Süleyman Demirel Üniversitesi
Sağlık Bilimleri Dergisi
Cilt 15, Sayı 1, 29 - 36, 2024

Suleyman Demirel University
Journal of Health Sciences
Volume 15, Issue 1, 29 - 36, 2024

Fractal Dimension Analysis of Cervical Vertebra on Cone-Beam Computed Tomography Scans of Smoker Males

Sigara İçen Erkeklerin Konik Işınlı Bilgisayarlı Tomografi Taramalarında Servikal Vertebranın Fraktal Boyut Analizi

Aslıhan ARTAŞ [1*], Elif Meltem ASLAN ÖZTÜRK [2]

[1] Department of Dentomaxillofacial Radiology, Faculty of Dentistry, Gaziantep University, Gaziantep, Türkiye
[2] Department of Dentomaxillofacial Radiology, Faculty of Dentistry, Lokman Hekim University, Ankara, Türkiye

ABSTRACT

Objective: This study aimed to comparison of vertebral fractal dimension (FD) values among smoker and non-smoker males.

Material and Methods: Cone-beam computed tomography (CBCT) images of 144 male patients were evaluated, 72 smokers constituted the study group, while 72 non-smokers formed the healthy control group in this study. In all CBCT images, the region of interest (ROI) assessing the second cervical vertebra (C2) was chosen as a 45x45 pixel size for ROI-v with reference to the coronal view of C2.

Results: While the mean FD value of ROI-v in the smoker group was 1.118±0.85, the mean FD value of ROI-v in the non-smoker group was 1.221±1.12. This difference between ROI-v values is also statistically significant ($p < 0.05$).

Conclusion: Fractal analysis of cervical vertebrae may help to evaluate osteoporotic changes in smoker males.

Keywords: Cigarette, fractal analysis, cone-beam computed tomograhy, cervical vertebra

Alınış / Received: 09.11.2023 Kabul / Accepted: 18.03.2024 Online Yayınlanma / Published Online: 22.04.2024

DOI: 10.22312sdusbed.1388544
ARAŞTIRMA MAKALESİ

*Corresponding author: dt.aslihanartas@gmail.com

Ö Z E T

Amaç: Bu çalışmada, sigara içen ve içmeyen erkeklerde vertebral fraktal boyut (FB) değerlerinin karşılaştırılması amaçlandı.

Gereç ve Yöntemler: Bu çalışmada 144 erkek hastanın konik ışınlı bilgisayarlı tomografi (KIBT) görüntüleri değerlendirilmiş, sigara içen 72 kişi çalışma grubunu, sigara içmeyen 72 kişi ise sağlıklı kontrol grubunu oluşturmuştur. Tüm KIBT görüntülerinde, ikinci servikal vertabrayı (C2) değerlendiren ilgi alanı (region of interest) (ROI), C2'nin koronal görünümü referans alınarak ROI-v için 45x45 piksel boyutu olarak seçildi.

Bulgular: Sigara içen grupta ROI-v'nin ortalama FB değeri 1,118±0,85 iken, sigara içmeyen grupta ROI-v'nin ortalama FB değeri 1,221±1,12 idi. ROI-v değerleri arasında bulunan fark istatistiksel açıdan anlamlıdır. ($p < 0.05$)

Sonuç: Servikal omurların fraktal analizi, sigara içen erkeklerde osteoporotik değişikliklerin değerlendirilmesine yardımcı olabilir.

Anahtar Kelimeler: Sigara, fraktal analiz, konik ışınlı bilgisayarlı tomografi, servikal vertebra

1. Introduction

Cigarette smoking is common around the world, despite the large number of deterrent measures that have been put in place for many years [1]. It has been reported that tobacco consumption causes the death of approximately 7 million people worldwide [2]. In addition to, cigarette smoking is the most common form of tobacco consumption [3]. There is a relationship between smoking and cardiovascular diseases, certain types of tumors, chronic obstructive pulmonary diseases, osteoporosis [1, 4].

Osteoporosis is a disease of skeletal system in which there is an imbalance in bone remodeling and an increased the risk of fracture [5]. Fragility fractures, which occur due to mechanical forces as a result of low-level trauma that would not normally result in a fracture, are a clinical consequence of osteoporosis [6]. Osteoporosis is an important public health problem due to socioeconomic reasons caused by fragility fractures [7]. There are more than 200 million osteoporosis patients when the literature is reviewed [8]. Osteoporosis is categorized into two main groups as primary and secondary. Postmenopausal and senile osteoporosis are the most common clinical forms and are primary causes [9, 10]. Secondary osteoporosis develops due to some genetic diseases, malabsorption, rheumatic diseases, smoking, use of some drugs [11, 12]. Recent research has shown that smoking has devastating effects on bone mass. This effect is due to the toxic effect on osteoblasts and increased bone destruction by osteoclasts [13, 14]. Males tend to smoke at higher rates than females [15]. In studies, secondary osteoporosis was found to be more common in males [16, 17] and one study concluded that although some progress has been made in recognizing osteoporosis in males, more studies are needed [18].

Osteoporosis is associated with poor bone strength, and bone strength is determined by features such as bone mineral density (BMD), bone microstructure, geometry and quality. BMD is decreased, bone microarchitecture is deteriorated in osteoporosis. DEXA, based on BMD measurement, is considered the gold standard method for identifying and assessing osteoporosis, but its availability and effectiveness in detecting changing bone quality are limited [7, 19, 20]. Since fragility fractures may occur in patients defined as normal BMD or osteopenic according to DEXA, auxiliary techniques are needed to determine differences in bone microstructure [21]. One of the most significant component creating to bone strength is its complex structure [22]. Fractal analysis (FA) is a mathematical method used to identify complex structures and shapes quantitatively and is signifyed numerically as fractal dimension (FD) [23]. Trabecular bone demonstrates fractal features such as complexity, and characteristic length due to its natural architecture. Thus, FA may be used to define the complex structure of trabecular bone [24].

Authors have reported that texture analysis and gray values of radiographic images may be associated with bone microarchitecture [25, 26]. Cone-beam computed tomography (CBCT), in which three-dimensional images are obtained, has an important place in the detection of pathological structures in the maxillofacial region, examination of the temporomandibular joint, evaluation of implant placement areas and in many areas of dentistry. Conventional radiographic projections, such as panoramic and periapical radiography, provide two-dimensional representations of superimposed structures attenuating an X-ray within a limited field of view. These inherent limitations can manifest as blurring and distortion of bony anatomy, hindering detailed visualization. Conversely, CBCT and micro-computed tomography (micro-CT) offer superior three-dimensional visualization of hard tissues due to their high spatial resolution [27]. Three-dimensional and high-resolution imaging modalities, offer a significant advantage in facilitating the accurate assessment of bone quality [28]. When studies in literature are reviewed, effect of tobacco use on mandibular bone has been evaluated using FA on panoramic radiography [4]. As far as we know, there is no study evaluating the effect of smoking on bone using FA on CBCT scans. This study hypothesized that the microarchitecture of vertebrae would differ between smoker males and non-smoker males. This study aims to comparatively evaluate cervical vertebral trabecular bone structure using FA on CBCT scans in smoker males and non-smoker males.

2. Material and Method

Study Groups

This study was approved by the Ankara Medipol University Non-Invasive Clinical Research Ethics Committee (Protocol No: 111). CBCT images in the archive of Ankara Medipol University Faculty of Dentistry, Department of Dentomaxillofacial Radiology were retrospectively analyzed. In our study, CBCT images of 144 patients were evaluated. 72 smokers constituted the study group, while 72 non-smokers formed the healthy control group. Ages of patients in both groups were 18 years or older and consisted of male patients only. Patients with systemic or chronic diseases, drug intake affecting bone metabolism, and a history of radiotherapy and chemotherapy were not included in this study.

Image Analysis and CBCT Scans

All assessments were performed by two dentomaxillofacial radiologists, one with seven (AA) and the other with five years of experience (EMAO). When there was disagreement between the observers, consensus was reached through discussion. For inter-observer calibration and reliability of the evaluations, 20% of the images were reviewed by the same observers two weeks after the initial evaluation.

In this study, images obtained from Castellini X-Radius Trio Plus 3D (Italy) CBCT device at 90 kVp, 8mA parameters were used. The slice thickness of the images was 1 mm, voxel size was 0.2 mm^3, and field of view was 16x18 cm.

Fractal Analysis

In all CBCT images, region of interest (ROI) assessing C2 was chosen as a 45x45 pixel size for ROI-v with reference to coronal view of C2. This ROI-v was determined by centering C2 using sagittal (Figure 1A), axial (Figure 1B), and coronal (Figure 1C) planes.

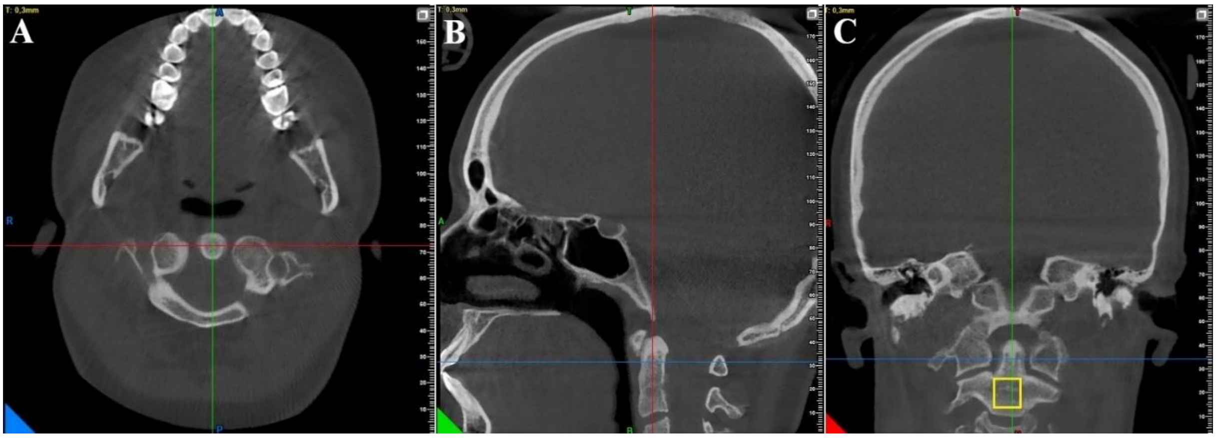

Figure 1: Second cervical vertebra

(C2); Its position is shown on axial (A), sagittal (B), and coronal (C) CBCT images. The determination of region of interest (ROI) in the coronal CBCT (C) image is demonstrated.

FD was calculated by box counting method using ImageJ version 15.2 (National Institutes of Health, Bethesda, MD, USA) program on it. Once ROI was selected, image was duplicated (Figure 2a). Gaussian filter was implemented on image to render blurred effect (Figure 2b). The resultant blurred image was later extracted from original image (Figure 2c). To develop specific features with differing brightness levels, such as trabeculae and bone marrow, an image was obtained by adding 128 gray values at each pixel position (Figure 2d). By implementing a brightness threshold of 128, the image was subsequently transformed into binary format (Figure 2e). To minimize noise, binary image was processed by erosion and dilation (Figure 2f, 2g). The image was further inverted, showing trabecular zones in black and bone marrow in white (Figure 2h). Lastly, image was submitted to skeletonization process that progressively removal pixels until only central pixel line remained (Figure 2i). The software used box counting algorithm that divided image into squares of 2, 3, 4, 6, 8, 12, 16, 32 and 64 pixels (Figure 2). The number of frames containing trabeculae and total number of frames were computed for each pixel size.

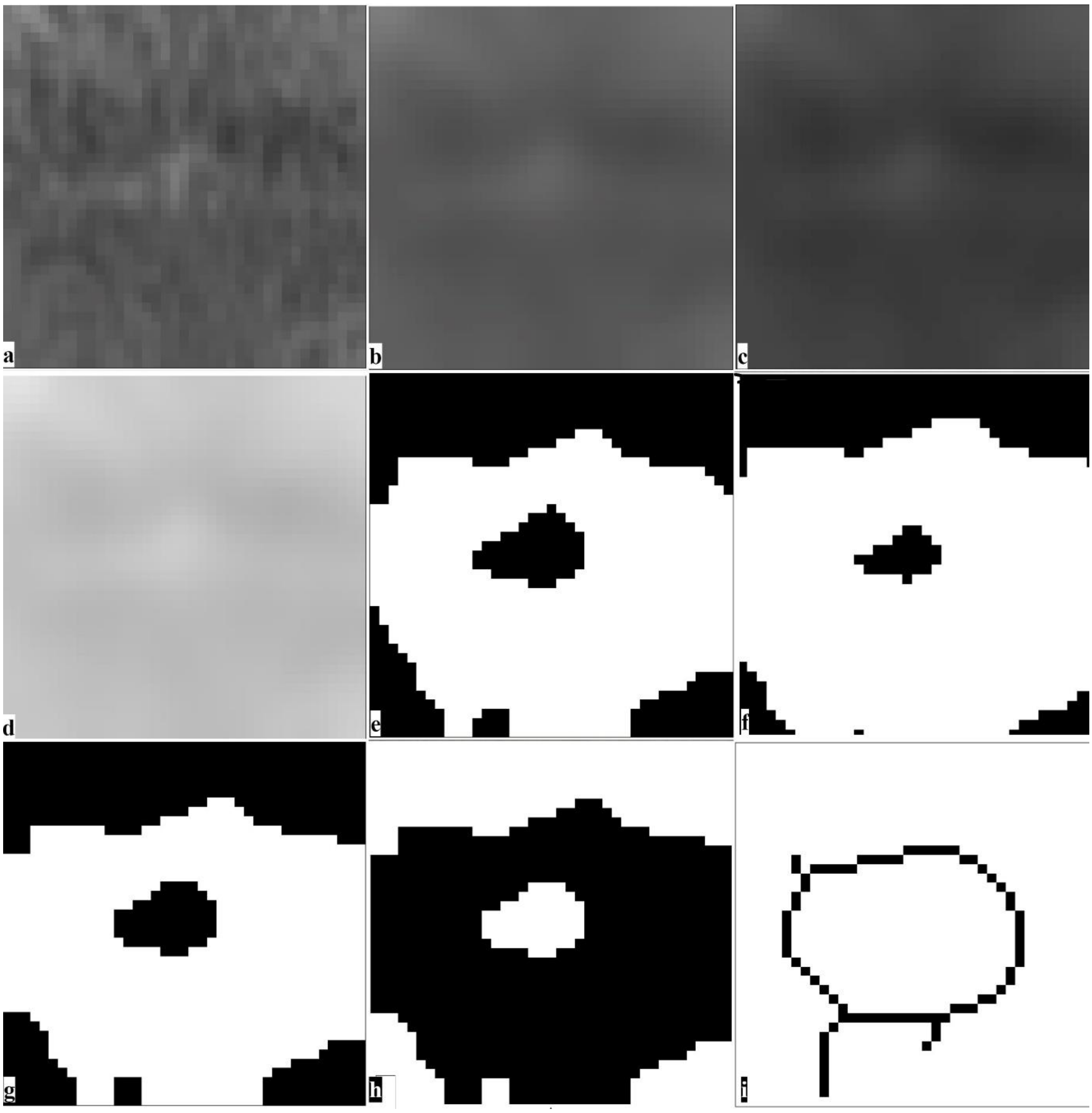

Figure 2: Fractal analysis methods

a. Selected ROI-v and duplicated, b. Gaussian filter, c. Subtraction, d. Addition of 128 pixels, e. Binarization, f. Erosion, g. Dilation, h. Inverted version, i. Skeletonization.

Their values were plotted on a logarithmic scale graph. The slope of line connecting plotted points on the chart supplied FD value.

Statistical Analyses

Data were analyzed using SPSS 22.0 (IBM Corp., New York). The Kolmogorov Smirnov test was performed to determine whether the study group was normally distributed, and it was determined that the data were normally distributed. The t-test was used to compare the mean FDs between the two groups. Results were reported as mean ± standard deviations and $p < 0.05$ was considered statistically significant.

3. Results

We found a high correlation (0.88-0.95) between repeated FD measurements, which implies a reliable inter-rater reliability of the measurements. The study included smoker males and non-smoker males aged 18-78 years. The mean ages of the smokers and non-smokers groups were 43.23 ± 16.39 and 42.53 ± 15.89, respectively. While the mean FD value of ROI-v in the smoker group was 1.118±0.85, the mean FD value of ROI-v in the non-smoker group was 1.221±1.12. This difference between ROI-v values is also statistically significant. ($p < 0.05$) (Table 1).

Table 1: Comparison of mean and standard deviation of variable among the groups

	Smoker Group		Non-smoker Group		P
	Mean±S.D.	Min.-Max.	Mean±S.D.	Min.-Max.	
ROI-v	1.118±0.85	0.852-1.273	1.221±1.12	0.996-1.472	0.004*

4. Discussion and Conclusion

In this study, vertebral FD on CBCT scans of smoker males were compared with non-smoker males. Vertebral measurements differed significantly between smoker males and non-smoker males. The mean FD values were found to be lower in smoker males. Previous studies examining the effect of drugs on the mandible bone considered low FD values as an indicator of osteoporotic changes [29, 30]. In the study of Basavarajappa et al. [4] using panoramic radiography images, lacunarity and FD of mandibular bone were evaluated in tobacco users and smokers. It was determined that FD decreased significantly in tobacco users and smokers. They interpreted this result of the study as meaning that the study groups had a less complex trabecular bone structure than healthy controls. In our study, we interpreted low values of FD at the vertebra as osteoporotic alterations in trabecular bone during smoking.

Smoking is associated with osteoporosis as well as with many other diseases [31]. Hou et al. [32] found that smoking was relationed with the prevalence of osteoporosis or osteopenia in their cross-sectional study. How smoking affects the skeletal system has not been fully resolved [31]. The effects of smoking on bone metabolism may result from indirect effects on weight, oxidative stress, hormone levels and/or direct effects on osteogenesis, such as collagen metabolism, the RANK-RANKL-OPG system, and bone angiogenesis [33].

FA is a mathematical procedure that provides the quantitative description of complex shapes and structures that cannot be defined by integral dimension and it is expressed numerically by the FD [23]. FD can be used to distinguish between normal bone density and osteoporotic changes [34]. There are different opinions about the relationship between FD and the complexity of the trabecular bone. While some studies [35, 36] have determined that the FD value increases as a result of osteoporotic changes, in some studies [4, 7, 37], it has been found that the FD value decreases in accordance with our study. Inconsistencies in reported FD values can be ascribed to a multitude of influencing factors. These factors encompass technical considerations such as exposure duration and image resolution, inherent anatomical variations within the sample population, the specific methodology employed for FA, and the diverse algorithms utilized for FD calculation [4, 38]. Therefore, further studies can be conducted in which standardization procedures are determined and strictly followed.

When the literature was evaluated, it was determined that there are many studies [37, 39] using FA on dental radiographs. In their study, Korkmaz et al. [37] determined that FA can be utilized on panoramic radiographs to define osteoporotic differences in the bones of individuals with vitamin D deficiency. Gülec et al. [39] in their study on panoramic radiographs, concluded that FA may be a suitable technique for distinguishing trabecular changes in the condyle of individuals with bruxism.

CBCT images of 51 patients diagnosed with osteoporosis according to DEXA and 52 patients with normal BMD (control group) were evaluated by Carvalho et al. [7]. FD values obtained from cervical vertebra and mandible were compared between the two groups. In the study group, FD values at the mandibular region were lower than in the control group, but the FD values at the vertebral bone did not differ significantly between the groups. The study concluded that FD at the vertebral region is not useful for referring women to be evaluated for osteoporosis. In this study, it was concluded that FD at the vertebral region may be useful in evaluating trabecular differences in smoker males. There are different opinions between our study and other study regarding the evaluation of the vertebral region using FA. A study using CBCT images revealed that change in voxel size significantly changes FD values. Larger voxel sizes were associated with lower FD values [40]. The voxel size in our study is different from the voxel size of the other study, and the inconsistency between the studies may be due to the situation.

Shrout et al. [41] suggested that FD calculations are insensitive to changes in film exposure, image alignment, and selected region of interest (ROI). In their other two studies, Shrout et al. [42, 43] stated a dependence of FD values on shape, size, and location of the ROI. In other study [44] and in the study conducted by Koh et al. [38] using panoramic images to predict age-related osteoporosis in postmenopausal women, the size and location of the ROI did not affect FD values. There is no similar study that can compare ROI features with our study. Therefore, further studies can be conducted on this subject.

In their meta-analysis, Ward et al. [45] found that smoking increases the risk of fracture more in men than in women. They speculated that this result might be due to the dose-dependent effect of smoking on bone loss. The duration and frequency of smoking were not evaluated in our study, which is among the limitations of our study. Also, our study had a small sample group. Further studies can be conducted in which fractal dimension analysis is performed using CBCT images, with a larger sample group, and the duration and frequency of smoking are also evaluated.

This study found that values of FD at the vertebra on CBCT scans decreased in smoker males and the low values of FD at the vertebra were concluded to indicate osteoporotic changes in the trabecular bone during smoking. Therefore, according to the results of our study, fractal analysis of cervical vertebrae may help to evaluate osteoporotic changes in smoker males.

Declaration of Ethical Code

In this study, we undertake that all the rules required to be followed within the scope of the "Higher Education Institutions Scientific Research and Publication Ethics Directive" are complied with, and that none of the actions stated under the heading "Actions Against Scientific Research and Publication Ethics" are not carried out.

This study was approved by the Ankara Medipol University Non-Invasive Clinical Research Ethics Committee (Protocol No: 111).

References

[1] Khalil MAM, Tan J, Khamis S, Khalil MAU, Azmat R, Ullah AR. 2017. Cigarette smoking and its hazards in kidney transplantation. Adv Med, 6213814.

[2] Organization WH.2017. WHO report on the global tobacco epidemic, 2017: monitoring tobacco use and prevention policies. World Health Organization.

[3] Celermajer DS, Sorensen KE, Georgakopoulos D, Bull, C, Thomas O, Robinson J, et al. 1993. Cigarette smoking is associated with dose-related and potentially reversible impairment of endothelium-dependent dilation in healthy young adults. Circulation, 88, 2149-55.

[4] Basavarajappa S, Ramachandra VK and Kumar S. 2021. Fractal dimension and lacunarity analysis of mandibular bone on digital panoramic radiographs of tobacco users. J Dent Res Dent Clin Dent Prospects, 15, 140.

[5] Aspray TJ and Hill TR. Osteoporosis and the ageing skeleton. 2019. Biochemistry and cell biology of ageing: Part II Clinical Science, 91, 453-76.

[6] Kanis JA, Oden A, Johnell O, Jonsson B, De Laet C, Dawson A. 2002. The burden of osteoporotic fractures: a method for setting intervention thresholds. Osteoporos Int, 12, 417-27

[7] Carvalho BF, de Castro JGK, de Melo NS, de Souza Figueiredo PT, Moreira-Mesquita CR, de Paula AP, et al. 2022. Fractal dimension analysis on CBCT scans for detecting low bone mineral density in postmenopausal women. Imaging Sci Dent, 52(1), 53.

[8] Sözen T, Özışık L, Başaran NÇ. 2017. An overview and management of osteoporosis. Eur J Rheumatol, 4(1), 46-56.

[9] Bijlsma A, Meskers C, Westendorp R, Maier A. 2012. Chronology of age-related disease definitions: osteoporosis and sarcopenia. Ageing Res Rev, 11, 320-4.

[10] Marcucci G, Brandi ML. 2015. Rare causes of osteoporosis. Clin Cases Miner Bone Metab, 12(2),151.

[11] Strehl C, Spies CM, Buttgereit F. 2011. Pharmacodynamics of glucocorticoids. Clin Exp Rheumatol, 5(68), 13-8.

[12] Ebeling, P.R., Nguyen, H.H., Aleksova, J., Vincent, A.J., Wong, P., Milat, F. 2022. Secondary osteoporosis. Endocrine Rev. , *43*, 240-313.

[13] Leslie WD, O'Donnell S, Jean S, Lagacé C, Walsh P, Bancej C, et al. 2009. Trends in hip fracture rates in Canada. JAMA, 302(8), 883-9,

[14] Ma D, Li Y, Hackfort B, Zhao Y, Xiao J, Swanson PC, et al. 2012. Smokeinduced signal molecules in bone marrow cells from altered lowdensity lipoprotein receptor-related protein 5 mice. J Proteome Res, 11(7), 3548-60.

[15] Perez-Warnisher MT, De Miguel MDPC, Seijo LM. 2018. Tobacco use worldwide: Legislative efforts to curb consumption. Ann Glob Health, 84,571-9

[16] Ryan C, Petkov V, Adler R. 2011. Osteoporosis in men: the value of laboratory testing. Osteoporos Int, 22(6), 1845-53.

[17] Pekkolay, Z., et al. 2023. *Secondary Causes of Osteoporosis: Tertiary Endocrine Center Experience.* Eurasıan Journal Of Medical Advances,**3**(1).

[18] Adler, R.A. 2014. Osteoporosis in men: a review. Bone research, 2(1), 1-8.

[19] Lewiecki, E.M. and K.E. Schmader, *Osteoporotic fracture risk assessment.* Cambridge, Massachusetts, EEUU. Obtenido de https://www. uptodate. com/contents/osteoporotic-fracture-riskassessment, 2013.

[20] Harrar, K., Hamami, L. 2008. The fractal dimension correlated to the bone mineral density. WSEAS Trans. Signal. Process, 4, 110-126.

[21] Schuit SCE, van der Klift M, Weel AEAM, de Laet CEDH, Burger H, Seeman E, Hofman A, Uitterlinden AG, van Leeuwen JPTM, Pols HAP. 2004. Fracture incidence and association with bone mineral density in elderly men and women: the Rotterdam Study. Bone, 34(1), 195-202

[22] Sanchez-Molina D, Velazquez-Ameijide J, Quintana V, Arregui-Dalmases C, Crandall JR, Subit D, et al. 2013. Fractal dimension and mechanical properties of human cortical bone. Med Eng Phys, 35(5), 576-82.

[23] Güleç M, Taşsöker M, Şener S. 2019. Tıpta ve Diş Hekimliğinde Fraktal Analiz. Ege Üniversitesi Diş Hekimliği Fakültesi Dergisi, 40(1), 17-31.

[24] Updike SX, Nowzari H. 2008. Fractal analysis of dental radiographs to detect periodontitis-induced trabecular changes. J Periodontal Res, 43(6), 658-64.

[25] Shokri A, Ghanbari M, Maleki FH, Ramezani L, Amini P, Tapak L. 2019. Relationship of gray values in cone beam computed tomography and bone mineral density obtained by dual energy X-ray absorptiometry. Oral Surg Oral Med Oral Pathol Oral Radiol,128(3), 319-31.

[26] Pachêco-Pereira C, Almeida FT, Chavda S, Major PW, Leite A, Guerra EN. 2019. Dental imaging of trabecular bone structure for systemic disorder screening: a systematic review. Oral Dis, 25(4), 1009-26.

[27] Kiljunen T, Kaasalainen T, Suomalainen A, Kortesniemi M. 2015. Dental cone beam CT: A review. Phys Med, 31(8), 844-60

[28] Otis L, Hong J, Tuncay O. 2004. Bone structure effect on root resorption. Orthod Craniofac Res, 7(3), 165-77.

[29] Temur, K.T., G. Magat, and S. Ozcan. 2023. A retrospective comparative fractal and radiomorphometric analysis of the effect of 3 generations of anti-epileptic drugs on the mandible. Oral Surg, Oral Med, Oral Pathol and Oral Radiol, 136(2), 255-62.

[30] Coşgunarslan A, Aşantoğrol F, Soydan Çabuk D, Canger EM. 2020. The effect of selective serotonin reuptake inhibitors on the human mandible. Oral Radiol, 37(1), 20-8.

[31] Yang, Y. H. et al. 2014. Oxidative damage to osteoblasts can be alleviated by early autophagy through the endoplasmic reticulum stress pathway–implications for the treatment of osteoporosis. Free Radic. Biol. Med, 77, 10-20.

[32] Hou W, Chen S, Zhu C, Gu Y, Zhu L and Zhou Z. 2023. Associations between smoke exposure and osteoporosis or osteopenia in a US NHANES population of elderly individuals. Front Endocrinol, 14, 1074574.

[33] Weng W, Li H, Zhu S. 2022. An overlooked bone metabolic disorder: cigarette smoking-induced osteoporosis. Genes, 13(5), 806.

[34] Mostafa RA, Arnout EA, Abo el-Fotouh MM. 2016. Feasibility of cone beam computed tomography radiomorphometric analysis and fractal dimension in assessment of postmenopausal osteoporosis in correlation with dual X-ray absorptiometry. Dentomaxillofac Radiol, 45, 20160212.

[35] Ruttimann UE, Webber RL, Hazelrig JB. 1992. Fractal dimension from radiographs of peridental alveolar bone: a possible diagnostic indicator of osteoporosis. Oral Surg Oral Med Oral Pathol, 74(1), 98-110.

[36] Hua Y, Nackaerts O, Duyck J, Maes F, Jacobs R. 2009. Bone quality assessment based on cone beam computed tomography imaging. Clin Oral Implants Res, 20(8), 767-71.

[37] Zihni Korkmaz M, Yemenoğlu H, Günaçar DN, Ustaoğlu G, Ateş Yildirim E. 2023. The effects of vitamin D deficiency on mandibular bone structure: a retrospective radiological study. Oral Radiol, 39(1), 67-74.

[38] Koh K-J, Park H-N, Kim K-A. 2012. Prediction of age-related osteoporosis using fractal analysis on panoramic radiographs. Imaging Sci Dent, 42(4), 231-5.

[39] Gulec M, Tassoker M, Ozcan S, Orhan K. 2021. Evaluation of the mandibular trabecular bone in patients with bruxism using fractal analysis. Oral Radiol, 37(1), 36-45.

[40] Pauwels R, Faruangsaeng T, Charoenkarn T, Ngonphloy N, Panmekiate S. 2015. Effect of exposure parameters and voxel size on bone structure analysis in CBCT. Dentomaxillofac Radiol, 44(8), 20150078–9.

[41] Shrout MK, Potter BJ, Hildebolt CF. 1997. The efect of image variations on fractal dimension calculations. Oral Surg Oral Med Oral Pathol Oral Radiol Endod, 84(1), 96-100.

[42] Shrout MK, Hildebolt CF, Potter BJ. 1997. The effect of varying the region of interest on calculations of fractal index. Dentomaxillofac Radiol, 26, 295-8.

[43] Shrout MK, Farley BA, Patt SM, Potter BJ, Hildebolt CF, Pilgram TK, et al. 1999. The effect of region of interest variations on morphologic operations data and gray-level values extracted from digitized dental radiographs. Oral Surg Oral Med Oral Pathol Oral Radiol Endod, 88(5), 636-9.

[44] Toghyani, S., Nasseh, I., Aoun, G., Noujeim, M. 2019. Effect of Image Resolution and Compression on Fractal Analysis of the Periapical Bone. Acta Inform. Medica, 27, 167-70.

[45] Ward KD, Klesges RC. 2001. A meta-analysis of the effects of cigarette smoking on bone mineral density. Calcif Tissue Int, 68, 259-70.