



**Variation in mandible shape and size due to osteoporosis:
Geometric morphometrics study**

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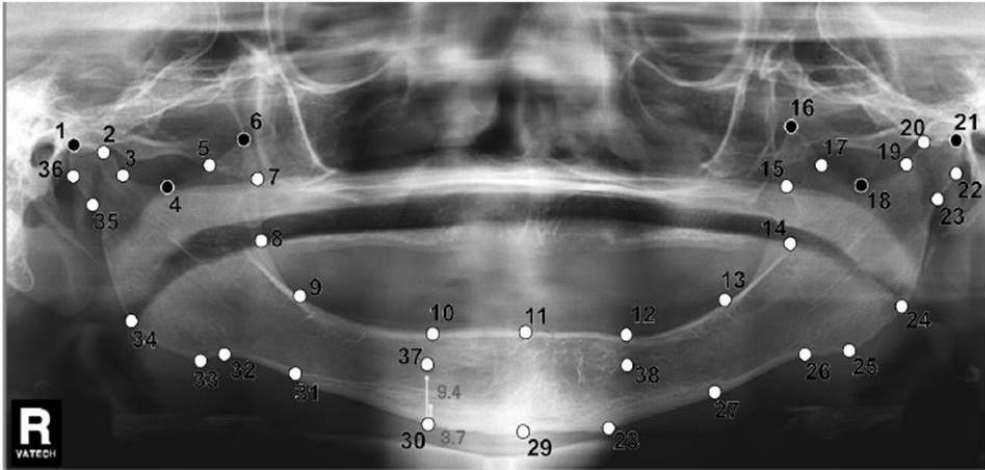


Figure 1

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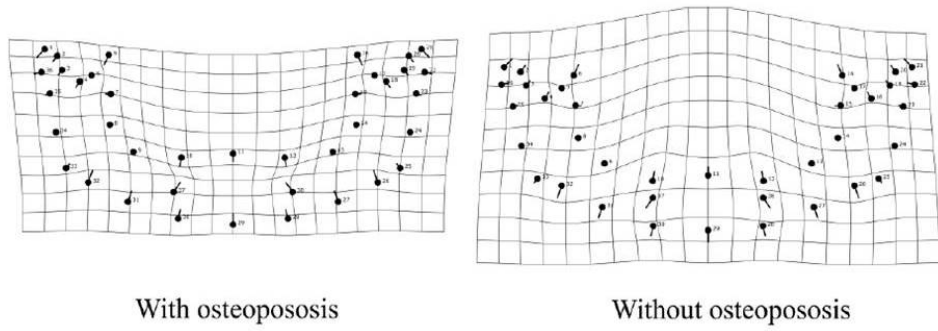


Figure 2

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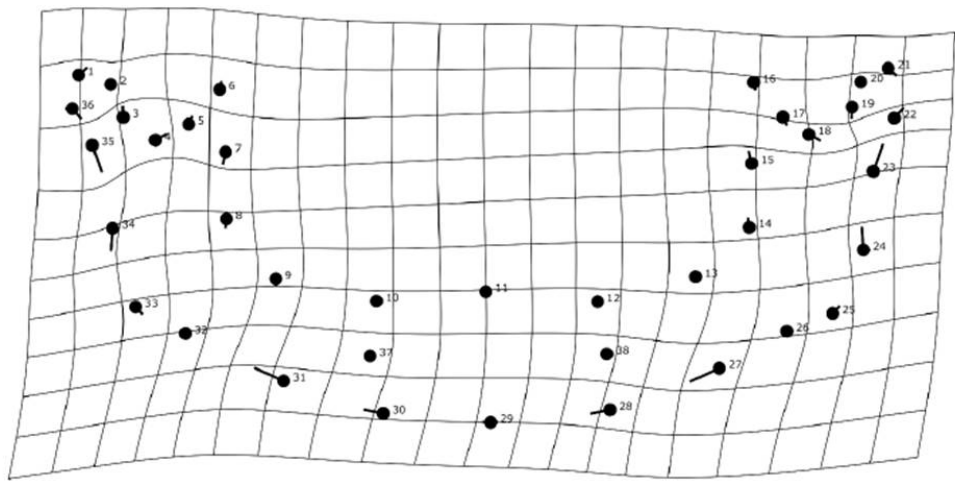


Figure 3
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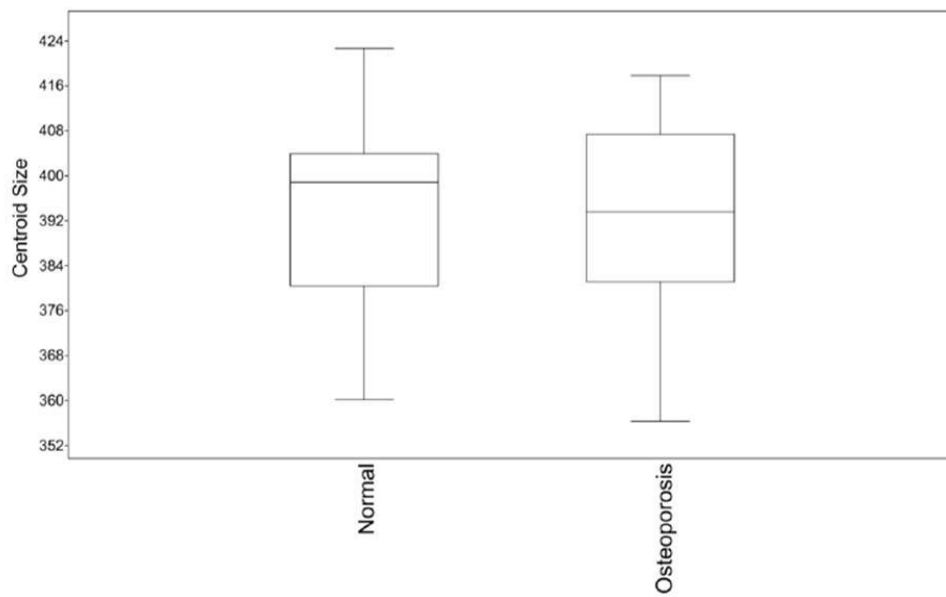


Figure 4

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Variation in mandible shape and size due to osteoporosis: Geometric morphometrics study

Variation in mandible with osteoporosis

ABSTRACT

Objective: Assessing whether it is possible screening women with osteoporosis through geometric morphometrics based on panoramic x-ray. **Materials and Methods:** Leukoderma women, after menopause, 40 years old (or older), with confirmed medical diagnosis of presence, or absence, of osteoporosis through bone densitometry examination. (N = 62). Measurements taken through panoramic X-ray based on geometric morphometrics. All x-rays were taken twice by the same researcher. Procrustes superimposition was assessed through Cartesian coordinates generated from anatomic landmark and semilandmarks. Regression Analysis, Multivariate Analysis of Variance (MANOVA), discriminant function and cross validation analysis, and Thin plate splines in MorphoJ software were carried out. Subsequently, Fluctuating Asymmetry Analysis (FA) was conducted and ANOVA was performed to assess differences in centroid size. **Results:** Significant values were recorded for mandible shape ($p < 0.01$) through MANOVA. Significant values ($P < 0.01$) were also found through discriminant function analysis between groups of women with, and without, osteoporosis. Fluctuating asymmetry analysis showed significant differences in mandible shape and size between sides ($p < 0.01$). **Conclusions:** Geometric morphometrics proved to be effective in screening and identifying elderly leukoderma women with, or without, osteoporosis based on panoramic x-rays. This is a promising technique to diagnose or identify patients with some health condition.

Keywords: osteoporosis, geometric morphometrics, mandible.

INTRODUCTION

Osteo Metabolic disease of multifactorial etiology, also known as osteoporosis, is featured by unbalance in bone remodeling process, which results in bone tissue density reduction to a level insufficient for important support functions - it worsens bone tissue fragility and increases the risk of fractures⁽¹⁾. Besides causing systemic manifestation, osteoporosis leads to issues in other parts of the body, among them, the face and its surroundings. Given its high prevalence, it is essential knowing and identifying all manifestations caused by this disease based on clinical aspects, as well as its buccal manifestation⁽²⁾. Bone resorption caused by osteoporosis accelerates volume reduction in the alveolar edges in the maxillomandibular complex, and also reduces the number and size of trabecular bone, and leads to cortical region thinning. Such loss in maxillomandibular bone support has straight influence on tooth fixation, since severe bone density loss can cause the loss of natural teeth and impair prosthesis fixation and dental implants. On the other hand, when osteoporosis is associated with periodontal disease, it is possible observing clinical framework worsening, which can potentiate tooth loss⁽³⁾.

According to Faisal-Cury and Zacchello⁽⁴⁾, the highest prevalence of osteoporosis in the Brazilian population is in women with age (61/70 and 71/96 years), time of amenorrhea (6/10 and 11/49 years), ethnicity (white and yellow) and with late menarche (13/15 and 16/21 years).

The main implications of osteoporosis to the buccal cavity include loss of periodontal insertion⁽⁵⁾, tooth loss⁽⁶⁾, loss in the height of the alveolar bone (due to resorption), erosion of lower cortical mandibular bone, reduction in lower cortical mandibular bone width, resorption of the two condyles and of the temporal components of the temporomandibular joints⁽⁷⁾.

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2 Changes resulting from osteoporosis in the mandibular anatomy are of great interest in
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4 dentistry, since progressive decrease in the jawbone substance reduces the possibility of
5
6 achieving effective rehabilitation of the buccal function - such process must be taken into
7
8 consideration at the time to plan dental treatments⁽⁸⁾. Thus, it is extremely important for dental
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10 surgeons to know the systemic conditions of their patients, such as osteoporosis cases, since
11
12 it is the way to avoid complications during clinical protocols⁽⁹⁾.
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15
16 Panoramic x-ray (PR) has been used as complementary examination to diagnose
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18 buccal pathologies. Nowadays, studies have suggested its adoption to diagnose
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20 osteoporosis, since some scholars have associated osteoporosis with changes in the
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22 trabecular bone of the human mandible⁽¹⁰⁾. Therefore, the aim of the present study was to
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24 assess whether it is possible screening the morphological features and patterns of
25
26 osteoporosis in elderly women through geometric morphometrics based on panoramic x-ray.
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29 30 **MATERIALS AND METHODS**

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33 In total, 62 leukoderma women after the menopause, in the age group 40 years or
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35 older, with confirmed medical diagnosis of presence or absence of osteoporosis through bone
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37 densitometry examination, who demanded dental treatment, were selected for the study.
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39 These women were divided into two groups: Group 1 – 31 women without osteoporosis; and
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41 Group 2 – 31 women diagnosed with osteoporosis. This study was approved by the Ethics
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43 committee from the of, under protocol number (CAAE: 0057.0.454.000-11).
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47 Digital panoramic x-ray was taken in PaX 400 Vatech equipment; patients were placed
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49 at horizontal Frankfurt Plane position and vertical median sagittal plane – the equipment was
50
51 calibrated to 76 kV, 10 mA and exposure time was set in 20 seconds. All images from the
52
53 panoramic x-rays were loaded in the tpsUtil software to generate a file in TPS format. The x-
54
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1
2 rays allowed selecting 38 anatomic landmarks and semilandmarks of the whole mandible;
3
4 measurements were taken in the tpsDig2 software (Figure 1).
5

6 All measurements were performed twice by the same researcher; Procrustes ANOVA
7
8 was conducted to assess whether the highest variation was between individuals or in results
9
10 deriving from meter error, based on Rowe (1997)⁽¹¹⁾. Semilandmarks were aligned in the
11
12 tpsRelw software by using the least-square method applied to Procrustes; semilandmarks
13
14 become reliable landmarks - the analyses are progressive. From the alignment on,
15
16 semilandmarks slide on its curve or surface and remove the effects of arbitrary spacing. This
17
18 process optimizes the position due to the mean shape of the total sample, which allows
19
20 quantifying curves and analyzing them along with the landmarks.
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25 The Procrustes superimposition analysis was conducted according to Cartesian
26
27 coordinates generated from the anatomic landmarks and semilandmarks. This methodology
28
29 turns the coordinates of original data into shape coordinates and eliminates scale effect,
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31 position and orientation. The Regression analysis was performed to assess the allometry
32
33 effect due to development (shape x size), which was caused by the fact that the assessed
34
35 individuals were at different ages. Multivariate analysis variance (MANOVA) was carried out
36
37 to assess variation in the assessed structures; discriminant function analysis and cross
38
39 validation, as well as Thin plate splines were conducted in the MorphoJ software.
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43 The Fluctuating Asymmetry (FA) was performed; the right and left sides of the
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45 mandible were compared through ANOVA, which was applied to Procrustes in the MorphoJ
46
47 software¹⁶. The Procrustes method provides adjustment based on minimal square values by
48
49 comparing dots corresponding to orthogonal changes. Procrustes ANOVA allows quantifying
50
51 shape variation at different levels - it is broadly used in asymmetric studies⁽¹¹⁾. Fluctuating
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53 Asymmetry assesses stressing conditions (for example, food and disease) that can affect the
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1
2 normal development of body structures. Thus, it emerges as a useful technique to assess
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4 morphological changes in humans associated with different health conditions throughout
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6 ontogeny.
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9 Centroid size or the size of the very core of the edge is the square root of the square
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11 distances added to all landmarks and to their centroids; in other words, it is the mean of all
12
13 landmarks. Patients in the present study agreed on participating in the research and signed
14
15 the Informed Consent Form. The research project was submitted to, and approved by, the
16
17 Research Ethics Committee (REC) (Protocol n. 2008/0235).
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20 21 22 **RESULTS**

23
24 The comparison among women with and without osteoporosis did not show allometry
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26 effect ($p>0.05$). Thus, the shape of the assessed structures was not influenced by size
27
28 because sampling did not include children or adolescents whose bone structure remains
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30 under formation. Allometry is related to changes in shape features due to size; this is an
31
32 essential concept for studies focused on assessing the development of certain structures.
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36 MANOVA evidenced significant values ($p<0.01$) that have pointed towards
37
38 morphological differences between the assessed groups. Significant values ($p<0.01$) were
39
40 also recorded through discriminant function analysis applied to the groups of women with and
41
42 without osteoporosis. Women were properly classified through cross validation within their
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44 group in 72% of the cases with 10,000 permutations.
45
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47
48 The Thin plate splines of participants with osteoporosis showed greater changes,
49
50 mainly in the region of the right and left coronoid processes (dots 6 and 16) and also in the
51
52 chin region, where it was possible observing bone resorption trend. Such fact was highlighted
53
54 by dots corresponding to the mental foramen (dots 37 and 38), according to which, patients
55
56

1
2 who do not have osteoporosis tend to present longer distance between the foramen and the
3
4 bone crest (dots 10 and 12) - the group with osteoporosis recorded the opposite result: trend
5
6 to shorten the distance between mental foramen and the bone crest (Figure 2).
7

8
9 The fluctuating asymmetry analysis through Procrustes ANOVA showed significant
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11 differences in shape and size between sides ($p < 0.01$). According to the Thin plate splines and
12
13 based on the panoramic x-ray, the distance between the right side of the mandibular branch
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15 (dots 34 and 35) and the body of the mandible (dots 30 and 31) was clearly shorter. Besides,
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17 it was possible observing that the left side of the condyle region of the mandible was also
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19 shorter (dots 21 and 23).
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22
23 ANOVA applied to assess size based on the size of the centroid did not show
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25 significant values ($p > 0.05$); however, the boxplot allowed seeing that women with
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27 osteoporosis presented lower size means than the ones who did not have bone resorption
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29 disease.
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32 33 34 35 **DISCUSSION**

36
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38 Geometric morphometrics (GM) is a tactic adopted for human health diagnostics, since
39
40 it uses quantitative approach to assess changes and variations in the shape of individuals'
41
42 morphologic structures - it allows describing the association between diseases and the
43
44 human body^(12, 13). It represents a method with the potential to assess the effects of
45
46 environmental factors and diseases on organs and organisms⁽¹⁴⁾.
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49
50 With respect to conventional morphometry (anthropometry), features found through
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52 measurements did not take into account the allometric variation or differences in growth
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54 stages - these features happen naturally in individuals, a fact that makes anthropometric data
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1
2 lead to error. Such process impairs data interpretation and does not reveal the reality of
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4 organisms. The use of GM has been an effective biomarker in early diagnostics and in
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6 monitoring events that can lead to Alzheimer's Disease⁽¹⁵⁾. According to Nunes et al.,
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8 (2018)⁽¹⁶⁾, it is possible identifying elderly individuals with diagnostic of diabetes and high
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10 blood pressure - both diseases or no illness at all – based on the morphology of the right side
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12 of the face by using geometric morphometrics. Ferreira et al., (2019)⁽¹³⁾ found differences in
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14 the telemetry of patients with sickle cell anemia, non-affected sickle cell trait; this outcome
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16 shows that the geometric morphometrics is more effective than conventional anthropometry.
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20 Similarly, the use of this technique to identify variation in shape due to certain diseases
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22 allowed observing that osteoporosis has morphologic features and patterns that can help its
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24 identification through the analysis of panoramic x-ray of elderly women. This finding is only
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26 possible to be used for shape variation (not for size) because it is in compliance with the fact
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28 that GM is more recommended than anthropometry, which only assesses size. Geometric
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30 morphometrics provides an efficient analysis and is statistically powerful; besides, it gathers
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32 geometric information about the validated structures and is capable of identifying subtle
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34 variations in shape change⁽¹⁷⁾.
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39 The Thin plate splines of patients with osteoporosis showed shorter distance between
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41 the mental foramen and the alveolar ridge, which indicates greater bone resorption trend.
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43 According to Benson; Prihoda and Glass (1991)⁽¹⁸⁾, the consequences of osteoporosis in the
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45 buccal cavity are highlighted by smaller alveolar ridge, jawbone mass and density reduction
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47 and by teeth loss. There are reports about decrease in cortical bone thickness, which is
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49 represented by increased porosity of the cortical mandible - it depends on patients' age and
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51 on the presence of bone loss.
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2 Studies such as those by Moeintaghavi et al. (2014)⁽¹⁹⁾ and Mostafa et al. (2016)⁽²⁰⁾
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4 have been using radio-morphometric indices to assess osteoporosis. Although bone
5
6 densitometry is the golden standard examination to assess bone loss, panoramic x-ray can
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8 point out changes in the mandible and help identifying patients with low bone loss without
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10 diagnostic, mainly with osteoporosis. Therefore, it can suggest the need of further in-depth
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12 investigation and make it possible intercepting disease progression⁽²¹⁾. The use of GM
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14 analysis in the present study has shown that each woman was properly classified within her
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16 group in 72% of the cases through cross validation. This outcome highlights that this
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18 technique also has good ability to help osteoporosis diagnostic.
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23 Pallagatti et al. (2017)⁽²²⁾ have assessed the effectiveness of panoramic x-ray to detect
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25 osteoporosis in women after menopause in comparison to dual energy X-ray adsorption. They
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27 used the Klemetti Index (KI) to detect osteoporosis in patients' initial phase. Their sample
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29 comprised 60 women after menopause - a panoramic x-ray was performed to classify the
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31 mandibular cortex based on the Klemetti Index. All x-rays were subjected to evaluation by 5
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33 experts with major degree in Oral Medicine and Radiology. Subsequently, the Dual Energy X-
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35 Ray Absorptiometry (DEXA) exam was carried out with all patients to assess mineral bone
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37 density. The mean accuracy of the 5 experts to show normal bone, osteopenia and
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39 osteoporosis in comparison to DEXA was 58.08%, 63.3% and 64.74%, respectively. The
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41 analyses have shown that observations by the 5 experts, based on KI, were not statistically
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43 different from that of the Bone mineral density (BMD)DMO evaluation conducted with the aid
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45 of the DEXA Scan. The aforementioned authors got to the conclusion that panoramic x-ray
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47 can be used as screening tool, as well as to the early detection of osteoporosis with the
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49 application of the Klemetti Index.
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Besides the observations above, an in-depth analysis of a panoramic x-ray allows identifying the presence of difference in the size and shape of the structure either on the right or on the left side⁽²³⁾. Even if the distortion caused by the radiographic method is one of the possible causes of the asymmetry between sides, the fact that there is bilateral physiological skeletal asymmetry is another important factor. This information corroborates results in the current study, since the GM of the panoramic x-ray of the mandible showed significant differences in the shape and size of the right and left sides of elderly women with and without osteoporosis.

The limitation of the present study lies on the fact that it only evaluated leukoderma women and that it did not take into consideration women with leucopenia. Thus, further studies must be conducted with individuals of both sexes, at different phases of the health-disease process and from different ethnic groups in order to assess whether the morphological change pattern in the mandible can be extrapolated to other groups.

CONCLUSION

Thus, the geometric morphometrics proved to be a technique capable of screening and of possibly identifying leukoderma elderly women with or without osteoporosis based on panoramic x-ray, which is a low cost method. ~~Geometric morphometrics only needs images, since software are free, which makes this method more advantageous than the others.~~ The panoramic x-ray can provide more information than methods often used for this purpose; therefore, GM is a promising technique to diagnose or identify patients with some health condition.

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1
2 ~~studies must be conducted with individuals of both sexes, at different phases of the health-~~
3 ~~disease process and from different ethnic groups in order to assess whether the~~
4 ~~morphological change pattern in the mandible can be extrapolated to other groups.~~
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13 **ACKNOWLEDGMENTS**

14 **Conflict of Interest**

15 None

16 **Funding**

17 None

18 **Sponsor's Role:** None.

19 **Regulatory Statement**

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21 This study was approved by the Ethics committee from the of, under protocol number
22 077/2011 (CAAE: 0057.0.454.000-11).
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29 LEGENDS

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34 **Figure 1.** Panoramic x-ray presenting anatomic landmarks (white dots) and semilandmarks
35 (hollow dots) used to compare morphological differences in women with osteoporosis.
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39 **Figure 2.** Thin plate spliness showing the place of variation in the mandible shape of women
40 with and without osteoporosis.
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44 **Figure 3.** Thin plate spliness highlighting the place of variation in mandible shape in women
45 with fluctuating asymmetry.
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49 **Figure 4.** Boxplot pointing towards variations in size based on the centroid size of women
50 with and without (normal) osteoporosis.
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Figure 1. Panoramic x-ray presenting anatomic landmarks (white dots) and semilandmarks (hollow dots) used to compare morphological differences in women with osteoporosis.

Figure 2. Thin plate splines showing the place of variation in the mandible shape of women with and without osteoporosis.

Figure 3. Thin plate splines highlighting the place of variation in mandible shape in women with fluctuating asymmetry.

Figure 4. Boxplot pointing towards variations in size based on the centroid size of women with and without (normal) osteoporosis.

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