



## Evaluation of Cortical and Trabecular Bone Structure of the Mandible in Oral Contraceptive Users

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### Research Article

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### ABSTRACT

**Objectives:** Oral contraceptives (OCs) are widely prescribed hormonal agents that may influence bone homeostasis due to their estrogen content. Estrogen is essential for maintaining skeletal integrity, primarily by modulating osteoblast and osteoclast activity. This study aimed to evaluate whether combined oral contraceptive (COC) use affects mandibular bone microarchitecture using fractal dimension (FD) analysis and panoramic mandibular index (PMI) assessments.

**Materials and Methods:** A case-control design was employed, analyzing digital panoramic radiographs from 290 women aged 18–50, including 145 COC users and 145 age-matched controls. FD values were determined from three mandibular sites: the condyle, angle, and interdental region. PMI values were also computed. Data were analyzed using SPSS software version 21.0 (IBM Corp., Armonk, NY, USA),  $p < 0.05$  was considered significant.

**Results:** There were no statistically significant variations in FD values observed between the COC user group and the control group in the condylar ( $p = 0.183$ ), angular ( $p = 0.603$ ), or interdental ( $p = 0.159$ ) areas. Likewise, there was no significant difference in PMI values between the two groups ( $p = 0.183$ ). Additionally, neither FD nor PMI values were significantly associated with estimated duration of contraceptive use.

**Conclusions:** Based on FD and PMI measurements, the study found no evidence that COC use leads to notable alterations in mandibular bone structure. These results suggest that estrogen-containing contraceptives may not adversely affect jawbone health in premenopausal women.

**Keywords:** Fractal analysis, mandible, oral contraceptives, panoramic radiography

## Oral Kontraseptif Kullananlarda Mandibulanın Kortikal ve Trabeküler Kemik Yapısının Değerlendirilmesi

### Araştırma Makalesi

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### ÖZ

**Amaç:** Oral kontraseptifler (OK), östrojen içerikleri nedeniyle kemik metabolizmasını etkileyebilen yaygın olarak kullanılan hormonal ilaçlardır. Östrojen, osteoblast ve osteoklast aktivitesini düzenleyerek kemik yoğunluğunun korunmasında önemli bir rol oynar. Bu çalışma, fraktal analiz ve panoramik mandibular indeks (PMI) ölçümleri kullanarak kombine oral kontraseptiflerin (KOK) mandibular kemik yapısı üzerindeki etkilerini araştırmayı amaçlamıştır.

**Gereç ve Yöntemler:** 18-50 yaş aralığında 290 kadın hastanın (145 KOK kullanıcısı ve 145 yaş eşleştirilmiş kontrol) dijital panoramik radyografileri kullanılarak bir vaka-kontrol çalışması yürütülmüştür. Fraktal boyut (FB) değerleri mandibular kondil, angulus ve interdental bölgeden ölçülürken, PMI değerleri hesaplanmıştır. İstatistiksel analiz için SPSS v21.0 (IBM Corp, Armonk, NY, ABD) kullanıldı ve anlamlılık düzeyi  $p < 0,05$  olarak belirlenmiştir.

**Bulgular:** Kondiler ( $p = 0,183$ ), gonial ( $p = 0,603$ ) ve interdental ( $p = 0,159$ ) bölgelerde KOK kullanıcıları ve kontroller arasında FB değerlerinde anlamlı bir fark gözlenmemiştir. Benzer şekilde, PMI değerleri de vaka-kontrol arasında istatistiksel açıdan anlamlı bir ilişki göstermemiştir ( $p = 0,183$ ). Ayrıca, FB ve PMI değerleri KOK kullanım süresiyle anlamlı bir ilişki göstermemiştir.

**Sonuçlar:** Bu çalışmada, FB ve PMI ölçümlerine dayanarak, KOK kullanımının mandibular kemik yapısını önemli ölçüde etkilediğine dair bir kanıt bulunamamıştır. Bu bulgular, östrojen içeren kontraseptiflerin menopoz öncesi kadınlarda kemik sağlığını olumsuz etkileyebileceğini düşündürmektedir.

**Anahtar Kelimeler:** Fraktal analiz, mandibula, oral kontraseptifler, panoramik radyografi

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### Introduction

A large number of women rely on contraceptive methods to prevent unplanned pregnancies. Oral contraceptives (OCs) are among the most widely used forms of contraception globally.<sup>1</sup> Fifty percent of women aged 20 to 24 in the United States are known to use oral contraceptives.<sup>2</sup> OCs can be

either combined oral contraceptives (COCs) or progestin-only pills (POPs).<sup>1</sup> Combined preparations containing estrogen and progesterone are most commonly used.<sup>3</sup>

Estrogen is the main regulator of bone metabolism and prevents osteoporosis.<sup>1,4</sup> Estrogen exerts its influence on

bone by directly modulating the activity of osteocytes, osteoclasts, and osteoblasts, resulting in decreased bone breakdown and the maintenance of bone formation processes.<sup>5</sup> Estrogen deficiency is frequently associated with a decline in bone mineral density (BMD), increasing susceptibility to skeletal weakening. In such cases, hormonal therapy or OCs are commonly prescribed.<sup>1</sup> In postmenopausal women, the risk of osteoporosis rises due to a combination of factors, including elevated levels of follicle-stimulating hormone (FSH), a lack of estrogen and reduced calcium absorption.<sup>6</sup>

Various studies have been conducted with different age groups to clarify the effects of OCs on BMD. It is known that the majority of the millions of OC users are younger than 30 years old.<sup>7</sup> Shoepe and Snow<sup>2</sup> reported that OC users had significantly greater BMD than controls in their study of young women. They indicated that using OC in adolescence and early adulthood could be linked to reduced bone mineral density. Similarly, Scholes et al.<sup>7</sup> demonstrated that young adult women experienced adverse effects on bone density when using OCs. On the other hand, in healthy, premenopausal women, COCs are either neutral or beneficial for bone health, as assessed by BMD and fracture risk.<sup>8</sup>

Recent advancements in dental imaging have enabled researchers to investigate jawbone characteristics with greater precision, offering new perspectives on systemic bone health. As the mandible is subject to both mechanical forces and hormonal modulation, it may provide early indicators of metabolic alterations that precede clinically detectable bone loss. Understanding the potential impact of hormonal agents, such as oral contraceptives, on craniofacial bone structures is essential not only for dental health professionals but also for broader preventive healthcare strategies. Such interdisciplinary insights may support the development of imaging-based screening tools that complement traditional methods used in osteoporosis risk assessment. Fractal analysis is a mathematical technique that quantifies the complexity of trabecular bone patterns based on the concept of self-similarity. It provides a numerical descriptor, known as the fractal dimension (FD), which reflects the degree of structural complexity within the trabecular network. Higher FD values correspond to more intricate and dense trabecular patterns, indicating variations in bone quality and mineral density. Therefore, fractal analysis serves as an important imaging-based quantitative method for assessing the trabecular bone pattern by measuring the geometric intricacies visible within radiographic images.<sup>9</sup> De Assis et al.<sup>6</sup> reported that FD values of women receiving hormone replacement therapy (HRT) were greater than those of the control group in their fractal analysis using panoramic radiographs of postmenopausal women receiving antiresorptive HRT. In addition to fractal analysis of the trabecular structure, radiographic findings of resorption of the lower mandibular cortex can be detected by panoramic radiography. The aim of this study was to compare mandibular cortical resorption findings and FD

values of the mandibular trabecular bone in women using COCs with those of an age-matched control group using panoramic radiography. It was hypothesized that women using combined oral contraceptives would demonstrate differences in the fractal dimension and PMI values of the mandibular bone compared to age-matched controls, potentially reflecting microstructural alterations associated with hormonal influence. FD analysis was selected as the primary method because it quantitatively captures the complexity of trabecular bone patterns. This approach enables the detection of subtle microarchitectural variations that may not be evident through conventional morphometric indices.

## Materials and Methods

### Sample and Study Design

The research was conducted in accordance with the principles outlined in the Declaration of Helsinki and was approved under protocol number 2024/459 by the Ethics Committee of Necmettin Erbakan University. The study was conducted retrospectively using digital panoramic radiographs of individuals who were examined at Necmettin Erbakan University Faculty of Dentistry between January 2020 and July 2024 and whose COC use was recorded in their anamnesis record.

Central pathology in the jaw bones, fractures, use of medications that influence bone metabolism (bisphosphonates, etc.), bone diseases, and artifactual images that did not meet diagnostic requirements didn't include in the study. The study involved individuals who were between the ages of 18-50 and systemically healthy. None of the women in the sample were in menopause. In line with these criteria, 145 individuals were included in the case group and 145 individuals were included in the control group. All individuals in the case group were using 30-35 µg formulations (low-dose).

### Image Processing: Fractal Analysis

Every digital panoramic image analyzed in this study was acquired using a 2D Veraviewpocs digital panoramic X-ray machine (J MORITA MFG Corp., Kyoto, Japan) with exposure settings of 5 mA, 70 kV, and an irradiation time of 15 seconds. For fractal analysis, digital panoramic images were saved in jpeg format and standardized to a resolution of 1920 × 1080 pixels.

Region of interest (ROI) sizes selected from 6 regions on the right and left of the trabecular bone, excluding the cortical bone, inferior alveolar canal cortical border, lamina dura, and dental tissues, are as follows (Figure 1):

- 50 × 50 pixels from the interdental region between the first molar and mandibular second premolar
- 100 × 100 pixels from mandibular angulus
- 50 × 50 pixels from condyle

The FD values were calculated using the box-count method outlined by White and Rudolph.<sup>10</sup> Fractal analysis was conducted using ImageJ version 1.41, a software developed by the National Institutes of Health and compatible with 64-bit Java on Windows systems. The program was downloaded from the official NIH website at <https://imagej.nih.gov/ij/download.html>. To assess

reliability, 20% of the dataset was reanalyzed by the same examiner after a 15-day interval to evaluate intraobserver consistency. The steps of this approach are shown in Figure 2.

#### **Panoramic Mandibular Index**

First defined by Benson et al.,<sup>11</sup> PMI values were obtained by dividing the mandibular cortex thickness by the distance from the mental foramen to the lower border of the mandibular cortex (Figure 3).

#### **Power Analysis**

A power analysis was performed using G\*Power 3.1 (Heinrich Heine University, Düsseldorf, Germany). Assuming a two-tailed test with  $\alpha = 0.05$  and an expected small-to-moderate effect size (Cohen's  $d = 0.33$ ), a sample size of 145 participants per group yielded approximately

80% statistical power to detect between-group differences. This analysis confirmed that the study design was adequately powered to identify meaningful differences in FD and PMI values, if present.

#### **Statistical Analysis**

The statistical analysis was performed using SPSS version 21.0 (IBM Corp., Armonk, NY, USA). Mean and standard deviation values were determined through descriptive statistical methods. Spearman's Rank Correlation Coefficient was used to determine the relationship between age and FD values. The Wilcoxon Signed-Rank Test was used to compare right and left FD values. The Mann-Whitney U test was employed to assess differences in FD and PMI values between the case and control groups, with a significance threshold set at  $p < 0.05$ .

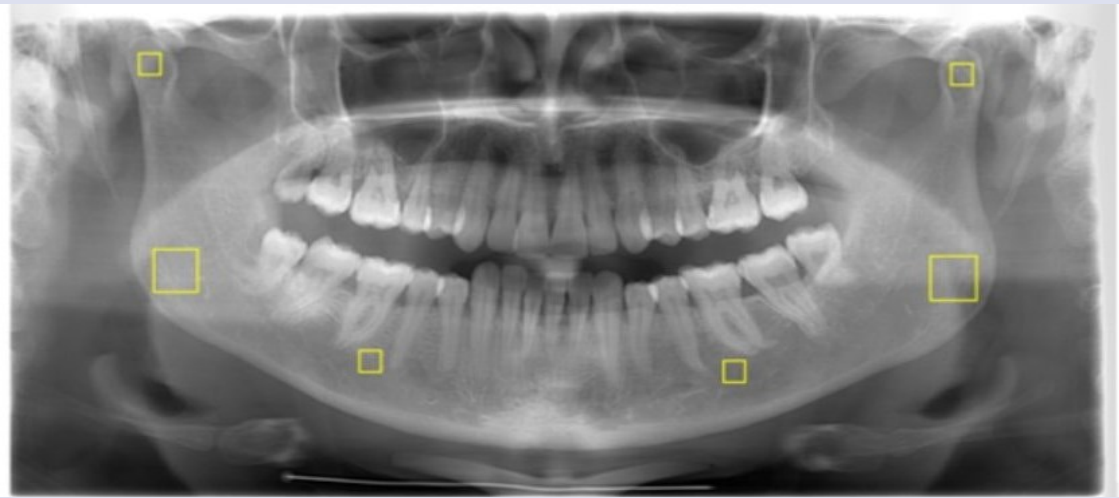


Figure 1. Selected ROIs on a panoramic image.

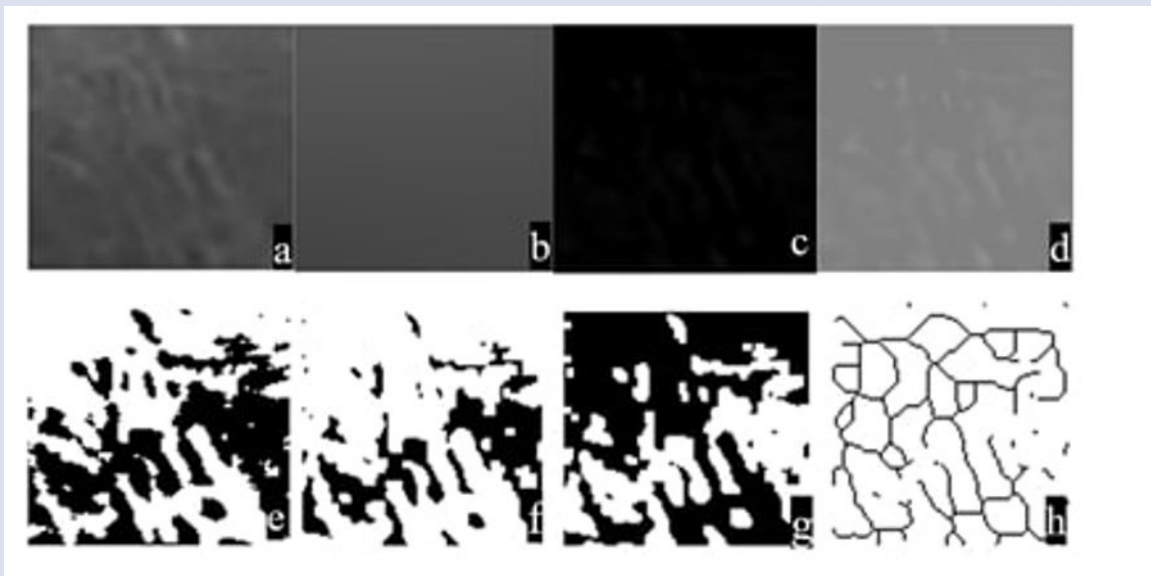


Figure 2. (a) Selected ROI. (b) Blurring. (c) Subtracting the blurry image from the original image. (d) Adding 128 shades of gray. (e) Converting to black and white image. (f) Noise reduction with Erode. (g) Invert colors. (h) Conversion to skeleton format.

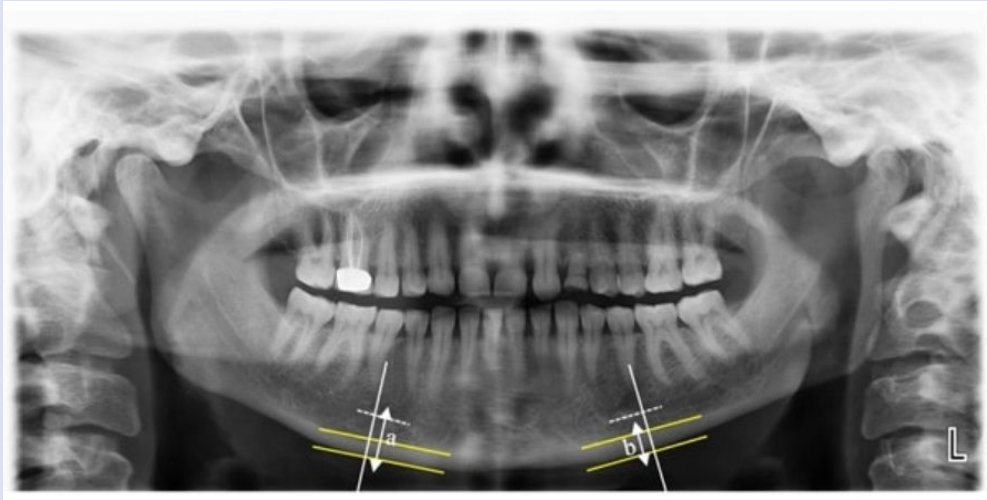


Figure 3. 'b/a' ratio gives the PMI.

## Results

The study included 290 female participants, with 145 in both the case and control groups, and a mean age of  $35.9 \pm 8.5$  years (ranging from 18 to 50). No statistically significant correlation was found between age and FD values ( $p > 0.05$ ). There were no statistically significant differences between the groups in the measurements obtained from the condylar, interdental, and angular regions ( $p > 0.05$ ; Table 1). A statistically significant difference was observed in the comparison of FD values between the right and left interdental regions of individuals ( $p < 0.05$ ). FD values in the right interdental region were found to be higher than those in the left.

No meaningful statistical difference in PMI measurements was observed between the case and control groups ( $p > 0.05$ ; Table 2).

No definitive medical information could be obtained regarding the duration of OC use of the participants in the case group. The approximate duration of use was evaluated in three groups: under 2 years, between 2 and 5 years, and exceeding 5 years; it was determined that FD and PMI did not show a statistically significant relationship according to the duration of OC use Table 3 shows the relationship between the duration of OC use and FD values.

Table 1. Comparison of the FD values between cases and controls

ROI		Sample size	Mean FD	p values
Condylar	Controls	145	$1.40 \pm 0.07$	0.183
	Cases	145	$1.41 \pm 0.07$	
	Total	290		
Angular	Controls	145	$1.37 \pm 0.07$	0.603
	Cases	145	$1.37 \pm 0.07$	
	Total	290		
Interdental	Controls	145	$1.45 \pm 0.05$	0.159
	Cases	145	$1.44 \pm 0.05$	
	Total	290		

Table 2. Comparison of the PMI values between cases and controls

	Sample size	PMI	p values
Controls	145	$0.330 \pm 0.063$	0.183
Cases	145	$0.374 \pm 0.361$	
Total	290		

Table 3. FD values according to the duration of OC use ( $p > 0.05$ )

Duration of OC use		Minimum	Maximum	Mean	Std. Deviation
<2 years	Condylar	1.2450	1.5005	1.400200	0.0688561
	Angular	1.1585	1.5052	1.384695	0.0924102
	Interdental	1.2717	1.5270	1.422520	0.0720825
2-5 years	Condylar	1.2193	1.5516	1.421379	0.0716527
	Angular	1.2059	1.5100	1.370347	0.0832018
	Interdental	1.1743	1.5551	1.439203	0.0705619
>5 years	Condylar	1.2297	1.5131	1.428691	0.0670391
	Angular	1.2254	1.5004	1.404382	0.0732424
	Interdental	1.3341	1.5260	1.446014	0.0505771

## Discussion

The impact of OCs on bone metabolism remains a topic of debate, with previous studies reporting conflicting findings regarding their effects on BMD. While estrogen, a key component of COCs, is known to regulate bone turnover and prevent osteoporosis, its influence on mandibular bone structure has not been thoroughly explored. This study is the first to our knowledge to investigate whether COC use affects the cortical and trabecular structure of the mandible by analyzing FD values and PMI measurements.

Fractal analysis is a quantitative technique used to measure intricate geometric structures that display repeating patterns across an image.<sup>12</sup> A higher FD value signifies greater structural complexity. It has been reported that fractal analysis may be a useful tool in the diagnosis of osteoporotic bone defects.<sup>13,14</sup> There are several studies in the literature reporting a correlation between low BMD and reduced FD.<sup>12,15</sup> Dental radiographs are commonly used imaging tools and they could serve as a potential screening method for detecting osteoporosis.<sup>12</sup> This study revealed no significant differences in FD values between COC users and controls across different mandibular regions (condylar, angular, and interdental). These results align with prior studies that found no impact of hormonal contraception on bone health in premenopausal women.<sup>16-18</sup> In addition to group comparisons, this study also demonstrated a statistically significant asymmetry between the right and left interdental regions, with higher FD values on the right side. This finding may reflect differences in functional loading or masticatory dominance, which can influence trabecular bone architecture. While previous studies rarely addressed right–left asymmetry in mandibular FD, our results suggest that local biomechanical factors may contribute to structural variability. Moreover, no age-related differences in FD were observed, indicating that interdental trabecular patterns remain relatively stable across the studied age range.

The condylar, angular (gonial), and interdental regions were selected as regions of interest because they represent distinct functional and load-bearing areas of the mandible, similar to many previous studies<sup>9,19-21</sup> investigating mandibular bone microarchitecture using fractal analysis. The condyle undergoes adaptive remodeling in response to masticatory forces and is sensitive to systemic hormonal influences; the angular region reflects cortical stress distribution patterns generated during mastication; and the interdental alveolar region includes metabolically active trabecular bone that responds to both local mechanical and systemic metabolic factors.

PMI has been used in many studies to evaluate mandibular morphometry<sup>22-25</sup> and has been reported to be positively correlated with BMD.<sup>26,27</sup> In this study, PMI measurements—which assess the ratio between the thickness of the mandibular cortex and the vertical distance from the mental foramen to the inferior mandibular border—did not differ significantly between

COC users and controls. These findings indicate that COC use is unlikely to cause notable changes in mandibular bone architecture.

Oestrogens and progestins are essential for maintaining bone metabolism and overall bone health. The loss of natural oestrogens results in a marked rise in the process of bone remodeling and increased bone deterioration, a common occurrence in early postmenopausal women.<sup>24</sup> In this study, women who had not yet started menopause and using COCs (has two components, the estrogen and the progestagen) were examined. It can be said that these pills, widely used by women across the globe, do not affect the jaw bones.

In addition to traditional BMD evaluations, exploring localized skeletal structures such as the mandible provides a unique perspective on bone metabolism, particularly in relation to hormonal influences. The mandible, as both a load-bearing and hormone-sensitive bone, may reflect subtle systemic changes that standard axial skeletal assessments could overlook. Although this study did not reveal significant differences, it still contributes to the literature by testing debated assumptions about the skeletal effects of COCs and by emphasizing the value of advanced image-based methodologies like FD and PMI within dental research. These methods also show that mandibular radiographs may serve as practical and accessible tools for detecting subtle bone changes beyond what conventional BMD measures can capture.

## Limitations

Despite these results, several limitations must be acknowledged. First, the retrospective design relied on anamnesis records, making it difficult to determine the exact duration and consistency of COC use. Second, bone structure assessments were based solely on 2D panoramic radiographs, which have inherent limitations in evaluating bone quality compared to more advanced imaging techniques like dual-energy X-ray absorptiometry (DXA) or cone-beam computed tomography (CBCT). Third, since the study was retrospective, it was not possible to evaluate the participants' nutritional habits, which could influence bone metabolism, as well as lifestyle factors such as dietary calcium intake, exercise, smoking, and alcohol consumption.

## Conclusions

This study suggests that COC use does not significantly impact mandibular bone structure based on fractal analysis and PMI measurements. However, variations in bone metabolism due to individual hormonal responses cannot be entirely ruled out. Longitudinal studies with larger sample sizes and advanced imaging techniques, such as CBCT or DXA, could help determine whether prolonged COC use has cumulative effects on bone metabolism. Future studies should take into account additional contributing factors—such as nutrition, exercise routines, and genetic background—to offer a more holistic perspective on how hormonal contraceptive use may affect mandibular bone health.

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None.

## Conflicts of Interest Statement

The authors declare no conflict of interest.

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