

Bone Microarchitecture by Dentistry Digital X-Ray (BμA-DDX) Software: A Pilot Study of the Analysis of Bone Density using Digital Dental X-Rays

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Article history

Received: 25-08-2015

Revised: 19-02-2016

Accepted: 20-02-2016

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Abstract: The Bone Microarchitecture by Dentistry Digital X-Ray (BμA-DDX) software was designed to determine jaw bone quality using digital dental X-rays. In order to identify patients with a suspicion of low bone density, a system was developed to evaluate bone microarchitecture through the analysis of samples collected in digital panoramic X-rays. The samples were collected at two sites of the mandible: alveolar ridge near the mental foramen and mandibular angle beneath the mandibular canal, bilaterally. These samples were submitted to a sequence of image processing operations to measure trabecular bone density. A total of 115 digital panoramic X-rays, corresponding to 460 samples, were processed digitally for trabecular pixel counting. This count was used to identify cases of normal or abnormal bone density based on values established in their lower limit. In conclusion, the method developed permitted the evaluation of samples of the mandibular body and ramus, indicating cases of normal and abnormal bone density. However, readjustment of the software parameters using a new set of X-rays is necessary when the images were submitted to pre-processing or suffered changes in the X-ray emission source.

Keywords: Bone Density, Dentistry, Image Processing, Computer Assisted, Radiography

Introduction

Bone mineral density can be measured using different techniques, such as single-photon absorptiometry, dual-photon absorptiometry, or dual-energy X-ray absorptiometry (DEXA) and quantitative computed tomography (Horner *et al.*, 1996; Corten *et al.*, 1993; Hildebolt *et al.*, 1993). DEXA is well established as a bone densitometry technique to measure bone mineral density at the spine and hip. Although bone densitometry is the gold standard imaging method for the diagnosis of osteoporosis and prevention of fractures, its high cost and lack of access of the population (Costa-Paiva *et al.*, 2003) impair its use as an assessment method of bone density in the jaws.

Quantitative computed microtomography (μCT) is another technique used for the characterization of bone tissue (Muller, 2002). The advantage of this technique is that it permits to measure small bone structures and unprocessed biopsy specimens, a fact rendering it a

nondestructive, rapid and accurate imaging method (Muller *et al.*, 1996). In small anesthetized living animals, bone tissue can be evaluated repeatedly at successive sites for changes in bone volume and architecture (Stenstrom *et al.*, 1998). Another potential application is the use of μCT data to create finite element models (van Rietbergen *et al.*, 1998). Van Oosterwyck *et al.* (2000) used μCT to qualitatively compare histological sections of peri-implant tissues and to correlate them with CT scans. Analysis of trabecular structures was similar for the two techniques.

Some authors found a correlation between trabecular bone changes and bone mineral density measured by optical densitometry, pixel intensity on X-rays and analysis of fractal dimension (Geraets *et al.*, 2007; Law *et al.*, 1996; Bollen *et al.*, 2001). However, no such correlations have been observed by other investigators (Yasar and Akgunlu, 2006).

Although different techniques are available for the evaluation of bone density on digital images, there are no

well-established methods for measuring bone density in the jaws. Panoramic radiography is frequently used for dental office patients, especially in cases of dental implant treatment. Several studies have reported a correlation between radiomorphometric indices on dental radiographs and bone mineral density at the lumbar spine, femoral neck and mandible (Geraets *et al.*, 2007; Devlin and Horner, 2002; Drozdowska *et al.*, 2001; White *et al.*, 2005; Taguchi *et al.*, 2006). It is therefore important to evaluate the use of panoramic radiography for the screening of individuals with low bone mineral density in order to aid in the referral of patients for bone densitometry.

Since osteoporosis affects trabecular bone and there are no standardized techniques for the evaluation of mandibular bone density, the analysis of bone density on panoramic X-rays may contribute to the investigation of this disease in alveolar bone. In an attempt to assist dental professionals, we developed a software designed to analyze bone density in samples collected in digital panoramic X-rays.

Materials and Methods

A total of 115 radiographs from 36 patients were analyzed to determine the parameters of an automatic system for the evaluation of mandibular bone density on panoramic dental X-rays. The study was approved by the Ethics Committee of the State University of Western Parana (Process No. 1088/2011-CEP). The 36 patients were between 20 and 34 years old. This age range was chosen since 90% of bone mass in humans is acquired by the age of 18, with a peak at 35 years of age (Kingsmill and Boyde, 1998). Patients in the range of 18 to 34 years are considered to be healthy in terms of bone density. A process of brightness and contrast standardization was used to standardize the panoramic dental X-rays for subsequent analysis of bone density in the patients (Leonardi *et al.*, 2003). This process matches the brightness and contrast of the image to be adjusted to a reference image that exhibits good definition of bone structures. The reference image was submitted to an auto-scaling process (Gonzalez and Woods, 2011) using Equation 1:

$$I_r(x, y) = \frac{255}{(f_{\max} - f_{\min})} (f(x, y) - f_{\min}) \quad (1)$$

where, $I_r(x, y)$ is the reference image after auto-scaling, $f(x, y)$ is the selected reference image and $f_{\min}$ and $f_{\max}$ are the tones corresponding to the 1st and 99th percentiles, respectively, of the grey tone distribution of the reference image.

After the auto-scaling process, the mean (μ_r) and variance (σ_r^2) of the reference image were calculated.

The standardization of brightness and contrast consisted of a linear transformation applied to the image to be adjusted (I_a) according to Equation 2:

$$I(x, y) = \text{gain} \cdot I_a(x, y) + \text{offset} \quad (2)$$

Where:

$$\text{gain} = \sqrt{\frac{\sigma_r^2}{\sigma_a^2}} \quad (3)$$

$$\text{offset} = \mu_r - \left(\sqrt{\frac{\sigma_r^2}{\sigma_a^2}} \cdot \mu_a \right) \quad (4)$$

where, μ_a and σ_a^2 are the mean and variance of the image to be adjusted (I_a), respectively. $I(x, y)$ is a standardized image used to evaluate the patient's bone density.

Samples were collected in the 115 X-ray adjusted by the brightness and contrast standardization process. Four samples were collected in each radiograph using a standard marker of 30×50 pixels in the areas highlighted in Fig. 1, for a total of 460 samples. All samples were submitted to auto-scaling (Equation 1), with $f_{\min}$ and $f_{\max}$ corresponding to the intensities of the darkest and clearest pixel of the sample, respectively. Thus, the histogram of each sample has acquired a maximum amplitude, enhancing its contrast.

The samples collected in the region of the mandibular ramus (LR and RR) and alveolar ridge (LA and RA) were pooled and the mean intensity of their pixels (μ) and variance of intensities (σ^2) were calculated for each sample. Mean intensities were analyzed in the two groups of samples using the Anderson-Darling test and ANOVA, adopting a level of significance of 5%. The tests were statistically significant for both normality of distribution and equality of means (μ), i.e., the user can analyze bone density in samples collected either in the region of the ramus or mandibular body, irrespective of the side chosen.

The mean (μ_g) and variance (σ_g^2) of pixel intensity of the samples was calculated for each group (mandibular ramus and alveolar ridge). Thus, there are distinct values of μ_g and σ_g^2 for these two regions.

The collected samples were then standardized in terms of brightness and contrast (Equation 2) using $\mu_r = \mu_g$ and $\sigma_r^2 = \sigma_g^2$.

The next step consisted of the counting of trabecular pixels. These pixels correspond to denser regions of mandibular bone in the samples collected. To classify a pixel as trabecular, its intensity should be equal to or higher than μ_{gs} and three or more of its 8-neighbors should have the same property, with μ_{gs} corresponding to the mean pixel intensity of the samples collected in 36 X-rays from healthy patients ranging in age from 20 to 34 years.

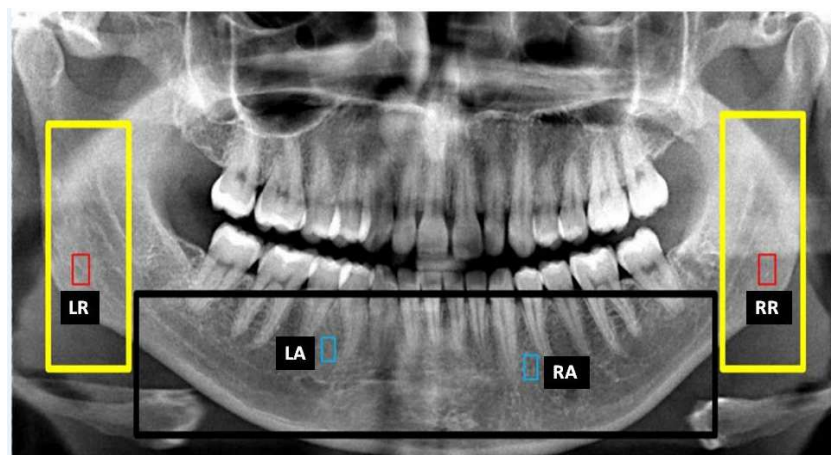


Fig. 1. Sampling areas in the mandible: Left Ramus (LR), Right Ramus (RR), Left Alveolar Ridge (LA) and Right Alveolar Ridge (RA)

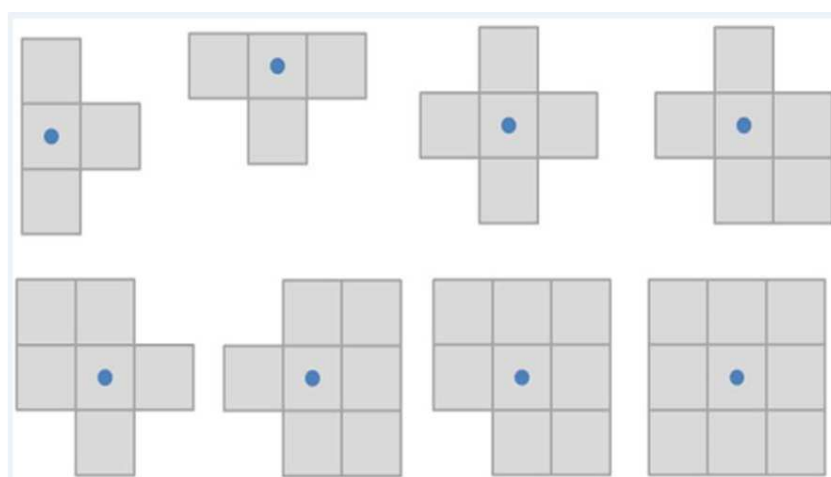


Fig. 2. The highlighted pixels correspond to trabecular pixels

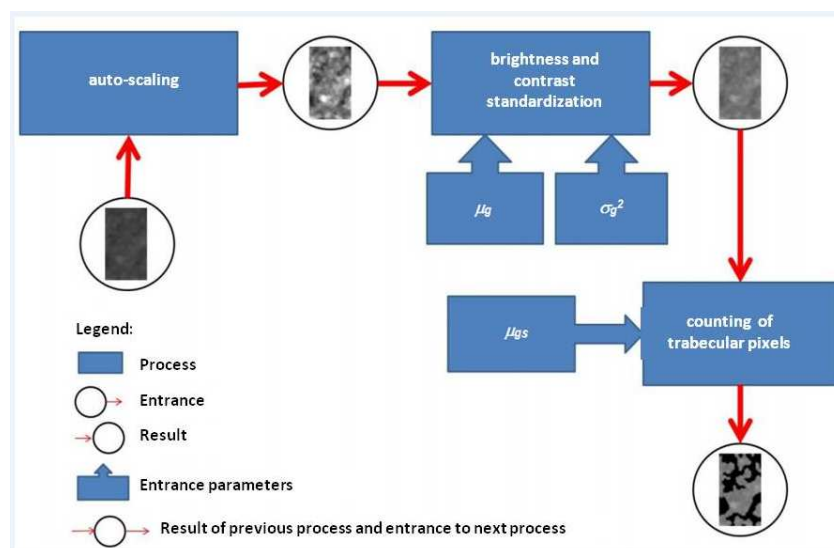


Fig. 3. Processes applied to the samples collected in the X-rays

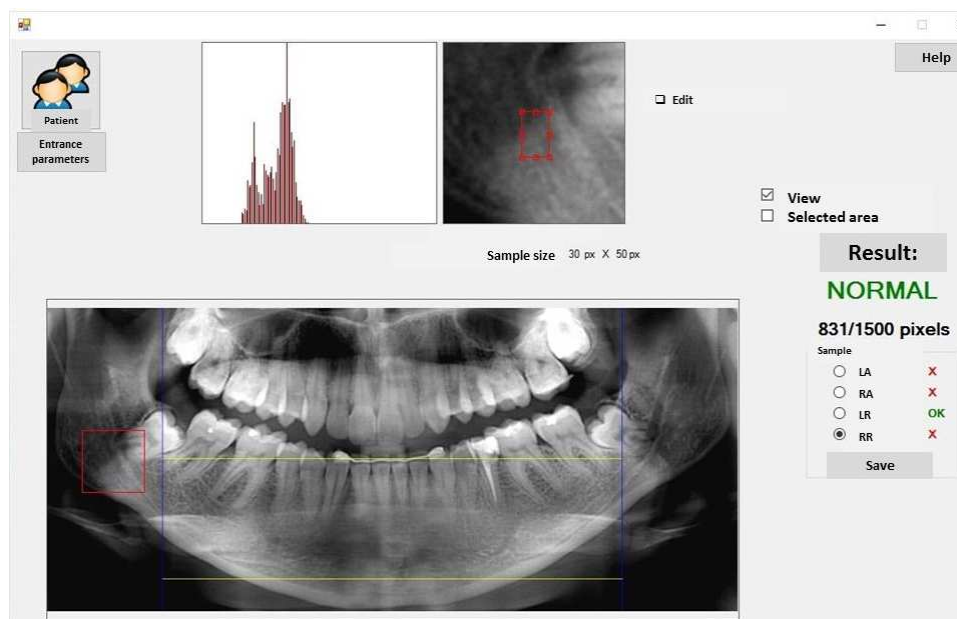


Fig. 4. The BμA-DDx software

Table 1. Parameters used with the BμA-DDx software

Region	μ_r	σ_r^2	μ_g	σ_g^2	μ_{gr}	$N_{pt_{min}}$
Alveolar ridge	96,33	3558,12	123	206	123	635
Mandibular ramus	96,33	3558,12	121	225	123	547

Trabecular pixels maintain their intensity, while a value of 0 is attributed to the other pixels. At the end of the process, the number of trabecular pixels is determined (N_{pt}).

The N_{pt} values obtained for the samples collected in the 36 X-rays of patients aged 20 to 34 years were tabulated. Next, the mean ($\mu_{N_{pt}}$) and standard deviation ($\sigma_{N_{pt}}$) of N_{pt} were calculated for samples obtained from the mandibular ramus and body. The minimum value of N_{pt} to classify a sample as having normal bone density was calculated using Equation 5:

$$N_{pt_{min}} = \mu_{N_{pt}} - 2 \cdot \sigma_{N_{pt}} \quad (5)$$

Since the N_{pt} values show a normal distribution, $N_{pt_{min}}$ is the lower limit that points to 2.5% of the samples collected, i.e., samples of X-rays with N_{pt} values less than $N_{pt_{min}}$ are indicated by the software as abnormal bone density.

Figure 2 shows some examples of spatial arrangements for trabecular pixels. Figure 3 summarizes the process to which the samples were submitted (collection to the final result), where the trabecular pixels are counted. Figure 4 illustrates the BμA-DDx software.

Results

The radiographic bone density in the region of the alveolar ridge was considered to be normal, with an N_{pt}

higher than 635 pixels. The bone density in the region of the mandibular ramus was also considered to be normal, with an N_{pt} higher than 547 pixels. Table 1 shows the parameters obtained from the analysis of the samples collected and used with the BμA-DDx software.

Discussion

The BμA-DDX software digitally processes the panoramic radiographic image for the analysis of trabecular structures of the samples collected in the two regions of interest. The standardized marker at the site of interest is positioned in these regions to delimit the size of the samples. The processes to which the samples are submitted are designed to expose the trabeculae and thus to permit the detection of orifices in the trabecular structure in order to establish bone density as normal or abnormal based on a lower limit of normality. The values obtained in this study can still not be used to quantify bone density on panoramic X-rays, but will permit the healthcare professional to identify cases that require a more detailed assessment.

In dentistry, bone density needs to be evaluated in surgical-prosthetic treatment used to replace lost teeth. Controversy exists regarding the effect of tooth loss on mandibular bone density. Schwartz-Dabney and Dechow (2002) observed no significant difference in cortical

bone density of edentulous mandibles between the buccal and lingual sites, but differences were found between the mandibular ramus and body. Areas in the lingual ramus, condyle and masseter were less dense. However, there were no differences between dentate and edentulous mandibles. Similarly, Henrikson and Wallenius (1974) found no differences in bone density between dentate and edentulous individuals or between men and women. The lack of differences suggests that cortical bone density following edentulation can be maintained despite changes in structure, resistance and anisotropy. Many of the discrepancies between studies are therefore due to methodological differences. Most studies evaluate bone density using two-dimensional scanning techniques (Horner and Devlin, 1992; Klemetti *et al.*, 1994; Ulm *et al.*, 1994). These methods are unable to remove the effects of tissue thickness and density and often assess cortical thickness instead of trabecular structure as done in the present study.

Computerized examination of digital images permits uniform, standardized and operator-independent analysis of bone quality (Karrbrink *et al.*, 2008). Most studies applying radiographic densitometry to measure mandibular bone density have used intraoral radiography (Kribbs, 1990; Mohajery and Brooks, 1992). The advantages of intraoral radiographic images include less overlap of bone structures and the absence of empty spaces. However, overlap of soft tissue can occur on intraoral film. In order to identify patients with a suspicion of low bone density, such as postmenopausal women, our team is developing another system to evaluate bone microarchitecture through the analysis of samples collected in intraoral periapical digital radiographs. Mohajery and Brooks (1992) used panoramic X-rays for bone densitometry and had the same difficulty as observed in the present study in establishing an image in the panoramic X-ray that was devoid of overlap. In an attempt to avoid these overlaps and to permit the use of panoramic X-rays as a reliable alternative to measure bone mineral density, the following regions of interest were evaluated in this study: alveolar ridge and mandibular ramus.

The characterization of trabecular bone quantity and quality is mainly based on its sensitivity to stimuli, such as hormonal (Gouveia *et al.*, 1997; Gallet *et al.*, 2013), mechanical (Huiskes *et al.*, 2000) and therapeutic effects (Chesnut *et al.*, 2005; van Rietbergen *et al.*, 2002). Trabecular bone structure is one aspect of bone quality that is known to affect bone strength and its quantification has become an important area of research. With the technical advances in imaging and image processing, clinical studies in humans and animal experiments have become a standard part of skeletal characterization for phenotyping (Bouxsein *et al.*, 2004; Kohler *et al.*, 2005), assessment of skeletal status (Boutroy *et al.*, 2005;

Khosla *et al.*, 2006) and treatment monitoring (Chesnut *et al.*, 2005; van Rietbergen *et al.*, 2002).

Following this reasoning, bone mass is the main determinant of bone mechanical resistance, accounting for 30 to 40%. Other factors are also involved such as bone quality, which depends on bone mineralization, bone turnover and bone micro architecture. The simplest parameters (Parfitt's parameters) are trabecular count, size and separation. A binary image (two grey levels) of bone tissue can be expanded and used to determine the trabecular bone pattern factor. This method tends to overestimate the number of convex surfaces, which are characteristic of trabecular network disruption. The binary image can be simplified (skeletonized) and used to determine the number of nodes (anastomoses between trabeculae) or free ends (segments disconnected from the network). The bone marrow star volume, the marrow interconnectivity index and the Euler-Poincaré number are useful parameters to characterize the bone marrow. These parameters can be measured on a bone specimen in various planes or on a digitized image in a single plane, as done in studies using microscopic or histological techniques (Kingsmill and Boyde, 1998) which demonstrate variations in bone density between sections. Two-dimensional analysis is still widely used, although three-dimensional studies provide better resolution and volumetric measures.

Another technique used to measure radiographic bone density is fractal analysis. In this procedure, fractal dimension measurements are used to determine the degree of trabecular network disruption. Histomorphometric data from experimental animal studies suggest that micro architecture-related factors can explain 10 to 30% of the variability in bone mechanical resistance, a proportion lower than that explained by bone mass.

Similar results have been obtained in studies using three-dimensional measurements such as μ CT, CT and Magnetic Resonance Imaging (MRI). Discrepancies exist between studies when the strength of the relationship between bone mass and bone mechanical resistance is evaluated, which can be attributed to differences in the sites of measurement and to errors in the measurement of variables that characterize bone mechanical resistance. The finite element method may be a means to overcome these problems. This method can be used to calculate Young's modulus of elasticity from three-dimensional bone segment reconstructions. Few cross-sectional studies have used a clinical approach to compare bone architecture between patients with osteoporotic fractures and controls with normal bone mass. Evaluation of bone architecture by histomorphometry, CT or MRI indicated that trabecular network disruption is more severe in patients with fractures (Cortet and Marchandise, 2001).

Shwartz-Dabney and Dechow (2002) reported the volumetric representation of bone density and the results differed from those of other studies using a microscopic scale. In the case of three-dimensional measurements, the results are influenced by the number of microporosities and spaces of bone resorption and mineralization.

Karrbrink *et al.* (2008) analyzed jaw bone density on digital radiographic images and correlated the results with DEXA values. The trabecular density values obtained were related to a scale that indicated whether the patient had osteoporosis, osteopenia, or was healthy. The bone density scale ranged from 3500, corresponding to a very dense structure, to 9500, corresponding to a very thin trabecular structure. The authors suggested values higher than 6500 to indicate a risk of osteoporosis, values of 6500-6200 to indicate a risk of osteopenia, and values less than 6200 to indicate that the patient is healthy. The present study was not designed with sufficient power to demonstrate other bone conditions such as osteoporosis. Further studies evaluating other bone conditions and osteoporosis may help confirm that the BuA-DDX software can identify cases of abnormal bone density based on values established in the lower limit. One future application of the software proposed in this study is to define a bone density scale.

A variety of structural indices used to quantitatively characterize the geometric properties of trabecular bone are available in the literature. These indices include volume and surface fractions (BV/TV and BS/BV) and metrics such as Trabecular Thickness (Tb.Th), number of trabeculae (Tb.N) and trabecular spacing (Tb.Sp). Additionally, non-metric indices such as the Structure Model Index (SMI), connectivity density (Conn.D) and Degree of Anisotropy (DA) have been introduced to describe topographic features of bone microstructure. The predictive powers of these indices for mechanical strength of trabecular bone have been demonstrated by several authors (Ito *et al.*, 2002; MacNeil and Boyd, 2007; Mittra *et al.*, 2005), providing information that is relevant for bone quality. SMI, which is derived from surface connectivity, has been proposed as a parameter to classify the type of trabecular bone structure, specifically the degree to which the structural elements resemble plate-like or rod-like geometries. A rod-like trabecular bone structure is characteristic of an osteoporotic patient (Hildebrand and Ruegsegger, 1997) and is strongly correlated with bone strength (Mittra *et al.*, 2005). The degree of trabecular connectivity, measured by Conn. D, can alter structural integrity and results in an elevated fracture risk due to the loss of connectivity (Davison *et al.*, 2006). The degree of anisotropy is a measure of directional variation of a structure and is calculated by the ratio of

maximum to minimum values of the mean intercept length tensor (Odgaard, 1997). With age, trabecular bone becomes more rod-like (Ding and Hvid, 2000), with connectivity being lost by disruption of thin horizontal trabeculae, and increasingly anisotropic (Mosekilde *et al.*, 2000).

Despite the existence of different complex processes as discussed in the previous section, this study reported a simple metric based on the calculation of mean pixel intensity (μ), variance of intensities (σ^2) and determination of the number of trabecular pixels (N_{pt}).

Conclusion

The method developed permitted the evaluation of samples collected in the regions of the alveolar ridge and mandibular ramus, identifying cases of normal and abnormal bone density on digital dental X-rays. However, readjustment of the software parameters is necessary when the X-rays were submitted to pre-processing or suffered changes in the X-ray emission source. In conclusion, the software designed to evaluate bone density on dental X-rays could be a practical and low-cost alternative for maxillofacial surgeons, periodontists and implantologists.

Acknowledgement

The authors would like to thank State University of Western Parana (Unioeste) for support and CNPq Research Foundation for fellowship.

Author Contributions

Adriane Yaeko Togashi: Contributed to the development of this study; suggested the concept and methods for designing the research; supervised all research activities; proposed this study; prepared the manuscript; read and approved the final manuscript.

Adair Santa Catarina: Contributed to the development of this study; suggested the concept and methods for designing the research; supervised all research activities; conducted the experiment, participated in acquiring and analyzing the data; read and approved the final manuscript.

Lucas Renato Piana Batistussi: Contributed to the development of this study; suggested the concept and methods for designing the research; conducted the experiment, participated in acquiring and analyzing the data; read and approved the final manuscript.

Guilherme Coelho: Contributed to the development of this study; suggested the concept and methods for designing the research; conducted the experiment, participated in acquiring and analyzing the data; read and approved the final manuscript.

Conflict of Interest

The authors have no financial interest in any company or any of the products mentioned in this article.

Ethics

This article is original and it contains the unpublished material. No other ethical issues are involved.

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