-counting method

N/A not applicable, *ROI* region of interest

methodological differences between the selected studies and the conflicting results. To verify the dissimilarity of the studies, we used a hierarchical clustering analysis according to Ward's method. To more clearly examine this area of investigation, five variables were divided into three clusters.

The first and second clusters were mainly composed of studies that used digitized intraoral radiographs [24–27, 29]. Nevertheless, the methods for calculating FD were different in these clusters, as all articles in the first cluster used the power spectrum method [24, 26] and all articles in the second cluster used the caliper method [25, 27, 29]. A significant association was only found in the method for calculating FD and the first and second clusters. This result may be related to the number of studies with the same authors in these clusters.

In some articles, the FD increased in postmenopausal women [24], osteoporotic patients [26, 28], and patients with a thinner and severely eroded mandibular cortex [26, 32]. Conversely, some previous studies showed a strong correlation between simulated osteoporosis in the maxillae and decreased FD [25], and also for decreased FD with low BMD [33–37]. In addition, we found some articles in which the FD on the jaw bones was not related to the density of the spine, hip, or radius [29], or the FD did not differ significantly between normal and osteoporotic patients [30, 31].

The conflicting results of the clinical studies have been mentioned previously in the literature [42]. However, the small sample sizes in the above three studies that found no relationship between FD and low BMD should be emphasized. Moreover, two of these studies were performed in younger populations [29, 31], while BMD was only measured in the lumbar spine in the other study [30].

Most of the clinical studies were in the third cluster, which primarily consisted of studies that used the box-counting method to calculate FD on panoramic radiographs. In our review, only three studies evaluated FD on the mandibular cortical bone, with different methodologies for selecting the cortex [32, 35, 37]. The first of these studies showed a significant difference in the mean FD of the mandibular cortex for groups of patients classified as C1, C2, and C3 by the MCI index [32]. Nevertheless, BMD was not evaluated in that study. Other authors found a decreased FD on the mandibular cortex in patients with low BMD [36]. A recent study found that the odds of having lower mean values for the mandibular cortical width and FD on the cortical bone were higher in osteoporotic patients [37]. These results may be explained by resorption of the inferior border of the mandibular cortical bone, which is often seen in patients with low BMD [34, 38, 39].

The conflicting data regarding trabecular bone, as suggested by some authors, may be explained by anatomical

Fig. 2 Panoramic image provided to illustrate the variability in the sizes and locations of the ROIs in the previous clinical studies. The ROIs marked with an asterisk were selected on intraoral radiographs
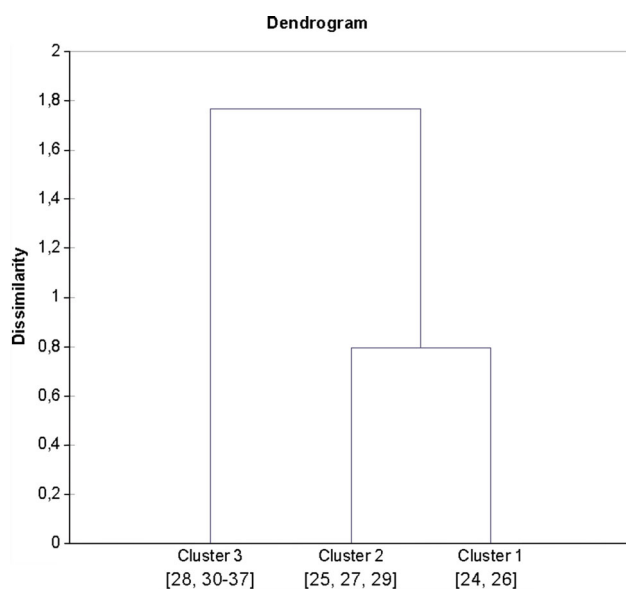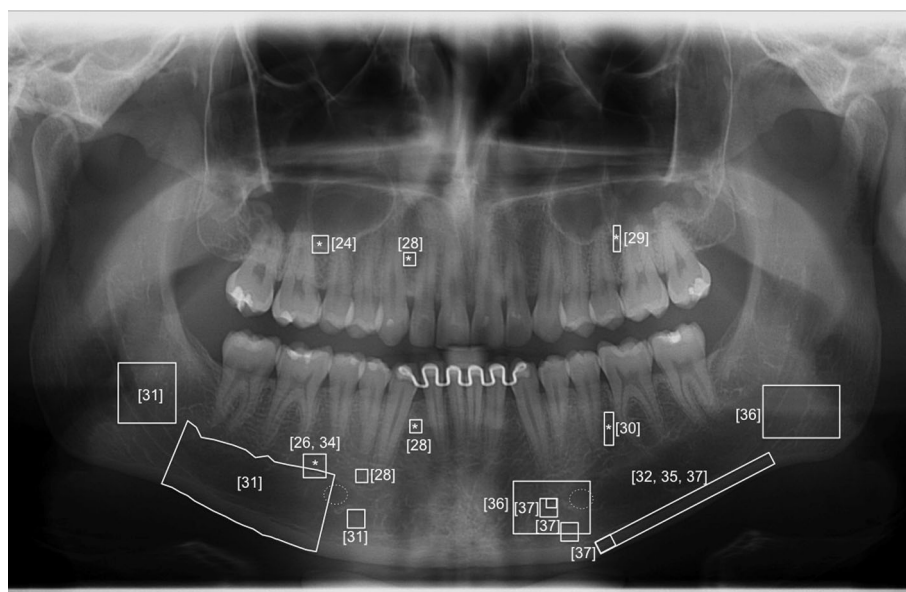

Fig. 3 Dendrogram showing the dissimilarity in the clusters of the selected articles (cophenetic correlation coefficient = 0.80)

most recent studies, a tendency toward a reduction in the FD on trabecular bone was seen in patients with osteoporosis compared with individuals with normal BMD [33–37]. This may explain the significant association found in our systematic review between the variable relationship between FD and low BMD and the clusters. The FD on cortical and trabecular bone should be further investigated with a view to use for osteoporosis screening.

Our systematic review also showed that some clinical studies used different imaging modalities such as intraoral radiography [24, 26, 28–30], panoramic radiography [26, 28, 30–32, 34–37], and CBCT [33]. Therefore, comparison of the results in these studies was difficult, as FD can only be reliably compared when using imaging modalities at the same spatial resolution [43]. Each imaging modality may have its own non-linear artifacts such as sampling frequency, noise, and spatial resolution. A previous study also verified that FD values estimated from digitized films on radiographs of rat bones were significantly greater than those produced by direct digital images [44]. Regarding our sample of studies, digitized forms of conventional dental radiographs (intraoral or panoramic) were generally used. This means that the FD may have been overestimated in most studies. FD analysis of CBCT images warrants further investigation, as only one study used this imaging modality.

Many methods exist for measuring FD, and each method has its own theoretical basis. This fact often leads to the acquisition of different dimensions based on different methods for the same feature [5]. The most commonly used procedure for calculating FD on dental radiographs was the box-counting method, probably because of its simplicity and availability [30–37]. When using the box-counting

variations, discrepancies in the imaging methods used to obtain two-dimensional or three-dimensional bone images, differences in selecting the areas to be measured, and/or differences in techniques for measuring FD [42]. Further, a recent study suggested that the performance of FD on the cortical bone was different from that of FD on the trabecular bone in women [37]. The same authors stated that cortical bone measurements might be considered as auxiliary tools to referring patients for DXA examinations, while the FD on the mandibular trabecular bone still cannot be used as an osteoporosis predictor [37]. However, in the

Fig. 4 Relationships between the variables and the clusters. a Kind of study (in vitro, in vivo with patients, in vivo with animals). b Relationship between FD and low BMD (increase in FD, decrease in FD, absence of change/correlation). c Method for calculating FD (power spectrum method, caliper method, box-counting method, dilation method). d Kind of digital image (direct using digital technologies/receptors, indirect using analog techniques/scanned images). e Kind of dental radiography (intraoral, extraoral, intraoral and extraoral, and CBCT)
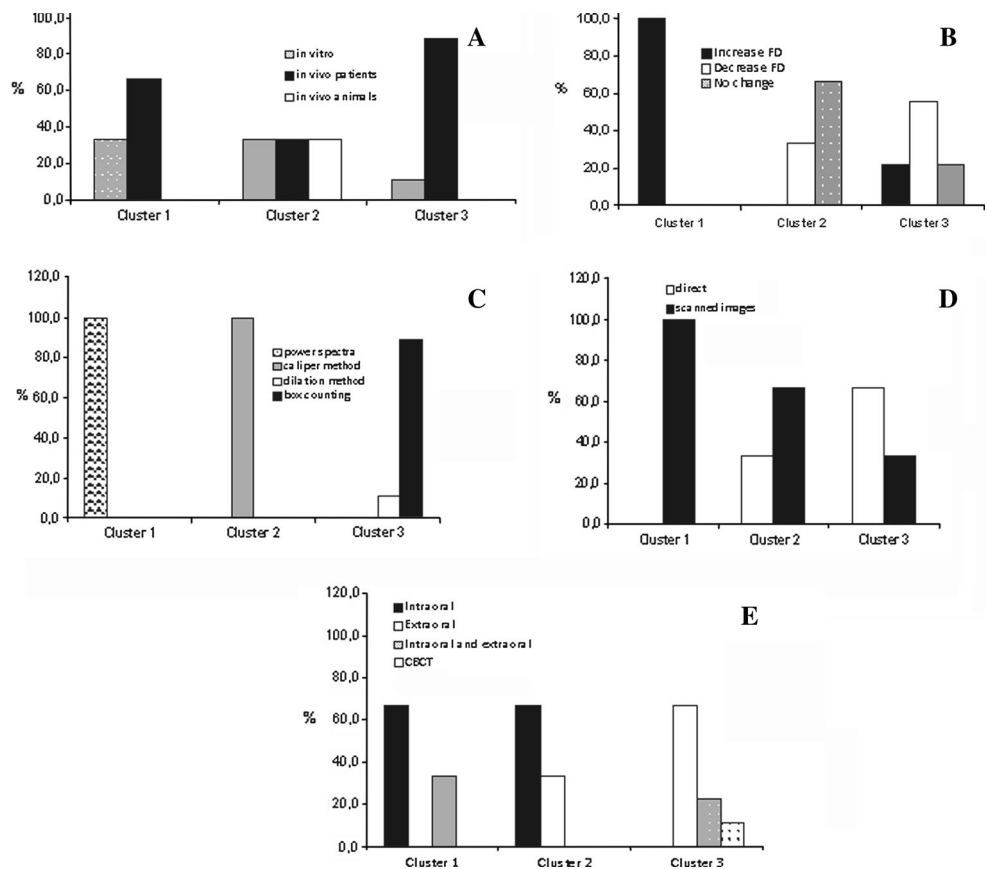
method for calculating FD, the studies generally used ImageJ software, a public domain program that can be downloaded from http://rsb.info.nih.gov/ij/. In fractal analysis, a box-counting algorithm is mainly used to quantify the trabecular pattern by counting the trabecular bone and bone marrow interface. The method also assesses the boundary of the trabecular bone and bone marrow, and a higher box-counting value indicates a more complex structure [4]. However, the results of the selected studies using the box-counting method were not in line with the above-mentioned statement.

Although fractals are very useful, calculation of quantitative properties like the FD is elusive and challenging. Therefore, several attempts have been made to investigate the reliability of FD estimation with different algorithms applied to different fractal functions [45]. Despite being the most commonly used procedure, the box-counting method has several limitations, such as the difficulty in obtaining error bounds [46], possibility of overestimation or underestimation [45], construction of empty boxes, box-size dependency of the FD computation, grid effect, and process of signal binarization required for this method [5]. The box-counting method may not cover the image surface very well, and hence cannot capture the FD for a rough-textured surface [2]. Further, disadvantages of the box-counting

dimension are the choice of initial and final sizes of the magnification factor and the longer time required for computation [47].

Some authors have demonstrated that large systematic errors can occur for a variety of estimator techniques, such as the box-counting method and power spectrum method, over a wide range of input FD values. When applied to Takagi and Brownian motion curves, these authors demonstrated the roles of resolution and quantization as limiting factors in the estimation process [45]. Since no estimators work well universally, the best outcome is to observe and explain the relative discrepancies of all estimators simultaneously to gain insights [42]. Therefore, further radiographic studies should be performed with combinations of different estimators at a standardized resolution to minimize the aforementioned limitations.

Our study has strengths and limitations. Owing to the scarcity and heterogeneity of relevant studies in the literature, it was not possible to perform a meta-analysis of the data in the selected studies. Consequently, it was decided to select the variables that could influence the dissimilarities found in the few published studies. Regarding the choice of areas to be analyzed by FD, the sizes and locations of the ROIs were extremely variable in the studies, and were not included in the hierarchical clustering analysis. Some

authors described that absolute ROI placement might not be necessary, since the FD values determined from ROIs on digital radiographic images of alveolar bone were insensitive to small variations in X-ray exposure, beam alignment, and ROI position [48].

In conclusion, this review has highlighted directions in which further research could help to determine the potential of detecting low BMD in patients based on FD analysis of dental radiographs. However, the kind of study, method for calculating FD, relationship between FD and low BMD, and imaging modality should be better standardized to minimize the controversies found in published studies. Future studies may also clarify the differences in performance between FD on the cortical and trabecular bone for osteoporosis screening.

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