Original Article

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Investigating the Effects of Smoking on Trabecular Bone Structure Using Fractal Analysis: A Pilot Case-control Study

Sigara İçen Bireylerdeki Trabeküler Kemik Değişikliklerinin Fraktal Analiz Yöntemiyle Araştırılması: Pilot Olgu-kontrol Çalışması

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ABSTRACT

Objective: Fractal analysis (FA) is a method that performs the evaluation of complex and irregular body structures through mathematics. The aim of this study is to use the FA approach to determine how smoking affects mandibular trabecular bone structure on panoramic radiographs.

Methods: While 55 smokers constituted the study group, 55 non-smokers constituted the control group. The study and control groups were paired for age and sex. Two region of interest (ROIs) with a pixel size of 100x100 were determined from the right mandibular angulus and the trabecular bone region between the right second premolar and first molar roots (interdental). Utilizing the box-counting technique, FA was conducted on the ROIs identified by the panoramic radiography. SPSS 21.0, developed by IBM Corp in Armonk, NY, USA, was used for the data analysis. At the 0.05 threshold, p-value was regarded as significant.

Results: The mean age of 74 male and 36 female individuals included in the study was 23.54±3.57 years. Fractal dimension (FD) values of gonial (p=0.528) and interdental regions (p=0.490) did not differ statistically from each other between the study-control groups (p>0.05). When the correlation analysis of pack-year values of smoking exposure and FD measurements was performed, a negative correlation that was not statistically significant was found (p>0.05).

Conclusion: As cigarette exposure increases, FD values tend to decrease. No effect of smoking on mandibular trabecular bone FD values was observed.

Keywords: Fractal, panoramic image, smoking

ÖZ

Amaç: Fraktal analiz (FA), karmaşık ve düzensiz vücut yapılarının değerlendirilmesini matematik yoluyla gerçekleştiren bir yöntemdir. Bu çalışmanın amacı, FA yaklaşımını panoramik radyografiler üzerinde sigaranın mandibuler trabeküler kemik yapısını nasıl etkilediğini belirlemede kullanmaktır.

Yöntemler: Sigara içen 55 kişi olgu grubunu oluştururken, sigara içmeyen 55 kişi kontrol grubu olarak belirlendi. Çalışma ve kontrol grupları yaş ve cinsiyet açısından eşleştirildi. Sağ mandibuler angulus ve sağ ikinci premolar ile birinci molar kökler (interdental) arasındaki trabeküler kemik bölgesinden 100x100 piksel boyutunda iki ilgi alanı (ROI) belirlendi. Panoramik radyografi ile belirlenen ROI'lar üzerinde kutu sayma tekniği kullanılarak FA yapıldı. Verilerin analizinde IBM Corp tarafından Armonk, NY, ABD'de geliştirilen SPSS 21.0 programı kullanıldı. P değeri 0,05 eşiğinde anlamlı olarak kabul edildi.

Bulgular: Çalışmaya dahil edilen 74 erkek ve 36 kadın bireyin yaş ortalaması 23,54±3,57 idi. Gonial (p=0,528) ve interdental bölgenin (p=0,490) fraktal boyut (FB) değerleri olgu-kontrol grupları arasında istatistiksel olarak birbirinden farklı değildi (p>0,05). Sigara maruziyetine ilişkin paket-yıl değerleri ile FB ölçümlerinin korelasyon analizi yapıldığında istatistiksel olarak anlamlı olmayan negatif ilişki saptandı (p>0,05).

Sonuç: Sigara maruziyeti arttıkça, FB değerleri azalma eğilimi gösterir. Sigara içmenin mandibuler trabeküler kemik FB değerlerine etkisi gözlenmemiştir.

Anahtar Sözcükler: Fraktal, panoramik görüntü, sigara içmek

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Introduction

Fractal analysis (FA) is a way of using math to study complex and irregular physical shapes. The fractal dimension (FD) provides a numerical representation of the FA value. By calculating how similar a structure is to itself, FD illustrates the intricate nature of the structure (1). The measurements of the area and length of fractals differ from the measurements of classical geometric shapes. Examples of geometric shapes are that a point has 0 (zero), a straight line has 1 (one), a square has 2 (two) dimensions, and a cube has 3 (three) dimensions. However, FD values cannot take integer values. Considering the FD of England's coastline, the value 1.25 indicates that the structure occupies more area than a straight line and is more complex but does not take up as much space as a plane (2).

Trabecular bone plays an important role in understanding how the structure of the bone has changed because cortical bone has a lower metabolic rate compared to this bone (3). The FD shown on radiographstakes into account differences in the intensity of trabecular bone and the loss of minerals from the bone. The fact that the FA method is not affected by the projection angle and the selection of the region to be examined in the alveolar bone increases the applicability of the technique in clinical conditions, making it easier for the clinician to evaluate the radiographs (4-6). Cigarette smoke contains more than 4,800 identified chemicals known to be carcinogenic, toxic and mutagenic (7). It is reported that smoking initiates inflammatory events by increasing oxygen radicals and therefore causes cancer and inflammatory diseases (8). Oxidative stress is the disruption of the balance between free radicals and antioxidants in favor of free radicals. It causes endothelial cell damage by initiating oxidative stress caused by smoking (9). Healthy endothelium produces vasodilators such as nitric oxide, prostacyclin, and endothelium-derived hyperpolarizing factor. When the endothelium is damaged, the balance between vasodilators/vasoconstrictors is destroyed, and atherosclerotic change begins. Even smoking just one cigarette increases blood pressure by around 20 mmHg acutely and temporarily via sympathetic nerve activation (10). It has been reported that smoking is an important risk factor for the pathogenesis of a number of neuroinflammatory and neurovascular disorders (11). Chronic smoking poses a risk for neurological diseases such as dementia, Parkinson's disease, and Alzheimer's disease (11), increasing amyloid deposition in a dose-dependent manner, leading to the formation of senile plaques (12).

The effect of smoking on bone metabolism occurs in various ways. It has been reported that nicotine, the main active component of cigarette smoke, has a direct effect on osteoblast proliferation and induces the expression of the bone matrix protein osteopontin. This means that nicotine has a direct toxic effect on osteoblasts. Other explained mechanisms of smoking on bone metabolism are due to antiestrogenic effects, hypercortisolism, decreased calcium absorption and decreased body weight (13).

Although there are various hypotheses regarding the mechanisms of bone resorption caused directly and indirectly by smoking (14), there is not enough data reporting the effect of smoking on the FD value of the mandibular trabecular bone. The usage of FA is growing daily since it is convenient and affordable. Although it has several drawbacks, the fact that it is non-invasive and unaffected by factors like projection geometry and radiodensity has led to an increase in its application in medicine and dentistry (15). Studies using FA have been conducted in a variety of fields, including the examination of alveolar bone loss caused by periodontitis (16), examining periapical lesions that develop following root canal treatment (17), the success of osteointegration of the bone surrounding implants (18), and the examination of the mandibular condyle's trabecular structure in patients with bruxism (19). The goal of this research is to use FA on digital panoramic radiographs to examine the impact of smoking on the mandibular trabecular bone structure.

Methods

Sample

The study received ethical approval from the Scientific Research Evaluation Ethics Committee at Necmettin Erbakan University's Faculty of Dentistry and its compliance with ethical principles was approved (decision no: 2020/02-06). The study was conducted in conformity with all rules and regulations as well as the principles stated in the Helsinki Declaration. Before the examination, the participants in the study received thorough information about it, and everyone who agreed to take part in it completed an "informed consent form".

• Systemically healthy (in particular without conditions that influence bone metabolism, such as Paget's disease, hyperparathyroidism, hypoparathyroidism, osteomalacia, renal osteodystrophy, and osteogenesis imperfecta) individuals between the ages of 20-35, without bruxism habit, without temporomandibular joint disease, with Angle class 1 bite, and without tooth deficiency were included in the study.

• The patients with pathology in the maxillofacial region, severe periodontal disease, a history of prior or ongoing orthodontic treatment, prosthetic restorations in any of their teeth, restorations with early contact in occlusion, and radiographs lacking diagnostic competence as a result of improper patient positioning or irradiation were excluded from the study.

Fifty-five individuals who met the specified conditions and smoked constituted the control group while 55 non-smokers constituted the control group. Both the study and control groups consisted of individuals of the same age and gender. The study's effectiveness was assessed to be 90.4% at a valuable level of 0.05 and a 95% range of confidence for the power analysis that was carried out to define the appropriateness of the sample size.

Pack-year Calculation

Smokers in the study group had their exposure calculated using a pack-year measure. There are 20 cigarettes in 1 pack of cigarettes. An example calculation is as follows (20):

It is calculated as (15/20)x40=30 for the person in question who has been a daily smoker of 15 cigarettes for a span of 40 years.

Image Acquisition

Every single panoramic radiograph utilized in the study was taken with a digital panoramic X-ray apparatus called the 2D Veraviewpocs. It was used to assist in the study (manufactured by J MORITA MFG Corp in Kyoto, Japan) at a 70 kVp, 5 mA, and 15 sec irradiation.

Image Processing

By using Adobe Photoshop CS5 from Adobe Systems Inc. in San Jose, CA, the sizes of all photos were changed to 2,800x1,500 pixels in order to standardize panoramic photographs recorded in the "TIF" (Tagged Image File) format. FA was carried out by means of the ImageJ v1.52 program, which was available to be downloaded for free online at https://imagej.nih.gov/ij/download.html.

For FA, two ROIs with 100x100 pixel sizes were determined on a panoramic image, from the right mandibular angulus and the trabecular bone region between the right second premolar and first molar roots (interdental) (Figure 1). The box-counting approach ....created by White and Rudolph (21) (1999) was used to carry out the phases of the FA procedure (Figure 2).

Statistical Analysis

The data was analyzed using the SPSS 21.0 program from IBM Corporation in Armonk, New York. Two observers conducted FD measures twice, with a 14-day gap between each measurement. Cronbach's alpha analysis was applied to interpret intra- and inter-observer agreement. The Mann-Whitney U test was used to make comparisons of the FD measures between the study and control groups. To investigate the connections between FD measures and smokers' pack-year values and to ascertain the connection between FD measurements and age, Spearman's rho analysis was utilized. At the 0.05 threshold, it was regarded as significant.

Results

The mean age of 74 male and 36 female individuals included in the study was 23.54±3.57 years, the average age of women was 24.39±3.4, and the mean age of men was 23.19±3.6 years. Table 1 lists the distribution of participants by gender, study-control groups, and their average age.

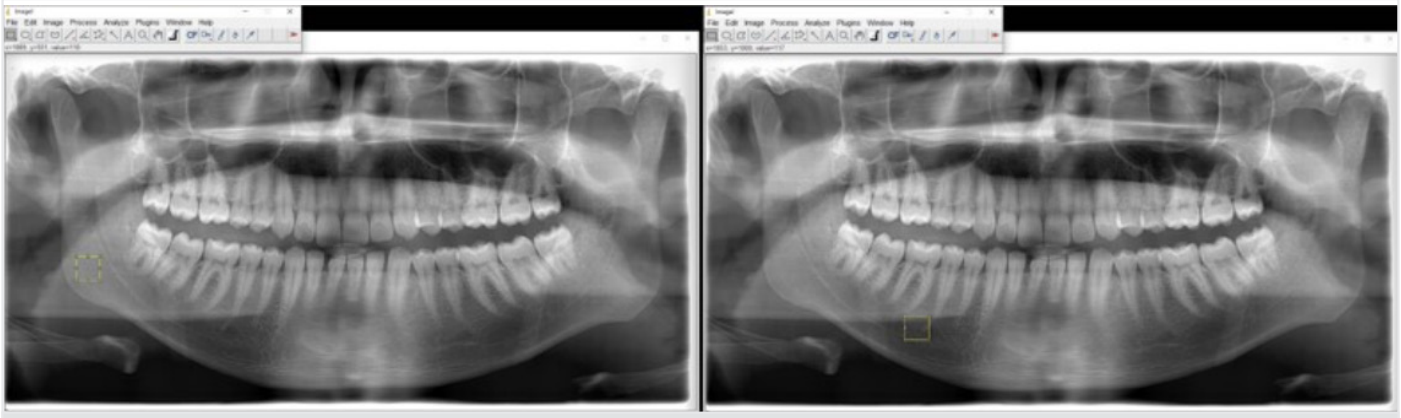

Figure 1. Selection of ROI
ROI: region of interest

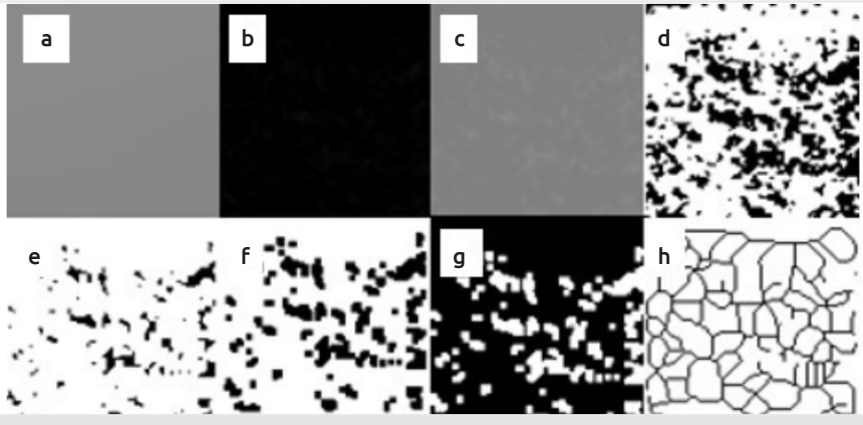

Figure 2. a) Blurring; **b)** Removing the blurred image from the original image; **c)** Adding 128 shades of gray; **d)** Black-and-white image conversion; **e)** Noise reduction with Erode; **f)** Expansion with Dilate; **g)** Color inversion; **h)** Convert to skeletal format

In our study, FA measurements made on a total of 220 (110x2) ROIs determined on panoramic radiographs of 110 individuals were repeated twice, with two-week intervals, on 22 patients by two observers. Cronbach's Alpha compatibility values were found to be 0.93-0.95 for the interdental region and 0.79-0.80 for the gonial region. The FD values estimated from the interdental area were lower than the FD values estimated from the gonial region (p=0.033) (Table 2).

The study group's gonial region FD value had the highest mean and the study group's interdental region FD value had the lowest mean (Table 3). FD values of gonial (p=0.528) and interdental region (p=0.490) did not differ statistically from each other between the study and control groups (p>0.05).

Pack-year values of cigarette consumption of the study group ranged from 0.3 to 26, with an average of 4.69±4.57. In the investigation of the correlation between FD measures and cigarette pack-year values; FD measures of the interdental (p=0.306, Spearman's Rho r=-0.141) and gonial regions (p=0.450, Spearman's Rho r=-0.104) and pack-year values showed a negative correlation, although statistical significance was not established (p>0.05). As cigarette exposure increased (pack-year values), FD values decreased (Table 4). When FD values of 110 individuals were reviewed in order to evaluate the correlation of FD values with age, there was a negative correlation between FD values of the interdental region (Spearman Rho, r=-0.40, p=0.676) and gonial region (Spearman Rho, r=-0.010, p=0.919); however, such correlation was not statistically significant (p>0.05). FD values tended to decrease along with the age increased (Table 5).

Discussion

Although two-dimensional projections used to view the trabecular structure are non-invasive, they are not sufficient to show the full detail of the trabecular structure. Therefore, FA of radiological images may be used to investigate the trabecular structural pattern (22). FA may be used to assess the trabecular structure of the alveolar bone objectively because, when viewed on radiographs, it exhibits a self-similar fractal pattern (18). Other advantages of this method are that it is not affected by

Table 1. Gender distribution and average age of the study and control groups

	Women			Men			
	Study	Control	Total	Study	Control	Total	Total
Number of patients	18	18	36	37	37	74	110
The mean age ± SD	24.39±3.4			23.19±3.6			23.54±3.57

SD: Standard Deviation

Table 2. The average FD values of the participants

ROI	FD (mean ± SD)	P value
Interdental	1.40±0.07	
Gonial	1.42±0.09	*0.033**

ROI: Region of interest, SD: Standard Deviation, FD: Fractal dimension
*p<0.05

Table 3. The average FD values of the individuals in the study and control groups

	ROI	FD mean ± SD
Study (n=55)	**Interdental**	1.399±0.071
	Gonial	1.424±0.110
Control (n=55)	**Interdental**	1.409±0.068
	Gonial	1.428±0.081

ROI: Region of interest, SD: Standard Deviation, FD: Fractal dimension

Table 4. Spearman's rho analysis to show correlation between FD measurements and smokers' pack-year values

FD values			Pack-year
Spearman's rho	**Interdental**	**Correlation coefficient**	-.141
		Sig. (p)	.306
		N	55
	Gonial	**Correlation coefficient**	-.104
		Sig. (p)	.450
		N	55

Sig: Significance

Table 5. Spearman's rho analysis to show correlation between FD measurements and age

FD values			Age
Spearman's rho			
	Interdental	Correlation coefficient	-.040
		Sig. (p)	.676
		N	110
	Gonial	Correlation coefficient	-.010
		Sig. (p)	.919
		N	110

Sig: Significance

changes of kVp, tube current and projection angles between -10° and +30° in periapical radiographs (3). This study used FA to investigate how smoking affected the mandibular trabecular bone structure.

The reason for the widespread use of trabecular bone for FA is that its regeneration rate is quite high and it is metabolically active compared to compact bone (3,23). It has been suggested that dental components should not be involved within the ROI limitations for research examining the trabecular bone structure (24). In this study, two ROIs with 100x100 pixel sizes were determined on a panoramic image, from the right mandibular angulus (gonial) and the trabecular bone region between the right second premolar and first molar roots (interdental). In the literature, there were several studies in which FD analysis was conducted on unilaterally selected ROIs similar to our study (25,26). In many recent studies (23,27-30) it has been stated that FD measurements in the right-left mandible do not differ. Based on this, unilateral measurement was made in the present study.

Ruttimann et al. (31) showed that FD was different for different anatomical locations on the mandibular bone (incisors, premolars and molars region), similar to this study. The gonial area's FD values (1.42±0.09) were higher than the FD values estimated from the interdental regions (1.40±0.07), according to the analysis of the FD values of the 110 participants in this study ($p=0.033$, $p<0.05$). Researchers theorise that this variation may be caused by individuals' unilateral eating patterns and radiographic positioning problems (32). A low value of FD indicates more cavities in the bone, and a high value of FD indicates fewer cavities within the bone and more complex bone architecture (33). Considering this information, among the regions examined in our study groups, it can be concluded that trabecular complexity is higher in the gonial region than in the interdental area. Yasar and Akgünlü (34) explained in their research conducted to examine the difference in trabecular formation of the toothed and toothless regions that lower FD values of toothed regions were associated with regular trabecular alignment in order to resist occlusal forces. Consequently, toothed and toothless regions have different trabecular bone structure and toothless regions have more complex and homogenous trabecular structure than toothed regions. The homogenous structure mentioned here defines the regular trabecular architecture with proper dimensions. These findings are consistent with our study.

Studies have shown that smoking has effects on bone metabolism and bone cells (35). Nicotine, the main active ingredient of cigarettes, reduces calcium absorption in the body (36). It is stated that smoking reduces vitamin D storage and osteoblast activity (37) and cortisol, which increases after smoking, can also reduce bone density (38).

The direct effect of smoking on bone is formed by the nuclear factor-kappa B ligand (RANKL)/RANK/osteoprotegerin (OPG) cytokine system, which is responsible for bone destruction (14). Smoking causes bone resorption by disrupting the balance in the RANKL/RANK/OPG pathway (39). The indirect effects of smoking on bone density are as follows: it causes weight loss, disrupts the parathyroid hormone-vitamin D axis, increases testosterone and lowers estrogen, and due to oxidative stress it induces osteoclastic activity and suppresses osteoblastic activity (40).

Smoking has a stronger impact on trabecular bone structure than cortical bone, and its impact is more strongly correlated with smoking duration than cigarette consumption (41). In our study, FD measurement values from gonial and interdental regions showed no noticeable difference between smokers and non-smokers. On the other hand, when 55 patients' pack-year values for cigarettes in the study group were examined, a decreasing trend was observed in the FD values as the cigarette exposure (pack-year values) increased. Smoking has negative effects on the skeleton, including increased bone resorption and osteoclast activity, disturbance of collagen metabolism, and a directly toxic influence on osteogenesis (42). It has been reported that smoking causes oral cavity bone to mend more slowly, reduces bone height, accelerates bone loss, and lowers bone quality (43). The fact that there was no difference between the study-control groups in our study can be better understood by revealing the differences in the chewing habits of the individuals. It has been reported that occlusal forces during chewing will cause differences in the trabecular structure of the mandible (34). Future studies should be conducted on larger samples, where the unilateral chewing patterns of individuals are also recorded.

In comparison to control group, mice exposed to secondhand smoking in experiments had reduced bone mineral density (44,45). The fact that individual differences that may affect bone health such as passive cigarette smoke exposure, nutrition (alcohol consumption, vitamin deficiencies such as vitamin D

and mineral deficiencies such as calcium) and sports habits of individuals were not evaluated in our study may affect the results and should be considered as a limitation.

The age range of the participants was limited (20 to 35 years of age) in order to minimize the age-based effect on FDs. When the correlation between FD values and age was analyzed, a negative correlation was found, but not statistically significant difference was detected between FD values of the interdental region (Spearman Rho, r=-0.40, p=0.676) and gonial region (Spearman Rho, r=-0.010, p=0.919) (p>0.05) (Table 5). The FD values tend to decrease along with the age increase. This result may be interpreted that trabecular complexity decreases with aging. A decrease may occur in the structure of bone trabeculae as a result of more bone resorption than bone remodeling and exposure of the bone to local stresses (46).

Conclusion

Within the limitations of the study, as cigarette exposure increased, FD values tended to decrease. No effect of smoking on mandibular trabecular bone FD values was observed. Future research with larger samples may be used to trackindividual characteristics including feeding patterns, unilateral chewing habits, and passive smoking.

Ethics

Ethics Committee Approval: The study received ethical approval from the Scientific Research Evaluation Ethics Committee at Necmettin Erbakan University's Faculty of Dentistry and its compliance with ethical principles was approved (decision no: 2020/02-06).

Informed Consent: Obtained.

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: D.A., M.T., Design: D.A., M.T., Data Collection or Processing: D.A., M.T., Analysis or Interpretation: M.T., Literature Search: D.A., M.T., Writing: D.A., M.T.

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